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Consequences of Oxidative Stress on Proteins

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Verfasserin / Verfasser:	Mag. Verena Haudek
Matrikel-Nummer:	9801779
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Betreuerin / Betreuer:	Univ.-Prof. Dr. Andreas Richter

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Zwei Dinge sind zu unserer Arbeit nötig: Unermüdliche Ausdauer und die
Bereitschaft, etwas, in das man viel Zeit und Arbeit gesteckt hat, wieder
wegzuwerfen.

Albert Einstein

Contents

1. Summary/Zusammenfassung	5
2. List of Abbreviations	7
3. Introduction	8
3.1. General scope and background	8
3.2. Aims and study design	16
3.3. Proteome analysis	18
3.4. Significance of the study	23
3.5. References to Introduction	25
4. Results and Discussion	31
4.1. Paper I	33
4.2. Paper II	105
4.3. Paper III	141
4.4. Paper VI	151
5. Curriculum Vitae	163

1. Summary

In organisms oxidative stress is generated, when the concentration of free radicals and other reactive oxygen species (ROS) exceeds the capacity of the antioxidant defense system. This may result in biological damage which is characteristic for arteriosclerosis and other diseases associated with chronic inflammation, e.g. cancer. There is strong evidence, that proteins are the main targets of oxidative stress and free radical action, and therefore proteome analysis represents a suitable method to investigate biological effects of oxidative stress.

In the first part of this study, human peripheral blood mononuclear cells (PBMCs) were exposed to hydrogen peroxide in autologous plasma, imitating *in vivo* conditions. The metabolically labeled cells were fractionated and the isolated cytosolic protein fractions were separated by 2-dimensional polyacrylamid gel electrophoresis (2D-PAGE). Protein spots were quantified by fluorography and autoradiography in order to reveal protein amounts and synthesis rates. Peptides from tryptic digestion of isolated proteins were separated by nano-liquid-chromatography and identified by peptide fragmentation analysis with a nano-electrospray ion trap mass spectrometer. Further, proteins were identified by shotgun analysis (1D-PAGE). As a result cells displayed a distinct stress response compared to control and down-regulated manganese superoxide dismutase. Additionally, PBMCs were isolated from cancer patients to analyze primary cells exposed to chronic oxidative stress. Plasma peroxidation levels of the patients were significantly higher than those of age and sex-matched controls. The corresponding cells displayed significant proteome alterations compared to control which appear to be related to inflammation and apoptosis regulation.

In the second part, the main aim was the identification of proteome maps of the different cell types of PBMCs (T-cells, monocytes, platelets, granulocytes, erythrocytes) and plasma. By means of these proteome maps, further evaluation of the impact of oxidative stress on the different cell types and plasma is performed in ongoing studies.

With this PhD-thesis, proteome reference maps of several cell types have been established and the identification of putative biomarkers for oxidative stress became possible.

1. Zusammenfassung

Oxidativer Stress entsteht, wenn die Konzentration von freien Sauerstoff-Radikalen oder anderer Radikale die Kapazität der körpereigenen Abwehrmechanismen übersteigt. Daraus kann eine biologische Schädigung des Organismus erfolgen, was wiederum zu Erkrankungen wie Arteriosklerose oder anderen mit chronischer Entzündung verbundenen Krankheiten, wie z.B. Krebs, führen kann. Proteine gelten als Hauptziele von oxidativem Stress, weshalb Proteom-Analysen passende Methoden zur Untersuchung von biologischen Effekten sind, die durch oxidativen Stress ausgelöst werden.

Im ersten Teil dieser Arbeit wurden menschliche periphere mononukleare Blutzellen Wasserstoffperoxid ausgesetzt. Durch diese Behandlung im eigenen Plasma wurden *in vivo* Konditionen nachgeahmt. Die Zellen wurden metabolisch markiert und die isolierten zytosolischen Proteine mit Hilfe von zwei-dimensionaler Polyacrylamid-Gelelektrophorese aufgetrennt. Die Quantifizierung von Proteinspots erfolgte mit Hilfe von Fluorographie und Autoradiographie wodurch Proteinmengen und Syntheseraten ermittelt wurde. Die durch den tryptischen Verdau der isolierten Proteine erhaltenen Peptide wurden mit Hilfe der nano-Hochdruck-Flüssigchromatographie getrennt und durch Peptidfragmentations-Analysen mit einem Elektrospray-Ionenfallen-Massenspektrometer identifiziert. Zusätzlich wurden die Proteine noch durch „Shotgun“-Proteomics (ein-dimensionale Polyacrylamid-Gelelektrophorese) identifiziert. Die Zellen zeigten eine deutliche Antwort auf den oxidativen Stress und die Synthese von Mangan-Superoxid Dismutase wurde vermindert. Weiters wurden Blutzellen von Krebspatienten isoliert und analysiert. Dies geschah in der Annahme, dass diese Zellen durch die Krebserkrankung einem internen, chronischen oxidativen Stress ausgesetzt sind. Die ermittelte Plasmaperoxidation der Krebspatienten war im Gegensatz zu der Kontrollgruppe gleichen Geschlechts und Alters erhöht. Die korrespondierenden Blutzellen zeigten Proteomveränderungen, die mit Entzündungsparametern und Apoptose in Zusammenhang gebracht werden können.

Im zweiten Teil der Arbeit wurden Proteom-Profile der verschiedenen im Blut vorhandenen Zelltypen (T-Zellen, Monozyten, Blutplättchen, Granulozyten und Erythrozyten) und des Blutplasmas erstellt. Mit Hilfe dieser Profile soll es ermöglicht werden die Auswirkungen von oxidativem Stress auf die einzelnen Zelltypen zu evaluieren.

Im Zuge dieser Arbeit war es möglich, Referenz-Proteom-Profile von mehreren verschiedenen Zelltypen zu erstellen, und potentielle Biomarker für oxidativen Stress aufzuzeigen.

2. List of Abbreviations

1/2D-PAGE: 1/2dimensional polyacrylamide gel-electrophoresis

CPL/MUW: Clinical Proteomics Laboratories at the Medical University of Vienna

Cu/Zn-SOD: copper/zinc superoxide dismutase

ESI: electrospray ionization

GPX: glutathione peroxidase

Hsp70: heat shock protein 70 kDa

LC-MS/MS: liquid chromatography tandem mass spectrometry

m/z: mass-to-charge ratio

MALDI: matrix assisted laser desorption/ionization

Mn-SOD: manganese superoxide dismutase

PBMC: peripheral blood mononuclear cells

pI: isoelectric point

PRIDE: Proteomics Identification Database (<http://www.ebi.ac.uk/pride>)

ROS: reactive oxygen species

RuBPS: Ruthenium II tris (bathophenanthroline disulfonate)

SDS: sodium dodecyl sulphate

SQL: Structured Query Language

TBA: thiobarbituric acid

3. Introduction

3.1. General scope and background

Ecotoxicology is the branch of toxicology that particularly focuses on the toxic effects of constituents of an ecosystem. Both natural and synthetic pollutants contribute to these toxic effects. Environmental toxicology is considered as a part of ecotoxicology which studies the effects on individuals, especially on human species.

Generation of oxidative stress

In the physiological context, reactive oxygen species (ROS) are generated endogenously by the respiratory chain of mitochondria or by peroxisomes. Yet, the exposure to xenobiotics, radiation, ultrasound, pollution, infections, drugs or smoking is considered as exogenous source for the production of ROS in an organism. If the concentration of free radicals or other ROS overrides the capacity of the antioxidant defense system of an organism, this can lead to the generation of oxidative stress [1]. ROS induce oxidative damage in lipids, DNA and proteins [2], which may result in biological damage leading to arteriosclerosis and other diseases associated with chronic inflammation, such as e.g. cancer [3] (*cf.* Figure 1).

Several studies dealing with environmental exposures to for example lead [4] or polycyclic aromatic hydrocarbons (PAHs) in urban environment [5], revealed that the production of ROS and the following oxidative stress increases the risk for elevated DNA damage or cancer.

Consequences of oxidative stress

As mentioned above, persistent oxidative stress leads to DNA damage, mutations and consequently to the activation of signal transduction pathways which stimulate the proliferation of cells [6]. This aberrant DNA synthesis and cell growth are important steps in carcinogenesis and belong to the hallmarks of cancer [7] (*cf.* Figure 2, 3). Carcinogenesis is a multistage process, in which at least three distinct steps can be recognized: initiation phase, promotion phase and progression phase [2].

In this regard, inflammatory events represent the main source of radicals and oxidative stress, which most frequently correlate with the pathogenesis of solid tumors [6, 8, 9]. In particular, elevated ROS generation and persistent oxidative stress have been recognized as characteristic features of carcinoma cells both *in vitro* and *in vivo* [3, 10].

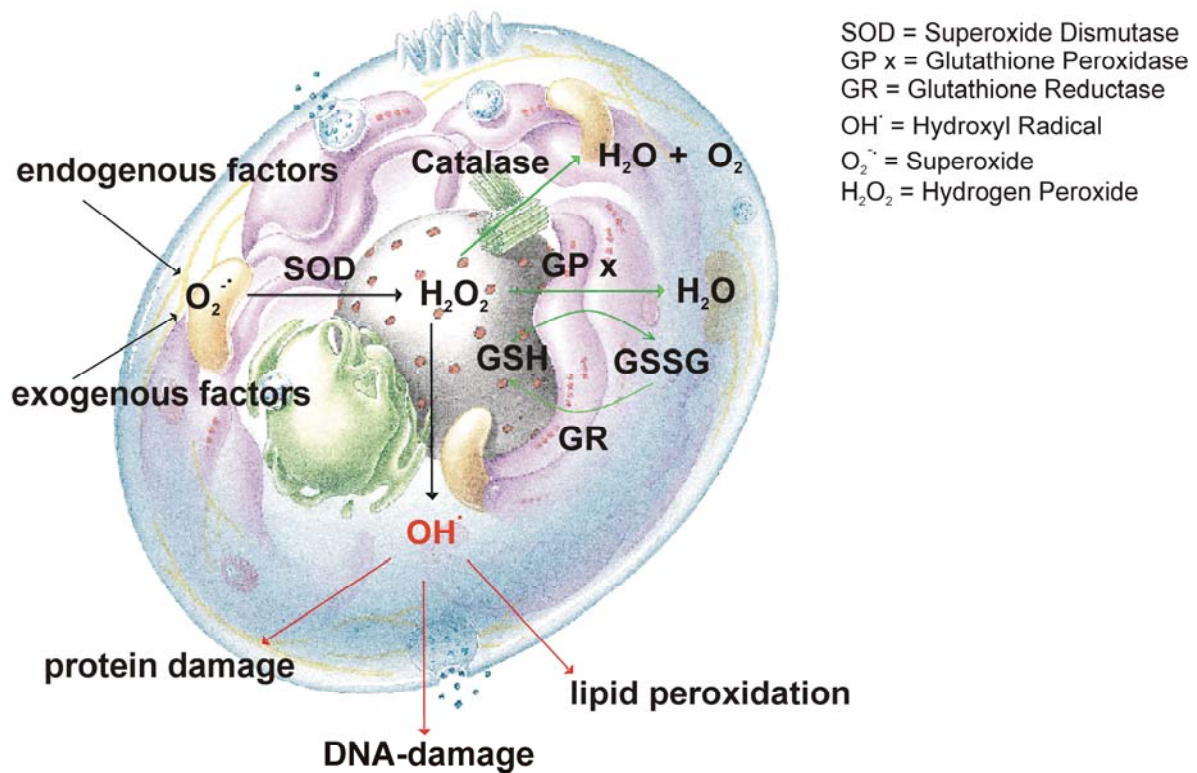


Figure 1: Scheme of the generation of oxidative stress in a eukaryotic cell (modified after IMD, Berlin). Endogenous and exogenous factors may lead to the generation of superoxide ($O_2^{\cdot -}$). Superoxide is decomposed by superoxide dismutase to hydrogen peroxide (H_2O_2), which is further processed through catalase and glutathione peroxidase to water and oxygen. Yet, the generation of hydroxyl radical ($OH^{\cdot}$) is possible and may lead further to protein damage, DNA damage and lipid peroxidation.

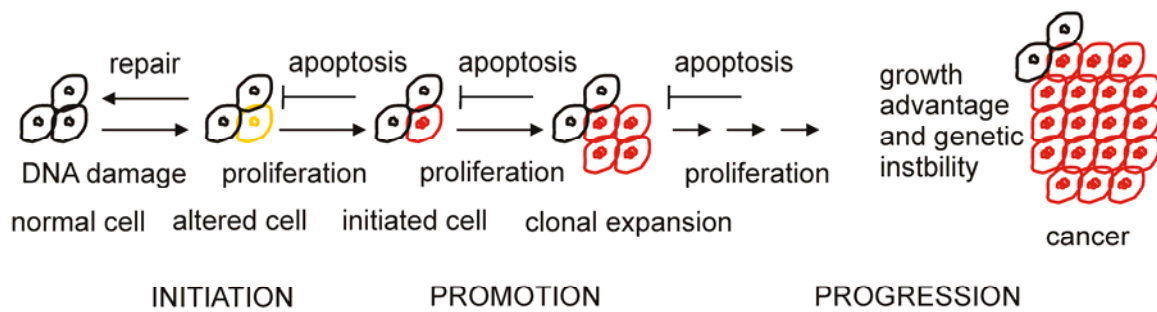


Figure 2: Multistage process of carcinogenesis [2]. After one round of DNA synthesis, the DNA mutation is determined and leads to an initiated cell (initiation). By induction of cell proliferation or inhibition of apoptosis, the initiated cell clonally expands to a focal lesion (promotion). By further DNA damage and genetic instability, the malignant stage may be reached (progression).

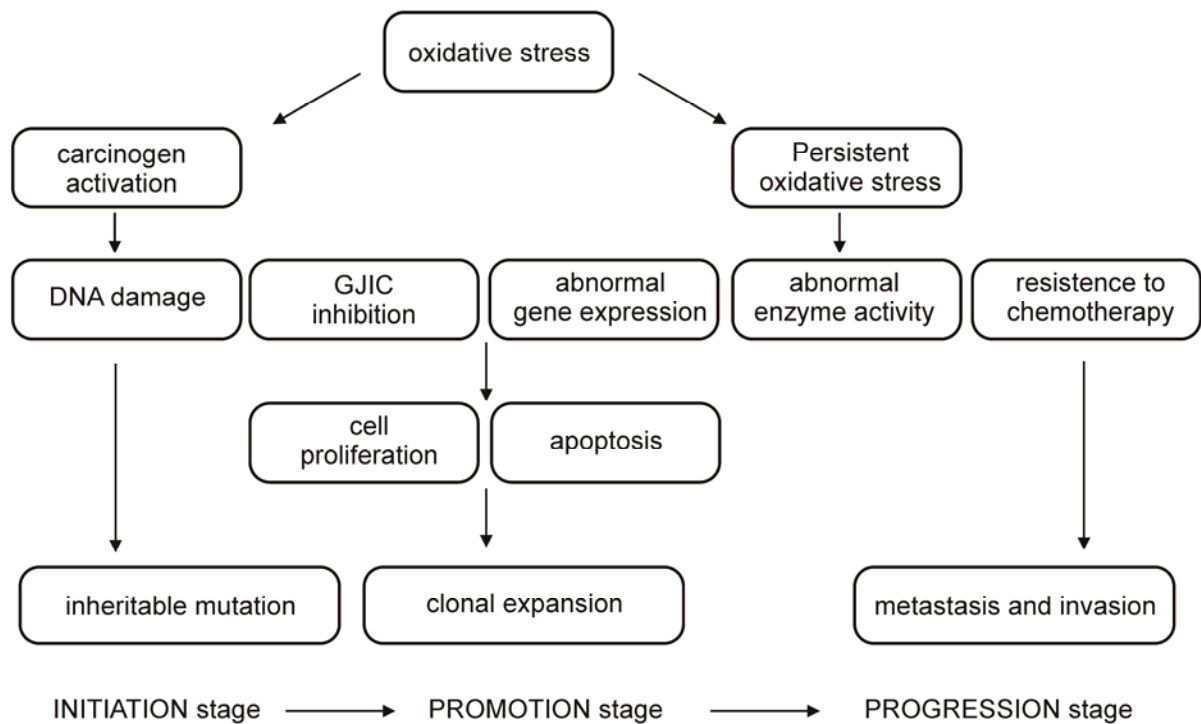


Figure 3: Oxidative stress and cancer [2]. Oxidative stress involves all three stages of the cancer process. During initiation it may contribute to DNA damage and chemical modifications of the DNA. This may result in a heritable mutation. During promotion, oxidative stress can contribute to abnormal gene expression, disturbance of cell-to-cell communication, and modification of second messenger systems. This could result in an increase in cell proliferation or a decrease in apoptosis in the initiated cell population which may further lead to clonal expansion of the initiated cells to preneoplastic focal lesions. During progression, oxidative stress facilitates additional DNA alterations in the initiated cell population. These may result in changes of enzymatic activities and provide resistance to normal growth regulation (e.g. apoptosis). GJIC = gap junctional intercellular communication

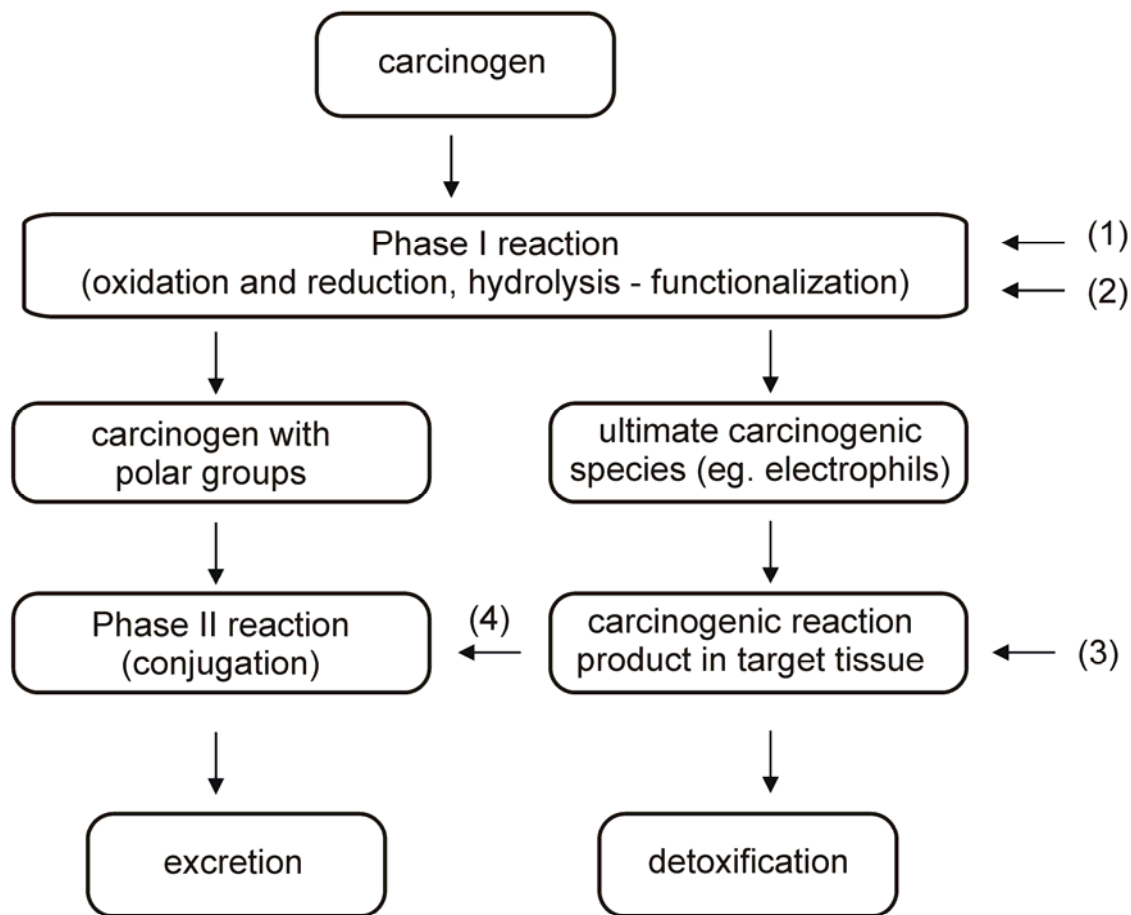
Chemoprotective properties of vegetables

It has been reported that several types of vegetables contain a large number of potentially anticarcinogenic agents [11]. These include allicin in garlic [12], isoflavones in soybean [13], lycopene in tomatoes [14], flavonoids in tea [15], carotinoids in carrots [16], lignans in flax seed [17], sulforaphane and other glucosinolates in cruciferous plants [18]. Although these plant ingredients have toxic effects when ingested in large amounts, as it was shown in animal experiments, smaller subtoxic doses facilitate their role as chemoprotective agents [19].

Numerous epidemiological studies indicated that consumption of cruciferous vegetables appears to protect against the incidence of various forms of cancer, such as e.g. colorectal, lung, prostate and breast cancer [16, 20-22]. The chemoprotective properties of cruciferous vegetables were attributed to breakdown products of glucosinolates (e.g. indoles, nitriles and isothiocyanates) [23].

Foreign compounds, such as toxic materials or carcinogens, enter the body and are metabolized by endogenous Phase I and Phase II enzymes for further excretion. In some cases these electrophils which are directly acting on macromolecules, can lead to the formation of cancer. However, the ability of carcinogens to exert their effects depends on the balance between the different activating enzymes. It is suggested that the anticarcinogenic mechanism of glucosinolates and their metabolites is triggered by induction of Phase I and Phase II enzymes, selective inhibition of enzyme activation and scavenging of electrophils and thus protecting against oxidative damage [19] (*cf.* Figure 4). By inducing Phase I and Phase II enzymes they facilitate detoxification of carcinogens. Some enzymes of Phase I reactions are known to activate xenobiotics to carcinogens, but it is further suggested that they are inhibited selectively by glucosinolate metabolites [24]. Additionally, the induction of cell cycle arrest and apoptosis may play a role in the cancer protective properties of cruciferous vegetables [20].

In a study it was shown, that the consumption of cruciferous vegetables, in this case Brussels sprouts, leads to inhibition of sulfotransferases in humans which finally protects against the heterocyclic amine 2-amino-1-methyl-6-phenyl-imidazo-[4,5-*b*]pyridine (PhIP) and oxidative DNA-damage [25].



glucosinulates:

- (1) induction of Phase I reactions
- (2) selective inhibition of the activating enzymes
- (3) induction of Phase II reactions
- (4) detoxification by trapping the electrophils

Figure 4: Common mechanism of carcinogen metabolism with the chemopreventive effects of glucosinulates [19]. Foreign compounds such as toxic materials or carcinogens enter the body and are metabolized by endogenous Phase I and Phase II enzymes for further excretion. Phase I enzymes contribute by means of oxidation, reduction and hydrolysis to the functionalization of substances, which means that they are transformed from lipophilic to more hydrophilic molecules. Phase II enzymes conjugate substances to larger molecules for further detoxification and excretion.

Methods for the detection of oxidative stress

The detection of oxidative stress can be performed on three basic levels: (1) the direct measurement of free radicals, (2) the detection and measurement of the resulting biological effects on macromolecules, and (3) the response of cells to oxidative stress.

The short half-life and the high reactivity of ROS limit the direct detection of free radicals *in vivo* [26]. The *ex vivo* measurement in cultured cells and preparations from isolated organs or tissues allows a better direct determination of oxygen-derived free radicals. There are several methods to measure free radicals such as e.g. by general fluorescent assays [27], spectrophotometric methods [28], the dichlorofluorescein assay [29], fluorescence-activated cell staining [30] or with flow cytometry [31]. The basic principle of all these assays is the reaction between the radical and the tracer, generating a measurable product. Radicals possess an unpaired electron and because of this another suitable method is the electron spin resonance technique [26].

The biological effect of radicals on macromolecules has been studied for many years and due to this investigation certain molecules which are prone to react with ROS and therefore might be used as indicators for oxidative stress have been identified [26]. These are for example the oxidative modification of proteins, which can be detected by carbonyl- or 3-nitrotyrosine-formation [32] or the generation of peroxides measured by means of lipid peroxide assays [33, 34].

The response of cells to radical mediated oxidative stress can be detected on different levels: on DNA-, mRNA- and protein-level. Proteins present the translational output of a cell and are considered as the main targets of oxidative stress and free radical action [35]. The term proteome describes the protein pool of a cell expressed at a given time [36], so its investigation provides an insight into biological processes, allowing the comparison of physiological and pathological states of a cell. Comprehensive studies investigating ROS and their effects on the proteome of organisms have already been performed on various systems as rice [37], yeast [38, 39] and cultured human cells [40-42].

Introduction of a model for measuring the response of cells to oxidative stress

In this PhD thesis the main focus laid on the investigation of the effect of oxidative stress on the proteome of human peripheral blood mononuclear cells (PBMCs). Different biological sources are accessible to proteome analysis, such as e.g. body fluids, blood plasma and urine, or primary cells such as PBMCs. PBMCs are known to present an optimal source for the investigation of primary human cells [43]. In this regard, PBMCs represent an accurate model for detecting the consequences of oxidative stress on the proteome since these cells (1) show a response to ROS generated in the body, (2) can be efficiently prepared within a short time which minimizes an experimental delay that could generate artifacts, and (3) are primary cells and therefore not subjected to drawbacks arising from long-term cell culturing, immortalization or even processes of malignant transformation [44].

PBMCs consist of lymphocytes and monocytes, which are interspersed to a varying degree with platelets, neutrophils, erythrocytes and plasma. Lymphocytes mainly comprise T cells (75%), B cells and natural killer cells. T cells and B cells are the major cellular components of the adaptive immune response. T cells are involved in the cell-mediated immunity, whereas B cells are primarily responsible for the humoral immunity. Natural killer cells are part of the innate immune system and play a major role in the rejection of tumors and cells infected by viruses as by initiating cell death [45]. Monocytes are also part of the immune system. They can move quickly to sites of infection and there differentiate into macrophages or dendritic cells [46]. The main function of erythrocytes is the delivery of oxygen to body tissues via the blood flow and transport carbon dioxide back to the lung. They also play a role in immune response and can influence the vessel walls by means of dilatation [47]. Platelets are small cytoplasmic bodies derived from megakaryocytes and are mainly involved in hemostasis and wound repair [48, 49]. Neutrophils are also essential for the immune system. They follow inflammation derived chemical signals and migrate towards the site of inflammation into the tissue to defend the body against pathogens [50]. Blood plasma makes up about 55% of the total blood volume. It is composed mainly of water (90%) with a high protein concentration, and contains dissolved glucose, mineral ions and hormones [51].

Due to this huge number of various features of the different blood cells and plasma, an assignment of proteins to the different cell types may help for further evaluation of clinical samples. There already exist several proteome maps of the different cell types and plasma, but an in-depth comparison by means of the same proteomic method has not been performed until now.

3.2. Aims and study design

Comparison of acute and chronic oxidative stress

The major aim of this study was the identification of differences between acute and chronic oxidative stress by means of different proteome expression patterns of PBMCs.

The further evaluation of PBMCs and their reaction towards oxidative stress are based on the generation of proteome maps of main blood components, such as monocytes, T cells, platelets, neutrophils, erythrocytes and plasma. By comparing the proteome profiles of these purified cell types and plasma, the assignment of a marker protein to a specific cell type or plasma is possible. By means of this, it should be easier to identify indicative proteins which then may serve as putative marker proteins for possible contaminations of purified cell samples. Additionally, the information can be used for systematic comparison of tissues and may further help for the detection of pathologic states. Reference proteome profiles of different cell types, or a specific set of proteins, such as common occurring proteins in several different cell types, may also be helpful for quality control or for further interpretation of proteome profiles of other cells. With such proteome maps the in-depth analysis of PBMCs and the interpretations of their cellular response will be improved.

Experiments for the investigation of acute or chronic oxidative stress were designed at conditions simulating the situation *in vivo*. For the acute response experiment, we imitated such physiological conditions by resuspending cells in autologous plasma for treatment with hydrogen peroxide (H₂O₂) at concentrations which have been reported to occur *in vivo* [52]. Hydrogen peroxide was used for the *in vitro* approach due to its capacity to cross cell membranes and diffuse through mitochondria, thereby causing many types of cellular injuries [3]. By using metabolic labeling and subsequent two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) analysis, we investigated the immediate response of cells to the oxidative challenge *in vitro*. This experimental strategy was combined with shotgun proteomics in order to achieve optimal reliability of data. Furthermore, we hypothesized that some oxidative stress-induced proteins may accumulate in cells and could therefore be useable as biomarkers. It is assumed that oxidative stress may occur in cancer patients *in vivo* and therefore primary cells from such patients represent a model for the long-term exposition to oxidative stress, namely a chronic physiological situation. To pursue this strategy, we determined the level of lipid peroxides in plasma derived from tumor patients by standard lipid peroxidation assays and found them elevated in comparison to plasma derived from

healthy age and sex-matched individuals. PBMCs were also subjected to comprehensive proteome profiling and compared to cells from the control persons.

Brussels sprout intervention study

In a second step, the putative protecting effects of glucosinulates, in this case in the terms of Brussels sprouts, against oxidative stress should be examined by means of a proteomic approach.

A consumption of sprouts (300 g/per person/d) over a period of five days was performed and the impact of sprouts consumption on the protein expression profile of PBMCs was investigated. It has been frequently emphasized that proteomics is an important tool to improve the current knowledge of cancer prevention by dietary factors [53-57], but only few investigations have been published using this technique to investigate the impact of dietary factors on the basis of animal models [58-60] or cell cultures [21, 22, 24].

3.3. Proteome analysis

Proteome versus Genome

The goal of proteomics is a comprehensive and quantitative description of protein expression and its changes under the influence of biological dysfunctions such as disease or drug treatment [61]. Protein expression depends on three different levels: (1) transcription of DNA, (2) translation of mRNA, and (3) posttranslational modification. For investigating the translational output of a cell, proteins have to be analyzed, which can be achieved by different strategies.

The main advantage of mRNA analysis represents its completeness of the accessibility to all genes which can be transcribed. A disadvantage of the use of mRNA expression profiles in characterizing cellular phenotypes is that the transcriptome does not effectively represent the proteome [61]. Just as well, mRNA abundance represents a poor indicator for the levels of corresponding protein [62, 63] and might vary by up to 30-fold and conversely [64]. Proteome analyses have the advantage to proof the expression of proteins rather than indicate that a given gene might become translated. The main limitation is due to the huge difference in protein abundance, resulting in an enormous analytical challenge [61, 65].

However, to examine the molecular phenotype of a particular cell population, proteome analysis represents a proper approach to gain insight into the network of proteins expressed at a given time and after a specific response [66].

Proteomics

Proteomics is a standardized technique for detection, identification and quantification of thousands of different proteins in various cells, tissues and body fluids. It provides the methodological basis for the analysis of aberrant, disease-related proteins [61]. The proteins of a cell represent the “molecular machinery” that reacts to altered conditions. Consequently, cells that are involved in diseases express different proteins compared to those under healthy conditions. According to the complexity of biological samples, protein analyses represent an enormous challenge. Proteins may alter their function depending on sub-cellular localization, interaction partners and amino acid modification.

Furthermore, there may be dramatic differences in the relative amounts of proteins. Within one cell, cytoskeletal proteins may be million-fold more abundant compared to e.g. signaling proteins. Within body fluids, such as blood plasma, differences in protein abundance may exceed 10-15 orders of magnitude [44].

To overcome the problem of high complexity of samples, it might be an advantage to analyze sub-cellular fractions. The protein content of a cell can be roughly divided into several compartments, which are the cytoplasmic, nuclear, mitochondrial, membrane and secreted fractions. These purified sub-cellular protein fractions represent the protein composition in a more detailed way [67]. Another advantage of working with cell fractions is that this strategy allows a better detection of low abundant proteins.

However, proteomics represent a reliable tool for the discovery of potential biomarkers for cancer and other inflammatory diseases [68-74]. Biomarkers are molecular signatures that indicate physiological and pathological changes [75], allowing early detection of disease or therapy control. As mentioned above, in contrast to methods focusing on DNA or mRNA, approaches considering proteins as potential biomarker candidates have the advantage that those are more reflective for changes in biological systems [76]. There is also strong evidence that proteins are the main initial targets of oxidative stress and free radical action [35, 77], as already described for Alzheimer, asthma, atherosclerosis, Diabetes Mellitus and other diseases [78].

For the investigation of the proteome of a cell, we focused on a combination of established proteome analysis methods, as described in the following.

2D-Polyacrylamide gel-electrophoresis (2D-PAGE)

One of the most common techniques for proteome profiling is based on the separation of proteins by means of high resolution two-dimensional gel-electrophoresis [79] (*cf.* Figure 5). The 2D-PAGE technique consists of two steps – the separation by (1) the different isoelectric point (pI) and (2) the different molecular weight. In combination with liquid chromatography tandem mass spectrometry (LC-MS/MS) it constitutes a powerful method for quantitative proteome analysis.

First dimension: Isoelectric focusing on an immobilized pH-gradient

Proteins can be separated due to their different charges, whereas the state of their charge is determined by the amino acid composition. The pH, at which the positive and negative charges of amino acids are neutral, is called the isoelectric point or pI-value. At this point, a single polypeptide is trapped in the gel-matrix during isoelectric focusing. The proteins become electrically neutral and do not migrate in the electric field anymore.

The immobilized pH-gradients are generated by means of co-polymerisation of a mixture of acrylamide derivatives composed of sulfonyl-, amino- and carboxyl groups and a gel matrix.

Second dimension: Gel electrophoresis, separation by different molecular weight

Proteins are treated with sodium dodecyl sulphate (SDS), which denatures the proteins and attaches SDS molecules to the protein proportional to its molecular weight. Due to the negative charge of the SDS molecules, all proteins acquire approximately the same mass-to-charge ratio. This is important, because after isoelectric focusing the proteins are uncharged and thus will not move in an electric field. After application of an electric field, the proteins migrate to the anode according to their mass, which are slowed by frictional forces, appearing inversely proportional to the molecular weight.

Fluorescence detection versus autoradiography

There are different methods that enable spot quantification. The quantification may be based on a two-color fluorescence labeling system [80], dual metabolic labeling with stable isotopes [81, 82] or on post-isolation isotopic protein labeling with isotope-coded affinity tags [83, 84]. Here, we used the combination of fluorescence detection and autoradiography in order to measure the protein amount of cells and to determine protein synthesis rates (*cf.* Figure 6). Furthermore, the combination of metabolic labeling of cells, sub-cellular fragmentation and subsequent 2D-analysis allows the detection of alterations in protein synthesis [67], modification and sub-cellular localization [85].

1D-Polyacrylamide gel-electrophoresis – liquid chromatography mass spectrometry (1D-PAGE - shotgun)

Another very powerful approach for proteome profiling is represented by 1D-PAGE (shotgun proteomics) with subsequent LC-MS/MS analysis. Although 2D-PAGE is the method of choice for quantitative analysis, 1D-PAGE represents a qualitative technique with high protein identification throughput.

In 1D-PAGE, complex protein mixtures are separated according to their molecular weight. The gel is then cut into several slices and digested with trypsin. The peptides are separated by nano-flow liquid chromatography and subsequently identified and quantified by mass spectrometry.

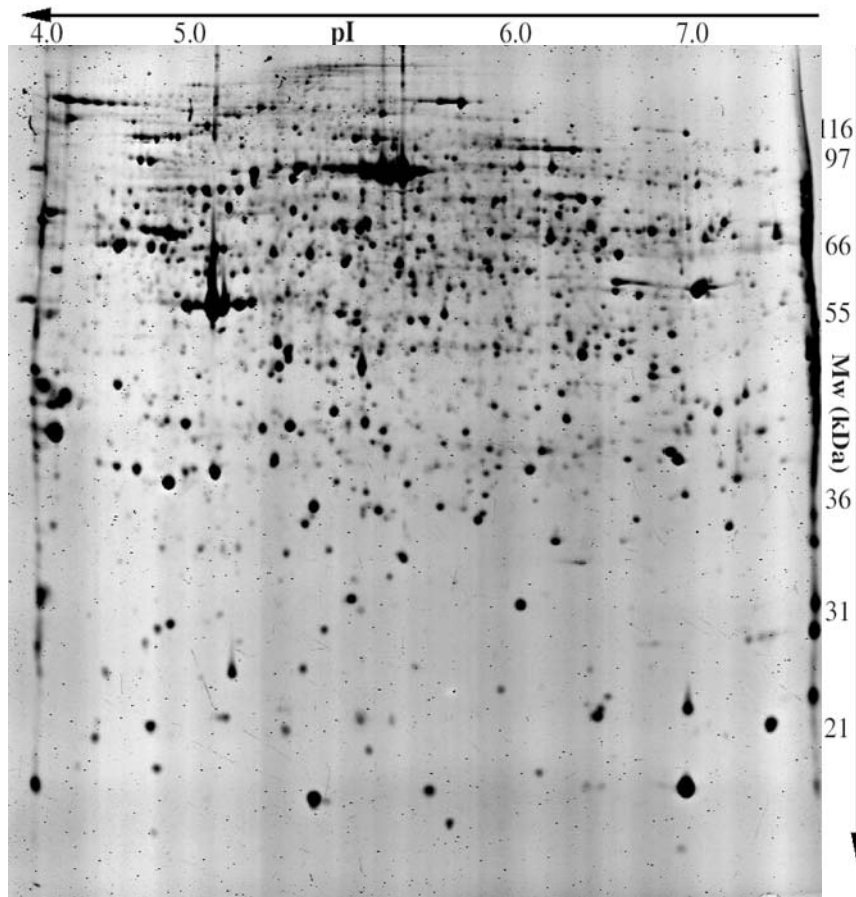


Figure 5: Fluorescence detection of a 2D-gel after separation of cellular extracts obtained from PBMCs. First dimension – separation by different pI; second dimension – separation by different molecular weight (unpublished data)

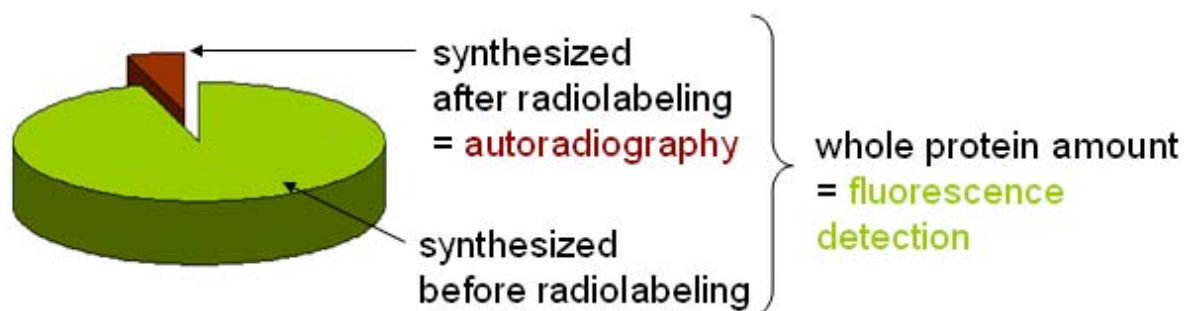


Figure 6: Fluorography versus autoradiography. The whole protein amount of a given sample can be measured by fluorescence detection, whereas autoradiography detects proteins that have been newly synthesized during the labeling period.

Protein Identification by Mass Spectrometry (MS)

Mass spectrometry represents the method of choice for the reliable and sensitive identification of proteins and peptides [86]. It is the most potent technology in proteomics and important for the global understanding of cellular functions [87].

Mass spectrometry is based on three principle components: an ion source, a mass analyzer and an ion detector. The molecules have to be charged and transferred into the gaseous phase by ionization, which can be accomplished e.g. by matrix assisted laser desorption/ionization (MALDI) or electrospray ionization (ESI) [88]. Under atmospheric pressure, ESI is based on spraying an electrically generated fine mist of ions into the mass spectrometer [87, 89].

In a second step, the ionized sample reaches the mass analyzer, where the ions are separated due to their different mass-to-charge (m/z) ratio. For mass analysis, we used an ion trap. The ions are first accumulated for several milliseconds and afterwards scanned from low to high m/z [87, 89]. In the detector the ions are detected by a photomultiplier, which results in a MS^1 spectrum or mass fingerprint, displaying an overview of peptide masses. The ion trap, however, also allows further analysis. Based on the data of MS^1 , ions with defined electrochemical properties are exclusively selected to enter the ion trap, where they get fragmented by collision with helium. Single peptide bounds are broken and the resulting peptide fragments are displayed in the MS^2 spectrum [90].

The resulting peak sequence indicates the amino acid sequence of the peptide, which can be read by combining the y- and the b-series. The y-series starts from the C-terminal and the b-series from the N-terminal end of the peptide sequence. Due to the uniqueness of many amino acid sequences of single peptides, some proteins can already be identified from one peptide sequence (*cf.* Figure 7).

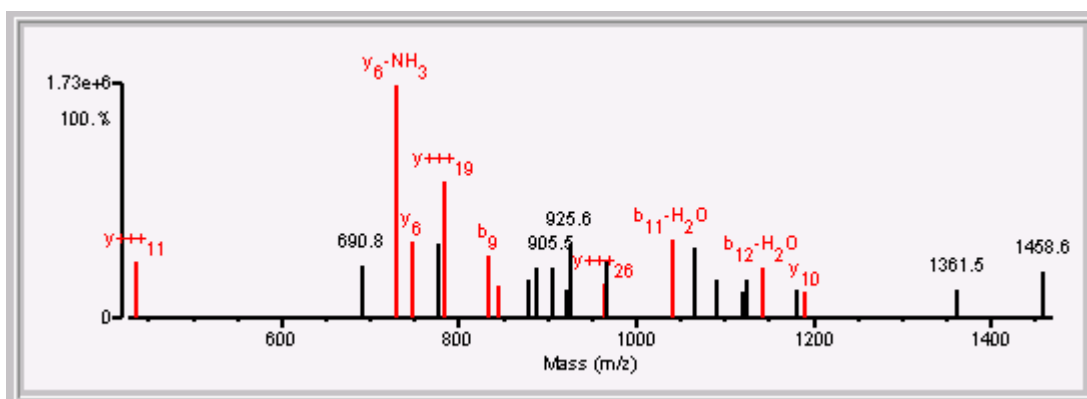


Figure 7: MS^2 spectra of one peptide. The amino acid sequence of the peptide can be reconstructed by sorting the peaks and assign the m/z differences to fitting amino acids. Y- and b-series differ in their starting points, one starts from the C-terminal and the other from the N-terminal end of the peptide sequence.

3.4. Significance of the study

To assess the impact of oxidative stress on the proteome of a cell in an accurate fashion, we combined 2D-PAGE and 1D-PAGE analyses of human PBMCs. The obtained data were further processed and analyzed by a home made SQL-database, recently designed as database of the “Clinical Proteomics Laboratories at the Medical University of Vienna” (CPL/MUW-database, Wimmer H. et al., manuscript in preparation).

The major aim of this PhD thesis was the identification of potential oxidative stress biomarkers in PBMCs and the investigation of their relation to a physiologic state (hydrogen peroxide treated, cancer patient, intervention with Brussel sprouts) or to cellular sub-populations (monocytes, T-cells, neutrophils, platelets, plasma) of the derived blood samples. In total, we detected more than 1400 different proteins in PBMCs. Out of this list we found 25 regulated proteins, either (1) by treatment with hydrogen peroxide, or (2) by comparing healthy persons (controls) versus patients with cancer, or (3) as the result of the Brussels sprout intervention.

One of the most important results was the distinct down-regulation of manganese superoxide dismutase (Mn-SOD), which has been reported to be specific for oxidative stress. One potential explanation might be the inactivation of this enzyme by hydrogen peroxide followed by proteasomal degradation as described for Cu/Zn-SOD (copper/zinc superoxide dismutase) in red blood cells by Salo et al. [91]. Furthermore, it might be that this down-regulation is part of the cells’ survival strategy. Mn-SOD decomposes superoxide to hydrogen peroxide, which is then processed to molecular oxygen and water by catalase, glutathione peroxidase and peroxiredoxin [3]. If the capacity of the hydrogen peroxide processing enzymes such as catalase is insufficient, the catalysis of the reverse conversion of H_2O_2 to superoxide by Mn-SOD will predominate. Immediate down-regulating Mn-SOD synthesis may be a strategy to reduce superoxide production under acute oxidative stress [92]. In other studies the down-regulation of Mn-SOD was also described in association with tumor suppressor activity of this protein [93-95].

Quite notably, under conditions designed to reduce oxidative stress which were introduced in the controlled Brussels sprouts intervention study, Mn-SOD was found to be significantly up-regulated. This was accompanied by the down-regulation of heat shock 70 kDa protein (hsp70). Both proteins play a role in malignant transformation of cells. Hsp70 is involved in the regulation of apoptosis, which leads to elimination of cancer cells. These findings indicate that the alteration of the synthesis of these proteins may be involved in the anticarcinogenic

effects of cruciferous vegetables, which was observed in earlier laboratory studies with animals [19].

Additionally, it was possible to generate proteome reference maps of the different PBMC cell types and plasma. With this information it should be possible to gain more detailed information about the cellular origin of potential biomarkers in PBMCs and use them for systematic comparison of tissues. Also, common occurring proteins in several different cell types can be used for quality control or for further interpretation of proteome profiles of other cell types.

In summary, these data suggests that the down-regulation of Mn-SOD might be a specific response and thus an indicator for oxidative stress. This thesis further demonstrates that the advanced methods of proteomics used in this study are highly suitable tools to identify putative markers of oxidative stress and their cellular occurrence. The reliability of those different regulated proteins such as Mn-SOD as potential biomarkers has to be evaluated by further studies.

3.5. References

1. Abuja, P.M. and R. Albertini, *Methods for monitoring oxidative stress, lipid peroxidation and oxidation resistance of lipoproteins*. Clin Chim Acta, 2001. **306**(1-2): p. 1-17.
2. Klaunig, J.E., et al., *The role of oxidative stress in chemical carcinogenesis*. Environ Health Perspect, 1998. **106 Suppl 1**: p. 289-95.
3. Karihtala, P. and Y. Soini, *Reactive oxygen species and antioxidant mechanisms in human tissues and their relation to malignancies*. Apmis, 2007. **115**(2): p. 81-103.
4. Siddiqui, M.K., S. Srivastava, and P.K. Mehrotra, *Environmental exposure to lead as a risk for prostate cancer*. Biomed Environ Sci, 2002. **15**(4): p. 298-305.
5. Singh, R., et al., *The relationship between biomarkers of oxidative DNA damage, polycyclic aromatic hydrocarbon DNA adducts, antioxidant status and genetic susceptibility following exposure to environmental air pollution in humans*. Mutat Res, 2007. **620**(1-2): p. 83-92.
6. Klaunig, J.E. and L.M. Kamendulis, *The role of oxidative stress in carcinogenesis*. Annu Rev Pharmacol Toxicol, 2004. **44**: p. 239-67.
7. Hanahan, D. and R.A. Weinberg, *The hallmarks of cancer*. Cell, 2000. **100**(1): p. 57-70.
8. Pryor, W.A., *Cancer and free radicals*. Basic Life Sci, 1986. **39**: p. 45-59.
9. Diplock, A.T., *Defense against reactive oxygen species*. Free Radic Res, 1998. **29**(6): p. 463-7.
10. Brown, N.S. and R. Bicknell, *Hypoxia and oxidative stress in breast cancer. Oxidative stress: its effects on the growth, metastatic potential and response to therapy of breast cancer*. Breast Cancer Res, 2001. **3**(5): p. 323-7.
11. Ramos, S., *Cancer chemoprevention and chemotherapy: dietary polyphenols and signalling pathways*. Mol Nutr Food Res, 2008. **52**(5): p. 507-26.
12. Nagini, S., *Cancer chemoprevention by garlic and its organosulfur compounds-panacea or promise?* Anticancer Agents Med Chem, 2008. **8**(3): p. 313-21.
13. Messina, M.J. and C.E. Wood, *Soy isoflavones, estrogen therapy, and breast cancer risk: analysis and commentary*. Nutr J, 2008. **7**: p. 17.
14. Ellinger, S., J. Ellinger, and P. Stehle, *Tomatoes, tomato products and lycopene in the prevention and treatment of prostate cancer: do we have the evidence from intervention studies?* Curr Opin Clin Nutr Metab Care, 2006. **9**(6): p. 722-7.
15. Ramos, S., *Effects of dietary flavonoids on apoptotic pathways related to cancer chemoprevention*. J Nutr Biochem, 2007. **18**(7): p. 427-42.
16. Steinmetz, K.A. and J.D. Potter, *Vegetables, fruit, and cancer prevention: a review*. J Am Diet Assoc, 1996. **96**(10): p. 1027-39.
17. Power, K.A. and L.U. Thompson, *Can the combination of flaxseed and its lignans with soy and its isoflavones reduce the growth stimulatory effect of soy and its isoflavones on established breast cancer?* Mol Nutr Food Res, 2007. **51**(7): p. 845-56.
18. Hayes, J.D., M.O. Kelleher, and I.M. Eggleston, *The cancer chemopreventive actions of phytochemicals derived from glucosinolates*. Eur J Nutr, 2008. **47 Suppl 2**: p. 73-88.
19. Dan, S., A.K. Tyagi, and H. Kaur, *Cancer modulation by glucosinolates: A review*. Current Science, 2000. **79**(12): p. 1665-1671.
20. Lynn, A., et al., *Cruciferous vegetables and colo-rectal cancer*. Proc Nutr Soc, 2006. **65**(1): p. 135-44.

21. Talalay, P. and J.W. Fahey, *Phytochemicals from cruciferous plants protect against cancer by modulating carcinogen metabolism*. J Nutr, 2001. **131**(11 Suppl): p. 3027S-33S.
22. Higdon, J.V., et al., *Cruciferous vegetables and human cancer risk: epidemiologic evidence and mechanistic basis*. Pharmacol Res, 2007. **55**(3): p. 224-36.
23. Hoelzl, C., et al., *Proteome alterations induced in human white blood cells by consumption of Brussel sprouts: Results of a pilot intervention study*. Proteomics Clin. Appl., 2008. **2**(1): p. 108-117.
24. Verhoeven, D.T., et al., *A review of mechanisms underlying anticarcinogenicity by brassica vegetables*. Chem Biol Interact, 1997. **103**(2): p. 79-129.
25. Hoelzl, C., et al., *Consumption of Brussels sprouts protects peripheral human lymphocytes against 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and oxidative DNA-damage: results of a controlled human intervention trial*. Mol Nutr Food Res, 2008. **52**(3): p. 330-41.
26. Brandes, R.P. and M. Janiszewski, *Direct detection of reactive oxygen species ex vivo*. Kidney Int, 2005. **67**(5): p. 1662-4.
27. Georgiou, C.D., et al., *An ultrasensitive fluorescent assay for the in vivo quantification of superoxide radical in organisms*. Anal Biochem, 2005. **347**(1): p. 144-51.
28. Howell, A.L., et al., *HIV-1-infected monocytes and monocyte-derived macrophages are impaired in their ability to produce superoxide radicals*. Int J Clin Lab Res, 1997. **27**(2): p. 111-7.
29. Hafer, K., K.S. Iwamoto, and R.H. Schiestl, *Refinement of the dichlorofluorescein assay for flow cytometric measurement of reactive oxygen species in irradiated and bystander cell populations*. Radiat Res, 2008. **169**(4): p. 460-8.
30. Chen, J., et al., *Enrichment of hematopoietic stem cells with SLAM and LSK markers for the detection of hematopoietic stem cell function in normal and Trp53 null mice*. Exp Hematol, 2008. **36**(10): p. 1236-43.
31. Volk, J., et al., *Oxidative burst measurement in patients treated with cytostatics: influence of G-CSF and role as a prognostic factor*. Ann Hematol, 2000. **79**(4): p. 187-97.
32. Murray, J., et al., *Monitoring oxidative and nitrative modification of cellular proteins: a paradigm for identifying key disease related markers of oxidative stress*. Adv Drug Deliv Rev, 2008. **60**(13-14): p. 1497-503.
33. Gay, C., J. Collins, and J.M. Gebicki, *Hydroperoxide assay with the ferric-xylenol orange complex*. Anal Biochem, 1999. **273**(2): p. 149-55.
34. Gay, C.A. and J.M. Gebicki, *Measurement of protein and lipid hydroperoxides in biological systems by the ferric-xylenol orange method*. Anal Biochem, 2003. **315**(1): p. 29-35.
35. Du, J. and J.M. Gebicki, *Proteins are major initial cell targets of hydroxyl free radicals*. Int J Biochem Cell Biol, 2004. **36**(11): p. 2334-43.
36. Wilkins, M.R., et al., *Progress with proteome projects: why all proteins expressed by a genome should be identified and how to do it*. Biotechnol Genet Eng Rev, 1996. **13**: p. 19-50.
37. Wan, X.Y. and J.Y. Liu, *Comparative proteomic analysis reveals an intimate protein network provoked by hydrogen peroxide stress in rice seedling leaves*. Mol Cell Proteomics, 2008.
38. Kusch, H., et al., *Proteomic analysis of the oxidative stress response in Candida albicans*. Proteomics, 2007. **7**(5): p. 686-97.
39. Kusch, H., et al., *A proteomic view of Candida albicans yeast cell metabolism in exponential and stationary growth phases*. Int J Med Microbiol, 2008. **298**(3-4): p. 291-318.

40. Lee, C.K., et al., *Proteomic profiling and identification of cofilin responding to oxidative stress in vascular smooth muscle*. Proteomics, 2006. **6**(24): p. 6455-75.
41. Seong, J.K., et al., *Proteomic analysis of the cellular proteins induced by adaptive concentrations of hydrogen peroxide in human U937 cells*. Exp Mol Med, 2002. **34**(5): p. 374-8.
42. Yamamoto, T., et al., *Identification of oxidative stress-related proteins for predictive screening of hepatotoxicity using a proteomic approach*. J Toxicol Sci, 2005. **30**(3): p. 213-27.
43. Nazarian, S.H., et al., *Tropism of Tanapox virus infection in primary human cells*. Virology, 2007. **368**(1): p. 32-40.
44. Thadikkaran, L., et al., *Recent advances in blood-related proteomics*. Proteomics, 2005. **5**(12): p. 3019-34.
45. Larosa, D.F. and J.S. Orange, 1. *Lymphocytes*. J Allergy Clin Immunol, 2008. **121**(2 Suppl): p. S364-9; quiz S412.
46. Jin, M., et al., *Two-dimensional gel proteome reference map of blood monocytes*. Proteome Sci, 2006. **4**: p. 16.
47. Pasini, E.M., et al., *In-depth analysis of the membrane and cytosolic proteome of red blood cells*. Blood, 2006. **108**(3): p. 791-801.
48. Garcia, A., et al., *Extensive analysis of the human platelet proteome by two-dimensional gel electrophoresis and mass spectrometry*. Proteomics, 2004. **4**(3): p. 656-68.
49. Garcia, A., N. Zitzmann, and S.P. Watson, *Analyzing the platelet proteome*. Semin Thromb Hemost, 2004. **30**(4): p. 485-9.
50. de Souza Castro, M., et al., *Proteome analysis of resting human neutrophils*. Protein Pept Lett, 2006. **13**(5): p. 481-7.
51. Schenk, S., et al., *A high confidence, manually validated human blood plasma protein reference set*. BMC Med Genomics, 2008. **1**: p. 41.
52. Stone, J.R., *An assessment of proposed mechanisms for sensing hydrogen peroxide in mammalian systems*. Arch Biochem Biophys, 2004. **422**(2): p. 119-24.
53. Daniel, H., *Genomics and proteomics: importance for the future of nutrition research*. Br J Nutr, 2002. **87 Suppl 2**: p. S305-11.
54. Davis, C.D. and J. Milner, *Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention*. Mutat Res, 2004. **551**(1-2): p. 51-64.
55. Go, V.L., R.R. Butrum, and D.A. Wong, *Diet, nutrition, and cancer prevention: the postgenomic era*. J Nutr, 2003. **133**(11 Suppl 1): p. 3830S-3836S.
56. Go, V.L., et al., *Diet and cancer prevention: evidence-based medicine to genomic medicine*. J Nutr, 2004. **134**(12 Suppl): p. 3513S-3516S.
57. Guengerich, F.P., *Functional genomics and proteomics applied to the study of nutritional metabolism*. Nutr Rev, 2001. **59**(8 Pt 1): p. 259-63.
58. Breikers, G., et al., *Potential protein markers for nutritional health effects on colorectal cancer in the mouse as revealed by proteomics analysis*. Proteomics, 2006. **6**(9): p. 2844-52.
59. Lee, S.C., et al., *Functional proteomics of resveratrol-induced colon cancer cell apoptosis: caspase-6-mediated cleavage of lamin A is a major signaling loop*. Proteomics, 2006. **6**(8): p. 2386-94.
60. Rowell, C., D.M. Carpenter, and C.A. Lamartiniere, *Chemoprevention of breast cancer, proteomic discovery of genistein action in the rat mammary gland*. J Nutr, 2005. **135**(12 Suppl): p. 2953S-2959S.
61. Anderson, N.L. and N.G. Anderson, *Proteome and proteomics: new technologies, new concepts, and new words*. Electrophoresis, 1998. **19**(11): p. 1853-61.

62. Anderson, L. and J. Seilhamer, *A comparison of selected mRNA and protein abundances in human liver*. Electrophoresis, 1997. **18**(3-4): p. 533-7.
63. Gygi, S.P., et al., *Correlation between protein and mRNA abundance in yeast*. Mol Cell Biol, 1999. **19**(3): p. 1720-30.
64. Futcher, B., et al., *A sampling of the yeast proteome*. Mol Cell Biol, 1999. **19**(11): p. 7357-68.
65. Schramm, A., et al., *Proteomics: techniques and applications in cancer research*. Klin Padiatr, 2003. **215**(6): p. 293-7.
66. Celis, J.E. and P. Gromov, *Proteomics in translational cancer research: toward an integrated approach*. Cancer Cell, 2003. **3**(1): p. 9-15.
67. Gundacker, N., et al., *Knowledge-based proteome profiling: considering identified proteins to evaluate separation efficiency by 2-D PAGE*. Electrophoresis, 2006. **27**(13): p. 2712-21.
68. Birrer, M.J., et al., *Proteomics as a tool for biomarker discovery*. Dis Markers, 2007. **23**(5-6): p. 411-7.
69. Wilkey, D.W. and M.L. Merchant, *Proteomic methods for biomarker discovery in urine*. Semin Nephrol, 2007. **27**(6): p. 584-96.
70. Devarajan, P., *Proteomics for Biomarker Discovery in Acute Kidney Injury*. Semin Nephrol, 2007. **27**(6): p. 637-651.
71. Maurya, P., et al., *Proteomic approaches for serum biomarker discovery in cancer*. Anticancer Res, 2007. **27**(3A): p. 1247-55.
72. Bharti, A., P.C. Ma, and R. Salgia, *Biomarker discovery in lung cancer--promises and challenges of clinical proteomics*. Mass Spectrom Rev, 2007. **26**(3): p. 451-66.
73. deVera, I.E., J.E. Katz, and D.B. Agus, *Clinical proteomics: the promises and challenges of mass spectrometry-based biomarker discovery*. Clin Adv Hematol Oncol, 2006. **4**(7): p. 541-9.
74. Choe, L.H., B.G. Werner, and K.H. Lee, *Two-dimensional protein electrophoresis: from molecular pathway discovery to biomarker discovery in neurological disorders*. NeuroRx, 2006. **3**(3): p. 327-35.
75. Zhang, H. and D.W. Chan, *Cancer biomarker discovery in plasma using a tissue-targeted proteomic approach*. Cancer Epidemiol Biomarkers Prev, 2007. **16**(10): p. 1915-7.
76. Meyer, H.E. and K. Stuhler, *High-performance Proteomics as a Tool in Biomarker Discovery*. Proteomics, 2007. **7 Suppl 1**: p. 18-26.
77. Gieseg, S., S. Duggan, and J.M. Gebicki, *Peroxidation of proteins before lipids in U937 cells exposed to peroxy radicals*. Biochem J, 2000. **350 Pt 1**: p. 215-8.
78. Dalle-Donne, I., et al., *Proteins as biomarkers of oxidative/nitrosative stress in diseases: the contribution of redox proteomics*. Mass Spectrom Rev, 2005. **24**(1): p. 55-99.
79. Gerner, C., et al., *Concomitant determination of absolute values of cellular protein amounts, synthesis rates, and turnover rates by quantitative proteome profiling*. Mol Cell Proteomics, 2002. **1**(7): p. 528-37.
80. Unlu, M., M.E. Morgan, and J.S. Minden, *Difference gel electrophoresis: a single gel method for detecting changes in protein extracts*. Electrophoresis, 1997. **18**(11): p. 2071-7.
81. Oda, Y., et al., *Accurate quantitation of protein expression and site-specific phosphorylation*. Proc Natl Acad Sci U S A, 1999. **96**(12): p. 6591-6.
82. Regnier, F.E., et al., *Comparative proteomics based on stable isotope labeling and affinity selection*. J Mass Spectrom, 2002. **37**(2): p. 133-45.
83. Gygi, S.P., et al., *Quantitative analysis of complex protein mixtures using isotope-coded affinity tags*. Nat Biotechnol, 1999. **17**(10): p. 994-9.

84. Cagney, G. and A. Emili, *De novo peptide sequencing and quantitative profiling of complex protein mixtures using mass-coded abundance tagging*. Nat Biotechnol, 2002. **20**(2): p. 163-70.
85. Gerner, C., et al., *The Fas-induced apoptosis analyzed by high throughput proteome analysis*. J Biol Chem, 2000. **275**(50): p. 39018-26.
86. Schuchardt, S. and A. Sickmann, *Protein identification using mass spectrometry: a method overview*. Exs, 2007. **97**: p. 141-70.
87. Guerrero, I.C. and O. Kleiner, *Application of mass spectrometry in proteomics*. Biosci Rep, 2005. **25**(1-2): p. 71-93.
88. Fenn, J.B., et al., *Electrospray ionization for mass spectrometry of large biomolecules*. Science, 1989. **246**(4926): p. 64-71.
89. Yates, J.R., 3rd, *Mass spectral analysis in proteomics*. Annu Rev Biophys Biomol Struct, 2004. **33**: p. 297-316.
90. Marzo, A. and L.D. Bo, *Tandem mass spectrometry (LC-MS-MS): a predominant role in bioassays for pharmacokinetic studies*. Arzneimittelforschung, 2007. **57**(2): p. 122-8.
91. Salo, D.C., et al., *Superoxide dismutase undergoes proteolysis and fragmentation following oxidative modification and inactivation*. J Biol Chem, 1990. **265**(20): p. 11919-27.
92. Haudek, V.J., et al., *Consequences of Acute and Chronic Oxidative Stress upon the Expression Pattern of Proteins in Peripheral Blood Mononuclear Cells*. J Proteome Res, 2008.
93. Chuang, T.C., et al., *Human manganese superoxide dismutase suppresses HER2/neu-mediated breast cancer malignancy*. FEBS Lett, 2007. **581**(23): p. 4443-9.
94. Oberley, L.W., *Mechanism of the tumor suppressive effect of MnSOD overexpression*. Biomed Pharmacother, 2005. **59**(4): p. 143-8.
95. Soini, Y., et al., *MnSOD expression is less frequent in tumour cells of invasive breast carcinomas than in in situ carcinomas or non-neoplastic breast epithelial cells*. J Pathol, 2001. **195**(2): p. 156-62.

4. Results and Discussion

Paper I

Proteome Maps of the Main Human Peripheral Blood Constituents

Verena J. Haudek, Nina C. Gundacker, Astrid Slany, Helge Wimmer, Christopher Gerner
Journal of Proteome Research, accepted with minor modifications

Paper II

Introducing a New Parameter for Quality Control of Proteome Profiles: Consideration of Commonly Expressed Proteins

Astrid Slany, **Verena J. Haudek**, Nina C. Gundacker, Johannes Griss, Thomas Mohr, Helge Wimmer, Maria Eisenbauer, Leonilla Elbling, Christopher Gerner
Electrophoresis 2009, in press

Paper III

Consequences of Acute and Chronic Oxidative Stress upon the Expression Pattern of Proteins in Peripheral Blood Mononuclear Cells

Verena J. Haudek, Nina C. Gundacker, Astrid Slany, Helge Wimmer, Editha Bayer, Karoline Pablé, Christopher Gerner
Published in Journal of Proteome Research 2008, 7(12), 5138-5147

Paper IV

Proteome alterations induced in human white blood cells by consumption of Brussels sprouts: Results of a pilot intervention study

Christine Hoelzl, Olga Lorenz, **Verena Haudek**, Nina Gundacker, Siegfried Knasmüller, Christopher Gerner
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Proteome Maps of the Main Human Peripheral Blood Constituents

Verena J. Haudek¹⁺, Astrid Slany¹⁺, Nina C. Gundacker¹, Helge Wimmer², Johannes Drach³,
Christopher Gerner^{1*}

¹Department of Medicine I, Institute of Cancer Research, Medical University of Vienna,
Austria

²Section Biomedical Laboratory Science, University of Applied Science, Vienna, Austria

³Department of Medicine I, Department of Clinical Oncology, Medical University of Vienna,
Austria

⁺ contributed equally

^{*} Correspondence: Christopher Gerner, Department of Medicine I, Institute of Cancer
Research, Medical University of Vienna, Austria

Email: Christopher.Gerner@meduniwien.ac.at

Phone: 0043-1-4277-65230

Abstract

Clinical proteome analysis will almost inevitably be confronted with blood constituents. Purified plasma, serum, cell or tissue samples may easily be contaminated with some other constituents, affecting the final proteome analysis result. In order to recognize proteins which are potentially indicative for the presence of major blood constituents, we purified T cells, monocytes, neutrophils, erythrocytes, platelets and plasma and performed comparative proteome profiling employing 2D-PAGE in addition to shotgun proteomics. By mass analysis, 605 different proteins were identified in the 2D gels. Seven of those displayed a highly specific expression pattern. A total of 1889 proteins were identified by shotgun proteomics, including 34 proteins with highly specific expression patterns. Indeed, proteins specific for each of the constituents were successfully identified. The corresponding genes displayed compatible expression specificities as determined by the use of GENATLAS. The present protein maps of each of the constituents may serve as references for comparative analyses and will aid the interpretation of proteome profiles of clinical materials.

Keywords:

proteome profiling, peripheral blood mononuclear cells, 2D-PAGE, shotgun proteomics, plasma, platelets, T cells, monocytes, neutrophils, erythrocytes

Introduction

Human blood represents an optimal source for discovery and analysis of biomarker. Proteins derived from diseased tissue compartments may leak into lymph and blood, eventually becoming detectable in plasma and serum. Many diseases accompanied by e.g. inflammation may directly affect the protein expression profile of blood compartments such as immune cells or platelets.¹ Such characteristic alterations may as well give rise to clinical biomarkers. Another important approach for biomarker discovery is the comparison of tissue specimen derived from healthy and diseased organs.² Differences in the finally obtained protein lists, however, may be due to epiphenomena accompanying disease states such as leukocyte invasion, platelet and fibrin deposition³ or alterations of the blood supply. It is not trivial to recognize such events from differential analysis of proteome profiles.⁴ To support data interpretation of clinical proteome profiling results, reference proteome maps might be very helpful.⁵ The knowledge of proteins expressed in a healthy background and the assignment of proteins to their potential source of origin could render comparative analyses searching for disease marker proteins easier to interpret.

Much effort has already been spent on the establishment of proteome profiles of blood constituents. Amongst others, these include the analysis of peripheral blood mononuclear cells (PBMCs),^{6, 7} lymphocytes,⁸ monocytes,⁹ neutrophils,¹⁰ erythrocytes,^{5, 11} platelets,¹²⁻¹⁴ T cells,¹⁵ and plasma.¹⁶⁻¹⁸ Proteome studies of blood constituents were employed to investigate various diseases such as atopic dermatitis,¹⁹ rheumatoid arthritis,²⁰ or to perform *in vivo* intervention studies with soy isoflavones,²¹ Brussels sprouts,²² or vitamin C supplementation.²³ Despite the large number of studies already performed, there is still a lack of standardization and it is hard to conclude for specificities in protein expression by comparing results obtained from different research teams. Therefore, systematic comparative studies employing different laboratories have been performed.²⁴ Obviously, apparent

differences are derived from variations in methods employed for the purification of constituents, for protein isolation, protein and peptide separation and protein identification. This may be not surprising, considering the large number of diverse molecules in biological samples. Thousands of different proteins occur in concentration spans up to 8-10 orders of magnitude,^{25, 26} and are mixed with metabolites, lipids, polysaccharides and nucleic acids. We have described recently that protein isolation strategies may be critical to obtain representative and reproducible results.²⁷

Here, we present a comparative proteome study of the most abundant blood constituents including plasma, lymphocytes, monocytes, platelets, neutrophils and erythrocytes. We purified each of those constituents and the analysis was confined to cytoplasmic proteins. The major aim was a reliable assignment of specific proteins to each of the different constituents. On one hand, we used 2D-PAGE and performed comparative pattern analysis. Spots were cut out and identified by mass spectrometry. On the other hand, we analyzed the same samples by shotgun proteomics^{28,29} resulting in many more protein identifications. Database-assisted analysis allowed us to identify several specifically expressed proteins which may serve as marker proteins for the respective blood constituents.

Experimental section

Isolation of PBMCs (peripheral blood mononuclear cells)

PBMCs were isolated from heparinized whole blood of different healthy donors by standard density gradient centrifugation with Ficoll-Paque (GE Healthcare Bio-Sciences AB, Uppsala, Sweden).^{8, 30} The cells were subsequently washed with HBSS (Hanks` Buffered Salt Solution, 1:1).

Isolation of plasma

2 ml of the heparinized whole blood were used for plasma isolation by centrifugation for 10 min at room temperature at 8000 g. The supernatant plasma was carefully isolated and stored at -80°C.

Monocyte and T cell separation

T cells and monocytes were separated by magnetic sorting using the MACS technique (Miltenyi Biotec, Bergisch Gladbach, Germany). Purified T cells were obtained through negative depletion of CD11b, CD14, CD16, CD19, CD33, and MHC class II-positive cells with the respective monoclonal antibody. Monocytes were enriched by using the biotinylated CD14 mAb VIM13 (achieving a cell purity 95 %) as previously described.³¹

Neutrophil and Erythrocyte separation

After standard density gradient centrifugation with Ficoll-Paque the resulting soft pellet was put on ice. 200 µl of the pellet were resuspended in 200 µl of sample buffer (7.5 M urea, 1.5 M thiourea, 4% CHAPS, 0.05% SDS, 100 mM DDT) to gain the erythrocytes. The rest of the pellet was resuspended in haemolysis buffer (0.16 M ammonium chloride, 0.01 M

potassium hydrogen carbonate, 1 μ M EDTA) to destroy erythrocytes and centrifuged to pellet neutrophils. The procedure was repeated two times to isolate the neutrophils.

Platelet separation

Whole blood of healthy donors was collected in Acid-Citrate-Dextrose-A tubes and was centrifuged at 110g for 30 minutes at room temperature. The supernatant was washed with RPMI 0 medium by centrifugation. Prostaglandin E1 (0.1 μ g/ml) (98% (HPLC) Synthetic, Sigma, Steinheim, Germany) was added during all steps to keep the thrombocytes inactivated. The pellet was resuspended in RPMI 0, an aliquote was taken for control and another aliquote was activated by Thrombin (1 μ g/ml) (Sigma, Steinheim, Germany). The platelets were then sonicated.

Sub-cellular fractionation

The isolation of cytoplasmic proteins was performed as described by Gundacker et al.²⁷ Cells were lysed in hypotonic lysis buffer (10 mM HEPES/NaOH, pH 7.4, 0.25 M sucrose, 10 mM NaCl, 3 mM MgCl₂, 0.5% Triton X-100) supplemented with protease inhibitors and pressed through a 26 g syringe to induce cell lysis. The cytoplasmic fraction was separated from nuclei by centrifugation and precipitated by addition of ethanol. Afterwards, all protein samples were dissolved in sample buffer (7.5 M urea, 1.5 M thiourea, 4% CHAPS, 0.05% SDS, 100 mM DDT).

2D polyacrylamid gel electrophoresis (2D-PAGE)

Proteins were loaded by passive rehydration on IPG strips pH 5–8, 17 cm (BioRad, Hercules, CA) at room temperature. Alternatively, IPG immobiline strips (GE) were used, which gave similar results (not shown). IEF was performed in a stepwise fashion (1 h 0– 500 V linear; 5 h 500 V; 5 h 500–3500 V linear; 12 h 3500 V). After IEF, the strips were equilibrated with 100

mM DTT and 2.5% iodacetamide according to the instructions of the manufacturer (BioRad). For SDS-PAGE using the Protean II xi electrophoresis system (BioRad), IPG strips were placed on top of 1.5 mm 12% polyacrylamide slab gels and overlaid with 0.5% low-melting agarose. The gels were stained with a 400 nM solution of Ruthenium II tris (bathophenanthroline disulfonate) (RuBPS) as described.³² Fluorography scanning was performed with the FluorImager 595 (GE Healthcare, Fairfield, CT) at a resolution of 100 μm .³³ All 2D gel data were independently reproduced two times. Gels were warped to a reference gel with the TT900 S2S software (version 2006.0.2389, Nonlinear dynamics, Carlsbad, CA) and evaluated with the Progenesis software PG200 (version 2006, Nonlinear) using the “same spot” algorithm.

1D-PAGE for subsequent shotgun analysis

Cytoplasmic protein fractions were loaded on 13% polyacrylamide gels, electrophoresis was performed until complete separation of a pre-stained molecular marker (Dual Color, Biorad, Hercules, CA) was visible. After fixation with 50% methanol/10% acetic acid and subsequent silver staining, gel lanes were cut out of the gel and digested with trypsin as described below.

MS-compatible silver staining procedure

2D gels were fixed with 50% methanol, washed and sensitized with 0.02% $\text{Na}_2\text{S}_2\text{O}_3$. The gels were stained with 0.1% AgNO_3 ice cold for 20 minutes, rinsed with bi-distilled water and subsequently developed with 3% Na_2CO_3 /0.05% formaldehyde as previously described.³⁴

Tryptic digest

Protein spots were cut out of the gel, the gel-pieces were de-stained with 15 mM $\text{K}_3\text{Fe}(\text{CN})_6$ /50 mM $\text{Na}_2\text{S}_2\text{O}_3$ and intensively washed with 50% methanol/10% acetic acid. The pH was adjusted with 50 mM NH_4HCO_3 , proteins were reduced with 10 mM DTT/50 mM

NH₄HCO₃ for 30 minutes at 56°C and alkylated with 50 mM iodoacetamide/50 mM NH₄HCO₃ 20 minutes in the dark. Afterwards the gel-pieces were treated with acetonitrile (ACN) and dried in a vacuum centrifuge. Between each step, the tubes were shaken for 5-10 minutes (Eppendorf Thermomixer comfort). Dry gel-spots were treated with trypsin 0.1 mg/ml (Trypsin sequencing grade, Roche Diagnostics, Germany)/50 mM NH₄HCO₃ for 20 minutes on ice, afterwards covered with 50 mM NH₄HCO₃ and subsequently incubated over night at 37°C. The digested peptides were eluted by adding 50 mM NH₄HCO₃, the supernatant was transferred into silicon-coated tubes, and this procedure was repeated two times with 5% formic acid/50% ACN. Between each elution step the gel-spots were ultrasonicated for 10 minutes. Finally the peptide solution was concentrated in a vacuum centrifuge to an appropriate volume.

Mass spectrometry analysis

For the identification of 2D spots, peptides were loaded on a Zorbax 300SB-C8 (5 µm, 0.3 mm, 5 mm) column and separated by nanoflow LC (1100 Series LC system, Agilent, Palo Alto, CA) with a Zorbax 300SB-C18 (5 µm, 75 mm, 150 mm) column at a flow rate of 250 nl/min using a gradient from 0.2% formic acid and 3% ACN to 0.2% formic acid and 45% ACN over 12 minutes. In case of shotgun analysis, peptides were also separated by nano-flow LC (1100 Series LC system, Agilent, Palo Alto, CA) using the HPLC-Chip technology (Agilent) equipped with a 40 nl Zorbax 300SB-C18 trapping column and a 75 µm x 150 mm Zorbax 300SB-C18 separation column at a flow rate of 400 nl/min, using a gradient from 0.2% formic acid and 3% ACN to 0.2% formic acid and 50% ACN over 80 minutes. Peptide identification was accomplished by MS/MS fragmentation analysis with an iontrap mass spectrometer (XCT-Ultra, Agilent) equipped with an orthogonal nanospray ion source. The MS/MS data, including peak list-generation and search engine, were interpreted by the Spectrum Mill MS Proteomics Workbench software (Version A.03.02, Agilent)

allowing for two missed cleavages and searched against the SwissProt Database for human proteins (Version 20080409 containing 19038 entries or, alternatively, version 14.3 containing 20328 entries) allowing for precursor mass deviation of 1.5 Da, a product mass tolerance of 0.7 Da and a minimum matched peak intensity (%SPI) of 70%. Due to previous chemical modification, carbamidomethylation of cysteine was set as fixed modification. No other modifications were considered here.

Construction of proteome reference maps

For the generation of the final protein list of all different cell types and plasma, the following protein selection algorithm was applied. Peptide scores were considered to select appropriate sequence assignments. To assess the reliability of the peptide scores, searches were performed against the corresponding reversed database. 5.9% positive hits were found with peptides scoring >9.0, while 0.21% positive hits were found with peptides scoring >13.0. Only peptides scoring higher than 9.0 were considered for protein identification. Identification details for each protein including all identified peptides, sequence coverage, peptide scores and MS2 spectra are fully accessible via PRIDE database (<http://www.ebi.ac.uk/pride/>).^{35, 36} In the final protein list (see supplementary data) the sums of all peptides related to the single proteins from the corresponding cell type are listed. Proteins derived from obvious contaminants such as fetal calf serum were deleted. Proteins were selected based on the expression of specific peptides. Selection of protein isoforms was performed as described by Zhang et al.³⁷ In case a definite assignment was not possible due to sequence homologies, the biologically most plausible candidate was selected. The derived data was further arranged and analyzed by a home made SQL-database, recently designed as database of the Clinical Proteomics Laboratories at the Medical University of Vienna (CPL/MUW-database, Wimmer H. et al, manuscript in preparation).

Results

2D-PAGE analysis of purified blood constituents

In order to assess the specificity of protein expression patterns, we employed 2D-PAGE to analyze the cytoplasmic protein fraction of three to six individual samples each of purified T cells, monocytes, neutrophils, erythrocytes and platelets in addition to blood plasma (Figure 1). Furthermore, we analyzed PBMCs which consist of lymphocytes (mainly T cells) and monocytes, interspersed to a varying degree with platelets, neutrophils, erythrocytes and plasma. Referring to previously published data, several commonly expressed proteins were readily identified.³⁸ Including proteins previously identified in PBMCs,⁷ a total of 1445 spots were cut out of the gels, resulting in the identification of 605 proteins (Table S1).

Shotgun analysis of purified blood constituents

All protein fractions analyzed by 2D-PAGE were also investigated by shotgun proteomics. Here, proteins were pre-fractionated via SDS-PAGE and the sliced gels digested with trypsin. Mass analysis was similar as applied for isolated 2D gel spots. A total of 1887 proteins were identified. All complete data analyzed in the present study is publicly accessible via PRIDE database (<http://www.ebi.ac.uk/pride/>),^{35, 36} PRIDE accessions 8884-8908. The number of proteins identified in the purified constituents is depicted in Figure 2.

In comparison, shotgun proteomics proved to be more sensitive than protein identification in 2D gels. All proteins identified in 2D gel spots were independently identified by shotgun proteomics as indicated in Table S1.

Comparative analysis searching for specifically expressed proteins

In order to find specifically expressed proteins, we compared 2D gel spot patterns of the purified constituents. It was our aim to identify proteins occurring in one, but not in any other of the purified blood constituents.

In T cells no specific protein was identified in 2D gels. Plasminogen activator inhibitor 2 (P05120) was found to be specific for monocytes; annexin A3 (P12429) for neutrophils; hemoglobin subunit beta (P68871) for erythrocytes and Integrin alpha-IIb (P08514) for platelets (Figure 1). Erythrocytes additionally displayed other specific proteins (Table 1). By means of shotgun analysis, these data were confirmed and extended. In Figure 2, the number of proteins which were only identified in the respective constituent, but not in any other, are indicated in brackets. The expression pattern of each identified protein can be retrieved from Table S1. Comparative analysis was supported by a home-made SQL-database (CPL/MUW-database, Wimmer et al., manuscript in preparation). To further evaluate the specificity of these proteins, we referred to the gene expression databases GENATLAS (<http://genatlas.medecine.univ-paris5.fr/>). In Table 1 we listed only those 34 proteins whose gene expression has been described to be specific for the particular constituent.

Database-assisted interpretation of cell samples:

The presented protein specificities can be used to assess the presence or absence of blood constituents in any protein sample of interest. The identification of a specifically expressed protein may give a strong indication for the presence of the corresponding constituent. This is exemplified for PBMCs treated *in vitro* with hydrogen peroxide (Table S2). The purified leukocyte fraction contained integrin alpha-IIb and Hemoglobin subunit alpha and beta which indicate contamination with platelets and erythrocytes.

Discussion

Enormous effort has been spent on proteome profiling of blood constituents such as serum and plasma.³⁹ The value of that effort is not doubted, as it holds great promise for biomarker discovery. The proteome profile of plasma or other body fluids, however, may be affected by a large variety of contaminants, which may occur at varying degrees. Within serum or plasma, lysed erythrocytes or platelets may be considered as contaminants which may significantly affect the final proteome profile. Otherwise, plasma and other blood constituents may be considered as potential contaminants when analyzing primary cells or tissue specimen.

According to our own experience, it is not trivial to recognize potential contaminants, which may render subsequent data interpretation inappropriate. Although a large number of proteome profiling studies have been performed on blood constituents, as mentioned above, clear specificities of protein expression can hardly be derived from these data. This is mainly due to the heterogeneity of study designs and methods.

Here, we performed a comprehensive comparative proteome profiling study of the purified blood constituents T cells, monocytes, neutrophils, erythrocytes and platelets in addition to blood plasma and PBMCs. We employed both 2D-PAGE and shotgun proteomics in order to make the final data applicable to a broad variety of proteome studies.

As expected, a large number of proteins were found to be expressed by more than one constituent (Table S1). Specific proteins of each of the purified constituents, however, were successfully identified (Table 1).

We have applied the same identification methodology to all constituents, ensuring optimal compatibility for comparative analysis. This allows as well comparison to other published data as follows.

PBMCs

Of the 174 different proteins identified in 2D gels of PBMCs by Vergara et al.,⁶ we also identified 156 proteins by shotgun analysis, representing 90% of these recently published results. In a formerly published reference 2D gel,⁷ we were able to detect 519 different proteins. 138 of these listed proteins correspond to the published data of Vergara et al..⁶

T cells

Till now, no proteome map of purified T cells has been published. We were able to detect 934 different proteins in primary human T cells by means of shotgun analysis. 95 of them were only found in this cell type. In Table 1, two specific T cell proteins are listed.

Monocytes

In a study using 2D gels for the investigation of the monocyte proteome, 231 protein spots have been identified, which corresponded to 164 different proteins.⁹ In 2D-gels we detected 391 different proteins, 108 overlap with the published data. By means of shotgun analysis, we were able to identify 837 different proteins, 85% of the 164 proteins were found in this data set. We listed three proteins as specific for monocytes (Table 1).

Platelets

2D gel platelet proteome profiles were established in several studies,^{12, 13} identifying about 800 different proteins. We detected 632 proteins by means of shotgun analysis and 328 proteins in 2D gels. In a further study, 10 potential biomarkers of platelet contaminations in PBMCs were presented.²⁴ Nine of these 10 proteins have been also found in our dataset not displaying the claimed specificity. Furthermore, their specificity for platelets could not be confirmed by means of the database GENATLAS. We listed nine other proteins as putative markers for platelet contamination (Table 1).

Erythrocytes

In an in-depth analysis of red blood cells, 587 different membrane and soluble proteins have been identified.¹¹ By shotgun analysis, we were able to identify 212 different proteins. The data overlap is about 15%. This may be mainly due to the fact that Pasini et al.¹¹ spent more

effort on pre-fractionation and focused on membrane and cytoplasmic proteins, whereas we focussed only cytoplasmic proteins.

Neutrophils

In a 2D gel based study, 102 different spots were reproducibly detected in neutrophils, 22 of them were successfully identified.¹⁰ We were able to identify 326 in 2D gels and 542 different proteins by means of shotgun proteomics. Eleven of them were found specific for neutrophils (Table 1).

Plasma

We detected 203 different proteins in plasma. A recent manually validated human blood plasma protein reference set listed 679 proteins.¹⁶ The overlap was 167 different proteins representing about 24%.

Conclusion

By means of 2D-PAGE and shotgun analysis we were able to define a set of specifically expressed proteins, which may serve as markers for one of the main blood constituents T cells, monocytes, neutrophils, erythrocytes, platelets and blood plasma. Some proteins were detectable in 2D gels, but many more were identified by shotgun proteomics. The present data may serve as reference for proteome profiling studies dealing with materials potentially contaminated with blood constituents. Furthermore, pathologic events such as tissue invasion by lymphocytes, monocytes and neutrophils or platelet aggregation may be detected in tissue samples by the use of the presently identified marker proteins.

Acknowledgments

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Supporting Information Available

Table S1: List of all detected proteins in PBMCs and purified constituents.

This table represents the total list of identified proteins in PBMCs, T cells, monocytes, neutrophils, platelets, erythrocytes and plasma. Proteins are sorted according to protein names and identified by their SwissProt Accession numbers. The numbers listed in rows indicate the number of distinct peptides identified by mass spectrometry corresponding to each constituent. Proteins which were also identified in 2D gels are marked (X)

Table S2: Example of database-assisted interpretation of a single sample. The table lists all proteins identified in a sample of PBMCs treated *in vitro* with 100 μ M hydrogen peroxide. It was chosen to show the use of database-assisted interpretation of cell samples. It is immediately possible to read the potential origins of each of the identified proteins with respect to the single constituents. This information may be used for the interpretation of differently regulated proteins in any kind of clinical sample.

This information is available free of charge via the internet at <http://pubs.arc.org>.

References

1. Lescuyer, P.; Hochstrasser, D.; Rabilloud, T., How shall we use the proteomics toolbox for biomarker discovery? *J Proteome Res* **2007**, 6, (9), 3371-6.
2. Celis, J. E.; Gromov, P., Proteomics in translational cancer research: toward an integrated approach. *Cancer Cell* **2003**, 3, (1), 9-15.
3. Gerner, C.; Steinkellner, W.; Holzmann, K.; Gsur, A.; Grimm, R.; Ensinger, C.; Obrist, P.; Sauermann, G., Elevated plasma levels of crosslinked fibrinogen gamma-chain dimer indicate cancer-related fibrin deposition and fibrinolysis. *Thromb Haemost* **2001**, 85, (3), 494-501.
4. Gerner, C., Screening for disease-markers and investigating drug effects by proteome profiling: can it meet expectations? *Comb Chem High Throughput Screen* **2004**, 7, (1), 1-9.
5. Zhang, Y.; Zhang, Y.; Adachi, J.; Olsen, J. V.; Shi, R.; de Souza, G.; Pasini, E.; Foster, L. J.; Macek, B.; Zougman, A.; Kumar, C.; Wisniewski, J. R.; Jun, W.; Mann, M., MAPU: Max-Planck Unified database of organellar, cellular, tissue and body fluid proteomes. *Nucleic Acids Res* **2007**, 35, (Database issue), D771-9.
6. Vergara, D.; Chiriaco, F.; Acierno, R.; Maffia, M., Proteomic map of peripheral blood mononuclear cells. *Proteomics* **2008**, 8, (10), 2045-51.
7. Haudek, V. J.; Gundacker, N. C.; Slany, A.; Wimmer, H.; Bayer, E.; Pable, K.; Gerner, C., Consequences of Acute and Chronic Oxidative Stress upon the Expression Pattern of Proteins in Peripheral Blood Mononuclear Cells. *J Proteome Res* **2008**.
8. Traxler, E.; Bayer, E.; Stockl, J.; Mohr, T.; Lenz, C.; Gerner, C., Towards a standardized human proteome database: quantitative proteome profiling of living cells. *Proteomics* **2004**, 4, (5), 1314-23.
9. Jin, M.; Diaz, P. T.; Bourgeois, T.; Eng, C.; Marsh, C. B.; Wu, H. M., Two-dimensional gel proteome reference map of blood monocytes. *Proteome Sci* **2006**, 4, 16.
10. de Souza Castro, M.; de Sa, N. M.; Gadelha, R. P.; de Sousa, M. V.; Ricart, C. A.; Fontes, B.; Fontes, W., Proteome analysis of resting human neutrophils. *Protein Pept Lett* **2006**, 13, (5), 481-7.
11. Pasini, E. M.; Kirkegaard, M.; Mortensen, P.; Lutz, H. U.; Thomas, A. W.; Mann, M., In-depth analysis of the membrane and cytosolic proteome of red blood cells. *Blood* **2006**, 108, (3), 791-801.
12. Garcia, A.; Prabhakar, S.; Brock, C. J.; Pearce, A. C.; Dwek, R. A.; Watson, S. P.; Hebestreit, H. F.; Zitzmann, N., Extensive analysis of the human platelet proteome by two-dimensional gel electrophoresis and mass spectrometry. *Proteomics* **2004**, 4, (3), 656-68.
13. O'Neill, E. E.; Brock, C. J.; von Kriegsheim, A. F.; Pearce, A. C.; Dwek, R. A.; Watson, S. P.; Hebestreit, H. F., Towards complete analysis of the platelet proteome. *Proteomics* **2002**, 2, (3), 288-305.
14. Garcia, A.; Zitzmann, N.; Watson, S. P., Analyzing the platelet proteome. *Semin Thromb Hemost* **2004**, 30, (4), 485-9.
15. Caron, M.; Imam-Sghiouar, N.; Poirier, F.; Le Caer, J. P.; Labas, V.; Joubert-Caron, R., Proteomic map and database of lymphoblastoid proteins. *J Chromatogr B Analyt Technol Biomed Life Sci* **2002**, 771, (1-2), 197-209.
16. Schenk, S.; Schoenhals, G. J.; de Souza, G.; Mann, M., A high confidence, manually validated human blood plasma protein reference set. *BMC Med Genomics* **2008**, 1, 41.
17. Stempfer, R.; Kubicek, M.; Lang, I. M.; Christa, N.; Gerner, C., Quantitative assessment of human serum high-abundance protein depletion. *Electrophoresis* **2008**, 29, (21), 4316-23.

18. Hortin, G. L.; Sviridov, D.; Anderson, N. L., High-abundance polypeptides of the human plasma proteome comprising the top 4 logs of polypeptide abundance. *Clin Chem* **2008**, 54, (10), 1608-16.
19. Kim, W. K.; Cho, H. J.; Ryu, S. I.; Hwang, H. R.; Kim, D. H.; Ryu, H. Y.; Chung, J. W.; Kim, T. Y.; Park, B. C.; Bae, K. H.; Ko, Y.; Lee, S. C., Comparative proteomic analysis of peripheral blood mononuclear cells from atopic dermatitis patients and healthy donors. *BMB Rep* **2008**, 41, (8), 597-603.
20. Schulz, M.; Dotzlaw, H.; Mikkat, S.; Eggert, M.; Neeck, G., Proteomic analysis of peripheral blood mononuclear cells: selective protein processing observed in patients with rheumatoid arthritis. *J Proteome Res* **2007**, 6, (9), 3752-9.
21. Fuchs, D.; Vafeiadou, K.; Hall, W. L.; Daniel, H.; Williams, C. M.; Schroot, J. H.; Wenzel, U., Proteomic biomarkers of peripheral blood mononuclear cells obtained from postmenopausal women undergoing an intervention with soy isoflavones. *Am J Clin Nutr* **2007**, 86, (5), 1369-75.
22. Hoelzl, C.; Lorenz, O.; Haudek, V.; Gundacker, N.; Knasmüller, S.; Gerner, C., Proteome alterations induced in human white blood cells by consumption of Brussel sprouts: Results of a pilot intervention study. *Proteomics Clin. Appl.* **2008**, 2, (1), 108-117.
23. Griffiths, H. R.; Willetts, R. S.; Grant, M. M.; Mistry, N.; Lunec, J.; Bevan, R. J., In vivo vitamin C supplementation increases phosphoinositol transfer protein expression in peripheral blood mononuclear cells from healthy individuals. *Br J Nutr* **2008**, 1-8.
24. de Roos, B.; Duthie, S. J.; Polley, A. C.; Mulholland, F.; Bouwman, F. G.; Heim, C.; Rucklidge, G. J.; Johnson, I. T.; Mariman, E. C.; Daniel, H.; Elliott, R. M., Proteomic methodological recommendations for studies involving human plasma, platelets, and peripheral blood mononuclear cells. *J Proteome Res* **2008**, 7, (6), 2280-90.
25. Shen, Y.; Jacobs, J. M.; Camp, D. G., 2nd; Fang, R.; Moore, R. J.; Smith, R. D.; Xiao, W.; Davis, R. W.; Tompkins, R. G., Ultra-high-efficiency strong cation exchange LC/RPLC/MS/MS for high dynamic range characterization of the human plasma proteome. *Anal Chem* **2004**, 76, (4), 1134-44.
26. Thadikkaran, L.; Siegenthaler, M. A.; Crettaz, D.; Queloz, P. A.; Schneider, P.; Tissot, J. D., Recent advances in blood-related proteomics. *Proteomics* **2005**, 5, (12), 3019-34.
27. Gundacker, N.; Bayer, E.; Traxler, E.; Zwickl, H.; Kubicek, M.; Stockl, J.; Gerner, C., Knowledge-based proteome profiling: considering identified proteins to evaluate separation efficiency by 2-D PAGE. *Electrophoresis* **2006**, 27, (13), 2712-21.
28. Chen, E. I.; Hewel, J.; Felding-Habermann, B.; Yates, J. R., 3rd, Large scale protein profiling by combination of protein fractionation and multidimensional protein identification technology (MudPIT). *Mol Cell Proteomics* **2006**, 5, (1), 53-6.
29. Nesvizhskii, A. I.; Aebersold, R., Interpretation of shotgun proteomic data: the protein inference problem. *Mol Cell Proteomics* **2005**, 4, (10), 1419-40.
30. Gerner, C.; Sauermann, G., Nuclear matrix proteins specific for subtypes of human hematopoietic cells. *J Cell Biochem* **1999**, 72, (4), 470-82.
31. Pickl, W. F.; Majdic, O.; Kohl, P.; Stockl, J.; Riedl, E.; Scheinecker, C.; Bello-Fernandez, C.; Knapp, W., Molecular and functional characteristics of dendritic cells generated from highly purified CD14⁺ peripheral blood monocytes. *J Immunol* **1996**, 157, (9), 3850-9.
32. Rabilloud, T.; Strub, J. M.; Luche, S.; van Dorsselaer, A.; Lunardi, J., A comparison between Sypro Ruby and ruthenium II tris (bathophenanthroline disulfonate) as fluorescent stains for protein detection in gels. *Proteomics* **2001**, 1, (5), 699-704.
33. Zwickl, H.; Traxler, E.; Staettner, S.; Parzefall, W.; Grasl-Kraupp, B.; Karner, J.; Schulte-Hermann, R.; Gerner, C., A novel technique to specifically analyze the secretome of cells and tissues. *Electrophoresis* **2005**, 26, (14), 2779-85.

34. Mortz, E.; Krogh, T. N.; Vorum, H.; Gorg, A., Improved silver staining protocols for high sensitivity protein identification using matrix-assisted laser desorption/ionization-time of flight analysis. *Proteomics* **2001**, 1, (11), 1359-63.
35. Jones, P.; Cote, R. G.; Cho, S. Y.; Klie, S.; Martens, L.; Quinn, A. F.; Thorneycroft, D.; Hermjakob, H., PRIDE: new developments and new datasets. *Nucleic Acids Res* **2008**, 36, (Database issue), D878-83.
36. Jones, P.; Cote, R. G.; Martens, L.; Quinn, A. F.; Taylor, C. F.; Derache, W.; Hermjakob, H.; Apweiler, R., PRIDE: a public repository of protein and peptide identifications for the proteomics community. *Nucleic Acids Res* **2006**, 34, (Database issue), D659-63.
37. Zhang, B.; Chambers, M. C.; Tabb, D. L., Proteomic parsimony through bipartite graph analysis improves accuracy and transparency. *J Proteome Res* **2007**, 6, (9), 3549-57.
38. Slany, A.; Haudek, V. J.; Gundacker, N., C.; Griss, J.; Mohr, T.; Wimmer, H.; Eisenbauer, M.; Elbling, L.; Gerner, C., Introducing a New Parameter for Quality Control of Proteome Profiles: Consideration of Commonly Expressed Proteins *Electrophoresis* **2008**, (in press).
39. Omenn, G. S.; Aebersold, R.; Paik, Y. K., 7(th) HUPO World Congress of Proteomics: Launching the Second Phase of the HUPO Plasma Proteome Project (PPP-2) 16-20 August 2008, Amsterdam, The Netherlands. *Proteomics* **2008**.

Legend to the figures/tables

Figure 1:

Specific proteins indicated in 2D gel sections of PBMCs, monocytes, platelets, neutrophils, plasma and erythrocytes. For each constituent except T cells, one potential marker protein was exemplified to demonstrate specific expression. For orientation on the gels, actin (P60709) was marked with a pentagon. The following proteins, detected by fluorescence staining, were depicted on the 2D gel sections: plasminogen activator inhibitor 2, P05120 (monocytes), annexin A3, P12429 (neutrophils), hemoglobin subunit alpha, P69905 (erythrocytes), integrin alpha-IIb, P08514 (platelets) and serum albumin, P02768 (plasma). Full circles indicate expressed proteins, whereas dashed circles indicate the localization of the absent proteins.

Figure 2:

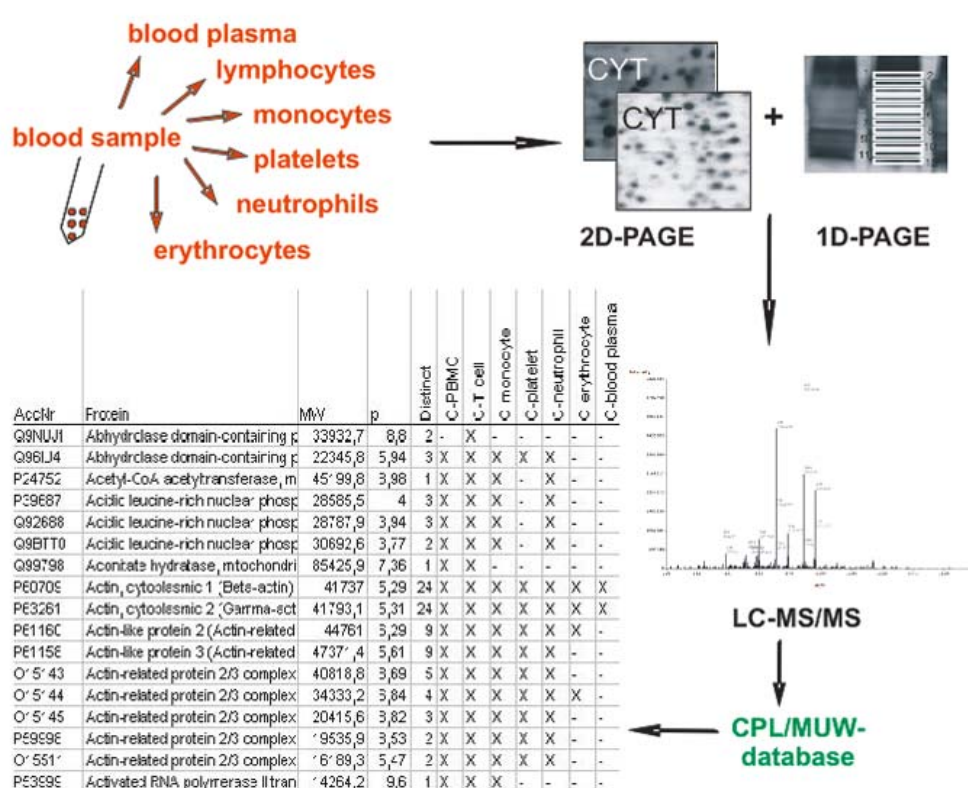
Number of proteins in PBMCs, T cells, monocytes, platelets, neutrophils, erythrocytes and plasma identified by shotgun proteomics. In total, 1887 proteins have been identified. In the figure the total number of identified proteins for each constituent is listed, the X-axis represents the corresponding percentage with respect to the total number of proteins. The dark gray bar represents ubiquitous proteins, the dashed bar represents the numbers of proteins which were only identified in the respective constituent, but not in any others. The corresponding number for each constituent is also indicated in brackets.

Table 1:

Proteins specifically occurring in the purified constituents as indicated. Proteins were identified by shotgun proteomics, the observed specificity was also found to apply to the corresponding genes according to gene expression data. Proteins which were also detectable on 2D gels are listed under “2D”.

Synopsis:

Blood mainly consists of lymphocytes, monocytes, neutrophils, erythrocytes, platelets and plasma. We purified these constituents and applied 2D-PAGE in addition to shotgun proteomics, resulting in the identification of 1887 proteins. For each constituent we present specifically expressed marker proteins. These data provide validated reference proteome maps of each constituent and may aid the interpretation of clinical proteome data.



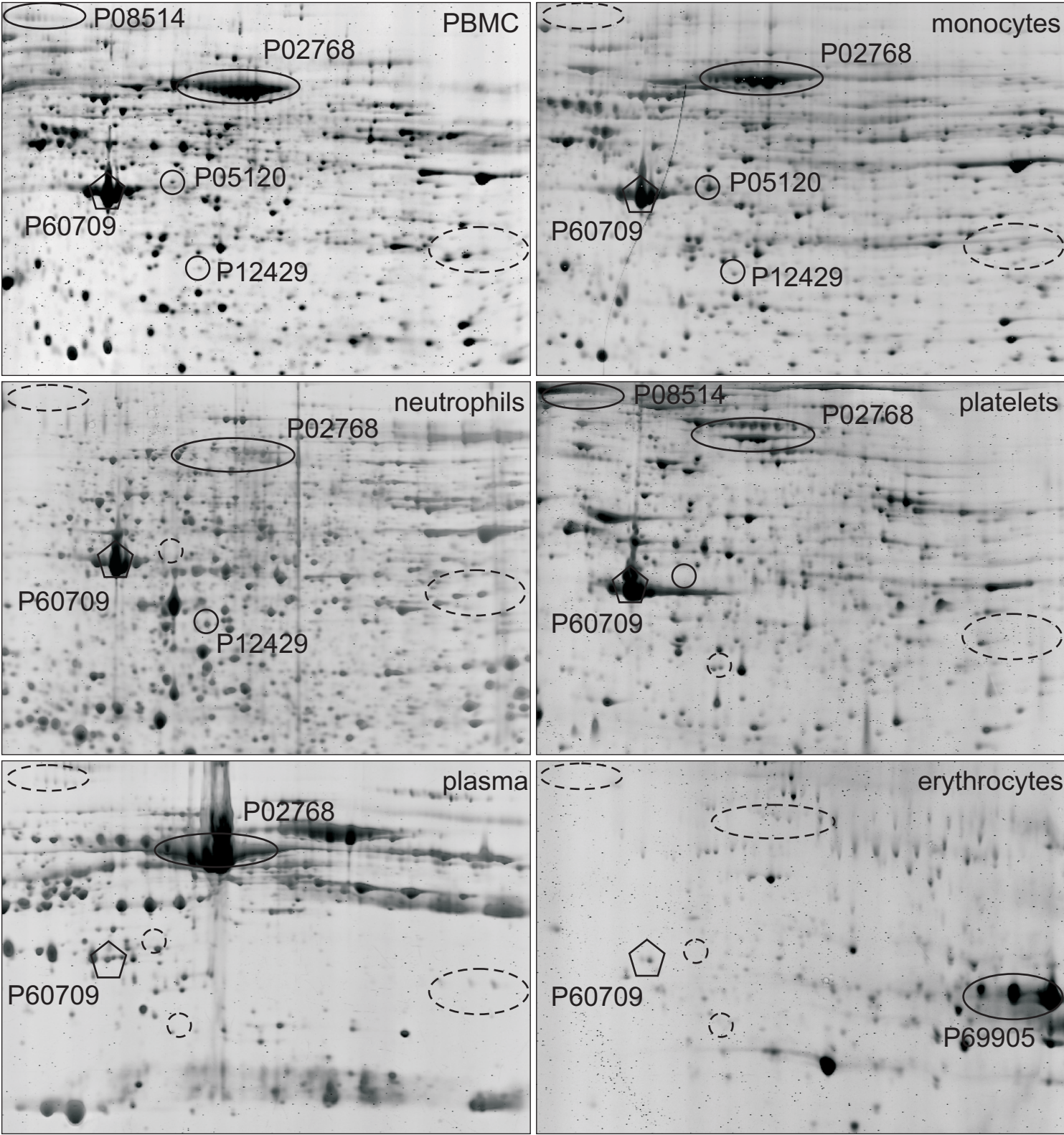


Figure 1

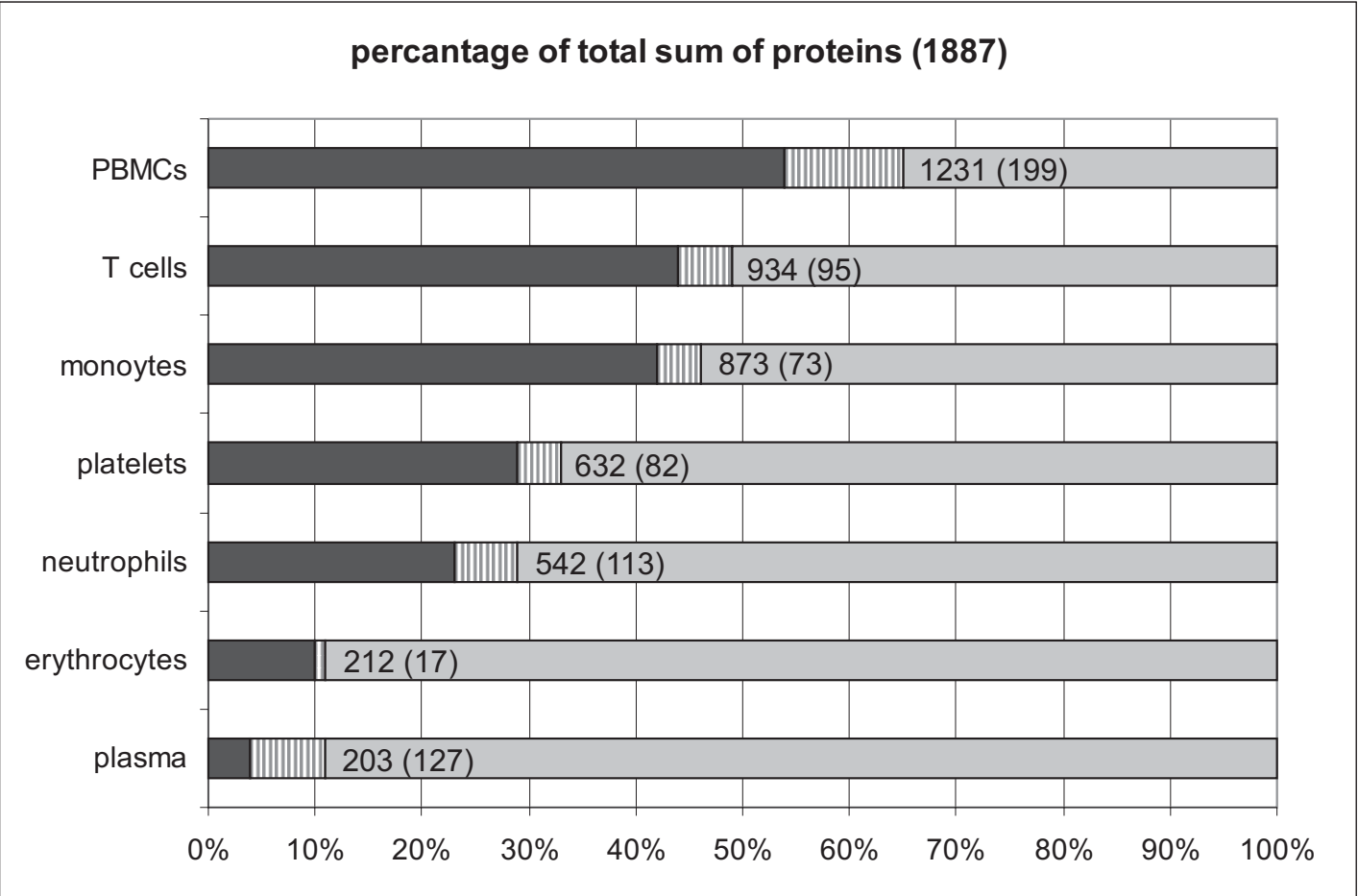


Figure 2

cell-specific proteins (without plasma)			
cell type	AccNr	Protein	2D
monocytes	P05120	Plasminogen activator inhibitor 2 precursor	x
	Q9Y336	Sialic acid-binding Ig-like lectin 9 precursor	
	O60603	Toll-like receptor 2 precursor	
T cells	P23743	Diacylglycerol kinase alpha	
	P14151	L-selectin precursor	
platelets	P08514	Integrin alpha-IIb precursor	x
	P22064	Latent-transforming growth factor beta-binding protein, isoform 1S precursor	
	Q14766	Latent-transforming growth factor beta-binding protein, isoform 1L precursor	
	Q13201	Multimerin-1 precursor	
	P02776	Platelet factor 4 precursor	
	P10720	Platelet factor 4 variant precursor	
	P07359	Platelet glycoprotein Ib alpha chain precursor	
	P40197	Platelet glycoprotein V precursor	
	P16109	P-selectin precursor	
neutrophils	P49913	Cathelicidin antimicrobial peptide precursor	
	P20061	Transcobalamin-1 precursor	
	P12429	Annexin A3	x
	P17213	Bactericidal permeability-increasing protein precursor	
	P59665	Neutrophil defensin 1 precursor	
	Q08477	Cytochrome P450 4F3	
	P22894	Neutrophil collagenase precursor	
	P11678	Eosinophil peroxidase precursor	
	O15389	Sialic acid-binding Ig-like lectin 5	
	O75015	Low affinity immunoglobulin gamma Fc region receptor III-B precursor	
	Q8N6Q3	CD177 antigen	
erythrocytes	P02730	Band 3 anion transport protein	x
	P16452	Erythrocyte membrane protein band 4.2	
	P69905	Hemoglobin subunit alpha (Alpha-globin)	x
	P68871	Hemoglobin subunit beta (Beta-globin)	
	P02042	Hemoglobin subunit delta (Delta-globin)	
	P69891	Hemoglobin subunit gamma-1	x
	P11171	Protein 4.1	
	P02549	Spectrin alpha chain, erythrocyte	
	P11277	Spectrin beta chain, erythrocyte	x

Table 1

Supplementary Table 1

	AccNr	Protein	plasma	erythrocytes	platelets	neutrophils	T cells	monocytes	PBMCs	2D
1	Q04446	1,4-alpha-glucan branching enzyme (EC 2,4,1,18) (Gly	-	-	-	3	-	-	-	-
2	P61604	10 kDa heat shock protein, mitochondrial (Hsp10) (10	-	-	2	2	2	5	6	X
3	P42704	130 kDa leucine-rich protein (LRP 130) (GP130) (Leuc	-	-	-	1	-	1	16	X
4	Q9NRX4	14 kDa phosphohistidine phosphatase (EC 3.1.3.-) (Ph	-	-	-	-	2	-	-	-
5	P31946	14-3-3 protein beta/alpha (Protein kinase C inhibitor pr	-	-	8	4	10	9	13	-
6	P62258	14-3-3 protein epsilon (14-3-3E)	-	3	13	3	10	10	12	-
7	Q04917	14-3-3 protein eta (Protein AS1)	-	-	10	6	11	4	7	-
8	P61981	14-3-3 protein gamma (Protein kinase C inhibitor prote	-	-	9	-	10	9	9	X
9	P27348	14-3-3 protein theta (14-3-3 protein tau) (14-3-3 protei	-	-	8	2	12	8	12	-
10	P63104	14-3-3 protein zeta/delta (Protein kinase C inhibitor pro	-	-	19	7	23	14	17	X
11	O60613	15 kDa selenoprotein precursor	-	-	-	-	-	-	2	-
12	Q9Y4L1	150 kDa oxygen-regulated protein precursor (Orp150)	-	-	-	-	1	-	4	X
13	Q99943	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha	-	-	-	-	-	-	1	-
14	P09543	2*,3*-cyclic-nucleotide 3*-phosphodiesterase (EC 3,1,4	-	-	-	1	-	-	-	-
15	Q16698	2,4-dienoyl-CoA reductase, mitochondrial precursor (E	-	-	-	-	3	1	3	-
16	P62191	26S protease regulatory subunit 4 (P26s4) (Proteasom	-	1	-	-	-	-	-	X
17	P17980	26S protease regulatory subunit 6A (TAT-binding prote	-	-	-	-	2	-	3	X
18	P43686	26S protease regulatory subunit 6B (MIP224) (MB67-i	-	-	-	-	-	3	2	X
19	P62195	26S protease regulatory subunit 8 (Proteasome subun	-	-	-	-	1	1	2	X
20	P62333	26S protease regulatory subunit S10B (Proteasome su	-	1	-	-	3	1	5	X
21	Q99460	26S proteasome non-ATPase regulatory subunit 1 (26	-	1	-	-	-	1	3	-
22	O75832	26S proteasome non-ATPase regulatory subunit 10 (2	-	-	-	-	-	-	2	-
23	O00231	26S proteasome non-ATPase regulatory subunit 11 (2	-	-	1	-	1	1	1	X
24	O00232	26S proteasome non-ATPase regulatory subunit 12 (2	-	1	-	-	1	1	2	-
25	Q9UNM6	26S proteasome non-ATPase regulatory subunit 13 (2	-	-	1	-	2	1	1	X
26	O00487	26S proteasome non-ATPase regulatory subunit 14 (2	-	-	-	-	1	-	1	X
27	Q13200	26S proteasome non-ATPase regulatory subunit 2 (26	-	1	-	-	3	3	4	-
28	O43242	26S proteasome non-ATPase regulatory subunit 3 (26	-	-	-	-	2	10	3	-
29	Q15008	26S proteasome non-ATPase regulatory subunit 6 (26	-	-	-	-	-	2	-	-
30	P51665	26S proteasome non-ATPase regulatory subunit 7 (26	-	-	-	-	2	1	1	X
31	P48556	26S proteasome non-ATPase regulatory subunit 8 (26	-	-	-	-	1	2	1	X
32	Q13442	28 kDa heat- and acid-stable phosphoprotein (PDGF-a	-	-	-	-	-	-	2	-
33	Q02218	2-oxoglutarate dehydrogenase E1 component, mitoch	-	-	-	-	6	-	5	X
34	P42126	3,2-trans-enoyl-CoA isomerase, mitochondrial precurs	-	-	-	-	4	1	-	X
35	Q9Y3B7	39S ribosomal protein L11, mitochondrial precursor (L	-	-	-	-	-	-	2	-
36	P52815	39S ribosomal protein L12, mitochondrial precursor (L	-	-	-	-	1	1	-	X
37	Q7Z2W9	39S ribosomal protein L21, mitochondrial precursor (L	-	-	-	-	-	-	1	-
38	Q99714	3-hydroxyacyl-CoA dehydrogenase type II (EC 1.1.1.3	-	-	8	1	11	8	12	X
39	Q9BUT1	3-hydroxybutyrate dehydrogenase type 2 (EC 1.1.1.30	-	-	-	-	-	-	1	-
40	P31937	3-hydroxyisobutyrate dehydrogenase, mitochondrial pr	-	-	-	-	2	1	4	X
41	P42765	3-ketoacyl-CoA thiolase, mitochondrial (EC 2.3.1.16) (	-	-	-	-	2	-	1	-
42	P09110	3-ketoacyl-CoA thiolase, peroxisomal precursor (EC 2	-	-	-	1	-	-	-	-
43	P25325	3-mercaptopyruvate sulfurtransferase (EC 2.8.1.2) (M	-	-	1	1	1	-	-	X
44	P46783	40S ribosomal protein S10	-	-	-	-	6	1	5	-
45	P62280	40S ribosomal protein S11 - Homo sapiens (Human)	-	-	-	-	8	-	7	-
46	P25398	40S ribosomal protein S12 - Homo sapiens (Human)	-	-	-	-	1	-	4	X
47	P62277	40S ribosomal protein S13	-	-	-	-	5	-	6	-
48	P62263	40S ribosomal protein S14	-	-	-	-	7	1	9	-
49	P62841	40S ribosomal protein S15 (RIG protein) - Homo sapie	-	-	-	-	1	-	2	-
50	P62244	40S ribosomal protein S15a	-	-	-	-	3	2	7	-

51	P62249	40S ribosomal protein S16	-	-	-	-	7	1	8	-
52	P08708	40S ribosomal protein S17 - Homo sapiens (Human)	-	-	-	-	3	-	5	-
53	P62269	40S ribosomal protein S18 (Ke-3) (Ke3)	-	-	-	-	10	1	8	-
54	P39019	40S ribosomal protein S19	-	-	-	-	3	-	7	-
55	P15880	40S ribosomal protein S2 (S4) (LLRep3 protein) - Homo sapiens (Human)	-	-	-	-	3	1	5	-
56	P60866	40S ribosomal protein S20 - Homo sapiens (Human)	-	-	-	-	2	-	5	-
57	P63220	40S ribosomal protein S21	-	-	-	-	1	-	-	-
58	P62266	40S ribosomal protein S23 - Homo sapiens (Human)	-	-	-	-	1	-	-	-
59	P62847	40S ribosomal protein S24 - Homo sapiens (Human)	-	-	-	-	3	-	2	-
60	P62851	40S ribosomal protein S25	-	-	-	-	2	-	2	-
61	P62854	40S ribosomal protein S26	-	-	-	-	3	1	3	-
62	P62857	40S ribosomal protein S28	-	-	-	-	1	3	1	-
63	P23396	40S ribosomal protein S3 - Homo sapiens (Human)	-	2	-	-	9	1	12	-
64	P61247	40S ribosomal protein S3a - Homo sapiens (Human)	-	-	-	-	6	-	10	-
65	P62701	40S ribosomal protein S4, X isoform (Single copy abundant)	-	-	-	-	6	-	8	-
66	P46782	40S ribosomal protein S5	-	-	-	-	5	1	2	-
67	P62753	40S ribosomal protein S6 (Phosphoprotein NP33)	-	-	-	-	4	-	5	-
68	P62081	40S ribosomal protein S7	-	-	-	-	8	2	6	-
69	P62241	40S ribosomal protein S8	-	-	-	-	6	1	7	-
70	P46781	40S ribosomal protein S9 - Homo sapiens (Human)	-	-	-	-	4	-	3	-
71	P08865	40S ribosomal protein SA (p40) (34/67 kDa laminin receptor)	-	-	-	-	8	2	5	X
72	P08195	4F2 cell-surface antigen heavy chain (4F2hc) (Lymphocyte)	-	-	-	-	-	1	1	-
73	P49189	4-trimethylaminobutyraldehyde dehydrogenase (EC 1.2.1.10)	-	1	-	-	8	-	8	X
74	Q8TCD5	5*(3*)-deoxyribonucleotidase, cytosolic type (EC 3.1.3.1)	-	-	-	-	1	-	1	-
75	Q00013	55 kDa erythrocyte membrane protein (p55) (Membrane protein)	-	-	2	-	-	-	-	-
76	P10809	60 kDa heat shock protein, mitochondrial precursor (Hsp60)	-	-	15	1	26	15	21	X
77	P05388	60S acidic ribosomal protein P0 (L10E)	-	-	-	-	7	1	7	X
78	P05386	60S acidic ribosomal protein P1	-	-	-	-	-	1	1	-
79	P05387	60S acidic ribosomal protein P2	-	-	-	-	5	2	4	-
80	P27635	60S ribosomal protein L10 (QM protein) (Tumor suppressor)	-	-	-	-	1	-	5	-
81	P62906	60S ribosomal protein L10a (CSA-19) - Homo sapiens (Human)	-	-	-	-	1	-	1	-
82	P62913	60S ribosomal protein L11 (CLL-associated antigen KV)	-	-	-	-	6	1	5	-
83	P30050	60S ribosomal protein L12	-	-	-	-	6	3	5	-
84	P26373	60S ribosomal protein L13 (Breast basic conserved protein)	-	-	-	-	3	-	5	-
85	P50914	60S ribosomal protein L14 (CAG-ISL 7) - Homo sapiens (Human)	-	-	-	-	2	1	3	-
86	P61313	60S ribosomal protein L15 - Homo sapiens (Human)	-	-	-	-	2	-	2	-
87	P18621	60S ribosomal protein L17 (L23) - Homo sapiens (Human)	-	-	-	-	6	-	2	-
88	Q07020	60S ribosomal protein L18	-	-	-	-	1	-	3	-
89	Q02543	60S ribosomal protein L18a - Homo sapiens (Human)	-	-	-	-	4	-	3	-
90	P46778	60S ribosomal protein L21 - Homo sapiens (Human)	-	-	-	-	3	-	1	-
91	P35268	60S ribosomal protein L22 (Epstein-Barr virus small R protein)	-	-	-	-	1	1	5	-
92	P62829	60S ribosomal protein L23 (Ribosomal protein L17)	-	-	-	-	2	1	6	-
93	P62750	60S ribosomal protein L23a - Homo sapiens (Human)	-	-	-	-	5	1	2	-
94	P83731	60S ribosomal protein L24 (Ribosomal protein L30) - Homo sapiens (Human)	-	-	-	-	2	-	-	-
95	P61254	60S ribosomal protein L26	-	-	-	-	4	-	-	-
96	P61353	60S ribosomal protein L27 - Homo sapiens (Human)	-	-	-	-	3	-	-	-
97	P46776	60S ribosomal protein L27a - Homo sapiens (Human)	-	-	-	-	5	-	2	-
98	P46779	60S ribosomal protein L28 - Homo sapiens (Human)	-	-	-	-	3	-	2	-
99	P47914	60S ribosomal protein L29 (Cell surface heparin-binding protein)	-	-	-	-	2	-	1	-
100	P39023	60S ribosomal protein L3 (HIV-1 TAR RNA-binding protein)	-	-	-	-	4	-	7	-
101	P62888	60S ribosomal protein L30	-	-	-	-	3	1	3	-
102	P62910	60S ribosomal protein L32 - Homo sapiens (Human)	-	-	-	-	3	-	-	-
103	P42766	60S ribosomal protein L35 - Homo sapiens (Human)	-	-	-	-	3	1	-	-
104	P61513	60S ribosomal protein L37a - Homo sapiens (Human)	-	-	-	-	-	-	1	-
105	P63173	60S ribosomal protein L38 - Homo sapiens (Human)	-	-	-	-	2	2	4	-
106	P36578	60S ribosomal protein L4 (L1) - Homo sapiens (Human)	-	-	-	-	5	-	4	-

107	P46777	60S ribosomal protein L5 - Homo sapiens (Human)	-	1	-	-	2	-	5	-
108	Q02878	60S ribosomal protein L6 (TAX-responsive enhancer e	-	-	-	-	4	1	5	-
109	P18124	60S ribosomal protein L7 - Homo sapiens (Human)	-	-	-	-	2	-	5	-
110	P62424	60S ribosomal protein L7a (Surfeit locus protein 3) (PL	-	-	-	-	2	-	5	-
111	P62917	60S ribosomal protein L8 - Homo sapiens (Human)	-	-	-	-	4	-	2	-
112	P32969	60S ribosomal protein L9 - Homo sapiens (Human)	-	-	-	-	4	-	3	-
113	Q01813	6-phosphofructokinase type C (EC 2.7.1.11) (Phospho	-	3	3	-	-	-	1	-
114	P17858	6-phosphofructokinase, liver type (EC 2.7.1.11) (Phos	-	-	-	-	-	4	5	-
115	P52209	6-phosphogluconate dehydrogenase, decarboxylating	-	-	1	17	5	12	7	X
116	O95336	6-phosphogluconolactonase (EC 3.1.1.31) (6PGL)	-	-	4	8	7	10	9	X
117	P11021	78 kDa glucose-regulated protein precursor (GRP 78)	-	-	25	2	22	22	23	X
118	Q9NUJ1	Abhydrolase domain-containing protein 10, mitochond	-	-	-	-	1	-	-	-
119	Q8NFV4	Abhydrolase domain-containing protein 11 - Homo sap	-	-	3	1	-	1	1	-
120	Q96IU4	Abhydrolase domain-containing protein 14B (CCG1-in	-	-	2	2	6	5	6	X
121	P24752	Acetyl-CoA acetyltransferase, mitochondrial precursor	-	-	-	4	5	4	3	X
122	O00400	Acetyl-coenzyme A transporter 1 (AT-1) (Acetyl-CoA tr	-	-	-	-	-	-	1	-
123	Q13510	Acid ceramidase precursor (EC 3.5.1.23) (Acylsphingo	-	-	-	5	2	5	5	X
124	P39687	Acidic leucine-rich nuclear phosphoprotein 32 family m	-	-	-	1	5	5	7	X
125	Q92688	Acidic leucine-rich nuclear phosphoprotein 32 family m	-	-	-	1	3	5	3	-
126	O43423	Acidic leucine-rich nuclear phosphoprotein 32 family m	-	-	-	-	-	-	2	-
127	Q9BTT0	Acidic leucine-rich nuclear phosphoprotein 32 family m	-	-	-	-	4	5	5	-
128	Q99798	Aconitate hydratase, mitochondrial precursor (EC 4.2.1	-	-	-	-	6	-	13	X
129	P60709	Actin, cytoplasmic 1 (Beta-actin)	-	3	31	22	34	23	26	X
130	P63261	Actin, cytoplasmic 2 (Gamma-actin)	-	3	31	22	34	23	26	X
131	P61160	Actin-like protein 2 (Actin-related protein 2)	-	1	10	11	10	6	12	X
132	P61158	Actin-like protein 3 (Actin-related protein 3)	-	-	15	9	12	8	16	X
133	O15143	Actin-related protein 2/3 complex subunit 1B (ARP2/3	-	-	5	6	7	5	11	-
134	O15144	Actin-related protein 2/3 complex subunit 2 (ARP2/3 co	-	1	9	11	11	6	19	X
135	O15145	Actin-related protein 2/3 complex subunit 3 (ARP2/3 co	-	-	6	3	6	4	7	-
136	P59998	Actin-related protein 2/3 complex subunit 4 (ARP2/3 co	-	-	4	4	6	3	6	-
137	O15511	Actin-related protein 2/3 complex subunit 5 (ARP2/3 co	-	-	4	1	4	3	4	X
138	Q9BPX5	Actin-related protein 2/3 complex subunit 5-like protein	-	-	-	-	-	-	2	X
139	Q9P1U1	Actin-related protein 3B OS=Homo sapiens GN=ACTF	-	-	-	2	-	-	-	-
140	P53999	Activated RNA polymerase II transcriptional coactivator	-	-	-	-	3	4	5	-
141	O95433	Activator of 90 kDa heat shock protein ATPase homolog	-	-	1	-	-	1	-	X
142	P13798	Acylamino-acid-releasing enzyme (EC 3.4.19.1) (AAR	-	5	1	-	2	1	2	X
143	P45954	Acyl-CoA dehydrogenase, short/branched chain specif	-	-	-	-	2	-	-	X
144	P16219	Acyl-CoA dehydrogenase, short-chain specific, mitoch	-	-	1	-	3	1	-	X
145	P49748	Acyl-CoA dehydrogenase, very-long-chain specific, mi	-	-	-	-	-	8	2	X
146	P07108	Acyl-CoA-binding protein (ACBP) (Diazepam-binding i	-	-	-	2	2	2	4	-
147	O75608	Acyl-protein thioesterase 1 (EC 3.1.2.-) (Lysophospho	-	-	4	4	2	4	5	X
148	O95372	Acyl-protein thioesterase 2 (EC 3.1.2.-) (Lysophospho	-	-	-	-	2	-	4	X
149	Q7L5N7	Acyltransferase-like 1 (EC 2,3,1,-) - Homo sapiens (Hu	-	-	-	1	-	-	-	-
150	O14672	ADAM 10 precursor (EC 3.4.24.81) (A disintegrin and	-	-	3	-	-	-	-	-
151	O43184	ADAM 12 precursor - Homo sapiens (Human)	-	-	1	-	-	-	-	-
152	P07741	Adenine phosphoribosyltransferase (EC 2.4.2.7) (APR	-	2	7	7	10	9	10	X
153	P55263	Adenosine kinase (EC 2.7.1.20) (AK) (Adenosine 5*-p	-	1	-	-	2	-	2	X
154	P23526	Adenosylhomocysteinase (EC 3.3.1.1) (S-adenosyl-L-	-	1	-	3	2	1	4	X
155	P00568	Adenylate kinase isoenzyme 1 (EC 2.7.4.3) (ATP-AMF	-	6	5	-	4	-	1	-
156	P54819	Adenylate kinase isoenzyme 2, mitochondrial (EC 2.7.	-	-	7	4	9	11	11	X
157	P30566	Adenylosuccinate lyase (EC 4.3.2.2) (Adenylosuccinas	-	2	-	-	2	-	4	X
158	P30520	Adenylosuccinate synthetase isozyme 2 (EC 6.3.4.4) (	-	-	-	6	-	-	2	X
159	Q01518	Adenylyl cyclase-associated protein 1 (CAP 1)	-	-	12	17	17	15	22	X
160	Q9HDC9	Adipocyte plasma membrane-associated protein (BSC	-	-	-	7	1	-	5	X
161	Q9NZ08	Adipocyte-derived leucine aminopeptidase precursor (	-	-	-	2	3	7	8	-
162	Q15848	Adiponectin precursor (Adipocyte, C1q and collagen d	2	-	-	-	-	-	-	-

163	P12235	ADP/ATP translocase 1 (Adenine nucleotide translocase 1)	-	-	-	-	-	1	-	-
164	P05141	ADP/ATP translocase 2 (Adenine nucleotide translocase 2)	-	-	2	-	2	4	8	-
165	P12236	ADP/ATP translocase 3 (Adenine nucleotide translocase 3)	-	-	-	-	-	5	-	-
166	Q9BRR6	ADP-dependent glucokinase (EC 2.7.1.147) (ADPGK)	-	-	1	1	-	1	1	-
167	Q10588	ADP-ribosyl cyclase 2 precursor (EC 3.2.2.5) (Cyclic AMP 3-phosphatase)	-	-	-	1	-	-	-	-
168	P84077	ADP-ribosylation factor 1	-	3	12	-	12	9	11	-
169	P61204	ADP-ribosylation factor 3	-	-	-	-	-	-	10	-
170	P18085	ADP-ribosylation factor 4	-	-	7	-	6	4	5	-
171	P84085	ADP-ribosylation factor 5	-	-	-	-	7	4	-	-
172	P62330	ADP-ribosylation factor 6 - Homo sapiens (Human)	-	-	-	-	2	2	7	-
173	P40616	ADP-ribosylation factor-like protein 1	-	-	-	2	-	-	-	-
174	Q96BM9	ADP-ribosylation factor-like protein 8A (ADP-ribosylation factor-like protein 8A)	-	-	-	-	1	3	2	-
175	Q9NVJ2	ADP-ribosylation factor-like protein 8B (ADP-ribosylation factor-like protein 8B)	-	-	-	4	-	-	-	-
176	Q9UKK9	ADP-sugar pyrophosphatase (EC 3.6.1.13) (EC 3.6.1.13)	-	-	-	-	2	-	2	X
177	P43652	Afamin precursor (Alpha-albumin) (Alpha-Alb) - Homo sapiens	6	-	-	-	-	-	-	-
178	O43488	Aflatoxin B1 aldehyde reductase member 2 (EC 1.-.-.-)	-	1	5	-	4	-	2	X
179	O00170	AH receptor-interacting protein (AIP) (Aryl-hydrocarbon receptor-interacting protein)	-	-	-	-	2	-	3	X
180	P49588	Alanyl-tRNA synthetase (EC 6.1.1.7) (Alanine--tRNA ligase)	-	1	-	-	2	-	4	X
181	P14550	Alcohol dehydrogenase [NADP+] (EC 1.1.1.2) (Aldehyde dehydrogenase)	-	-	-	-	5	-	3	X
182	P11766	Alcohol dehydrogenase class 3 chi chain (EC 1.1.1.1)	-	-	-	-	3	-	3	X
183	Q8IZ83	Aldehyde dehydrogenase family 16 member A1 - Homo sapiens	-	-	1	1	1	2	4	-
184	P05091	Aldehyde dehydrogenase, mitochondrial precursor (EC 1.2.1.3)	-	-	-	-	-	6	4	X
185	P15121	Aldose reductase (EC 1.1.1.21) (AR) (Aldehyde reductase)	-	1	1	-	8	2	6	X
186	P55008	Allograft inflammatory factor 1 (AIF-1) (Ionized calcium binding adapter molecule 1)	-	-	-	1	1	1	-	X
187	P02763	Alpha-1-acid glycoprotein 1 precursor (AGP 1) (Orosomucoid)	5	-	-	2	-	-	1	-
188	P19652	Alpha-1-acid glycoprotein 2 precursor (AGP 2) (Orosomucoid)	3	-	-	-	-	-	-	-
189	P04217	Alpha-1B-glycoprotein precursor (Alpha-1-B glycoprotein)	11	-	-	-	-	-	1	-
190	P08697	Alpha-2-antiplasmin precursor (Alpha-2-plasmin inhibitor)	3	-	-	-	-	-	-	-
191	P02765	Alpha-2-HS-glycoprotein precursor (Fetuin-A) (Alpha-2-macroglobulin)	1	-	-	-	-	-	1	-
192	P01023	Alpha-2-macroglobulin precursor (Alpha-2-M)	61	-	24	-	-	-	42	-
193	P12814	Alpha-actinin-1 (Alpha-actinin cytoskeletal isoform) (Non-muscle alpha-actinin)	-	13	56	7	18	21	41	X
194	P35609	Alpha-actinin-2 (Alpha actinin skeletal muscle isoform) (Muscle alpha-actinin)	-	-	-	-	-	-	4	-
195	O43707	Alpha-actinin-4 (Non-muscle alpha-actinin 4) (F-actin binding protein)	-	15	23	-	14	24	33	X
196	P35611	Alpha-adducin (Erythrocyte adducin subunit alpha) - Homo sapiens	-	-	-	-	3	-	1	-
197	P61163	Alpha-centractin (Centractin) (Centrosome-associated protein)	-	-	4	-	-	1	1	X
198	P06733	Alpha-enolase (EC 4.2.1.11) (2-phospho-D-glycerate kinase)	-	4	17	16	30	25	27	X
199	P02771	Alpha-fetoprotein precursor (Alpha-fetoglobulin) (Alpha-fetoprotein)	-	-	-	1	-	2	1	X
200	P54920	Alpha-soluble NSF attachment protein (SNAP-alpha) (SNAP-25)	-	-	6	-	5	2	7	X
201	P37840	Alpha-synuclein (Non-A beta component of AD amyloid) (Synuclein)	-	6	6	-	6	-	1	X
202	Q8TCU4	Alstrom syndrome protein 1 - Homo sapiens (Human)	-	-	-	-	1	-	-	-
203	P02760	AMBIP protein precursor [Contains: Alpha-1-microglobulin]	10	-	-	-	-	-	2	-
204	Q9H4A4	Aminopeptidase B (EC 3.4.11.6) (Ap-B) (Arginyl aminopeptidase)	-	-	-	1	-	3	-	X
205	P15144	Aminopeptidase N (EC 3.4.11.2) (hAPN) (Alanyl aminopeptidase)	-	4	-	-	-	-	-	-
206	Q01432	AMP deaminase 3 (EC 3.5.4.6) (AMP deaminase isoform 3)	-	-	-	2	-	-	-	-
207	Q7Z5R6	Amyloid beta A4 precursor protein-binding family B member 1	-	-	-	-	-	-	2	-
208	P03950	Angiogenin precursor (EC 3.1.27.-) (Ribonuclease 5) (Angiogenin)	7	-	-	-	-	-	-	-
209	P01019	Angiotensinogen precursor [Contains: Angiotensin-1 (Angiotensin)]	3	-	-	-	1	-	4	X
210	P16157	Ankyrin-1 (Erythrocyte ankyrin) (Ankyrin-R) - Homo sapiens	-	29	6	-	9	-	-	-
211	P04083	Annexin A1 (Annexin I) (Lipocortin I) (Calpactin II) (Chordin)	-	-	-	23	22	19	27	X
212	P50995	Annexin A11 (Annexin XI) (Calcyclin-associated annexin)	-	-	1	4	11	4	8	X
213	P07355	Annexin A2 (Annexin II) (Lipocortin II) (Calpactin I head)	-	5	-	-	18	19	27	X
214	P12429	Annexin A3 (Annexin III) (Lipocortin III) (Placental antigen)	-	-	4	24	-	5	-	X
215	P09525	Annexin A4 (Annexin IV) (Lipocortin IV) (Endonexin)	-	-	1	10	4	4	7	X
216	P08758	Annexin A5 (Annexin V) (Lipocortin V) (Endonexin II) (Fetuin)	-	-	8	11	16	17	20	X
217	P08133	Annexin A6 (Annexin VI) (Lipocortin VI) (P68) (P70) (P71)	-	-	1	22	39	32	37	X
218	P20073	Annexin A7 (Annexin VII) (Synexin)	-	1	-	-	7	1	6	X

219	Q03518	Antigen peptide transporter 1 (APT1) (Peptide transpo	-	-	-	-	-	2	1	-
220	Q03519	Antigen peptide transporter 2 (APT2) (ATP-binding cas	-	-	-	-	-	-	2	-
221	P01008	Antithrombin-III precursor (ATIII) - Homo sapiens (Hun	8	-	-	-	-	-	1	-
222	Q10567	AP-1 complex subunit beta-1 (Adapter-related protein	-	-	3	-	-	2	4	-
223	O43747	AP-1 complex subunit gamma-1 (Adapter-related prote	-	-	-	-	-	-	1	-
224	P63010	AP-2 complex subunit beta-1 (Adapter-related protein	-	-	-	-	3	-	4	-
225	P02647	Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contai	31	-	-	-	-	1	27	X
226	Q8NCW5	Apolipoprotein A-I-binding protein precursor - Homo sa	-	-	-	-	-	-	2	-
227	P02652	Apolipoprotein A-II precursor (Apo-AII) (ApoA-II) [Cont	2	-	-	-	-	-	-	-
228	P06727	Apolipoprotein A-IV precursor (Apo-AIV) (ApoA-IV)	24	-	-	-	-	-	8	X
229	P04114	Apolipoprotein B-100 precursor (Apo B-100) [Contains	77	-	-	-	-	-	3	-
230	Q0VD83	Apolipoprotein B-100 receptor - Homo sapiens (Huma	-	1	-	2	-	2	4	-
231	P02656	Apolipoprotein C-III precursor (Apo-CIII) (ApoC-III) - H	1	-	-	-	-	2	3	-
232	P55056	Apolipoprotein C-IV precursor (Apo-CIV) (ApoC-IV) - H	3	-	-	-	-	-	-	-
233	P05090	Apolipoprotein D precursor (Apo-D) (ApoD) - Homo sa	5	-	-	-	-	-	-	X
234	P02649	Apolipoprotein E precursor (Apo-E) - Homo sapiens (H	16	-	-	-	-	-	5	-
235	Q13790	Apolipoprotein F precursor (Apo-F) (Lipid transfer inhib	2	-	-	-	-	-	-	-
236	O95445	Apolipoprotein M (Apo-M) (ApoM) (Protein G3a) - Hom	3	-	-	-	-	-	-	-
237	O14791	Apolipoprotein-L1 precursor (Apolipoprotein L-I) (Apoli	4	-	-	-	-	-	-	-
238	Q07812	Apoptosis regulator BAX, membrane isoform alpha	-	-	-	2	1	2	3	-
239	Q9ULZ3	Apoptosis-associated speck-like protein containing a C	-	-	-	7	4	12	9	X
240	O14727	Apoptotic protease-activating factor 1 (Apaf-1)	-	-	-	-	-	1	2	-
241	P18054	Arachidonate 12-lipoxygenase, 12S-type (EC 1.13.11.	-	-	2	-	-	-	-	-
242	P16050	Arachidonate 15-lipoxygenase (EC 1.13.11.33) (Arach	-	-	-	8	-	-	-	X
243	P09917	Arachidonate 5-lipoxygenase (EC 1.13.11.34) (5-lipox	-	-	-	-	-	2	-	-
244	P05089	Arginase-1 (EC 3.5.3.1) (Type I arginase) (Liver-type a	-	-	-	8	-	-	-	X
245	P55145	ARMET protein precursor (Arginine-rich protein) - Hom	-	-	3	-	1	4	4	-
246	O43681	Arsenical pump-driving ATPase (EC 3.6.3.16) (Arsenit	-	-	1	-	1	1	-	X
247	P17174	Aspartate aminotransferase, cytoplasmic (EC 2.6.1.1)	-	1	-	1	-	-	-	X
248	P00505	Aspartate aminotransferase, mitochondrial precursor (	-	-	1	1	4	2	8	-
249	Q9ULA0	Aspartyl aminopeptidase (EC 3.4.11.21) - Homo sapie	-	-	-	-	-	-	4	X
250	P14868	Aspartyl-tRNA synthetase (EC 6.1.1.12) (Aspartate--tF	-	-	2	-	3	-	-	X
251	Q6DD88	Atlantin-3 - Homo sapiens (Human)	-	-	-	-	-	5	1	-
252	P00846	ATP synthase a chain (EC 3.6.3.14) (ATPase protein f	-	-	-	-	-	1	-	-
253	P25705	ATP synthase alpha chain, mitochondrial precursor (E	-	-	16	8	22	17	23	X
254	P24539	ATP synthase B chain, mitochondrial precursor (EC 3.	-	-	1	-	2	2	6	-
255	P06576	ATP synthase beta chain, mitochondrial precursor (EC	-	-	17	6	21	18	20	X
256	O75947	ATP synthase D chain, mitochondrial (EC 3.6.3.14)	-	-	3	-	9	7	9	X
257	P30049	ATP synthase delta chain, mitochondrial precursor (EC	-	-	2	1	1	2	1	X
258	P56385	ATP synthase e chain, mitochondrial (EC 3.6.3.14) - H	-	-	-	-	1	2	-	-
259	P56134	ATP synthase f chain, mitochondrial (EC 3.6.3.14)	-	-	-	-	1	2	2	-
260	P36542	ATP synthase gamma chain, mitochondrial precursor (	-	-	2	1	7	1	5	-
261	P48047	ATP synthase O subunit, mitochondrial precursor (EC	-	-	5	2	8	7	11	-
262	O75964	ATP synthase subunit g, mitochondrial (EC 3.6.3.14) (	-	-	3	-	1	5	4	-
263	Q8N139	ATP-binding cassette sub-family A member 6 - Homo	-	-	-	1	-	-	-	-
264	Q8NE71	ATP-binding cassette sub-family F member 1 (ATP-bir	-	-	-	-	1	-	-	-
265	P53396	ATP-citrate synthase (EC 2.3.3.8) (ATP-citrate (pro-S-	-	2	-	1	1	4	8	-
266	P12956	ATP-dependent DNA helicase 2 subunit 1 (EC 3.6.1.-)	-	-	-	-	19	1	23	X
267	P13010	ATP-dependent DNA helicase 2 subunit 2 (EC 3.6.1.-)	-	-	-	-	16	5	17	-
268	Q08211	ATP-dependent RNA helicase A (EC 3.6.1.-) (Nuclear	-	-	-	-	-	-	1	-
269	Q9NUU7	ATP-dependent RNA helicase DDX19A (EC 3,6,1,-) (D	-	-	-	-	-	1	-	X
270	O00148	ATP-dependent RNA helicase DDX39 (EC 3.6.1.-) (DE	-	-	-	-	-	-	2	-
271	O14497	AT-rich interactive domain-containing protein 1A (ARIL	-	-	-	1	-	-	-	-
272	O75882	Attractin precursor (Mahogany homolog) (DPPT-L) - H	7	-	-	-	-	-	-	-
273	Q9NT62	Autophagy-related protein 3 (APG3-like) (hApg3) (Prot	-	-	-	-	-	4	-	-
274	O95352	Autophagy-related protein 7 (APG7-like) (Ubiquitin-act	-	-	-	-	-	-	1	-

275	P20160	Azurocidin precursor (Cationic antimicrobial protein CA	-	-	-	3	-	2	1	-
276	P17213	Bactericidal permeability-increasing protein precursor	-	-	-	6	-	-	-	-
277	P02730	Band 3 anion transport protein (Anion exchange protei	-	12	-	-	12	-	-	-
278	O75531	Barrier-to-autointegration factor (Breakpoint cluster reg	-	-	-	-	2	3	2	-
279	P51572	B-cell receptor-associated protein 31 (BCR-associated	-	-	-	2	1	1	4	-
280	Q13884	Beta-1-syntrophin (59 kDa dystrophin-associated prote	-	-	-	-	-	-	1	-
281	P02749	Beta-2-glycoprotein 1 precursor (Beta-2-glycoprotein I	6	-	-	-	-	-	3	-
282	P61769	Beta-2-microglobulin precursor [Contains: Beta-2-micr	1	-	3	1	-	2	3	X
283	P25098	Beta-adrenergic receptor kinase 1 - Homo sapiens (Hu	-	-	-	-	-	-	1	-
284	Q96KN2	Beta-Ala-His dipeptidase precursor (EC 3.4.13.20) (Ca	4	-	-	-	-	-	-	-
285	P49407	Beta-arrestin-1 (Arrestin, beta 1)	-	-	1	-	-	-	1	-
286	P32121	Beta-arrestin-2 (Arrestin beta 2) - Homo sapiens (Hum	-	-	-	-	1	-	-	-
287	P42025	Beta-centractin (Actin-related protein 1B) (ARP1B)	-	-	3	-	-	-	-	X
288	P13929	Beta-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hy	-	2	5	4	-	-	5	-
289	P16278	Beta-galactosidase precursor (EC 3.2.1.23) (Lactase)	-	-	-	-	-	3	1	-
290	P06865	Beta-hexosaminidase alpha chain precursor (EC 3.2.1	-	-	-	-	-	1	-	-
291	P07686	Beta-hexosaminidase beta chain precursor (EC 3.2.1.4	-	-	-	-	-	4	1	X
292	Q9HBI1	Beta-parvin (Affixin)	-	-	15	-	1	-	4	-
293	P55957	BH3 interacting domain death agonist (BID)	-	2	4	2	2	4	3	X
294	P07814	Bifunctional aminoacyl-tRNA synthetase [Includes: Glu	-	-	-	-	5	-	1	-
295	P31939	Bifunctional purine biosynthesis protein PURH [Include	-	3	-	-	5	-	4	X
296	P19835	Bile salt-activated lipase precursor - Homo sapiens (H	-	-	-	-	-	-	1	-
297	P53004	Biliverdin reductase A precursor (EC 1.3.1.24) (Biliver	-	-	1	1	4	3	1	X
298	P50583	Bis(5*-nucleosyl)-tetrphosphatase [asymmetrical] (EC	-	-	-	-	2	-	1	-
299	P07738	Bisphosphoglycerate mutase (EC 5.4.2.4) (2,3-bisphos	-	3	-	-	6	-	-	-
300	Q13867	Bleomycin hydrolase (EC 3.4.22.40) (BLM hydrolase)	-	1	-	-	-	-	1	X
301	Q9H3K6	BolA-like protein 2	-	-	-	-	2	3	2	X
302	P13727	Bone-marrow proteoglycan precursor (BMPG) (Proteo	-	-	-	5	-	1	-	-
303	P80723	Brain acid soluble protein 1 (BASP1 protein) (Neurona	-	-	-	1	-	-	1	-
304	Q9UBW5	Bridging integrator 2 (Breast cancer-associated protei	-	-	9	1	-	-	3	-
305	P11586	C-1-tetrahydrofolate synthase, cytoplasmic (C1-THF s	-	1	-	2	-	-	3	-
306	P04003	C4b-binding protein alpha chain precursor (C4bp) (Pro	9	-	-	-	-	-	-	-
307	P21730	C5a anaphylatoxin chemotactic receptor - Homo sapie	-	-	-	1	-	-	-	-
308	P49593	Ca(2+)/calmodulin-dependent protein kinase phosphat	-	-	2	-	1	1	1	-
309	P27708	CAD protein [Includes: Glutamine-dependent carbamo	-	-	-	-	-	1	-	-
310	P63098	Calcineurin subunit B isoform 1 (Protein phosphatase	-	-	-	-	1	-	-	-
311	O75746	Calcium-binding mitochondrial carrier protein Aralar1 (	-	-	-	-	2	-	-	-
312	Q6NUK1	Calcium-binding mitochondrial carrier protein SCA-MC-	-	-	-	1	-	2	3	-
313	Q9Y376	Calcium-binding protein 39 (Protein Mo25) - Homo sap	-	-	-	2	-	-	-	X
314	Q9ULU8	Calcium-dependent secretion activator 1 (Calcium-dep	-	-	-	-	-	-	1	-
315	Q9Y2V2	Calcium-regulated heat stable protein 1 (Calcium-regu	-	-	-	1	2	-	1	-
316	P06703	Calcyclin (Prolactin receptor-associated protein) (PRA	-	-	-	-	2	6	-	X
317	Q9HB71	Calcyclin-binding protein (CacyBP) (hCacyBP) (Siah-in	-	-	1	-	3	2	1	-
318	Q05682	Caldesmon (CDM)	-	1	7	-	-	-	-	X
319	P31949	Calgizzarin (S100 calcium-binding protein A11) (S100	-	-	-	3	2	6	3	-
320	P05109	Calgranulin A (Migration inhibitory factor-related protei	-	1	1	13	3	15	12	X
321	P06702	Calgranulin B (Migration inhibitory factor-related protei	-	-	-	14	5	16	11	X
322	P62158	Calmodulin (CaM)	-	1	3	1	3	5	4	-
323	P27824	Calnexin precursor (Major histocompatibility complex c	-	-	5	-	2	8	10	-
324	P60903	Calpactin I light chain (S100 calcium-binding protein A	-	-	-	-	-	4	2	X
325	P04632	Calpain small subunit 1 (CSS1) (Calcium-dependent p	-	1	7	4	10	4	7	X
326	P07384	Calpain-1 catalytic subunit (EC 3.4.22.52) (Calpain-1 k	-	2	6	3	3	4	11	-
327	P17655	Calpain-2 catalytic subunit precursor (EC 3.4.22.53) (C	-	-	-	-	2	2	7	-
328	P20810	Calpastatin (Calpain inhibitor) (Sperm BS-17 compone	-	-	-	-	-	2	7	-
329	Q99439	Calponin-2 (Calponin H2, smooth muscle) (Neutral cal	-	-	10	6	10	1	8	X
330	P27797	Calreticulin precursor (CRP55) (Calregulin) (HACBP) (	-	-	7	3	4	7	5	X

331	P10644	cAMP-dependent protein kinase type I-alpha regulator	-	-	3	-	1	2	2	X
332	P31323	cAMP-dependent protein kinase type II-beta regulatory	-	-	2	-	-	-	-	-
333	P17612	cAMP-dependent protein kinase, alpha-catalytic subunit	-	-	-	-	-	-	1	-
334	P22694	cAMP-dependent protein kinase, beta-catalytic subunit	-	-	-	-	-	-	1	-
335	Q6JBY9	Capz-interacting protein - Homo sapiens (Human)	-	-	-	-	-	-	1	-
336	P00915	Carbonic anhydrase 1 (EC 4.2.1.1) (Carbonic anhydrase 1)	-	11	6	-	16	5	1	X
337	P00918	Carbonic anhydrase 2 (EC 4.2.1.1) (Carbonic anhydrase 2)	-	7	9	-	12	2	4	X
338	P16152	Carbonyl reductase [NADPH] 1 (EC 1.1.1.184) (NADP-dependent carbonyl reductase 1)	-	1	5	-	8	2	9	X
339	O75828	Carbonyl reductase [NADPH] 3 (EC 1.1.1.184) (NADP-dependent carbonyl reductase 3)	-	-	-	-	-	-	3	X
340	Q96IY4	Carboxypeptidase B2 precursor (EC 3.4.17.20) (Carboxypeptidase B2)	2	-	-	-	-	-	-	-
341	P22792	Carboxypeptidase N subunit 2 precursor (Carboxypeptidase N subunit 2)	8	-	-	-	-	-	-	X
342	P13688	Carcinoembryonic antigen-related cell adhesion molecule 1	-	-	-	2	-	-	-	-
343	P40199	Carcinoembryonic antigen-related cell adhesion molecule 2	-	-	-	2	-	-	-	-
344	P31997	Carcinoembryonic antigen-related cell adhesion molecule 3	-	-	-	2	-	-	-	-
345	Q8N3K9	Cardiomyopathy-associated protein 5 - Homo sapiens	-	-	-	-	-	-	2	-
346	P67870	Casein kinase II subunit beta (CK II beta) (Phosvitin) (Casein kinase II subunit beta)	-	-	1	-	-	-	-	-
347	P29466	Caspase-1 precursor (EC 3.4.22.36) (CASP-1) (Interleukin-1 beta-converting enzyme)	-	-	-	-	2	1	-	X
348	P42574	Caspase-3 precursor (EC 3.4.22.-) (CASP-3) (Apoptin)	-	-	2	-	-	-	1	X
349	Q9BXW7	Cat eye syndrome critical region protein 5 precursor	-	-	-	-	-	-	1	-
350	P04040	Catalase (EC 1.11.1.6)	-	17	4	9	21	13	11	X
351	P21964	Catechol O-methyltransferase (EC 2.1.1.6)	-	-	-	-	2	6	3	X
352	P49913	Cathelicidin antimicrobial peptide precursor (18 kDa cathelicidin)	-	-	-	5	-	1	-	-
353	P07858	Cathepsin B precursor (EC 3.4.22.1) (Cathepsin B1) (Lysosomal aspartate protease B)	-	-	-	-	4	4	4	X
354	P07339	Cathepsin D precursor (EC 3.4.23.5) [Contains: Cathepsin D]	-	-	1	2	4	8	6	X
355	P08311	Cathepsin G precursor (EC 3.4.21.20) (CG) - Homo sapiens	-	-	-	6	-	1	-	-
356	P09668	Cathepsin H precursor (EC 3.4.22.16) [Contains: Cathepsin H]	-	-	-	-	1	1	2	-
357	P25774	Cathepsin S precursor (EC 3.4.22.27)	-	-	-	3	3	7	6	X
358	Q9UBR2	Cathepsin Z precursor (EC 3.4.22.-) (Cathepsin X) (Cathepsin Z)	-	-	-	1	-	2	2	X
359	Q8N6Q3	CD177 antigen OS=Homo sapiens GN=CD177 PE=1	-	-	-	1	-	-	-	-
360	Q15762	CD226 antigen precursor (DNAX accessory molecule 2)	-	-	1	-	-	-	-	-
361	P16070	CD44 antigen precursor (Phagocytic glycoprotein I) (P16070)	-	1	-	-	1	3	3	-
362	O43866	CD5 antigen-like precursor (SP-alpha) (CT-2) (IgM-associated protein)	1	-	-	-	-	-	-	-
363	P08962	CD63 antigen (Melanoma-associated antigen ME491)	-	-	-	2	-	-	-	-
364	P21926	CD9 antigen (p24) (Leukocyte antigen MIC3) (Motility-inhibitory protein)	-	-	2	-	-	-	2	-
365	P48960	CD97 antigen precursor (Leukocyte antigen CD97) - Homo sapiens	-	-	-	-	-	2	2	-
366	P14209	CD99 antigen precursor (T-cell surface glycoprotein E)	-	-	1	-	1	-	-	-
367	Q9NV96	Cell cycle control protein 50A (Transmembrane protein 50A)	-	-	-	1	-	-	-	-
368	P60953	Cell division control protein 42 homolog precursor (G2/M-specific cell cycle protein 42)	-	-	3	1	5	4	5	X
369	Q99741	Cell division control protein 6 homolog (CDC6-related protein)	1	-	-	-	-	-	-	-
370	P62633	Cellular nucleic acid-binding protein (CNBP) (Zinc finger protein)	-	-	-	-	2	4	5	-
371	Q15027	Centaurin-beta 1 (Cnt-b1) - Homo sapiens (Human)	-	1	2	-	4	-	1	-
372	Q96P48	Centaurin-delta 2 (Cnt-d2) (Arf-GAP, Rho-GAP, ankyrin-binding protein)	-	-	-	-	-	2	4	-
373	P00450	Ceruloplasmin precursor (EC 1.16.3.1) (Ferroxidase)	39	-	-	-	-	-	13	X
374	O76074	cGMP-specific 3*,5*-cyclic phosphodiesterase (EC 3.1.1.37)	-	-	1	-	-	-	-	-
375	Q9BY43	Charged multivesicular body protein 4a (Chromatin-modifying protein)	-	-	-	-	1	1	-	-
376	Q9H444	Charged multivesicular body protein 4b (Chromatin-modifying protein)	-	-	-	-	1	-	1	-
377	Q96FZ7	Charged multivesicular body protein 6 (Chromatin-modifying protein)	-	-	1	-	-	-	-	-
378	P36222	Chitinase-3-like protein 1 precursor (Cartilage glycoprotein 39)	-	-	-	11	-	-	-	-
379	Q13231	Chitotriosidase-1 precursor (EC 3.2.1.14) (Chitinase-1)	-	-	-	4	-	-	-	-
380	O00299	Chloride intracellular channel protein 1 (Nuclear chloride channel protein 1)	-	2	6	4	8	6	7	X
381	Q9Y696	Chloride intracellular channel protein 4 (Intracellular chloride channel protein 4)	-	-	6	-	-	-	1	X
382	Q9NZA1	Chloride intracellular channel protein 5 - Homo sapiens	-	-	-	-	-	1	-	-
383	Q8WWI5	Choline transporter-like protein 1 (Solute carrier family 3, Na+/dependent)	-	-	-	-	-	1	1	-
384	Q8IWA5	Choline transporter-like protein 2 (Solute carrier family 3, Na+/dependent)	-	-	-	3	-	-	-	-
385	P83916	Chromobox protein homolog 1 (Heterochromatin protein 1)	-	-	-	-	1	-	-	-
386	Q13185	Chromobox protein homolog 3 (Heterochromatin protein 3)	-	-	-	-	3	3	4	X

387	O75390	Citrate synthase, mitochondrial precursor (EC 2.3.3.1)	-	-	1	2	5	3	5	-
388	Q00610	Clathrin heavy chain 1 (CLH-17)	-	4	10	-	13	25	45	-
389	P53675	Clathrin heavy chain 2 (CLH-22)	-	-	-	-	-	-	11	-
390	Q14677	Clathrin interactor 1 (Epsin-4) (Epsin-related protein) (	-	-	-	-	1	-	1	-
391	O43809	Cleavage and polyadenylation specificity factor 5 (Clea	-	-	-	-	1	-	3	-
392	Q16630	Cleavage and polyadenylation specificity factor 6 (Clea	-	-	-	-	1	-	-	-
393	P10909	Clusterin precursor (Complement-associated protein S	17	-	7	-	-	-	7	X
394	Q99417	C-Myc-binding protein (Associate of Myc 1) (AMY-1)	-	-	-	-	-	1	1	-
395	O43598	c-Myc-responsive protein Rcl	-	-	-	-	3	1	1	X
396	Q14019	Coactosin-like protein	-	-	6	6	6	9	10	X
397	P00740	Coagulation factor IX precursor (EC 3,4,21,22) (Christ	4	-	-	-	-	-	-	-
398	P12259	Coagulation factor V precursor (Activated protein C co	3	-	7	-	-	-	-	-
399	P00742	Coagulation factor X precursor (EC 3,4,21,6) (Stuart fa	1	-	-	-	-	-	-	-
400	P00748	Coagulation factor XII precursor (EC 3,4,21,38) (Hage	4	-	-	-	-	-	-	-
401	P00488	Coagulation factor XIII A chain precursor (EC 2.3.2.13	-	-	29	-	4	6	14	X
402	P05160	Coagulation factor XIII B chain precursor (Protein-gluta	2	-	-	-	-	-	-	-
403	P53621	Coatomer subunit alpha (Alpha-coat protein) (Alpha-C	-	-	-	-	-	-	8	-
404	P53618	Coatomer subunit beta (Beta-coat protein) (Beta-COP	-	-	-	-	3	4	5	-
405	O14579	Coatomer subunit epsilon (Epsilon-coat protein) (Epsil	-	-	-	-	-	-	1	X
406	Q9Y678	Coatomer subunit gamma (Gamma-coat protein) (Gan	-	-	-	1	1	1	5	-
407	Q9UBF2	Coatomer subunit gamma-2 (Gamma-2 coat protein) (	-	-	-	-	-	-	2	-
408	P61923	Coatomer subunit zeta-1 (Zeta-1 coat protein) (Zeta-1	-	-	-	-	1	2	1	-
409	P23528	Cofilin-1 (Cofilin, non-muscle isoform) (18 kDa phosph	1	4	14	11	16	17	18	X
410	Q9Y281	Cofilin-2 (Cofilin, muscle isoform)	-	-	-	-	-	-	7	X
411	Q96CT7	Coiled-coil domain-containing protein 124 - Homo sapi	-	-	-	-	1	-	-	-
412	Q9Y6H1	Coiled-coil-helix-coiled-coil-helix domain-containing pr	-	-	-	-	-	1	1	-
413	Q9BWP8	Collectin-11 precursor - Homo sapiens (Human)	1	-	-	-	-	-	-	-
414	Q8N668	COMM domain-containing protein 1 (Protein Murr1) - H	-	-	-	-	-	1	-	-
415	Q9UBI1	COMM domain-containing protein 3 (Bup protein) (PIL	-	-	-	-	-	2	1	X
416	Q9P000	COMM domain-containing protein 9	-	-	-	-	1	1	1	-
417	P02745	Complement C1q subcomponent subunit A precursor	1	-	-	-	-	-	-	-
418	P02746	Complement C1q subcomponent subunit B precursor	7	-	1	-	-	-	-	-
419	P02747	Complement C1q subcomponent subunit C precursor	4	-	-	-	-	-	-	-
420	P00736	Complement C1r subcomponent precursor (EC 3,4,21	3	-	-	-	-	-	-	X
421	P09871	Complement C1s subcomponent precursor (EC 3,4,21	2	-	-	-	-	-	-	X
422	P06681	Complement C2 precursor (EC 3,4,21,43) (C3/C5 com	3	-	-	-	-	-	-	-
423	P01024	Complement C3 precursor [Contains: Complement C3	89	-	5	-	-	-	27	X
424	P0C0L4	Complement C4-A precursor (Acidic complement C4)	48	-	-	-	-	-	5	X
425	P0C0L5	Complement C4-B precursor (Basic complement C4) [	50	-	-	-	-	-	-	X
426	P01031	Complement C5 precursor [Contains: Complement C5	16	-	-	-	-	-	-	-
427	Q07021	Complement component 1 Q subcomponent-binding p	-	-	1	-	2	-	1	-
428	P13671	Complement component C6 precursor - Homo sapiens	8	-	-	-	-	-	-	-
429	P10643	Complement component C7 precursor - Homo sapiens	2	-	-	-	-	-	-	-
430	P07357	Complement component C8 alpha chain precursor (Co	2	-	-	-	-	-	-	-
431	P07358	Complement component C8 beta chain precursor (Cor	2	-	-	-	-	-	-	-
432	P07360	Complement component C8 gamma chain precursor	7	-	-	-	-	-	-	-
433	P02748	Complement component C9 precursor [Contains: Com	7	-	-	-	-	-	-	-
434	P00751	Complement factor B precursor (EC 3.4.21.47) (C3/C5	18	-	-	-	-	-	1	X
435	P00746	Complement factor D precursor (EC 3,4,21,46) (C3 co	5	-	-	-	-	-	-	-
436	P08603	Complement factor H precursor (H factor 1) - Homo sa	36	-	1	-	-	-	3	-
437	Q03591	Complement factor H-related protein 1 precursor (FHR	5	-	-	-	-	-	-	-
438	P36980	Complement factor H-related protein 2 precursor (FHR	3	-	-	-	-	-	-	-
439	Q9BXR6	Complement factor H-related protein 5 precursor (FHR	2	-	-	-	-	-	-	-
440	P05156	Complement factor I precursor (EC 3.4.21.45) (C3B/C	9	-	-	-	-	-	-	X
441	P78357	Contactin-associated protein 1 precursor (Caspr) (Cas	-	-	-	1	-	-	-	-
442	P61201	COP9 signalosome complex subunit 2 (Signalosome s	-	-	-	-	2	-	-	-

443	Q9BT78	COP9 signalosome complex subunit 4 (Signalosome s	-	1	-	-	2	-	-	X
444	Q7L5N1	COP9 signalosome complex subunit 6 (Signalosome s	-	-	1	-	1	-	-	X
445	Q99627	COP9 signalosome complex subunit 8 (Signalosome s	-	-	1	-	2	2	-	X
446	Q99829	Copine-1 (Copine I)	-	-	1	2	4	4	5	X
447	Q96FN4	Copine-2 (Copine II) - Homo sapiens (Human)	-	-	-	2	-	-	-	-
448	O75131	Copine-3 (Copine III)	-	-	-	5	3	3	2	-
449	Q96A23	Copine-4 (Copine IV) (Copine-8) - Homo sapiens (Hur	-	-	-	1	-	-	-	-
450	Q9NTM9	Copper homeostasis protein cutC homolog - Homo sa	-	-	-	-	1	-	-	-
451	O75367	Core histone macro-H2A.1 (Histone macroH2A1) (mH	-	-	-	1	-	-	1	-
452	Q13951	Core-binding factor subunit beta (CBF-beta) (Polyoma	-	-	-	-	2	1	-	X
453	P31146	Coronin-1A (Coronin-like protein p57) (Coronin-like pro	-	-	3	9	14	3	12	X
454	Q9ULV4	Coronin-1C (Coronin-3) (hCRNN4)	-	-	8	-	-	-	-	X
455	P57737	Coronin-7 (70 kDa WD repeat tumor rejection antigen	-	-	-	2	2	2	3	X
456	P08185	Corticosteroid-binding globulin precursor (CBG) (Trans	4	-	-	-	-	-	-	-
457	P02741	C-reactive protein precursor [Contains: C-reactive prot	1	-	-	-	-	-	-	-
458	P46109	Crk-like protein	-	-	4	-	-	-	1	X
459	Q13363	C-terminal-binding protein 1 (EC 1.1.1.-) (CtBP1) - Hor	-	-	-	-	2	-	-	-
460	Q9Y240	C-type lectin domain family 11 member A precursor (S	-	-	1	-	-	-	-	-
461	Q13620	Cullin-4B - Homo sapiens (Human)	-	-	-	-	1	-	1	-
462	Q86VP6	Cullin-associated NEDD8-dissociated protein 1 (Cullin	-	7	-	-	7	3	16	-
463	P55273	Cyclin-dependent kinase 4 inhibitor D (p19-INK4d) - H	-	-	1	-	-	-	-	-
464	P01040	Cystatin A (Stefin A) (Cystatin AS)	-	-	-	2	1	3	1	-
465	P04080	Cystatin B (Liver thiol proteinase inhibitor) (CPI-B) (Ste	-	-	-	2	3	5	4	X
466	P01034	Cystatin C precursor (Neuroendocrine basic polypeptid	4	-	-	-	-	-	-	-
467	Q15828	Cystatin M precursor (Cystatin E) - Homo sapiens (Hu	1	-	-	-	-	-	-	-
468	P21291	Cysteine and glycine-rich protein 1 (Cysteine-rich prote	-	-	8	-	2	-	1	X
469	P49589	Cysteinyl-tRNA synthetase, cytoplasmic (EC 6.1.1.16)	-	-	-	-	-	-	2	-
470	P32320	Cytidine deaminase (EC 3.5.4.5) (Cytidine aminohydro	-	-	-	2	-	2	1	-
471	P04839	Cytochrome b-245 heavy chain (p22 phagocyte B-cyto	-	-	-	5	1	12	7	-
472	P13498	Cytochrome b-245 light chain (p22 phagocyte B-cyto	-	-	-	1	-	1	-	-
473	O43169	Cytochrome b5 outer mitochondrial membrane isoform	-	-	1	-	3	2	2	-
474	P99999	Cytochrome c	-	-	1	-	1	2	7	-
475	P20674	Cytochrome c oxidase polypeptide Va, mitochondrial p	-	-	-	-	2	3	3	X
476	P10606	Cytochrome c oxidase polypeptide Vb, mitochondrial p	-	-	-	-	1	3	2	-
477	P12074	Cytochrome c oxidase polypeptide VIa-liver, mitochon	-	-	-	-	-	2	-	-
478	P14406	Cytochrome c oxidase polypeptide VIIa-liver/heart, mit	-	-	-	-	-	2	-	-
479	P00403	Cytochrome c oxidase subunit 2 (EC 1.9.3.1) (Cytochr	-	-	-	-	4	3	5	-
480	P13073	Cytochrome c oxidase subunit IV isoform 1, mitochond	-	-	-	-	3	3	2	-
481	P14854	Cytochrome c oxidase subunit VIb isoform 1 (EC 1.9.3	-	-	-	-	1	3	-	-
482	P08574	Cytochrome c1, heme protein, mitochondrial precursor	-	-	-	-	-	1	4	-
483	Q9HBI6	Cytochrome P450 4F11 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
484	P78329	Cytochrome P450 4F2 (EC 1.14.13.30) (CYPIVF2) (Le	-	-	-	1	-	-	-	-
485	Q08477	Cytochrome P450 4F3 - Homo sapiens (Human)	-	-	-	5	-	-	-	-
486	P98187	Cytochrome P450 4F8 OS=Homo sapiens GN=CYP4F	-	-	-	2	-	-	-	-
487	Q8IUI8	Cytokine receptor-like factor 3 - Homo sapiens (Huma	-	-	5	-	4	1	-	-
488	P50453	Cytoplasmic antiproteinase 3 (CAP3) (CAP-3) (Protea	-	-	1	-	7	4	11	X
489	O14576	Cytoplasmic dynein 1 intermediate chain 1 - Homo sap	-	1	-	-	-	-	-	-
490	Q13409	Cytoplasmic dynein 1 intermediate chain 2 (Dynein int	-	1	-	-	-	-	2	X
491	Q8NCM8	Cytoplasmic dynein 2 heavy chain 1 - Homo sapiens (	-	-	-	-	1	-	-	-
492	Q7L576	Cytoplasmic FMR1-interacting protein 1 - Homo sapier	-	-	-	-	-	3	1	-
493	Q96F07	Cytoplasmic FMR1-interacting protein 2 - Homo sapier	-	-	-	-	-	-	1	-
494	P28838	Cytosol aminopeptidase (EC 3.4.11.1) (Leucine amino	-	-	1	-	1	1	3	X
495	Q96KP4	Cytosolic nonspecific dipeptidase (Glutamate carbo	-	-	-	-	5	4	8	X
496	P47712	Cytosolic phospholipase A2 (cPLA2) (Phospholipase A	-	-	-	-	1	-	-	-
497	P49902	Cytosolic purine 5*-nucleotidase - Homo sapiens (Hum	-	-	-	1	-	-	-	-
498	Q8N465	D-2-hydroxyglutarate dehydrogenase, mitochondrial p	-	-	1	-	1	-	-	-

499	O43175	D-3-phosphoglycerate dehydrogenase (EC 1.1.1.95) (D-3-PGADH)	-	-	-	-	-	1	-	X
500	Q96EP5	DAZ-associated protein 1 (Deleted in azoospermia-associated gene 1)	-	-	-	-	2	-	1	-
501	Q5TDH0	DDI1 homolog 2 - Homo sapiens (Human)	-	1	-	-	-	-	-	-
502	P30046	D-dopachrome decarboxylase (EC 4.1.1.84) (D-dopachrome decarboxylase)	-	-	-	3	2	3	3	X
503	Q92608	Dedicator of cytokinesis protein 2	-	-	-	-	-	1	2	-
504	Q9BTZ2	Dehydrogenase/reductase SDR family member 4 (EC 1.1.1.179)	-	-	-	-	-	-	2	-
505	Q9Y394	Dehydrogenase/reductase SDR family member 7 precursor	-	-	-	-	-	1	-	-
506	Q8NBQ5	Dehydrogenase/reductase SDR family member 8 precursor	-	-	-	1	-	1	-	-
507	P54886	Delta 1-pyrroline-5-carboxylate synthetase (P5CS) (Ala1)	-	-	-	-	-	-	1	-
508	Q13011	Delta3,5-delta2,4-dienoyl-CoA isomerase, mitochondrial	1	-	6	1	10	8	8	X
509	P13716	Delta-aminolevulinic acid dehydratase (EC 4.2.1.24) (F	-	4	10	-	9	-	-	X
510	P27707	Deoxycytidine kinase (EC 2.7.1.74) (dCK) - Homo sap	-	-	-	-	-	1	1	-
511	P32321	Deoxycytidylate deaminase (EC 3.5.4.12) (dCMP deami	-	-	2	-	-	1	1	X
512	P33316	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mit	-	-	-	-	3	1	1	X
513	Q07507	Dermatopontin precursor - Homo sapiens (Human)	3	-	-	-	-	-	-	-
514	P60981	Destrin (Actin-depolymerizing factor) (ADF)	-	-	5	-	2	-	7	X
515	Q9Y295	Developmentally-regulated GTP-binding protein 1 (DR	-	-	-	-	-	1	1	-
516	Q9NR28	Diablo homolog, mitochondrial precursor (Second mito	-	-	2	-	2	2	3	-
517	P23743	Diacylglycerol kinase alpha (EC 2.7.1.107) (Diglycerid	-	-	-	-	3	-	4	-
518	P49619	Diacylglycerol kinase gamma - Homo sapiens (Human)	-	-	1	-	-	-	-	-
519	Q9H4E7	Differentially expressed in FDCP 6 - Homo sapiens (H	-	-	-	-	1	-	1	-
520	P09622	Dihydrolipoyl dehydrogenase, mitochondrial precursor	-	-	-	1	1	1	2	X
521	P36957	Dihydrolipoyllysine-residue succinyltransferase compo	-	-	-	-	3	-	-	X
522	P09417	Dihydropteridine reductase (EC 1.5.1.34) (HDHPR) (Q	-	-	-	-	1	-	1	X
523	Q16555	Dihydropyrimidinase-related protein 2 (DRP-2) (Collap	-	-	2	-	2	2	3	X
524	Q3LXA3	Dihydroxyacetone kinase (EC 2.7.1.29) (Glycerone kin	-	-	-	-	1	-	-	X
525	Q01459	Di-N-acetylchitobiase precursor - Homo sapiens (Hum	-	-	-	1	-	-	-	-
526	P53634	Dipeptidyl-peptidase 1 precursor (EC 3.4.14.1) (Dipep	-	-	1	4	1	2	4	-
527	Q9UHL4	Dipeptidyl-peptidase 2 precursor (EC 3.4.14.2) (Dipep	-	-	1	2	-	1	2	-
528	Q9NY33	Dipeptidyl-peptidase 3 (EC 3.4.14.4) (Dipeptidyl-peptid	-	-	-	-	-	1	2	-
529	Q95989	Diphosphoinositol polyphosphate phosphohydrolase 1	-	-	-	2	-	-	-	-
530	Q8NFP7	Diphosphoinositol polyphosphate phosphohydrolase 3	-	-	-	-	-	-	1	-
531	Q14689	Disco-interacting protein 2 homolog A - Homo sapiens	-	-	-	-	-	1	-	-
532	P26358	DNA (cytosine-5)-methyltransferase 1 (EC 2.1.1.37) (D	-	-	1	-	-	-	-	-
533	Q16531	DNA damage-binding protein 1 (Damage-specific DNA	-	-	-	-	1	2	3	-
534	Q9UBZ9	DNA repair protein REV1 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
535	Q13472	DNA topoisomerase 3-alpha (EC 5.99.1.2) (DNA topoi	-	-	-	-	1	-	-	-
536	P27695	DNA-(apurinic or apyrimidinic site) lyase (EC 4.2.99.18	-	-	-	3	7	1	9	-
537	Q9UBS4	DnaJ homolog subfamily B member 11 precursor (ER-	-	-	1	-	-	1	-	X
538	P59910	DnaJ homolog subfamily B member 13 - Homo sapien	-	-	-	-	-	1	-	-
539	Q9NVM6	DnaJ homolog subfamily C member 17 - Homo sapien	-	-	-	-	-	1	-	-
540	Q9H3Z4	DnaJ homolog subfamily C member 5 (Cysteine string	-	-	-	2	-	1	1	-
541	O75937	DnaJ homolog subfamily C member 8 (Splicing proteir	-	-	-	-	3	-	6	-
542	O60496	Docking protein 2 (Downstream of tyrosine kinase 2) (	-	-	3	-	-	-	1	X
543	Q7L591	Docking protein 3 (Downstream of tyrosine kinase 3) -	-	-	2	1	-	-	-	-
544	O60762	Dolichol-phosphate mannosyltransferase (EC 2.4.1.83)	-	-	-	-	-	-	2	-
545	P39656	Dolichyl-diphosphooligosaccharide--protein glycosyltra	-	-	-	1	-	4	3	-
546	P04844	Dolichyl-diphosphooligosaccharide--protein glycosyltra	-	-	1	1	1	10	-	X
547	P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltra	-	-	-	1	5	17	10	X
548	Q9C005	Dpy-30-like protein - Homo sapiens (Human)	-	-	-	-	-	1	1	-
549	Q16643	Drebrin (Developmentally-regulated brain protein) - Ho	-	-	2	-	-	-	-	-
550	Q9UJU6	Drebrin-like protein (SH3 domain-containing protein 7)	-	-	4	2	-	-	2	X
551	Q02750	Dual specificity mitogen-activated protein kinase kinas	-	-	-	-	-	-	2	-
552	P46734	Dual specificity mitogen-activated protein kinase kinas	-	-	-	1	2	-	-	-
553	P51452	Dual specificity protein phosphatase 3 (EC 3.1.3.48) (E	-	-	7	-	-	3	2	X
554	Q13561	Dynactin subunit 2 (Dynactin complex 50 kDa subunit)	-	-	3	-	-	-	1	X

555	Q14203	Dynactin-1 (150 kDa dynein-associated polypeptide) (I	-	-	1	-	-	-	2	-
556	O00429	Dynamamin-1-like protein (EC 3.6.5.5) (Dynamamin-like prot	-	-	10	-	-	1	4	-
557	P50570	Dynamamin-2 (EC 3,6,5,5)	-	-	-	-	-	2	-	-
558	Q14204	Dynein heavy chain, cytosolic (DYHC) (Cytoplasmic dy	-	-	-	-	-	6	-	-
559	Q96FJ2	Dynein light chain 2, cytoplasmic (Dynein light chain L	-	-	-	-	-	2	-	-
560	Q9NP97	Dynein light chain 2A, cytoplasmic (Dynein-associated	-	-	-	-	1	2	-	-
561	Q96C19	EF-hand domain-containing protein 2 (Swiprosin-1)	-	-	1	4	8	12	12	X
562	Q8N3D4	EH domain-binding protein 1-like protein 1 - Homo sap	-	-	-	-	-	1	-	-
563	Q9H4M9	EH-domain-containing protein 1 (Testilin) (hPAST1)	-	-	10	9	5	-	11	X
564	Q9NZN3	EH-domain-containing protein 3	-	-	14	-	-	-	-	-
565	Q15717	ELAV-like protein 1 (Hu-antigen R) (HuR) - Homo sapi	-	-	-	-	-	1	-	-
566	P13804	Electron transfer flavoprotein alpha-subunit, mitochond	-	-	7	-	8	4	13	X
567	P38117	Electron transfer flavoprotein beta-subunit (Beta-ETF)	-	-	1	-	8	5	5	-
568	P68104	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation	-	2	2	7	18	13	18	X
569	P24534	Elongation factor 1-beta (EF-1-beta)	-	-	2	-	2	3	3	-
570	P29692	Elongation factor 1-delta (EF-1-delta) (Antigen NY-CO	-	-	2	-	7	3	4	X
571	P26641	Elongation factor 1-gamma (EF-1-gamma) (eEF-1B ga	-	-	1	2	2	2	5	X
572	P13639	Elongation factor 2 (EF-2)	-	10	-	3	21	15	28	X
573	P49411	Elongation factor Tu, mitochondrial precursor (EF-Tu)	-	-	1	-	16	5	7	X
574	Q9Y6C2	EMILIN-1 precursor (Elastin microfibril interface-locate	-	-	3	-	-	-	-	-
575	Q9UI08	Ena/VASP-like protein (Ena/vasodilator-stimulated pho	-	-	-	-	1	-	2	-
576	O94919	Endonuclease domain-containing 1 protein precursor (	-	-	1	-	-	-	-	-
577	Q6P179	Endoplasmic reticulum aminopeptidase 2 - Homo sapi	-	-	-	-	-	-	1	-
578	P30040	Endoplasmic reticulum protein ERp29 precursor (ERp	-	-	6	2	6	8	8	X
579	P14625	Endoplasmin precursor (94 kDa glucose-regulated pro	-	3	14	-	14	19	23	X
580	Q96AP7	Endothelial cell-selective adhesion molecule precursor	-	-	2	-	-	-	-	-
581	O60869	Endothelial differentiation-related factor 1 (EDF-1) (Mu	-	-	-	-	-	1	2	-
582	Q9UHY7	Enolase-phosphatase E1 (EC 3.1.3.77) (2,3-diketo-5-r	-	-	1	-	1	1	-	-
583	Q9NTX5	Enoyl-CoA hydratase domain-containing protein 1 - Ho	-	-	-	-	-	-	2	-
584	P30084	Enoyl-CoA hydratase, mitochondrial precursor (EC 4.2	-	-	1	-	8	4	8	X
585	P12724	Eosinophil cationic protein precursor (EC 3.1.27.-) (EC	-	-	-	2	-	1	-	-
586	Q05315	Eosinophil lysophospholipase (EC 3.1.1.5) (Charcot-L	-	-	-	6	2	4	1	-
587	P11678	Eosinophil peroxidase precursor (EC 1.11.1.7) (EPO)	-	-	-	6	-	-	-	-
588	P61916	Epididymal secretory protein E1 precursor (Niemann-F	-	-	-	-	1	3	1	X
589	P12830	Epithelial-cadherin precursor (E-cadherin) (Uvomorulin	3	-	-	-	-	-	-	-
590	P07099	Epoxide hydrolase 1 (EC 3.3.2.9) (Microsomal epoxide	-	-	-	-	-	1	-	-
591	Q96HE7	ERO1-like protein alpha precursor (EC 1.8.4.-) (ERO1	-	-	-	-	2	4	1	-
592	P27105	Erythrocyte band 7 integral membrane protein (Stomat	-	5	13	2	6	1	8	-
593	P16452	Erythrocyte membrane protein band 4.2 (Erythrocyte p	-	14	-	-	1	-	-	-
594	P30042	ES1 protein homolog, mitochondrial precursor (Protein	-	-	2	-	4	-	4	X
595	P10768	Esterase D (EC 3.1.1.1)	-	1	4	2	4	3	6	X
596	Q92506	Estradiol 17-beta-dehydrogenase 8 (EC 1.1.1.62) (17-	-	-	-	-	1	-	-	X
597	O95571	ETHE1 protein, mitochondrial precursor (EC 3.-.-.-) (E	-	-	3	3	7	5	5	X
598	P60842	Eukaryotic initiation factor 4A-I (EC 3.6.1.-) (ATP-depe	-	1	3	-	8	4	7	X
599	Q14240	Eukaryotic initiation factor 4A-II (EC 3.6.1.-) (ATP-depe	-	-	-	-	5	-	5	X
600	O43324	Eukaryotic translation elongation factor 1 epsilon-1 (M	-	-	-	-	-	1	1	-
601	P41567	Eukaryotic translation initiation factor 1 (eIF1) (Protein	-	-	-	-	-	1	3	X
602	P47813	Eukaryotic translation initiation factor 1A, X-chromoso	-	-	-	-	3	-	-	X
603	P05198	Eukaryotic translation initiation factor 2 subunit 1 (Euk	-	-	1	-	2	-	2	X
604	O75822	Eukaryotic translation initiation factor 3 subunit 1 (eIF-	-	-	-	-	1	-	-	-
605	Q14152	Eukaryotic translation initiation factor 3 subunit 10 (eIF	-	-	-	-	3	-	14	-
606	Q9UBQ5	Eukaryotic translation initiation factor 3 subunit 12 (eIF	-	-	1	-	1	-	3	-
607	O15372	Eukaryotic translation initiation factor 3 subunit 3 (eIF-	-	-	-	-	-	-	1	X
608	O00303	Eukaryotic translation initiation factor 3 subunit 5 (eIF-	-	-	-	-	3	1	1	X
609	Q9Y262	Eukaryotic translation initiation factor 3 subunit 6-intera	-	-	-	-	-	4	1	-
610	P55884	Eukaryotic translation initiation factor 3 subunit 9 (eIF-	-	-	-	-	1	-	4	-

611	Q04637	Eukaryotic translation initiation factor 4 gamma 1 (eIF-4G1)	-	-	-	-	2	-	-	-
612	O43432	Eukaryotic translation initiation factor 4 gamma 3 (eIF-4G3)	-	-	-	-	-	-	1	-
613	P23588	Eukaryotic translation initiation factor 4B (eIF-4B)	-	-	-	-	1	-	-	X
614	P06730	Eukaryotic translation initiation factor 4E (eIF4E) (eIF-4E)	-	-	2	-	1	1	2	X
615	Q8N5X7	Eukaryotic translation initiation factor 4E type 3 - Homo sapiens	-	-	-	1	-	-	-	-
616	Q15056	Eukaryotic translation initiation factor 4H (eIF-4H) (Wilamowski factor)	-	-	1	-	3	1	2	X
617	P55010	Eukaryotic translation initiation factor 5 (eIF-5)	-	-	1	-	-	-	-	X
618	P63241	Eukaryotic translation initiation factor 5A (eIF-5A) (eIF-5A)	-	3	6	-	7	6	6	X
619	P56537	Eukaryotic translation initiation factor 6 (eIF-6) (B4 integrin)	-	-	-	1	1	1	3	-
620	P34910	EVI2B protein precursor (Ecotropic viral integration site 2B)	-	-	-	-	-	3	1	-
621	Q16394	Exostosin-1 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
622	O14980	Exportin-1 (Chromosome region maintenance 1 protein)	-	-	-	-	-	3	3	-
623	Q9UIA9	Exportin-7 (Exp7) (Ran-binding protein 16) - Homo sapiens	-	-	-	-	1	1	-	-
624	P15311	Ezrin (p81) (Cytovillin) (Villin-2)	-	-	3	7	12	9	14	X
625	O14745	Ezrin-radixin-moesin-binding phosphoprotein 50 (EBP50)	-	-	4	2	6	1	3	-
626	P52907	F-actin capping protein alpha-1 subunit (CapZ alpha-1)	-	2	7	7	8	6	9	X
627	P47755	F-actin capping protein alpha-2 subunit (CapZ alpha-2)	-	2	8	1	5	7	5	X
628	P47756	F-actin capping protein beta subunit (CapZ beta)	-	-	12	8	10	9	14	X
629	Q13158	FADD protein (FAS-associating death domain-containing protein)	-	-	-	-	-	-	1	-
630	Q96AE4	Far upstream element-binding protein 1 (FUSE-binding protein 1)	-	-	-	-	4	2	9	X
631	Q92945	Far upstream element-binding protein 2 (FUSE-binding protein 2)	-	1	-	-	5	7	11	X
632	Q96124	Far upstream element-binding protein 3 (FUSE-binding protein 3)	-	-	-	-	2	-	-	-
633	P14324	Farnesyl pyrophosphate synthetase (FPP synthetase)	-	-	1	1	-	-	1	-
634	P49327	Fatty acid synthase (EC 2.3.1.85) [Includes: [Acyl-carrier protein]]	-	-	4	-	1	1	7	-
635	Q01469	Fatty acid-binding protein, epidermal (E-FABP) (Psoriasis)	-	-	-	1	1	4	4	X
636	P02794	Ferritin heavy chain (EC 1.16.3.1) (Ferritin H subunit) (L-type)	-	-	-	-	3	2	6	X
637	P02792	Ferritin light chain (Ferritin L subunit)	-	-	-	7	4	6	7	X
638	P02671	Fibrinogen alpha chain precursor [Contains: Fibrinopeptide A]	9	-	15	-	-	-	15	X
639	P02675	Fibrinogen beta chain precursor [Contains: Fibrinopeptide B]	16	1	27	-	1	-	23	X
640	P02679	Fibrinogen gamma chain precursor	11	-	12	-	-	-	15	X
641	P02751	Fibronectin precursor (FN) (Cold-insoluble globulin) (C1G)	33	2	6	-	-	-	4	-
642	P23142	Fibulin-1 precursor	2	-	-	-	-	-	-	-
643	O00602	Ficolin-1 precursor (Collagen/fibrinogen domain-containing)	-	-	-	-	-	3	-	X
644	Q15485	Ficolin-2 precursor (Ficolin-B) (Ficolin-beta) (L-ficolin)	3	-	-	-	-	-	-	-
645	O75636	Ficolin-3 precursor (Collagen/fibrinogen domain-containing)	7	-	-	-	-	-	-	-
646	P20930	Filaggrin - Homo sapiens (Human)	-	-	-	-	-	-	2	-
647	P21333	Filamin-A (Alpha-filamin) (Filamin-1) (Endothelial actin-binding protein)	1	17	94	12	56	65	103	X
648	O75369	Filamin-B (FLN-B) (Beta-filamin) (Actin-binding-like protein)	-	23	-	-	1	3	9	-
649	Q14315	Filamin-C (Gamma-filamin) (Filamin-2) (Protein FLNc)	-	8	-	-	-	-	4	-
650	P62942	FK506-binding protein 1A (EC 5.2.1.8) (Peptidyl-prolyl isomerase)	-	-	1	-	-	2	2	-
651	P26885	FK506-binding protein 2 precursor (EC 5.2.1.8) (Peptidyl-prolyl isomerase)	-	-	1	-	-	2	2	X
652	Q00688	FK506-binding protein 3 (EC 5.2.1.8) (Peptidyl-prolyl isomerase)	-	-	-	-	1	-	2	-
653	Q02790	FK506-binding protein 4 (EC 5.2.1.8) (Peptidyl-prolyl isomerase)	-	-	-	-	1	-	1	X
654	Q13451	FK506-binding protein 5 (EC 5.2.1.8) (Peptidyl-prolyl isomerase)	-	-	-	-	4	-	2	X
655	P30043	Flavin reductase (EC 1.5.1.30) (FR) (NADPH-dependent)	-	11	2	-	8	6	7	X
656	O75955	Flotillin-1 - Homo sapiens (Human)	-	3	1	-	-	-	-	-
657	Q14254	Flotillin-2 - Homo sapiens (Human)	-	1	1	-	-	-	-	-
658	P41439	Folate receptor gamma precursor (FR-gamma) (Folate receptor)	-	-	-	3	-	-	-	-
659	Q96RU3	Formin-binding protein 1 (Formin-binding protein 17) (Formin)	-	-	-	-	4	-	-	-
660	O95466	Formin-like 1 protein (Formin-like protein) (Leukocyte formin)	-	-	-	-	2	4	9	-
661	Q13642	Four and a half LIM domains protein 1 (FHL-1) (Skeletal)	-	-	2	-	1	-	2	-
662	P09467	Fructose-1,6-bisphosphatase 1 (EC 3.1.3.11) (D-fructose-1,6-bisphosphatase)	-	-	-	1	2	2	5	X
663	P04075	Fructose-bisphosphate aldolase A (EC 4.1.2.13) (Muscle)	-	7	14	10	19	14	16	X
664	P09972	Fructose-bisphosphate aldolase C (EC 4.1.2.13) (Brain)	-	-	3	3	6	2	5	-
665	P07954	Fumarate hydratase, mitochondrial precursor (EC 4.2.1.2)	-	-	1	1	2	1	2	X
666	P16930	Fumarylacetoacetase (EC 3.7.1.2) (Fumarylacetoacetate hydrolase)	-	-	2	2	-	2	-	X

667	Q6P587	Fumarylacetoacetate hydrolase domain-containing protein	-	-	-	-	1	1	2	X
668	O15117	FYN-binding protein (FYN-T-binding protein) (FYB-120)	-	-	3	-	-	-	-	-
669	O95866	G6b protein precursor - Homo sapiens (Human)	-	-	3	-	-	-	-	-
670	P09382	Galectin-1 (Beta-galactoside-binding lectin L-14-I) (Lac	-	-	-	-	3	6	5	X
671	P17931	Galectin-3 (Galactose-specific lectin 3) (Mac-2 antigen	-	-	-	4	-	4	2	-
672	Q08380	Galectin-3-binding protein precursor (Lectin galactosid	-	-	2	-	-	-	-	-
673	Q3ZCW2	Galectin-related protein - Homo sapiens (Human)	-	-	6	-	-	-	-	-
674	O95166	Gamma-aminobutyric acid receptor-associated protein	-	-	-	1	-	2	-	-
675	P09104	Gamma-enolase (EC 4.2.1.11) (2-phospho-D-glycerate	-	-	-	-	6	-	-	X
676	Q92820	Gamma-glutamyl hydrolase precursor (EC 3.4.19.9) (G	2	-	-	1	-	1	1	-
677	P13284	Gamma-interferon-inducible lysosomal thiol reductase	-	-	-	-	-	1	1	-
678	Q9HBI0	Gamma-parvin - Homo sapiens (Human)	-	-	-	2	-	1	1	-
679	P17900	Ganglioside GM2 activator precursor (GM2-AP) (Cere	-	-	-	-	-	1	-	-
680	Q9NS71	Gastrokin-1 precursor - Homo sapiens (Human)	1	-	-	-	-	-	-	-
681	O95479	GDH/6PGL endoplasmic bifunctional protein precursor	-	-	-	1	-	-	1	-
682	Q13630	GDP-L-fucose synthetase (EC 1.1.1.271) (Protein FX)	-	2	-	-	-	-	-	X
683	P06396	Gelsolin precursor (Actin-depolymerizing factor) (ADF)	9	4	18	14	5	6	16	X
684	Q9P107	GEM-interacting protein (GMIP)	-	-	-	-	-	1	1	-
685	O60763	General vesicular transport factor p115 (Transcytosis-	-	-	-	-	-	3	1	-
686	P60983	Glia maturation factor beta (GMF-beta)	-	-	2	-	3	2	2	X
687	O60234	Glia maturation factor gamma (GMF-gamma)	-	-	2	1	6	3	5	X
688	P46926	Glucosamine-6-phosphate isomerase (EC 3.5.99.6) (G	-	-	-	-	2	1	2	X
689	P11413	Glucose-6-phosphate 1-dehydrogenase (EC 1.1.1.49)	-	-	4	11	3	9	5	X
690	P06744	Glucose-6-phosphate isomerase (EC 5.3.1.9) (GPI) (P	-	1	4	12	8	12	9	X
691	P14314	Glucosidase II beta subunit precursor (Protein kinase	-	-	-	1	1	-	6	-
692	P00367	Glutamate dehydrogenase 1, mitochondrial precursor	-	-	-	-	8	2	10	X
693	P48506	Glutamate--cysteine ligase catalytic subunit (EC 6.3.2.	-	3	-	-	-	-	-	-
694	P48507	Glutamate--cysteine ligase regulatory subunit (EC 6.3.	-	-	3	-	1	-	-	X
695	O94925	Glutaminase kidney isoform, mitochondrial precursor	-	-	-	-	1	-	1	X
696	P35754	Glutaredoxin-1 (Thioltransferase-1) (TTase-1)	-	-	-	2	-	3	-	-
697	P07203	Glutathione peroxidase 1 (EC 1.11.1.9) (GSHPx-1) (G	-	1	11	-	6	11	10	X
698	P22352	Glutathione peroxidase 3 precursor (EC 1.11.1.9) (GS	4	-	-	-	-	-	-	X
699	P00390	Glutathione reductase, mitochondrial precursor (EC 1.	-	1	2	3	9	2	5	-
700	Q9Y2Q3	Glutathione S-transferase kappa 1 (EC 2.5.1.18) (GST	-	-	5	-	8	4	11	-
701	P09488	Glutathione S-transferase Mu 1 (EC 2.5.1.18) (GSTM1	-	-	-	-	5	4	7	-
702	P28161	Glutathione S-transferase Mu 2 (EC 2.5.1.18) (GSTM2	-	-	1	-	5	-	4	-
703	P21266	Glutathione S-transferase Mu 3 (EC 2.5.1.18) (GSTM3	-	-	-	-	3	-	1	X
704	Q03013	Glutathione S-transferase Mu 4 (EC 2.5.1.18) (GSTM4	-	-	2	-	5	4	7	-
705	P09211	Glutathione S-transferase P (EC 2.5.1.18) (GST class-	-	-	8	8	6	9	8	X
706	P48637	Glutathione synthetase (EC 6.3.2.3) (Glutathione s	-	-	-	-	-	2	1	X
707	P78417	Glutathione transferase omega-1 (EC 2.5.1.18) (GSTC	-	-	9	5	5	4	6	X
708	P04406	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.	-	7	22	25	25	14	21	X
709	Q8N335	Glycerol-3-phosphate dehydrogenase 1-like protein - H	-	-	-	1	-	-	-	-
710	P43304	Glycerol-3-phosphate dehydrogenase, mitochondrial p	-	-	2	-	1	2	3	X
711	P35573	Glycogen debranching enzyme (Glycogen debrancher	-	-	-	1	-	-	2	-
712	P11216	Glycogen phosphorylase, brain form (EC 2.4.1.1)	-	-	2	-	5	-	9	X
713	P06737	Glycogen phosphorylase, liver form (EC 2.4.1.1) - Hon	-	-	-	28	-	4	4	-
714	P46976	Glycogenin-1 (EC 2.4.1.186) - Homo sapiens (Human)	-	-	-	1	-	-	-	-
715	P04921	Glycophorin C (PAS-2*) (Glycoprotein beta) (GLPC) (C	-	1	-	-	-	-	-	-
716	P30419	Glycylpeptide N-tetradecanoyltransferase 1 (EC 2.3.1.	-	-	-	-	-	-	1	-
717	P41250	Glycyl-tRNA synthetase (EC 6.1.1.14) (Glycine--tRNA	-	-	-	-	1	-	1	X
718	Q9HC38	Glyoxalase domain-containing protein 4 - Homo sapien	-	-	1	2	4	-	10	-
719	Q9UBQ7	Glyoxylate reductase/hydroxypyruvate reductase (EC	-	-	-	-	-	-	2	X
720	P36959	GMP reductase 1 (EC 1.7.1.7) (Guanosine 5*-monoph	-	-	1	-	1	-	-	-
721	Q9H4A6	Golgi phosphoprotein 3 (Coat-protein GPP34)	-	1	-	-	-	-	1	X
722	Q9H3P7	Golgi resident protein GCP60 (Acyl-CoA-binding doma	-	-	-	1	-	2	-	-

723	Q9H4G4	Golgi-associated plant pathogenesis-related protein 1	1	-	1	2	2	2	3	-
724	P28676	Grancalcin	-	-	1	4	3	5	3	X
725	P10144	Granzyme B precursor - Homo sapiens (Human)	-	-	-	-	-	-	1	-
726	O75791	GRB2-related adapter protein 2 (GADS protein) (Grow	-	-	1	-	1	-	-	-
727	Q12849	G-rich sequence factor 1 (GRSF-1)	-	-	-	-	1	1	1	X
728	Q4V328	GRIP1-associated protein 1 (GRASP-1) - Homo sapie	-	-	-	-	-	-	1	-
729	P62993	Growth factor receptor-bound protein 2 (Adapter prote	-	-	2	3	2	4	10	X
730	Q9UIJ7	GTP:AMP phosphotransferase mitochondrial (EC 2.7.4	-	-	2	-	2	1	1	-
731	P01112	GTPase HRas precursor (Transforming protein p21) (p	-	-	2	-	-	2	-	-
732	P01111	GTPase NRas precursor (Transforming protein N-Ras	-	-	2	-	1	-	-	-
733	Q8WWP7	GTPase, IMAP family member 1 (Immunity-associated	-	-	-	-	3	1	4	-
734	Q9NUV9	GTPase, IMAP family member 4 (Immunity-associated	-	-	-	-	7	1	5	-
735	P62826	GTP-binding nuclear protein Ran (GTPase Ran) (Ras-	-	4	4	4	10	10	12	X
736	P36406	GTP-binding protein ARD-1 (ADP-ribosylation factor d	-	-	-	-	1	-	-	-
737	Q15382	GTP-binding protein Rheb (Ras homolog enriched in b	-	-	2	-	-	-	-	-
738	Q9NR31	GTP-binding protein SAR1a (COPII-associated small G	-	-	8	3	2	2	4	X
739	Q9Y6B6	GTP-binding protein SAR1b (GTBPB)	-	-	-	-	-	-	2	X
740	Q03113	Guanine nucleotide-binding protein alpha-12 subunit (G	-	-	-	1	-	-	-	X
741	Q14344	Guanine nucleotide-binding protein alpha-13 subunit (G	-	-	-	-	-	-	2	-
742	P63244	Guanine nucleotide-binding protein beta subunit 2-like	-	1	-	-	11	3	13	X
743	P63096	Guanine nucleotide-binding protein G(i), alpha-1 subu	-	-	-	-	2	-	-	-
744	P04899	Guanine nucleotide-binding protein G(i), alpha-2 subu	-	-	8	8	7	8	9	X
745	P59768	Guanine nucleotide-binding protein G(l)/G(s)/G(o) sub	-	-	-	1	-	-	-	-
746	P62873	Guanine nucleotide-binding protein G(l)/G(s)/G(t) bet	-	-	6	-	5	2	-	X
747	P62879	Guanine nucleotide-binding protein G(l)/G(s)/G(t) bet	-	-	6	3	5	-	7	X
748	P09471	Guanine nucleotide-binding protein G(o) subunit alpha	-	-	-	2	-	-	-	-
749	P50148	Guanine nucleotide-binding protein G(q) subunit alpha	-	-	4	2	-	-	1	-
750	P19086	Guanine nucleotide-binding protein G(z) subunit alpha	-	-	3	-	-	-	-	-
751	Q16774	Guanylate kinase (EC 2.7.4.8) (GMP kinase)	-	-	-	-	2	-	2	X
752	Q9H0R5	Guanylate-binding protein 3 (GTP-binding protein 3) (G	-	-	-	-	2	-	-	-
753	Q96PP8	Guanylate-binding protein 5 (GTP-binding protein 5) (G	-	-	-	-	-	-	1	-
754	Q9H0R4	Haloacid dehalogenase-like hydrolase domain-contain	-	-	4	-	1	-	-	-
755	Q9BSH5	Haloacid dehalogenase-like hydrolase domain-contain	-	-	-	-	-	-	1	-
756	P00738	Haptoglobin precursor [Contains: Haptoglobin alpha ch	25	-	-	3	-	8	10	X
757	P00739	Haptoglobin-related protein precursor - Homo sapiens	18	1	-	-	-	5	-	-
758	Q7Z4H3	HD domain-containing protein 2 - Homo sapiens (Hum	-	-	-	-	1	-	1	-
759	Q8N4P3	HD domain-containing protein 3 - Homo sapiens (Hum	-	-	-	-	1	-	-	-
760	Q86WZ0	HEAT repeat-containing protein 4 - Homo sapiens (Hu	-	-	-	-	1	-	2	-
761	P08107	Heat shock 70 kDa protein 1 (HSP70.1) (HSP70-1/HS	-	1	8	16	12	13	16	X
762	P34931	Heat shock 70 kDa protein 1L (Heat shock 70 kDa pro	-	-	-	9	-	-	6	X
763	P34932	Heat shock 70 kDa protein 4 (Heat shock 70-related p	-	4	2	-	4	4	6	X
764	P17066	Heat shock 70 kDa protein 6 (Heat shock 70 kDa prote	-	-	-	5	-	2	4	X
765	P11142	Heat shock cognate 71 kDa protein (Heat shock 70 kD	-	7	16	8	24	15	25	X
766	Q12931	Heat shock protein 75 kDa, mitochondrial precursor (H	-	-	1	-	1	2	1	X
767	P07900	Heat shock protein HSP 90-alpha (HSP 86)	-	5	17	5	24	23	30	X
768	P08238	Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	-	3	9	5	18	21	29	X
769	P54652	Heat shock-related 70 kDa protein 2 (Heat shock 70 k	-	-	-	-	-	-	6	X
770	Q92598	Heat-shock protein 105 kDa (Heat shock 110 kDa prot	-	1	-	-	-	-	-	X
771	P04792	Heat-shock protein beta-1 (HspB1) (Heat shock 27 kD	-	-	6	-	1	-	4	X
772	Q9NQ75	HEF-like protein - Homo sapiens (Human)	-	-	4	-	-	-	-	-
773	P14317	Hematopoietic lineage cell-specific protein (Hematopo	-	1	-	-	8	2	3	X
774	Q9NRV9	Heme-binding protein 1 (p22HBP)	-	1	-	1	2	2	1	X
775	Q9Y5Z4	Heme-binding protein 2 (Protein SOUL) (Placental pro	-	-	1	3	1	3	-	-
776	P69905	Hemoglobin subunit alpha (Hemoglobin alpha chain) (G	4	19	-	6	-	11	9	-
777	P68871	Hemoglobin subunit beta (Hemoglobin beta chain) (Be	6	21	-	11	-	17	15	X
778	P02042	Hemoglobin subunit delta (Hemoglobin delta chain) (D	-	15	-	4	-	12	12	-

779	P69891	Hemoglobin subunit gamma-1 (Hemoglobin gamma-1	-	7	-	-	-	-	-	-	-
780	P69892	Hemoglobin subunit gamma-2 (Hemoglobin gamma-2	4	-	-	-	-	-	-	-	-
781	P02790	Hemopexin precursor (Beta-1B-glycoprotein)	13	-	-	-	-	-	-	5	-
782	Q9Y251	Heparanase precursor (EC 3.2.-.-) (Heparanase-1) (H	-	-	1	-	-	-	-	-	-
783	P05546	Heparin cofactor 2 precursor (Heparin cofactor II) (HC	9	-	-	-	-	-	-	-	-
784	Q04756	Hepatocyte growth factor activator precursor (EC 3,4,2	1	-	-	-	-	-	-	-	-
785	P26927	Hepatocyte growth factor-like protein precursor (Macro	1	-	-	-	-	-	-	-	-
786	P51858	Hepatoma-derived growth factor (HDGF) (High-mobilit	-	-	-	1	2	-	-	5	-
787	Q13151	Heterogeneous nuclear ribonucleoprotein A0 (hnRNP	-	-	-	-	-	1	1	-	-
788	P09651	Heterogeneous nuclear ribonucleoprotein A1 (Helix-de	-	-	-	3	6	2	7	-	-
789	Q32P51	Heterogeneous nuclear ribonucleoprotein A1-like prote	-	-	-	-	-	-	8	-	-
790	P51991	Heterogeneous nuclear ribonucleoprotein A3 (hnRNP	-	-	-	-	1	-	2	-	-
791	O60812	Heterogeneous nuclear ribonucleoprotein C-like 1 (hnf	-	-	-	-	-	3	2	-	-
792	Q14103	Heterogeneous nuclear ribonucleoprotein D0 (hnRNP	-	-	-	1	6	4	8	X	-
793	P52597	Heterogeneous nuclear ribonucleoprotein F (hnRNP F	-	-	-	-	6	2	5	X	-
794	P38159	Heterogeneous nuclear ribonucleoprotein G (hnRNP G	-	-	-	-	1	2	-	-	-
795	P31943	Heterogeneous nuclear ribonucleoprotein H (hnRNP H	-	-	-	-	6	2	4	X	-
796	P31942	Heterogeneous nuclear ribonucleoprotein H3 (hnRNP	-	-	-	-	1	1	-	X	-
797	P61978	Heterogeneous nuclear ribonucleoprotein K (hnRNP K	-	-	3	2	12	14	11	X	-
798	O60506	Heterogeneous nuclear ribonucleoprotein Q (hnRNP Q	-	-	-	-	3	2	2	-	-
799	O43390	Heterogeneous nuclear ribonucleoprotein R (hnRNP R	-	-	-	-	1	-	2	-	-
800	Q9BUJ2	Heterogeneous nuclear ribonucleoprotein U-like protei	-	-	-	-	1	-	-	-	-
801	Q1KMD3	Heterogeneous nuclear ribonucleoprotein U-like protei	-	-	-	-	-	-	1	-	-
802	P22626	Heterogeneous nuclear ribonucleoproteins A2/B1 (hnF	-	2	-	3	6	6	10	X	-
803	P07910	Heterogeneous nuclear ribonucleoproteins C1/C2 (hnF	-	-	-	-	2	4	3	X	-
804	Q00839	Heterogenous nuclear ribonucleoprotein U (hnRNP U)	-	-	-	-	9	2	8	-	-
805	P19367	Hexokinase-1 (EC 2.7.1.1) (Hexokinase type I) (HK I)	-	3	3	-	4	-	6	-	-
806	P52790	Hexokinase-3 (EC 2.7.1.1) (Hexokinase type III) (HK II	-	-	-	13	-	10	10	-	-
807	P30273	High affinity immunoglobulin epsilon receptor gamma-	-	-	1	1	-	3	1	-	-
808	P09429	High mobility group protein 1 (HMG-1) (High mobility g	-	-	-	-	16	11	19	-	-
809	Q9UGV6	High mobility group protein 1-like 10 (HMG-1L10)	-	-	-	-	-	-	7	-	-
810	P26583	High mobility group protein 2 (HMG-2)	-	-	-	1	7	8	16	-	-
811	O15347	High mobility group protein B3 (High mobility group pro	-	-	-	-	-	2	-	-	-
812	P37235	Hippocalcin-like protein 1 (Visinin-like protein 3) (VILIP	-	-	-	-	4	-	-	X	-
813	P49773	Histidine triad nucleotide-binding protein 1 (Adenosine	-	-	2	-	3	4	4	X	-
814	P04196	Histidine-rich glycoprotein precursor (Histidine-proline-	10	-	-	-	-	-	-	-	-
815	P12081	Histidyl-tRNA synthetase (EC 6.1.1.21) (Histidine--tRN	-	-	-	-	2	-	-	X	-
816	Q96QV6	Histone H2A type 1-A - Homo sapiens (Human)	-	-	-	-	-	-	3	-	-
817	P33778	Histone H2B type 1-B (H2B,f) (H2B/f) (H2B,1) - Homo	-	-	-	-	-	-	2	-	-
818	P62805	Histone H4	-	-	3	-	4	1	11	-	-
819	P30443	HLA class I histocompatibility antigen, A-1 alpha chain	-	1	4	-	2	-	5	-	-
820	P13746	HLA class I histocompatibility antigen, A-11 alpha chai	-	-	-	-	-	-	4	-	-
821	P01892	HLA class I histocompatibility antigen, A-2 alpha chain	-	-	5	-	-	-	6	-	-
822	P18462	HLA class I histocompatibility antigen, A-25 alpha chai	-	-	-	-	-	-	4	-	-
823	P16188	HLA class I histocompatibility antigen, A-30 alpha chai	-	-	-	-	-	-	6	-	-
824	P30455	HLA class I histocompatibility antigen, A-36 alpha chai	-	-	-	-	-	-	5	-	-
825	P30464	HLA class I histocompatibility antigen, B-15 alpha chai	-	-	-	-	-	-	8	-	-
826	P30685	HLA class I histocompatibility antigen, B-35 alpha chai	-	-	-	-	-	-	6	-	-
827	P30481	HLA class I histocompatibility antigen, B-44 alpha chai	-	-	-	-	-	-	3	-	-
828	P30491	HLA class I histocompatibility antigen, B-53 alpha chai	-	-	-	-	-	-	5	-	-
829	P01889	HLA class I histocompatibility antigen, B-7 alpha chain	-	-	-	3	-	-	-	-	-
830	P30460	HLA class I histocompatibility antigen, B-8 alpha chain	-	-	-	-	-	-	5	-	-
831	P30499	HLA class I histocompatibility antigen, Cw-1 alpha cha	-	-	-	-	-	-	1	-	-
832	Q07000	HLA class I histocompatibility antigen, Cw-15 alpha ch	-	-	-	-	-	-	2	-	-
833	P30501	HLA class I histocompatibility antigen, Cw-2 alpha cha	-	-	-	-	-	-	1	-	-
834	P04233	HLA class II histocompatibility antigen gamma chain (H	-	-	-	-	-	2	2	-	-

835	P28068	HLA class II histocompatibility antigen, DM beta chain	-	-	-	-	-	-	1	-
836	P01908	HLA class II histocompatibility antigen, DQ(1) alpha chain	-	-	-	-	-	-	1	X
837	P01903	HLA class II histocompatibility antigen, DR alpha chain	-	-	-	-	-	3	-	-
838	P01912	HLA class II histocompatibility antigen, DR-1 beta chain	-	-	-	-	-	2	-	-
839	P13761	HLA class II histocompatibility antigen, DRB1-7 beta chain	-	-	-	-	-	-	4	X
840	P50502	Hsc70-interacting protein (Hip) (Putative tumor suppressor)	-	1	4	-	2	-	3	X
841	Q16543	Hsp90 co-chaperone Cdc37 (Hsp90 chaperone protein)	-	1	1	-	2	2	3	-
842	Q16775	Hydroxyacylglutathione hydrolase (EC 3.1.2.6) (Glyoxalase I)	-	-	-	-	1	-	-	X
843	P35914	Hydroxymethylglutaryl-CoA lyase, mitochondrial precursor	-	-	-	1	-	-	-	-
844	Q6YN16	Hydroxysteroid dehydrogenase-like protein 2 - Homo sapiens	-	-	-	2	-	-	-	-
845	P00492	Hypoxanthine-guanine phosphoribosyltransferase (EC 2.7.1.3)	-	1	5	3	3	6	4	X
846	P01876	Ig alpha-1 chain C region - Homo sapiens (Human)	11	-	-	-	-	-	8	X
847	P01877	Ig alpha-2 chain C region - Homo sapiens (Human)	7	-	-	-	-	-	5	-
848	P01857	Ig gamma-1 chain C region - Homo sapiens (Human)	14	-	-	-	-	-	14	-
849	P01859	Ig gamma-2 chain C region - Homo sapiens (Human)	10	-	-	-	-	-	7	-
850	P01860	Ig gamma-3 chain C region (Heavy chain disease protein)	9	-	-	-	-	-	4	-
851	P01861	Ig gamma-4 chain C region - Homo sapiens (Human)	8	-	-	-	-	-	-	-
852	P01742	Ig heavy chain V-I region EU - Homo sapiens (Human)	-	-	-	-	-	-	1	-
853	P01743	Ig heavy chain V-I region HG3 precursor - Homo sapiens	2	-	-	-	-	-	-	-
854	P06331	Ig heavy chain V-II region ARH-77 precursor - Homo sapiens	2	-	-	-	-	-	-	-
855	P01825	Ig heavy chain V-II region NEWM - Homo sapiens (Human)	1	-	-	-	-	-	-	-
856	P01824	Ig heavy chain V-II region WAH - Homo sapiens (Human)	1	-	-	-	-	-	-	-
857	P01766	Ig heavy chain V-III region BRO - Homo sapiens (Human)	3	-	-	-	-	-	-	-
858	P01767	Ig heavy chain V-III region BUT - Homo sapiens (Human)	1	-	-	-	-	-	-	-
859	P01781	Ig heavy chain V-III region GAL - Homo sapiens (Human)	4	-	-	-	-	-	-	-
860	P01771	Ig heavy chain V-III region HIL - Homo sapiens (Human)	2	-	-	-	-	-	-	-
861	P01777	Ig heavy chain V-III region TEI - Homo sapiens (Human)	-	-	-	-	-	-	1	-
862	P01779	Ig heavy chain V-III region TUR - Homo sapiens (Human)	2	-	-	-	-	-	-	-
863	P01764	Ig heavy chain V-III region VH26 precursor - Homo sapiens	4	-	-	-	-	-	-	-
864	P01834	Ig kappa chain C region - Homo sapiens (Human)	7	6	-	2	-	-	7	-
865	P01593	Ig kappa chain V-I region AG	2	-	-	-	-	-	-	X
866	P04430	Ig kappa chain V-I region BAN - Homo sapiens (Human)	1	-	-	-	-	-	-	-
867	P01596	Ig kappa chain V-I region CAR - Homo sapiens (Human)	2	-	-	-	-	-	-	-
868	P01602	Ig kappa chain V-I region HK102 precursor (Fragment)	1	-	-	-	-	-	-	-
869	P01613	Ig kappa chain V-I region Ni - Homo sapiens (Human)	1	-	-	-	-	-	-	-
870	P01609	Ig kappa chain V-I region Scw - Homo sapiens (Human)	2	-	-	-	-	-	-	-
871	P01611	Ig kappa chain V-I region Wes - Homo sapiens (Human)	1	-	-	-	-	-	-	-
872	P01614	Ig kappa chain V-II region Cum - Homo sapiens (Human)	2	-	-	-	-	-	-	-
873	P04206	Ig kappa chain V-III region GOL (Rheumatoid factor)	-	-	-	-	-	-	4	-
874	P18135	Ig kappa chain V-III region HAH precursor	4	-	-	-	-	-	-	-
875	P01622	Ig kappa chain V-III region Ti - Homo sapiens (Human)	3	-	-	-	-	-	-	-
876	P04433	Ig kappa chain V-III region VG precursor (Fragment)	-	-	-	-	-	-	1	-
877	P01625	Ig kappa chain V-IV region Len - Homo sapiens (Human)	3	-	-	-	-	-	2	-
878	P01842	Ig lambda chain C regions - Homo sapiens (Human)	5	-	-	-	2	-	4	-
879	P04208	Ig lambda chain V-I region WAH - Homo sapiens (Human)	-	-	-	-	-	-	2	-
880	P80748	Ig lambda chain V-III region LOI - Homo sapiens (Human)	1	-	-	-	-	-	-	X
881	P01714	Ig lambda chain V-III region SH - Homo sapiens (Human)	1	-	-	-	-	-	-	-
882	P01717	Ig lambda chain V-IV region Hil - Homo sapiens (Human)	1	-	-	-	-	-	-	-
883	P01871	Ig mu chain C region - Homo sapiens (Human)	8	-	-	-	-	-	9	-
884	P04220	Ig mu heavy chain disease protein (BOT) - Homo sapiens	-	-	-	-	-	-	4	-
885	P01591	Immunoglobulin J chain - Homo sapiens (Human)	3	-	-	-	-	-	-	-
886	O00629	Importin alpha-4 subunit (Karyopherin alpha-4 subunit)	-	-	-	-	1	1	1	-
887	Q14974	Importin beta-1 subunit (Karyopherin beta-1 subunit) (Importin beta-1)	-	-	3	4	4	4	10	-
888	O00410	Importin beta-3 (Karyopherin beta-3) (Ran-binding protein 4)	-	-	-	-	3	-	6	-
889	Q8TEX9	Importin-4 (Importin 4b) (Imp4b) (Ran-binding protein 4)	-	-	-	-	1	-	-	-
890	Q96P70	Importin-9 (Imp9) (Ran-binding protein 9) (RanbP9) - Homo sapiens	-	-	-	-	-	1	-	-

891	P55060	Importin-alpha re-exporter (Chromosome segregation	-	-	-	-	-	6	2	-
892	Q5TEJ8	Induced by contact to basement membrane 1 protein (I	-	-	-	1	-	1	1	-
893	O14920	Inhibitor of nuclear factor kappa-B kinase subunit beta	-	-	1	-	-	1	-	-
894	Q15181	Inorganic pyrophosphatase (EC 3.6.1.1) (Pyrophosphat	-	-	-	2	6	1	5	X
895	Q9H2U2	Inorganic pyrophosphatase 2, mitochondrial precursor	-	-	1	1	4	-	5	X
896	Q9BY32	Inosine triphosphate pyrophosphatase (EC 3.6.1.19) (I	-	-	-	-	2	2	2	X
897	P20839	Inosine-5*-monophosphate dehydrogenase 1 (EC 1.1.	-	-	-	-	1	1	-	X
898	P12268	Inosine-5*-monophosphate dehydrogenase 2 (EC 1.1.	-	-	-	-	1	1	2	X
899	P29218	Inositol monophosphatase (EC 3.1.3.25) (IMPase) (IM	-	-	2	-	2	1	4	X
900	O14732	Inositol monophosphatase 2 (EC 3.1.3.25) (IMPase 2)	-	-	-	-	-	1	-	-
901	P17936	Insulin-like growth factor-binding protein 3 precursor (I	1	-	-	-	-	-	-	-
902	P24593	Insulin-like growth factor-binding protein 5 precursor (I	1	-	-	-	-	-	-	-
903	P35858	Insulin-like growth factor-binding protein complex acid	7	-	-	-	-	-	-	-
904	P17301	Integrin alpha-2 precursor (Platelet membrane glycopr	-	-	1	-	-	-	-	-
905	P23229	Integrin alpha-6 precursor (VLA-6) (CD49f antigen) [C	-	-	8	-	-	-	-	-
906	P08514	Integrin alpha-IIb precursor (Platelet membrane glycop	-	-	31	3	-	-	21	X
907	P20701	Integrin alpha-L precursor (Leukocyte adhesion glycop	-	-	-	-	2	3	4	-
908	P11215	Integrin alpha-M precursor (Cell surface glycoprotein M	-	-	-	33	9	32	22	-
909	P20702	Integrin alpha-X precursor (Leukocyte adhesion glycop	-	-	-	3	-	3	-	-
910	P05556	Integrin beta-1 precursor (Fibronectin receptor beta su	-	4	4	-	-	-	1	-
911	P05107	Integrin beta-2 precursor (Cell surface adhesion glycop	-	-	-	13	2	14	11	-
912	P05106	Integrin beta-3 precursor (Platelet membrane glycopro	-	-	23	1	-	-	9	-
913	P18084	Integrin beta-5 precursor - Homo sapiens (Human)	-	-	-	1	-	1	-	-
914	Q13418	Integrin-linked protein kinase (EC 2.7.11.1) (ILK-1) (IL	-	-	8	-	1	-	7	X
915	P05362	Intercellular adhesion molecule 1 precursor (ICAM-1) (	-	1	-	-	-	1	-	-
916	P13598	Intercellular adhesion molecule 2 precursor (ICAM-2) (	-	-	2	-	-	-	-	-
917	P32942	Intercellular adhesion molecule 3 precursor (ICAM-3) (	-	-	-	-	-	1	2	-
918	P48551	Interferon-alpha/beta receptor beta chain precursor - H	-	-	-	-	-	-	1	-
919	P05161	Interferon-induced 17 kDa protein precursor [Contains	-	-	-	-	-	-	1	-
920	P80217	Interferon-induced 35 kDa protein (IFP 35)	-	-	-	-	-	-	1	X
921	P20591	Interferon-induced GTP-binding protein Mx1 (Interfero	-	-	-	-	2	-	3	X
922	P32455	Interferon-induced guanylate-binding protein 1 (GTP-b	-	-	-	-	1	-	-	-
923	P32456	Interferon-induced guanylate-binding protein 2 (GTP-b	-	-	-	-	2	-	1	X
924	P09914	Interferon-induced protein with tetratricopeptide repeat	-	-	-	-	2	-	-	-
925	P13164	Interferon-induced transmembrane protein 1 (Interfero	-	-	-	1	1	-	1	-
926	Q96AZ6	Interferon-stimulated gene 20 kDa protein (EC 3.1.13.1	-	-	-	-	3	-	2	-
927	Q12905	Interleukin enhancer-binding factor 2 (Nuclear factor o	-	-	-	-	-	-	1	X
928	P01584	Interleukin-1 beta precursor (IL-1 beta) (Catabolin)	-	-	-	-	-	-	3	-
929	P18510	Interleukin-1 receptor antagonist protein precursor (IL-	-	-	-	-	-	-	1	X
930	Q14005	Interleukin-16 precursor (IL-16) (Lymphocyte chemoat	-	-	-	-	6	-	9	-
931	Q27J81	Inverted formin-2 - Homo sapiens (Human)	-	-	4	-	-	-	1	-
932	Q96CN7	Isochorismatase domain-containing protein 1 - Homo s	-	-	3	-	-	-	2	-
933	Q96AB3	Isochorismatase domain-containing protein 2, mitoch	-	-	1	-	2	1	2	-
934	P50213	Isocitrate dehydrogenase [NAD] subunit alpha, mitoch	1	-	1	-	3	2	4	X
935	O43837	Isocitrate dehydrogenase [NAD] subunit beta, mitoch	-	-	-	-	-	-	1	-
936	O75874	Isocitrate dehydrogenase [NADP] cytoplasmic (EC 1.1	-	-	1	7	-	7	2	X
937	P48735	Isocitrate dehydrogenase [NADP], mitochondrial precu	-	-	6	5	7	6	8	-
938	P41252	Isoleucyl-tRNA synthetase, cytoplasmic (EC 6.1.1.5) (I	-	-	-	-	-	2	1	-
939	Q9NSE4	Isoleucyl-tRNA synthetase, mitochondrial precursor (E	-	-	-	-	4	1	1	-
940	Q13907	Isopentenyl-diphosphate delta-isomerase 1 (EC 5.3.3.	-	-	-	1	-	-	-	X
941	P26440	Isovaleryl-CoA dehydrogenase, mitochondrial precursor	-	-	1	-	1	-	1	X
942	Q9Y624	Junctional adhesion molecule A precursor (JAM-A) (Ju	-	-	3	-	-	-	-	-
943	O60229	Kalirin RhoGEF - Homo sapiens (Human)	-	-	1	-	-	-	-	-
944	P29622	Kallistatin precursor (Serpins A4) (Kallikrein inhibitor) (F	2	-	-	-	-	-	-	-
945	P33176	Kinesin heavy chain (Ubiquitous kinesin heavy chain) (	-	1	-	-	-	-	-	-
946	Q86VH2	Kinesin-like protein KIF27 - Homo sapiens (Human)	1	-	1	-	-	-	1	-

947	P01042	Kininogen-1 precursor (Alpha-2-thiol proteinase inhibitor)	5	-	-	-	-	-	-	-	X
948	Q14657	L antigen family member 3 (ITBA2 protein) (ESO-3 protein)	-	-	-	-	-	1	2	-	-
949	P02788	Lactotransferrin precursor (EC 3.4.21.-) (Lactoferrin) (Human)	-	-	-	45	12	19	-	-	-
950	Q04760	Lactoylglutathione lyase (EC 4.4.1.5) (Methylglyoxal lyase)	-	-	3	1	6	4	6	X	-
951	Q6P4A8	LAMA-like protein 1 precursor - Homo sapiens (Human)	-	-	-	8	-	4	2	-	-
952	Q8NHP8	LAMA-like protein 2 precursor - Homo sapiens (Human)	-	-	-	-	-	-	1	-	-
953	P42166	Lamina-associated polypeptide 2 isoform alpha (Thymocyte)	-	-	-	-	-	-	2	-	-
954	P42167	Lamina-associated polypeptide 2, isoforms beta/gamma	-	-	-	-	-	-	2	-	-
955	Q14739	Lamin-B receptor (Integral nuclear envelope inner membrane)	-	-	-	1	-	-	-	-	-
956	P24043	Laminin alpha-2 chain precursor (Laminin M chain) (Mammalian)	-	-	-	-	-	1	-	-	-
957	P46379	Large proline-rich protein BAT3 (HLA-B-associated transmembrane)	-	-	-	-	-	1	1	X	-
958	Q14766	Latent-transforming growth factor beta-binding protein	-	-	11	-	-	-	1	-	-
959	P22064	Latent-transforming growth factor beta-binding protein	-	-	12	-	-	-	-	-	-
960	Q9BS40	Latexin (Endogenous carboxypeptidase inhibitor) (EC 3.4.21.100)	-	1	-	1	-	-	-	-	-
961	Q6P5Q4	Leiomodin-2 - Homo sapiens (Human)	-	-	-	1	-	-	-	-	-
962	P02750	Leucine-rich alpha-2-glycoprotein precursor (LRG) - Human	5	-	-	-	-	-	-	-	-
963	Q32MZ4	Leucine-rich repeat flightless-interacting protein 1 (LRR-FLIIP1)	-	-	2	-	4	4	9	-	-
964	Q8N1G4	Leucine-rich repeat-containing protein 47 - Homo sapiens	-	-	-	-	-	-	1	-	-
965	Q8N9N7	Leucine-rich repeat-containing protein 57 - Homo sapiens	-	-	-	1	-	-	2	-	-
966	Q96AG4	Leucine-rich repeat-containing protein 59 - Homo sapiens	-	-	1	-	-	-	1	-	-
967	Q9P2J5	Leucyl-tRNA synthetase, cytoplasmic (EC 6.1.1.4) (Leucyl-tRNA synthetase)	-	-	-	-	-	-	1	-	-
968	P08575	Leukocyte common antigen precursor (EC 3.1.3.48) (Leukocyte common antigen)	-	-	-	9	22	27	27	X	-
969	P30740	Leukocyte elastase inhibitor (LEI) (Serpine B1) (Monocyte)	-	1	10	16	10	14	11	X	-
970	P08246	Leukocyte elastase precursor (EC 3.4.21.37) (Elastase)	-	-	-	6	-	1	2	-	-
971	Q8N6C8	Leukocyte immunoglobulin-like receptor subfamily A member 1	-	-	-	2	-	-	-	-	-
972	Q8NHL6	Leukocyte immunoglobulin-like receptor subfamily B member 1	-	-	-	-	-	1	-	-	-
973	P09960	Leukotriene A-4 hydrolase (EC 3.3.2.6) (LTA-4 hydrolase)	-	-	-	14	8	15	11	X	-
974	Q15722	Leukotriene B4 receptor 1 (LTB4-R 1) (P2Y purinoceptor)	-	-	-	1	-	-	-	-	-
975	O60711	Leupaxin - Homo sapiens (Human)	-	-	-	-	1	-	-	X	-
976	P48059	LIM and senescent cell antigen-like-containing domain	-	-	10	-	-	-	8	-	-
977	Q14847	LIM and SH3 domain protein 1 (LASP-1) (MLN 50)	-	-	4	1	4	2	6	X	-
978	P18428	Lipopolysaccharide-binding protein precursor (LBP) - Human	1	-	-	-	-	-	-	-	-
979	P05451	Lithostathine 1 alpha precursor - Homo sapiens (Human)	1	-	-	-	-	-	-	-	-
980	P48304	Lithostathine 1 beta precursor - Homo sapiens (Human)	1	-	-	-	-	-	-	-	-
981	P23141	Liver carboxylesterase 1 precursor (EC 3.1.1.1) (Acyl-CoA esterase)	-	-	-	-	-	5	7	X	-
982	P00338	L-lactate dehydrogenase A chain (EC 1.1.1.27) (LDH-A)	-	1	14	14	18	9	20	-	-
983	Q9BYZ2	L-lactate dehydrogenase A-like 6B (EC 1.1.1.27) - Homo sapiens	-	-	-	-	-	1	1	-	-
984	P07195	L-lactate dehydrogenase B chain (EC 1.1.1.27) (LDH-B)	2	6	14	5	22	9	19	X	-
985	P36776	Lon protease homolog, mitochondrial precursor (EC 3.4.21.26)	-	-	-	-	-	-	3	X	-
986	P33121	Long-chain-fatty-acid--CoA ligase 1 (EC 6.2.1.3) (Long-chain-fatty-acid--CoA ligase)	-	-	-	1	-	-	-	-	-
987	P08637	Low affinity immunoglobulin gamma Fc region receptor 1	-	-	-	-	-	-	1	-	-
988	O75015	Low affinity immunoglobulin gamma Fc region receptor 1	-	-	-	1	-	-	-	-	-
989	P24666	Low molecular weight phosphotyrosine protein phosphatase	-	3	4	-	5	5	4	X	-
990	Q07954	Low-density lipoprotein receptor-related protein 1 precursor	-	-	-	-	-	3	-	-	-
991	P14151	L-selectin precursor (Lymph node homing receptor) (L-selectin)	-	-	-	-	1	-	-	-	-
992	P51884	Lumican precursor (Keratan sulfate proteoglycan lumican)	1	-	-	-	-	-	-	-	-
993	P05455	Lupus La protein (Sjogren syndrome type B antigen) (Sjogren syndrome type B antigen)	-	-	-	-	6	-	3	X	-
994	Q7Z4W1	L-xylulose reductase (EC 1.1.1.10) (XR) (Dicarbonyl/L-xylulose reductase)	-	-	2	-	4	-	3	-	-
995	Q13094	Lymphocyte cytosolic protein 2 (SH2 domain-containing)	-	-	1	-	2	4	2	-	-
996	P33241	Lymphocyte-specific protein 1 (Protein pp52) (52 kDa)	-	-	-	2	3	2	-	-	-
997	P10253	Lysosomal alpha-glucosidase precursor (EC 3.2.1.20) (Alpha-glucosidase)	-	-	-	-	-	5	1	X	-
998	O00754	Lysosomal alpha-mannosidase precursor (EC 3.2.1.24) (Alpha-mannosidase)	-	-	-	-	1	3	2	-	-
999	P10619	Lysosomal protective protein precursor (EC 3.4.16.5) (Protective protein)	-	-	1	3	-	2	3	-	-
1000	P42785	Lysosomal Pro-X carboxypeptidase precursor (EC 3.4.21.100)	-	-	-	2	-	2	-	-	-
1001	P11279	Lysosome-associated membrane glycoprotein 1 precursor	-	-	-	4	1	4	4	-	-
1002	P13473	Lysosome-associated membrane glycoprotein 2 precursor	-	-	-	-	-	2	-	X	-

1003	P61626	Lysozyme C precursor (EC 3.2.1.17) (1,4-beta-N-acetylglucosaminidase)	1	-	-	5	2	10	8	-
1004	Q15046	Lysyl-tRNA synthetase (EC 6.1.1.6) (Lysine--tRNA ligase)	-	-	-	-	-	-	1	-
1005	P40121	Macrophage capping protein (Actin-regulatory protein)	-	1	-	8	4	8	4	X
1006	P14174	Macrophage migration inhibitory factor (MIF) (Phenylphosphorylcholine hydrolase)	-	-	1	1	1	1	1	X
1007	P34810	Macrosialin precursor (GP110) (CD68 antigen)	-	-	1	-	-	-	1	-
1008	Q86V88	Magnesium-dependent phosphatase 1 (EC 3.1.3.-) (EC 3.1.3.1)	-	-	-	2	-	-	-	-
1009	Q14728	Major facilitator superfamily domain-containing protein	-	-	-	1	-	1	1	-
1010	P04156	Major prion protein precursor (PrP) (PrP27-30) (PrP33-36)	-	-	1	-	-	-	-	-
1011	Q14764	Major vault protein (MVP) (Lung resistance-related protein)	-	11	-	-	10	3	7	X
1012	P40925	Malate dehydrogenase, cytoplasmic (EC 1.1.1.37) (Cytoplasmic malate dehydrogenase)	-	3	6	5	12	3	10	X
1013	P40926	Malate dehydrogenase, mitochondrial precursor (EC 1.1.1.40)	-	-	11	6	16	10	16	-
1014	Q9ULC4	Malignant T cell amplified sequence 1 OS=Homo sapiens	-	-	-	1	-	-	-	-
1015	O43451	Maltase-glucoamylase, intestinal [Includes: Maltase (EC 3.2.1.20)]	-	-	-	5	-	-	-	-
1016	Q8NFP4	MAM domain-containing glycosylphosphatidylinositol anchor	-	-	-	-	-	1	-	-
1017	O00187	Mannan-binding lectin serine protease 2 precursor (EC 3.4.21.26)	3	-	-	-	-	-	-	-
1018	Q9Y5P6	Mannose-1-phosphate guanylttransferase subunit beta	-	-	-	-	-	-	1	-
1019	O60664	Mannose-6-phosphate receptor-binding protein 1 (Carbohydrate binding protein)	-	-	1	3	1	4	5	X
1020	P11226	Mannose-binding protein C precursor (MBP-C) (MBP1)	1	-	-	-	-	-	-	-
1021	Q96L34	MAP/microtubule affinity-regulating kinase 4 (EC 2.7.1.1)	-	-	1	-	-	1	-	-
1022	Q8IX19	Mast cell-expressed membrane protein 1 - Homo sapiens	-	-	-	1	-	1	-	-
1023	P43243	Matrin-3	-	-	-	-	-	-	3	-
1024	P08493	Matrix Gla-protein precursor (MGP) (Cell growth-inhibitory protein)	1	-	-	-	-	-	-	-
1025	P14780	Matrix metalloproteinase-9 precursor (EC 3.4.24.35) (Hs-MMP-9)	-	-	-	21	3	14	-	-
1026	Q9NVC6	Mediator of RNA polymerase II transcription subunit 17	-	-	-	2	-	-	-	-
1027	O00264	Membrane-associated progesterone receptor component 1	-	-	3	-	-	-	1	-
1028	O15173	Membrane-associated progesterone receptor component 2	-	-	-	-	-	-	1	-
1029	Q96N66	Membrane-bound O-acyltransferase domain-containing protein	-	-	-	-	-	3	-	-
1030	Q13255	Metabotropic glutamate receptor 1 precursor (mGluR1)	-	-	-	1	-	-	-	-
1031	P01033	Metalloproteinase inhibitor 1 precursor (TIMP-1) (Erythrocyte TIMP)	1	-	5	-	-	-	-	-
1032	P16035	Metalloproteinase inhibitor 2 precursor (TIMP-2) (Tissue inhibitor of metalloproteinases)	3	-	-	-	-	-	-	-
1033	Q2M296	Methenyltetrahydrofolate synthetase domain-containing protein	-	1	-	-	-	-	-	-
1034	Q9NZL9	Methionine adenosyltransferase 2 subunit beta - Homo sapiens	-	1	-	-	3	-	-	-
1035	P50579	Methionine aminopeptidase 2 (EC 3.4.11.18) (MetAP 2)	-	-	-	-	1	-	2	-
1036	Q9NZV6	Methionine-R-sulfoxide reductase B1 - Homo sapiens	-	-	-	1	-	-	-	-
1037	Q9H8H3	Methyltransferase-like protein 7A precursor (EC 2.1.1.1)	-	-	-	-	-	3	1	-
1038	O14880	Microsomal glutathione S-transferase 3 (EC 2.5.1.18)	-	-	-	1	-	-	-	-
1039	P67812	Microsomal signal peptidase 18 kDa subunit (EC 3.4.21.1)	-	-	-	-	-	2	2	-
1040	Q9UPN3	Microtubule-actin cross-linking factor 1, isoforms 1/2/3	-	1	-	-	-	-	-	-
1041	Q66K74	Microtubule-associated protein 1S - Homo sapiens (Htubulin)	-	-	-	-	-	-	1	-
1042	P27816	Microtubule-associated protein 4 (MAP 4)	-	1	-	-	-	-	-	-
1043	Q15691	Microtubule-associated protein RP/EB family member	-	-	6	-	6	4	4	X
1044	Q15555	Microtubule-associated protein RP/EB family member	-	-	9	-	-	-	-	-
1045	Q8TCT9	Minor histocompatibility antigen H13 (EC 3.4.99.-) (Signal peptide)	-	-	-	-	-	1	-	-
1046	Q9Y2B0	MIR-interacting saposin-like protein precursor (Transmembrane protein)	-	-	-	-	3	2	1	X
1047	Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein (Oxoglutarate/malate carrier)	-	-	-	-	-	-	2	-
1048	Q16540	Mitochondrial 39S ribosomal protein L23 (L23mt) (MRP)	-	-	-	-	-	-	1	-
1049	Q9Y6C9	Mitochondrial carrier homolog 2 (Met-induced mitochondrial carrier)	-	-	-	-	1	1	1	-
1050	Q9Y5J7	Mitochondrial import inner membrane translocase subunit	-	-	-	-	2	-	-	-
1051	Q9NS69	Mitochondrial import receptor subunit TOM22 homolog	-	-	1	-	1	1	2	-
1052	P28482	Mitogen-activated protein kinase 1 (EC 2.7.1.37) (Extracellular signal-regulated kinase)	-	-	-	3	2	1	1	X
1053	Q16539	Mitogen-activated protein kinase 14 (EC 2.7.11.24) (Mitogen-activated protein kinase)	-	-	-	1	1	-	-	-
1054	Q9UHA4	Mitogen-activated protein kinase kinase 1-interacting protein	-	-	-	1	1	2	2	X
1055	Q9Y2Q5	Mitogen-activated protein-binding protein-interacting protein	-	-	-	-	-	1	1	-
1056	Q96T76	MMS19-like protein (hMMS19) (MET18 homolog) - Homo sapiens	-	-	-	-	1	-	-	-
1057	P26038	Moesin (Membrane-organizing extension spike protein)	-	1	10	19	24	21	30	X
1058	O95396	Molybdenum cofactor synthesis protein 3 (Molybdopterin synthase)	-	-	1	1	1	-	1	-

1059	P50224	Monoamine-sulfating phenol sulfotransferase (EC 2.8.	-	-	4	-	-	-	1	X
1060	O15427	Monocarboxylate transporter 4 (MCT 4) (MCT 3) (Solu	-	-	-	-	-	2	2	-
1061	P08571	Monocyte differentiation antigen CD14 precursor (Myc	-	-	-	-	-	1	-	-
1062	Q99685	Monoglyceride lipase (EC 3.1.1.23) (MGL) (HU-K5) (L	-	-	10	1	-	-	-	-
1063	Q7L9L4	Mps one binder kinase activator-like 1A (Mob1 homolo	-	-	2	1	2	1	3	X
1064	Q9H8S9	Mps one binder kinase activator-like 1B (Mob1 homolo	-	-	-	-	-	-	4	-
1065	Q96BX8	Mps one binder kinase activator-like 2A (Mob1 homolo	-	-	-	-	1	-	1	-
1066	P22234	Multifunctional protein ADE2 [Includes: Phosphoribosy	-	-	1	-	3	-	2	X
1067	Q13201	Multimerin-1 precursor (Endothelial cell multimerin 1) (	-	-	15	-	-	-	5	-
1068	Q9H8L6	Multimerin-2 precursor (EMILIN-3) (Elastin microfibril i	5	-	-	-	-	-	-	-
1069	O00499	Myc box-dependent-interacting protein 1 (Bridging inte	-	-	-	-	1	-	1	-
1070	P24158	Myeloblastin precursor (EC 3.4.21.76) (Leukocyte prot	-	-	-	4	4	4	2	-
1071	P41218	Myeloid cell nuclear differentiation antigen	-	-	-	5	-	1	3	-
1072	P05164	Myeloperoxidase precursor (EC 1.11.1.7) (MPO) [Con	-	-	-	33	8	20	20	-
1073	Q9NZM1	Myoferlin (Fer-1-like protein 3) - Homo sapiens (Huma	1	-	-	-	-	-	-	-
1074	Q12965	Myosin Ie (Myosin Ic)	-	-	-	1	-	1	-	-
1075	O00160	Myosin If (Myosin-IE)	-	-	-	5	2	6	6	-
1076	P05976	Myosin light chain 1, skeletal muscle isoform (MLC1F)	-	-	-	-	-	-	1	-
1077	Q15746	Myosin light chain kinase, smooth muscle (EC 2.7.11.1	-	-	2	-	-	-	-	-
1078	P60660	Myosin light polypeptide 6 (Myosin light chain alkali 3)	-	-	10	1	8	8	8	-
1079	P19105	Myosin regulatory light chain 2, nonsarcomeric (Myosi	-	-	7	2	7	5	8	X
1080	P35580	Myosin-10 (Myosin heavy chain, nonmuscle IIb) (Nonr	-	-	-	-	8	-	20	-
1081	Q7Z406	Myosin-14 (Myosin heavy chain, nonmuscle IIc) (Nonr	-	1	-	3	5	3	-	-
1082	P35579	Myosin-9 (Myosin heavy chain, nonmuscle IIa) (Nonm	-	25	76	28	71	63	156	-
1083	P58546	Myotrophin (V-1 protein)	-	-	5	3	3	5	5	X
1084	P29966	Myristoylated alanine-rich C-kinase substrate (MARCK	-	-	-	-	-	-	3	-
1085	P20933	N(4)-(beta-N-acetylglucosaminy)-L-asparaginase prec	-	-	-	-	-	-	1	-
1086	Q9UJ70	N-acetylglucosamine kinase (EC 2.7.1.59) (GlcNAc kir	-	1	-	2	2	7	7	X
1087	P15586	N-acetylglucosamine-6-sulfatase precursor (EC 3.1.6.	-	1	-	-	-	1	-	-
1088	Q96PD5	N-acetylmuramoyl-L-alanine amidase precursor (EC 3	4	-	-	-	-	-	-	-
1089	Q9GZZ1	N-acetyltransferase 13 - Homo sapiens (Human)	-	-	-	-	2	1	2	-
1090	Q02083	N-acyl ethanolamine-hydrolyzing acid amidase precurs	-	-	-	-	-	-	1	-
1091	Q13423	NAD(P) transhydrogenase, mitochondrial precursor (E	-	-	-	-	-	6	3	-
1092	P23368	NAD-dependent malic enzyme, mitochondrial precurs	-	-	1	-	2	-	4	X
1093	Q86Y39	NADH dehydrogenase [ubiquinone] 1 alpha subcompl	-	-	-	-	-	-	2	-
1094	O00483	NADH dehydrogenase [ubiquinone] 1 alpha subcompl	-	-	-	-	2	2	1	-
1095	O95182	NADH dehydrogenase [ubiquinone] 1 alpha subcompl	-	-	-	-	-	1	2	-
1096	Q16795	NADH dehydrogenase [ubiquinone] 1 alpha subcompl	-	-	-	-	2	2	2	-
1097	O96000	NADH dehydrogenase [ubiquinone] 1 beta subcomple	-	-	-	-	1	4	2	-
1098	O95168	NADH dehydrogenase [ubiquinone] 1 beta subcomple	-	-	-	-	-	-	3	-
1099	O43920	NADH dehydrogenase [ubiquinone] iron-sulfur protein	-	-	-	-	-	-	2	-
1100	O75251	NADH dehydrogenase [ubiquinone] iron-sulfur protein	-	-	-	-	1	-	3	-
1101	P00387	NADH-cytochrome b5 reductase (EC 1.6.2.2) (B5R) (E	-	-	6	-	2	-	1	-
1102	O75380	NADH-ubiquinone oxidoreductase 13 kDa-A subunit, r	-	-	-	-	-	-	1	-
1103	Q16718	NADH-ubiquinone oxidoreductase 13 kDa-B subunit (E	-	-	1	-	1	1	1	X
1104	O00217	NADH-ubiquinone oxidoreductase 23 kDa subunit, mit	-	-	-	-	2	1	2	-
1105	P19404	NADH-ubiquinone oxidoreductase 24 kDa subunit, mit	-	-	-	-	1	1	-	X
1106	O75489	NADH-ubiquinone oxidoreductase 30 kDa subunit, mit	-	-	-	-	5	3	7	X
1107	O95299	NADH-ubiquinone oxidoreductase 42 kDa subunit, mit	-	-	-	-	2	1	1	-
1108	P28331	NADH-ubiquinone oxidoreductase 75 kDa subunit, mit	-	-	-	-	3	1	3	X
1109	P56556	NADH-ubiquinone oxidoreductase B14 subunit (EC 1.6	-	-	-	-	-	-	2	-
1110	Q9P0J0	NADH-ubiquinone oxidoreductase B16.6 subunit (EC	-	-	-	-	-	1	3	-
1111	Q9Y5S8	NADPH oxidase homolog 1 (NOX-1) (NOH-1) (NADH/	-	-	-	-	-	1	1	-
1112	Q13765	Nascent polypeptide-associated complex alpha subun	-	-	1	-	6	2	4	X
1113	P49279	Natural resistance-associated macrophage protein 1 (f	-	-	-	-	-	1	-	-
1114	P55160	Nck-associated protein 1-like (Membrane-associated p	-	-	-	-	1	-	1	-

1115	Q92597	NDRG1 protein (N-myc downstream-regulated gene 1	-	-	-	-	2	-	2	X
1116	Q15843	NEDD8 precursor (Ubiquitin-like protein Nedd8) (Nedd	-	-	-	1	1	2	-	-
1117	P61081	NEDD8-conjugating enzyme Ubc12 (EC 6.3.2.-) (Ubiq	-	-	2	-	-	4	2	X
1118	P08473	Neprilysin (EC 3.4.24.11) (Neutral endopeptidase) (NE	-	-	-	1	-	-	-	-
1119	Q8WXH0	Nesprin-2 (Nuclear envelope spectrin repeat protein 2)	-	-	-	-	-	1	-	-
1120	Q09666	Neuroblast differentiation-associated protein AHNAK (	-	-	-	-	-	16	13	-
1121	Q14697	Neutral alpha-glucosidase AB precursor (EC 3.2.1.84)	-	7	10	4	13	19	21	X
1122	P22894	Neutrophil collagenase precursor (EC 3.4.24.34) (Matr	-	-	-	9	-	4	-	-
1123	P14598	Neutrophil cytosol factor 1 (NCF-1) (Neutrophil NADPH	-	-	-	6	-	3	1	-
1124	P19878	Neutrophil cytosol factor 2 (NCF-2) (Neutrophil NADPH	-	-	-	4	-	3	-	-
1125	Q15080	Neutrophil cytosol factor 4 (NCF-4) (Neutrophil NADPH	-	-	-	4	-	3	-	-
1126	P59665	Neutrophil defensin 1 precursor (HNP-1) (HP-1) (HP1)	-	-	-	3	-	-	-	-
1127	P80188	Neutrophil gelatinase-associated lipocalin precursor (N	3	-	-	13	5	6	-	-
1128	Q0ZGT2	Nexilin - Homo sapiens (Human)	-	-	3	-	-	-	-	-
1129	O95865	NG,NG-dimethylarginine dimethylaminohydrolase 2 (E	-	-	-	-	2	-	-	X
1130	P55769	NHP2-like protein 1 (High mobility group-like nuclear p	-	-	-	-	-	-	2	-
1131	Q9BZQ8	Niban protein	-	-	-	-	-	-	1	-
1132	Q96TA1	Niban-like protein (Meg-3)	-	4	-	-	-	2	-	-
1133	P43490	Nicotinamide phosphoribosyltransferase (EC 2.4.2.12)	-	-	-	11	1	-	-	X
1134	Q6XQN6	Nicotinate phosphoribosyltransferase - Homo sapiens	-	1	1	2	-	1	2	-
1135	P14543	Nidogen-1 precursor (Entactin) - Homo sapiens (Huma	-	-	6	-	-	-	-	-
1136	Q86X76	Nitrilase homolog 1 (EC 3.5.-.-) - Homo sapiens (Huma	-	-	-	1	-	-	-	X
1137	Q9NQR4	Nitrilase homolog 2 - Homo sapiens (Human)	-	-	-	1	-	4	3	-
1138	P05204	Nonhistone chromosomal protein HMG-17 (High-mobi	-	-	-	-	-	-	1	-
1139	P10153	Nonsecretory ribonuclease precursor (EC 3.1.27.5) (R	-	-	-	5	1	3	-	-
1140	P22307	Nonspecific lipid-transfer protein, mitochondrial precur	-	-	-	1	-	-	2	X
1141	Q9UNZ2	NSFL1 cofactor p47 (p97 cofactor p47)	-	1	-	-	4	-	2	X
1142	P41227	N-terminal acetyltransferase complex ARD1 subunit h	-	-	-	-	1	-	-	-
1143	P49321	Nuclear autoantigenic sperm protein (NASP) - Homo s	-	-	-	-	1	1	1	-
1144	P82979	Nuclear protein Hcc-1 (Proliferation-associated cytokin	-	-	-	-	-	-	1	-
1145	P61970	Nuclear transport factor 2 (NTF-2) (Placental protein 1	-	-	-	-	3	3	4	X
1146	P67809	Nuclease sensitive element-binding protein 1 (Y-box-b	-	-	-	-	1	-	1	-
1147	P19338	Nucleolin (Protein C23)	-	-	-	1	10	-	4	-
1148	P06748	Nucleophosmin (NPM) (Nucleolar phosphoprotein B23	-	-	-	-	2	1	4	X
1149	P52594	Nucleoporin-like protein RIP (HIV-1 Rev-binding protei	-	-	1	-	-	-	-	-
1150	P15531	Nucleoside diphosphate kinase A (EC 2.7.4.6) (NDK A	-	4	8	5	7	8	7	X
1151	P22392	Nucleoside diphosphate kinase B (EC 2.7.4.6) (NDK B	-	-	9	7	10	9	8	-
1152	Q96DE0	Nucleoside diphosphate-linked moiety X motif 16 (EC	-	-	-	-	-	3	1	X
1153	P55209	Nucleosome assembly protein 1-like 1 (NAP-1-related	-	-	5	-	-	2	-	-
1154	Q99733	Nucleosome assembly protein 1-like 4 (Nucleosome a	-	-	-	-	2	-	3	-
1155	Q9Y5Y2	Nucleotide-binding protein 2 (NBP 2)	-	-	-	-	1	-	1	X
1156	Q8WVJ2	NudC domain-containing protein 2 - Homo sapiens (Hu	-	-	-	-	1	1	-	-
1157	Q56VL3	OCIA domain-containing protein 2 - Homo sapiens (Hu	-	-	-	-	-	-	2	-
1158	Q6UX06	Olfactomedin-4 precursor - Homo sapiens (Human)	-	-	-	6	-	-	-	-
1159	Q9NNT2	Opioid growth factor receptor (OGFr) (Zeta-type opioi	-	-	-	-	-	-	1	-
1160	Q92882	Osteoclast-stimulating factor 1	-	-	2	4	4	5	5	X
1161	P78380	Oxidized low-density lipoprotein receptor 1 - Homo sag	-	-	-	1	-	-	-	-
1162	P50897	Palmitoyl-protein thioesterase 1 precursor (EC 3.1.2.2	-	-	-	-	-	-	1	-
1163	O95497	Pantetheinase precursor (EC 3.5.1.92) (Pantetheine h	-	-	-	1	-	-	-	-
1164	P20962	Parathymosin - Homo sapiens (Human)	-	-	-	-	-	-	1	-
1165	P49023	Paxillin	-	-	-	-	-	-	3	-
1166	O00151	PDZ and LIM domain protein 1 (Elfin) (LIM domain pro	-	-	21	-	2	-	6	X
1167	Q9UBV8	Peflin (PEF protein with a long N-terminal hydrophobic	-	-	-	2	-	-	-	-
1168	Q9UJ68	Peptide methionine sulfoxide reductase (EC 1.8.4.11)	-	-	-	2	-	-	-	-
1169	O75594	Peptidoglycan recognition protein precursor (PGRP-S)	-	-	-	4	-	2	-	-
1170	P62937	Peptidyl-prolyl cis-trans isomerase A (EC 5.2.1.8) (PPI	2	5	10	6	14	12	12	X

1171	P23284	Peptidyl-prolyl cis-trans isomerase B precursor (EC 5.2.1.8) (PPIB)	1	-	14	5	7	10	14	X
1172	Q9UNP9	Peptidyl-prolyl cis-trans isomerase E (EC 5.2.1.8) (PPIE)	-	-	-	-	-	-	1	X
1173	Q13526	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (PIN1)	-	-	-	-	1	-	-	X
1174	Q9Y237	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 4 (PIN4)	-	-	-	-	-	-	2	-
1175	P30405	Peptidyl-prolyl cis-trans isomerase, mitochondrial precursor (PPIB)	-	-	5	-	-	1	-	-
1176	Q9Y3C6	Peptidyl-prolyl cis-trans isomerase-like 1 (EC 5.2.1.8) (PPIB)	-	1	-	-	-	-	2	-
1177	Q9H2H8	Peptidyl-prolyl cis-trans isomerase-like 3 (EC 5.2.1.8) (PPIB)	-	-	-	1	2	2	1	-
1178	Q9Y3E5	Peptidyl-tRNA hydrolase 2, mitochondrial precursor (EPT2)	-	-	-	-	-	1	-	X
1179	P14222	Perforin-1 precursor (P1) (Lymphocyte pore forming protein)	-	-	-	-	1	-	6	-
1180	Q06830	Peroxiredoxin-1 (EC 1.11.1.15) (Thioredoxin peroxidase)	-	5	7	2	17	15	19	X
1181	P32119	Peroxiredoxin-2 (EC 1.11.1.15) (Thioredoxin peroxidase)	-	16	5	5	15	12	11	X
1182	Q13162	Peroxiredoxin-4 (EC 1.11.1.15) (Prx-IV) (Thioredoxin peroxidase)	-	-	6	-	3	2	3	X
1183	P30044	Peroxiredoxin-5, mitochondrial precursor (EC 1.11.1.15) (Prx-V)	-	-	7	10	10	11	9	X
1184	P30041	Peroxiredoxin-6 (EC 1.11.1.15) (Antioxidant protein 2) (Prx-VI)	-	5	20	11	14	8	14	X
1185	P51659	Peroxisomal multifunctional enzyme type 2 (MFE-2) (PEX2)	-	-	2	-	-	1	1	-
1186	Q8WW12	PEST proteolytic signal-containing nuclear protein (PEST)	-	-	-	-	-	-	2	-
1187	Q00325	Phosphate carrier protein, mitochondrial precursor (PTC)	-	-	-	-	1	2	6	-
1188	P30086	Phosphatidylethanolamine-binding protein (PEBP) (Protein)	-	6	5	5	13	10	14	X
1189	Q9NTJ5	Phosphatidylinositol phosphatase SAC1 - Homo sapiens	-	-	1	-	-	-	-	-
1190	Q8TCU6	Phosphatidylinositol 3,4,5-trisphosphate-dependent Rac guanine nucleotide exchange factor 1 (PHOEX)	-	-	-	-	-	1	1	-
1191	P27986	Phosphatidylinositol 3-kinase regulatory subunit alpha (PI3K)	-	-	-	-	-	-	1	-
1192	Q00169	Phosphatidylinositol transfer protein alpha isoform (PtdITP)	-	1	-	-	1	1	1	X
1193	P48739	Phosphatidylinositol transfer protein beta isoform (PtdITP)	-	-	-	-	1	-	1	X
1194	P48426	Phosphatidylinositol-4-phosphate 5-kinase type-2 alpha (PIP2K)	-	-	2	-	3	-	3	-
1195	P80108	Phosphatidylinositol-glycan-specific phospholipase D 2 (PLD2)	5	-	-	-	-	-	-	-
1196	Q16822	Phosphoenolpyruvate carboxykinase [GTP], mitochondrial	-	-	-	-	-	1	1	X
1197	P36871	Phosphoglucosyltransferase-1 (EC 5.4.2.2) (Glucose phosphotransferase)	-	-	5	6	5	-	4	X
1198	Q96G03	Phosphoglucosyltransferase-2 (EC 5.4.2.2) (Glucose phosphotransferase)	-	-	-	1	6	1	7	-
1199	P00558	Phosphoglycerate kinase 1 (EC 2.7.2.3) (Primer recognition protein)	-	8	16	20	21	15	23	X
1200	P18669	Phosphoglycerate mutase 1 (EC 5.4.2.1) (EC 5.4.2.4)	-	-	7	9	15	12	15	X
1201	P36969	Phospholipid hydroperoxide glutathione peroxidase, mitochondrial	-	-	2	-	4	2	3	-
1202	P55058	Phospholipid transfer protein precursor (Lipid transfer protein)	1	-	-	-	-	-	-	-
1203	Q9H008	Phospholysine phosphohistidine inorganic pyrophosphatase	-	-	-	1	2	-	3	-
1204	Q15126	Phosphomevalonate kinase (EC 2.7.4.2) (PMKase)	-	-	2	-	1	1	-	X
1205	O60256	Phosphoribosyl pyrophosphate synthetase-associated protein	-	-	-	-	1	-	-	-
1206	O15067	Phosphoribosylformylglycinamide synthase (EC 6.3.5.1) (PRF)	-	-	-	-	-	-	2	X
1207	Q96BW5	Phosphotriesterase-related protein (Parathion hydrolase)	-	-	-	-	2	-	-	X
1208	P36955	Pigment epithelium-derived factor precursor (PEDF) (Secreted)	4	-	-	-	-	-	-	-
1209	P35237	Placental thrombin inhibitor (Cytoplasmic antiprotease)	-	-	3	2	2	6	3	X
1210	P03952	Plasma kallikrein precursor (EC 3.4.21.34) (Plasma prokallikrein)	5	-	-	-	-	-	-	-
1211	P23634	Plasma membrane calcium-transporting ATPase 4 - Homo sapiens	-	-	-	-	-	4	-	-
1212	P05155	Plasma protease C1 inhibitor precursor (C1 Inh) (C1In)	15	-	-	-	-	-	2	X
1213	P02753	Plasma retinol-binding protein precursor (PRBP) (RBP)	7	-	-	-	1	-	1	X
1214	P05121	Plasminogen activator inhibitor 1 precursor (PAI-1) (EPAI1)	-	-	2	-	-	-	-	X
1215	Q8NC51	Plasminogen activator inhibitor 1 RNA-binding protein	-	-	-	-	1	-	1	-
1216	P05120	Plasminogen activator inhibitor 2 precursor (PAI-2) (PI2)	-	-	-	-	-	1	1	X
1217	P00747	Plasminogen precursor (EC 3.4.21.7) [Contains: Plasminogen]	10	-	2	-	-	-	3	-
1218	Q02325	Plasminogen-related protein B precursor - Homo sapiens	1	-	-	-	-	-	-	-
1219	P13796	Plastin-2 (L-plastin) (Lymphocyte cytosolic protein 1) (LPL)	-	-	-	31	47	39	45	X
1220	P02775	Platelet basic protein precursor (PBP) (Small inducible coagulation protein)	2	-	9	2	-	-	6	-
1221	P16284	Platelet endothelial cell adhesion molecule precursor (PECAM-1)	-	5	5	-	-	1	2	-
1222	P02776	Platelet factor 4 precursor (PF-4) (CXCL4) (Oncostatin M)	1	-	6	-	-	-	6	-
1223	P10720	Platelet factor 4 variant precursor (PF4var1) (PF4alt) (PF4)	-	-	3	-	-	-	-	-
1224	P16671	Platelet glycoprotein 4 (Platelet glycoprotein IV) (GPVI)	-	-	5	-	-	1	1	-
1225	P07359	Platelet glycoprotein Ib alpha chain precursor (Glycophorin B)	-	-	8	-	-	-	-	-
1226	P13224	Platelet glycoprotein Ib beta chain precursor (GP-Ib beta)	-	-	4	-	-	-	2	-

1227	P14770	Platelet glycoprotein IX precursor (GPIX) (CD42a antigen)	-	-	5	-	-	-	2	-
1228	P40197	Platelet glycoprotein V precursor (GPV) (CD42D antigen)	-	-	7	-	-	-	1	-
1229	Q9HCN6	Platelet glycoprotein VI precursor - Homo sapiens (Human)	-	-	1	-	-	-	-	-
1230	Q9H7M9	Platelet receptor Gi24 precursor - Homo sapiens (Human)	-	-	1	-	-	1	1	-
1231	P43034	Platelet-activating factor acetylhydrolase IB alpha subunit	-	1	1	-	4	2	2	-
1232	P68402	Platelet-activating factor acetylhydrolase IB beta subunit	-	-	4	-	2	2	2	X
1233	Q15102	Platelet-activating factor acetylhydrolase IB gamma subunit	-	-	-	-	3	1	2	X
1234	P08567	Pleckstrin (Platelet p47 protein)	-	-	16	3	2	-	11	-
1235	Q96S99	Pleckstrin homology domain-containing family F member	-	-	-	-	-	-	1	-
1236	O15031	Plexin-B2 precursor (MM1) - Homo sapiens (Human)	-	-	-	-	-	1	-	-
1237	Q9UKK3	Poly [ADP-ribose] polymerase 4 (EC 2.4.2.30) (PARP-1)	-	-	-	-	-	1	-	-
1238	Q9NX46	Poly(ADP-ribose) glycohydrolase ARH3 - Homo sapiens	-	1	-	-	1	-	1	-
1239	Q15365	Poly(rC)-binding protein 1 (Alpha-CP1) (hnRNP-E1) (Nucleosome)	-	-	5	3	9	5	7	X
1240	Q15366	Poly(rC)-binding protein 2 (Alpha-CP2) (hnRNP-E2) (Nucleosome)	-	-	1	-	5	6	6	X
1241	P11940	Polyadenylate-binding protein 1 (Poly(A)-binding protein 1)	-	-	1	-	3	1	2	-
1242	P26599	Polypyrimidine tract-binding protein 1 (PTB) (Heterogeneous nuclear protein)	-	-	1	-	3	5	7	-
1243	P08397	Porphobilinogen deaminase (EC 2.5.1.61) (Hydroxymethylglutaryl-CoA lyase)	-	-	-	-	2	-	-	-
1244	Q96CX2	Potassium channel tetramerisation domain-containing protein 1	-	-	-	2	-	12	6	X
1245	O75915	PRA1 family protein 3 (ARL-6-interacting protein 5) (ARL6IP5)	-	-	-	-	2	1	4	-
1246	Q9UHV9	Prefoldin subunit 2	-	-	1	-	4	2	1	X
1247	P61758	Prefoldin subunit 3 (Von Hippel-Lindau-binding protein 1)	-	-	1	-	1	-	1	X
1248	Q9NQP4	Prefoldin subunit 4 (Protein C-1) - Homo sapiens (Human)	-	-	-	-	1	-	-	-
1249	Q99471	Prefoldin subunit 5 (C-myc-binding protein Mm-1) (Myc-binding protein)	-	-	-	-	2	1	1	X
1250	P20742	Pregnancy zone protein precursor	10	-	-	-	-	3	14	-
1251	Q5JRX3	Presequence protease, mitochondrial precursor (EC 3.4.21.10)	-	1	-	-	1	-	-	-
1252	P07602	Proactivator polypeptide precursor [Contains: Saposin B]	-	-	-	4	-	6	2	X
1253	P38919	Probable ATP-dependent RNA helicase DDX48 (EC 3.6.4.12)	-	-	-	-	4	1	2	X
1254	Q9HA77	Probable cysteinyl-tRNA synthetase, mitochondrial precursor	-	-	-	1	-	-	-	-
1255	Q8TEA8	Probable D-tyrosyl-tRNA(Tyr) deacylase 1 (EC 3.1.1.15)	-	-	1	-	-	-	-	-
1256	Q86Y34	Probable G-protein coupled receptor 97 precursor (GPR97)	-	-	-	2	-	-	-	-
1257	O96008	Probable mitochondrial import receptor subunit TOM40	-	-	-	-	1	-	1	X
1258	Q8N0Y7	Probable phosphoglycerate mutase 4 (EC 5.4.2.1) (EC 5.4.2.1)	-	-	-	-	-	1	-	-
1259	P98196	Probable phospholipid-transporting ATPase 1H (EC 3.6.3.1)	-	-	-	-	-	1	-	-
1260	Q86YV0	Probable Ras GTPase-activating protein FLJ00412 - Homo sapiens	-	-	-	-	-	-	1	-
1261	P07737	Profilin-1 (Profilin I)	3	-	17	11	12	15	14	X
1262	Q8WUM4	Programmed cell death 6-interacting protein (PDCD6-interacting protein)	-	1	1	-	8	8	10	X
1263	Q9BUL8	Programmed cell death protein 10 (TF-1 cell apoptosis-inducing factor)	-	-	5	-	3	-	3	-
1264	Q53EL6	Programmed cell death protein 4 (Nuclear antigen H73)	-	-	-	-	2	-	1	-
1265	O75340	Programmed cell death protein 6 (Probable calcium-binding protein)	-	-	2	2	4	5	5	X
1266	P35232	Prohibitin	-	-	7	1	7	7	8	X
1267	Q99623	Prohibitin-2 (B-cell receptor-associated protein BAP37)	-	-	7	-	8	2	11	-
1268	Q9HCU5	Prolactin regulatory element-binding protein (Mammalian)	-	-	-	1	-	-	-	-
1269	P12273	Prolactin-inducible protein precursor (Secretory actin-binding protein)	2	-	-	-	-	-	-	X
1270	P12004	Proliferating cell nuclear antigen (PCNA) (Cyclin) - Homo sapiens	-	-	-	-	1	-	-	-
1271	Q9UQ80	Proliferation-associated protein 2G4 (Cell cycle protein 2G4)	-	-	1	-	2	-	2	X
1272	O94903	Proline synthetase co-transcribed bacterial homolog protein	-	-	1	1	5	1	4	-
1273	Q9H939	Proline-serine-threonine phosphatase-interacting protein	-	-	5	-	1	-	-	-
1274	P48147	Prolyl endopeptidase (EC 3.4.21.26) (Post-proline cleaving enzyme)	-	-	1	-	1	-	1	X
1275	P27918	Properdin precursor (Factor P) - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1276	Q8NBP7	Proprotein convertase subtilisin/kexin type 9 precursor	2	-	-	-	-	-	-	-
1277	Q15185	Prostaglandin H synthase 3 (EC 5.3.99.3) (Cytosolic phospholipase A2)	-	-	2	1	5	4	5	X
1278	P41222	Prostaglandin-H2 D-isomerase precursor (EC 5.3.99.2)	1	-	-	-	-	-	-	-
1279	Q6S8J3	Prostate, ovary, testis-expressed protein on chromosome 1	-	-	-	8	-	-	9	-
1280	Q06323	Proteasome activator complex subunit 1 (Proteasome activator complex)	-	-	7	6	16	11	16	X
1281	Q9UL46	Proteasome activator complex subunit 2 (Proteasome activator complex)	-	1	6	5	12	9	11	X
1282	P61289	Proteasome activator complex subunit 3 (Proteasome activator complex)	-	-	-	-	1	-	-	X

1283	Q92530	Proteasome inhibitor PI31 subunit (hPI31) - Homo sap	-	-	-	-	2	-	-	-
1284	P25786	Proteasome subunit alpha type 1 (EC 3.4.25.1) (Protea	-	-	2	1	7	3	9	X
1285	P25787	Proteasome subunit alpha type 2 (EC 3.4.25.1) (Protea	-	1	4	2	6	6	5	X
1286	P25788	Proteasome subunit alpha type 3 (EC 3.4.25.1) (Protea	-	1	3	-	8	4	8	X
1287	P25789	Proteasome subunit alpha type 4 (EC 3.4.25.1) (Protea	-	-	2	-	7	4	6	X
1288	P28066	Proteasome subunit alpha type 5 (EC 3.4.25.1) (Protea	-	-	2	-	3	3	7	-
1289	P60900	Proteasome subunit alpha type 6 (EC 3.4.25.1) (Protea	-	1	2	-	6	5	10	X
1290	O14818	Proteasome subunit alpha type 7 (EC 3.4.25.1) (Protea	-	-	3	1	10	6	8	X
1291	Q8TAA3	Proteasome subunit alpha type 7-like (EC 3.4.25.1)	-	-	-	-	-	-	4	-
1292	P20618	Proteasome subunit beta type 1 (EC 3.4.25.1) (Protea	-	-	5	1	9	8	10	-
1293	P40306	Proteasome subunit beta type 10 precursor (EC 3.4.25	-	-	-	-	4	1	3	X
1294	P49721	Proteasome subunit beta type 2 (EC 3.4.25.1) (Protea	-	-	3	-	6	5	8	X
1295	P49720	Proteasome subunit beta type 3 (EC 3.4.25.1) (Protea	-	-	4	1	6	5	8	X
1296	P28070	Proteasome subunit beta type 4 precursor (EC 3.4.25.	-	-	1	-	1	2	4	X
1297	P28074	Proteasome subunit beta type 5 precursor (EC 3.4.25.	-	3	-	-	1	-	-	-
1298	P28062	Proteasome subunit beta type 8 precursor (EC 3.4.25.	-	-	5	1	8	7	6	-
1299	P28065	Proteasome subunit beta type 9 precursor (EC 3.4.25.	-	-	1	-	7	5	6	X
1300	Q5VYK3	Proteasome-associated protein ECM29 homolog (Ecm	-	-	-	-	-	-	2	-
1301	P11171	Protein 4.1 (Band 4.1) (P4.1) (EPB4.1) (4.1R) - Homo	-	11	1	-	-	-	1	-
1302	Q99873	Protein arginine N-methyltransferase 1 (EC 2.1.1.-) (In	-	-	-	-	1	-	-	-
1303	Q562R1	Protein beta-actin-like - Homo sapiens (Human)	-	-	10	6	9	7	8	-
1304	Q9NQ88	Protein C12orf5	-	-	-	-	-	1	2	-
1305	Q9Y224	Protein C14orf166	-	-	-	-	5	-	1	X
1306	Q969H8	Protein C19orf10 precursor (Stromal cell-derived grow	-	-	-	-	3	4	3	X
1307	Q9NQG5	Protein C20orf77	-	-	-	-	-	-	3	X
1308	Q9P1F3	Protein C6orf115	-	-	-	2	1	1	2	X
1309	O75223	Protein C7orf24	-	-	-	1	1	1	2	X
1310	Q9NZB2	Protein C9orf10	-	-	-	-	1	-	-	-
1311	Q9UKY7	Protein CDV3 homolog - Homo sapiens (Human)	-	-	-	-	2	-	1	-
1312	Q8WUX9	Protein CHMP7 - Homo sapiens (Human)	-	-	-	-	2	1	-	-
1313	Q2KHT3	Protein CLEC16A - Homo sapiens (Human)	-	-	1	-	-	-	-	-
1314	O75629	Protein CREG1 precursor (Cellular repressor of E1A-s	-	-	-	1	1	2	-	-
1315	O60888	Protein CutA precursor (Brain acetylcholinesterase pu	-	-	-	-	1	1	1	-
1316	O60610	Protein diaphanous homolog 1 (Diaphanous-related fo	-	-	13	-	12	5	24	-
1317	Q9NSV4	Protein diaphanous homolog 3 (Diaphanous-related fo	-	-	1	-	-	-	-	-
1318	P30101	Protein disulfide-isomerase A3 precursor (EC 5.3.4.1)	-	-	12	5	16	17	20	X
1319	P13667	Protein disulfide-isomerase A4 precursor (EC 5.3.4.1)	-	-	-	-	2	3	8	X
1320	Q15084	Protein disulfide-isomerase A6 precursor (EC 5.3.4.1)	-	-	11	-	7	7	6	X
1321	P07237	Protein disulfide-isomerase precursor (EC 5.3.4.1) (PD	-	-	13	10	5	14	16	X
1322	Q99497	Protein DJ-1 (Oncogene DJ1)	-	3	7	6	7	7	12	X
1323	Q9H098	Protein FAM107B - Homo sapiens (Human)	-	-	-	-	3	-	-	-
1324	Q8IZP2	Protein FAM10A4	-	-	3	-	-	-	3	-
1325	Q9BUR5	Protein FAM121B precursor - Homo sapiens (Human)	-	-	-	-	-	1	2	-
1326	Q9H0Q0	Protein FAM49A	-	-	-	-	-	-	2	-
1327	Q9NUQ9	Protein FAM49B (L1)	-	-	-	10	4	8	12	-
1328	Q9BSJ8	Protein FAM62A (Membrane-bound C2 domain-contai	-	1	2	-	10	6	18	-
1329	P49354	Protein farnesyltransferase/geranylgeranyltransferase	-	-	-	1	-	-	-	X
1330	Q13045	Protein flightless-1 homolog	-	-	-	-	-	-	6	-
1331	Q6NYC8	Protein KIAA1949 - Homo sapiens (Human)	-	-	-	-	1	-	2	-
1332	Q8N163	Protein KIAA1967 (Deleted in breast cancer gene 1 pr	-	-	-	-	-	-	6	-
1333	P17252	Protein kinase C alpha type (EC 2.7.11.13) (PKC-alpha	-	-	1	-	1	2	-	-
1334	P05771	Protein kinase C beta type (EC 2.7.11.13) (PKC-beta)	-	-	-	-	-	-	3	-
1335	Q05655	Protein kinase C delta type (EC 2.7.11.13) (nPKC-delt	-	-	-	1	-	1	1	-
1336	Q86UE4	Protein LYRIC (Lysine-rich CEACAM1 co-isolated prot	-	-	-	-	1	-	-	-
1337	P61326	Protein mago nashi homolog	-	-	-	-	-	2	3	-
1338	Q96A72	Protein mago nashi homolog 2	-	-	-	-	-	-	4	X

1339	Q9BPW8	Protein NipSnap1 - Homo sapiens (Human)	-	-	-	-	-	-	5	-
1340	O75323	Protein NipSnap2 (Glioblastoma amplified sequence)	-	-	-	-	-	1	2	-
1341	Q9UFN0	Protein NipSnap3A (NipSnap4) (Target for Salmonella)	-	-	3	2	2	3	6	-
1342	Q96FA3	Protein pellino homolog 1 - Homo sapiens (Human)	-	-	1	-	-	-	1	-
1343	O14974	Protein phosphatase 1 regulatory subunit 12A (Myosin)	-	-	-	-	-	-	1	-
1344	Q15435	Protein phosphatase 1 regulatory subunit 7 (Protein ph	-	-	-	-	1	-	2	X
1345	P35813	Protein phosphatase 2C isoform alpha (EC 3.1.3.16) (P	-	-	1	-	1	-	-	-
1346	O75688	Protein phosphatase 2C isoform beta (EC 3.1.3.16) (P	-	-	-	1	-	-	-	X
1347	Q96M27	Protein PPRC1 - Homo sapiens (Human)	-	-	-	-	1	-	-	-
1348	Q9P258	Protein RCC2 (Telophase disk protein of 60 kDa) (RC	-	-	-	-	1	-	1	-
1349	P80511	Protein S100-A12 (S100 calcium-binding protein A12)	-	-	-	3	-	3	-	X
1350	P25815	Protein S100-P (S100 calcium-binding protein P) - Hor	-	-	-	4	-	1	-	-
1351	Q01105	Protein SET (Phosphatase 2A inhibitor I2PP2A) (I-2PP	-	-	-	-	3	2	1	X
1352	Q15436	Protein transport protein Sec23A (SEC23-related prote	-	-	-	-	1	-	2	X
1353	O95486	Protein transport protein Sec24A (SEC24-related prote	-	-	-	-	-	1	-	-
1354	P53992	Protein transport protein Sec24C (SEC24-related prote	-	-	-	-	-	-	2	-
1355	O94979	Protein transport protein Sec31A - Homo sapiens (Hur	-	-	1	-	2	2	2	-
1356	P61619	Protein transport protein Sec61 subunit alpha isoform	-	-	-	-	1	1	-	-
1357	Q14761	Protein tyrosine phosphatase receptor type C-associat	-	-	-	-	1	-	3	-
1358	Q12974	Protein tyrosine phosphatase type IVA protein 2 (EC 3	-	-	1	-	1	-	2	-
1359	Q9BRP8	Protein wibg homolog - Homo sapiens (Human)	-	-	-	-	-	-	1	-
1360	Q9UK55	Protein Z-dependent protease inhibitor precursor (PZ-d	2	-	-	-	-	-	-	-
1361	Q9ULC6	Protein-arginine deiminase type-1 (EC 3.5.3.15) (Prote	-	-	1	-	1	1	1	-
1362	Q9Y2J8	Protein-arginine deiminase type-2 (EC 3.5.3.15) (Prote	-	-	-	1	-	1	-	-
1363	P21980	Protein-glutamine gamma-glutamyltransferase 2 (EC 2	-	5	-	-	-	-	-	X
1364	P22061	Protein-L-isoaspartate(D-aspartate) O-methyltransfera	-	1	3	2	6	3	9	X
1365	Q9Y2Y8	Proteoglycan 3 precursor (Eosinophil major basic prote	-	-	-	4	-	-	-	-
1366	Q92954	Proteoglycan-4 precursor (Lubricin) (Megakaryocyte-s	3	-	-	-	-	-	-	-
1367	Q04941	Proteolipid protein 2 (Intestinal membrane A4 protein)	-	-	2	1	1	2	1	-
1368	P00734	Prothrombin precursor (EC 3.4.21.5) (Coagulation fact	22	-	-	-	-	-	1	-
1369	P06454	Prothymosin alpha [Contains: Thymosin alpha-1]	-	-	-	-	-	1	-	-
1370	P01100	Proto-oncogene protein c-fos - Homo sapiens (Human)	-	-	-	-	-	1	-	-
1371	P09769	Proto-oncogene tyrosine-protein kinase FGR (EC 2.7.1	-	-	-	3	-	-	-	-
1372	P06241	Proto-oncogene tyrosine-protein kinase Fyn (EC 2.7.1	-	-	2	-	-	-	3	-
1373	P06239	Proto-oncogene tyrosine-protein kinase LCK (EC 2.7.1	-	-	-	-	1	-	2	-
1374	P12931	Proto-oncogene tyrosine-protein kinase Src (EC 2.7.10	-	-	7	-	-	-	5	-
1375	P15498	Proto-oncogene vav	-	-	-	-	-	-	1	-
1376	P16109	P-selectin precursor (Granule membrane protein 140)	-	-	6	-	-	1	1	-
1377	P61457	Pterin-4-alpha-carbinolamine dehydratase (EC 4.2.1.9	-	-	-	1	-	-	-	-
1378	P00491	Purine nucleoside phosphorylase (EC 2.4.2.1) (Inosine	-	4	17	14	16	11	16	X
1379	P55786	Puromycin-sensitive aminopeptidase (EC 3.4.11.-) (PS	-	1	-	-	1	3	5	-
1380	Q9NTK5	Putative GTP-binding protein PTD004	-	-	-	-	-	-	1	-
1381	Q14568	Putative heat shock protein HSP 90-alpha A2 - Homo	-	-	-	-	-	3	-	-
1382	Q6ZN80	Putative maltase-glucoamylase-like protein FLJ16351	-	-	-	3	-	-	-	-
1383	A6NI72	Putative neutrophil cytosol factor 1B OS=Homo sapier	-	-	-	2	-	-	-	-
1384	A8MVU1	Putative neutrophil cytosol factor 1C OS=Homo sapier	-	-	-	3	-	-	-	-
1385	O43143	Putative pre-mRNA-splicing factor ATP-dependent RN	-	-	-	-	-	-	3	-
1386	Q53FA7	Putative quinone oxidoreductase (EC 1.-.-.-) (Tumor p	-	-	-	2	-	-	-	-
1387	P98179	Putative RNA-binding protein 3 (RNA-binding motif pro	-	-	-	-	1	-	2	-
1388	Q9Y383	Putative RNA-binding protein Luc7-like 2 - Homo sapie	-	-	-	-	2	1	-	-
1389	Q8NFU3	Putative thiosulfate sulfurtransferase KAT (EC 2.8.1.1)	-	-	-	-	-	-	1	-
1390	Q9Y448	Putative TRAF4-associated factor 1 - Homo sapiens (H	-	-	-	-	-	-	1	-
1391	Q5T440	Putative transferase C1orf69, mitochondrial precursor	-	-	-	-	-	-	1	-
1392	Q9NTT1	Putative ubiquitin-conjugating enzyme E2 D3-like prote	-	-	2	-	-	2	2	-
1393	O00764	Pyridoxal kinase (EC 2.7.1.35) (Pyridoxine kinase)	-	-	-	3	3	2	3	X
1394	P08559	Pyruvate dehydrogenase E1 component alpha subunit	-	-	-	-	-	-	3	X

1395	P11177	Pyruvate dehydrogenase E1 component beta subunit	-	-	2	-	5	-	9	X
1396	Q8NCN5	Pyruvate dehydrogenase phosphatase regulatory subunit	-	-	-	-	1	-	-	-
1397	P14618	Pyruvate kinase isozymes M1/M2 (EC 2.7.1.40) (Pyruv	-	6	29	30	32	38	35	X
1398	Q08257	Quinone oxidoreductase (EC 1.6.5.5) (NADPH:quinon	-	1	-	-	2	-	2	-
1399	P31150	Rab GDP dissociation inhibitor alpha (Rab GDI alpha)	-	-	7	5	5	5	9	X
1400	P50395	Rab GDP dissociation inhibitor beta (Rab GDI beta) (G	-	4	10	11	13	13	21	X
1401	Q6WKZ4	Rab11 family-interacting protein 1 (Rab11-FIP1) (Rab-	-	-	-	1	-	-	-	-
1402	O60518	Ran-binding protein 6 (RanBP6)	-	-	-	-	-	-	1	-
1403	P43487	Ran-specific GTPase-activating protein (Ran-binding p	-	-	2	1	2	1	3	X
1404	P52306	Rap1 GTPase-GDP dissociation stimulator 1 (SMG P2	-	-	2	-	-	-	-	X
1405	Q8TB24	Ras and Rab interactor 3 (Ras interaction/interference	-	-	-	-	1	-	-	-
1406	Q14644	Ras GTPase-activating protein 3 (GAP1(IP4BP)) (Ins	-	-	2	-	-	-	1	-
1407	P46940	Ras GTPase-activating-like protein IQGAP1 (p195)	-	1	-	4	23	30	39	-
1408	Q13576	Ras GTPase-activating-like protein IQGAP2	-	-	3	-	7	2	19	-
1409	Q7LDG7	RAS guanyl-releasing protein 2 - Homo sapiens (Hum	-	-	-	-	-	-	1	-
1410	Q15404	Ras suppressor protein 1 (Rsu-1) (RSP-1)	-	-	13	2	3	-	10	-
1411	P63000	Ras-related C3 botulinum toxin substrate 1 precursor (	-	-	6	-	5	7	6	-
1412	P15153	Ras-related C3 botulinum toxin substrate 2 precursor (	-	-	7	4	10	7	10	X
1413	P61026	Ras-related protein Rab-10	-	-	4	2	5	5	4	-
1414	P62491	Ras-related protein Rab-11A (Rab-11) (YL8)	-	-	7	7	7	5	7	-
1415	Q15907	Ras-related protein Rab-11B (GTP-binding protein YP	-	-	-	-	8	5	8	-
1416	P61106	Ras-related protein Rab-14	-	-	10	3	4	8	9	-
1417	P59190	Ras-related protein Rab-15	-	-	2	-	2	2	2	-
1418	Q9NP72	Ras-related protein Rab-18 - Homo sapiens (Human)	-	-	-	3	-	5	3	-
1419	P62820	Ras-related protein Rab-1A (YPT1-related protein)	-	-	8	-	-	9	7	X
1420	Q9H0U4	Ras-related protein Rab-1B	-	-	10	5	7	10	9	-
1421	Q9UL25	Ras-related protein Rab-21 - Homo sapiens (Human)	-	-	-	3	1	2	3	-
1422	Q969Q5	Ras-related protein Rab-24 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1423	P51159	Ras-related protein Rab-27A (Rab-27) (GTP-binding p	-	-	-	6	2	5	3	-
1424	O00194	Ras-related protein Rab-27B (C25KG)	-	-	9	2	-	-	5	-
1425	P61019	Ras-related protein Rab-2A	-	-	2	5	5	9	6	-
1426	Q13636	Ras-related protein Rab-31 (Rab-22B)	-	-	-	5	-	4	-	-
1427	Q13637	Ras-related protein Rab-32 - Homo sapiens (Human)	-	-	1	2	-	3	-	-
1428	Q9H082	Ras-related protein Rab-33B	-	-	1	-	2	2	2	-
1429	Q15286	Ras-related protein Rab-35 (Rab-1C) (GTP-binding pr	-	-	2	1	2	2	2	-
1430	Q96AX2	Ras-related protein Rab-37	-	-	2	-	-	1	-	-
1431	Q14964	Ras-related protein Rab-39A (Rab-39)	-	-	-	-	2	2	2	-
1432	P20336	Ras-related protein Rab-3A	-	-	-	2	-	3	5	-
1433	P20337	Ras-related protein Rab-3B	-	-	-	1	-	-	-	-
1434	O95716	Ras-related protein Rab-3D	-	-	-	4	-	5	6	-
1435	P61018	Ras-related protein Rab-4B	-	-	-	-	-	-	2	-
1436	P20339	Ras-related protein Rab-5A	-	-	3	4	-	4	4	-
1437	P61020	Ras-related protein Rab-5B	-	-	3	4	2	-	-	-
1438	P51148	Ras-related protein Rab-5C (RAB5L) (L1880)	-	-	-	7	6	5	6	-
1439	P20340	Ras-related protein Rab-6A (Rab-6)	-	-	-	2	5	2	4	-
1440	Q9NRW1	Ras-related protein Rab-6B	-	-	9	-	-	-	-	-
1441	P51149	Ras-related protein Rab-7	-	-	11	10	10	10	10	X
1442	P61006	Ras-related protein Rab-8A (Oncogene c-mel)	-	-	5	3	6	6	6	-
1443	Q92930	Ras-related protein Rab-8B	-	-	-	3	4	4	7	-
1444	Q9NP90	Ras-related protein Rab-9B (Rab-9L) (RAB9-like prote	-	-	-	1	-	-	-	-
1445	P11233	Ras-related protein Ral-A - Homo sapiens (Human)	-	-	-	-	-	-	2	-
1446	P11234	Ras-related protein Ral-B - Homo sapiens (Human)	-	-	3	3	-	-	3	-
1447	P62834	Ras-related protein Rap-1A precursor (GTP-binding pr	-	-	-	-	8	8	11	-
1448	P61224	Ras-related protein Rap-1b precursor (GTP-binding pr	-	-	16	8	12	9	14	X
1449	A6NIZ1	Ras-related protein Rap-1b-like protein OS=Homo sap	-	-	-	9	-	-	-	-
1450	P61225	Ras-related protein Rap-2b precursor	-	-	2	-	2	2	-	-

1451	Q9Y3L5	Ras-related protein Rap-2c precursor	-	-	-	1	-	-	-	-
1452	Q00765	Receptor expression-enhancing protein 5 (Polyposis lo	-	-	-	1	-	-	1	-
1453	Q12913	Receptor-type tyrosine-protein phosphatase eta precu	-	-	-	1	-	2	-	-
1454	O43665	Regulator of G-protein signaling 10 (RGS10)	-	-	5	-	6	-	2	X
1455	Q9NS28	Regulator of G-protein signaling 18 (RGS18) - Homo s	-	-	4	-	-	-	-	-
1456	P49795	Regulator of G-protein signaling 19 OS=Homo sapiens	-	-	-	1	-	-	-	-
1457	P35244	Replication protein A 14 kDa subunit (RP-A) (RF-A) (R	-	-	-	-	2	-	4	-
1458	P15927	Replication protein A 32 kDa subunit (RP-A) (RF-A) (R	-	-	-	-	2	1	3	X
1459	P27694	Replication protein A 70 kDa DNA-binding subunit (RP	-	-	-	-	-	-	3	-
1460	Q9HD89	Resistin precursor (Cysteine-rich secreted protein FIZ2	-	-	-	3	-	2	-	X
1461	P30622	Restin (Cytoplasmic linker protein 170 alpha-2) (CLIP-	-	-	1	-	-	-	1	-
1462	O95197	Reticulon-3 (Neuroendocrine-specific protein-like 2) (N	-	-	-	2	-	2	-	-
1463	Q9NQC3	Reticulon-4 (Neurite outgrowth inhibitor) (Nogo protein	-	-	3	2	1	4	2	-
1464	P00352	Retinal dehydrogenase 1 (EC 1.2.1.36) (RdDH1) (RAL	-	6	-	-	-	-	-	X
1465	Q99969	Retinoic acid receptor responder protein 2 precursor (C	3	-	-	-	-	-	-	-
1466	Q9HB40	Retinoid-inducible serine carboxypeptidase precursor (	-	-	-	1	-	3	2	-
1467	Q8TC12	Retinol dehydrogenase 11 (EC 1.1.1.-) (Retinal reduct	-	-	4	-	-	-	1	-
1468	P52565	Rho GDP-dissociation inhibitor 1 (Rho GDI 1) (Rho-GI	-	-	4	5	6	5	7	X
1469	P52566	Rho GDP-dissociation inhibitor 2 (Rho GDI 2) (Rho-GI	-	-	10	13	17	13	18	X
1470	Q68EM7	Rho GTPase-activating protein 17 - Homo sapiens (Hu	-	-	-	-	-	-	1	-
1471	Q7Z616	Rho GTPase-activating protein 30 - Homo sapiens (Hu	-	-	-	-	1	-	2	-
1472	Q92888	Rho guanine nucleotide exchange factor 1 (p115-RhoG	-	-	-	-	7	-	5	-
1473	Q96PE2	Rho guanine nucleotide exchange factor 17 - Homo sa	-	-	-	-	2	-	-	-
1474	Q13464	Rho-associated protein kinase 1 (EC 2.7.11.1) (Rho-a	-	-	-	-	-	-	5	-
1475	Q07960	Rho-GTPase-activating protein 1 (GTPase-activating p	-	-	1	5	1	1	6	X
1476	Q8N392	Rho-GTPase-activating protein 18 (MacGAP) - Homo	-	-	1	-	-	-	-	-
1477	P42331	Rho-GTPase-activating protein 25 - Homo sapiens (Hu	-	-	-	-	1	-	1	-
1478	P98171	Rho-GTPase-activating protein 4 (Rho-GAP hematopo	-	-	-	-	5	4	4	-
1479	O43182	Rho-GTPase-activating protein 6 (Rho-type GTPase-a	-	-	1	-	-	-	-	-
1480	P62745	Rho-related GTP-binding protein RhoB precursor (H6)	-	-	-	3	-	-	-	X
1481	P08134	Rho-related GTP-binding protein RhoC precursor (H9)	-	-	7	-	-	-	9	-
1482	P84095	Rho-related GTP-binding protein RhoG precursor	-	-	2	7	6	8	8	-
1483	P34096	Ribonuclease 4 precursor (EC 3.1.27.-) (RNase 4) - H	1	-	-	-	-	-	-	-
1484	P13489	Ribonuclease inhibitor (Ribonuclease/angiogenesis inh	-	4	2	4	3	11	12	-
1485	O00584	Ribonuclease T2 precursor (EC 3.1.27.-) (Ribonucleas	-	-	-	1	1	-	1	-
1486	P49247	Ribose-5-phosphate isomerase (EC 5.3.1.6) (Phospho	-	-	1	2	3	-	1	X
1487	P60891	Ribose-phosphate pyrophosphokinase I (EC 2.7.6.1) (	-	5	-	-	5	-	1	X
1488	P11908	Ribose-phosphate pyrophosphokinase II (EC 2.7.6.1) (	-	-	-	-	-	-	2	X
1489	P51812	Ribosomal protein S6 kinase alpha-3 (EC 2.7.11.1) (S	-	-	-	-	1	2	5	-
1490	Q9P2E9	Ribosome-binding protein 1 (Ribosome receptor protei	-	-	-	-	-	-	1	-
1491	P16083	Ribosyl-dihydroxynicotinamide dehydrogenase [quinone]	-	-	-	2	-	-	-	X
1492	Q63HN8	RING finger protein 213 - Homo sapiens (Human)	-	-	-	-	-	2	-	-
1493	Q9Y5S9	RNA-binding protein 8A (RNA-binding motif protein 8A	-	-	1	-	2	-	1	X
1494	Q01844	RNA-binding protein EWS (EWS oncogene) (Ewing sar	-	-	-	-	-	-	1	-
1495	P35637	RNA-binding protein FUS (Oncogene FUS) (Oncogene	-	-	-	-	-	-	1	-
1496	Q96T51	RUN and FYVE domain-containing protein 1 (FYVE-fir	-	-	1	-	2	-	-	-
1497	Q9Y230	RuvB-like 2 (EC 3.6.1.-) (48-kDa TATA box-binding pr	-	1	-	-	1	-	1	X
1498	P26447	S100 calcium-binding protein A4 (Metastasin) (Mts1 pr	-	-	-	3	3	6	4	X
1499	Q9UH99	Sad1/unc-84-like protein 2 (Rab5-interacting protein) (	-	-	-	-	1	-	2	-
1500	P31153	S-adenosylmethionine synthetase isoform type-2 (EC	-	-	-	-	2	-	-	X
1501	Q9Y3Z3	SAM domain and HD domain-containing protein 1 (De	-	-	-	-	14	15	31	X
1502	Q9UPN7	SAPS domain family member 1	-	-	-	-	-	-	1	-
1503	P16615	Sarcoplasmic/endoplasmic reticulum calcium ATPase	-	-	-	-	-	1	6	-
1504	Q93084	Sarcoplasmic/endoplasmic reticulum calcium ATPase	-	-	7	3	3	1	8	-
1505	Q96C86	Scavenger mRNA decapping enzyme DcpS (EC 3.-.-.	-	-	-	-	4	1	-	X
1506	P55735	SEC13-related protein (SEC13-like protein 1)	-	-	1	-	-	-	1	X

1507	Q13103	Secreted phosphoprotein 24 precursor (Spp-24) (Secr	3	-	-	-	-	-	-	-	-
1508	Q96PL1	Secretoglobulin family 3A member 2 precursor - Homo s	1	-	-	-	-	-	-	-	-
1509	O15126	Secretory carrier-associated membrane protein 1 (Sec	-	-	-	-	-	1	-	-	-
1510	O15127	Secretory carrier-associated membrane protein 2 (Sec	-	-	-	-	-	2	-	-	-
1511	P49903	Selenide, water dikinase 1 (EC 2.7.9.3) (Selenophospi	-	-	-	-	1	-	-	-	X
1512	Q13228	Selenium-binding protein 1	-	6	-	-	6	-	-	-	X
1513	Q8IZQ5	Selenoprotein H - Homo sapiens (Human)	-	-	-	-	-	-	1	-	-
1514	P49908	Selenoprotein P precursor (SeP) - Homo sapiens (Hur	1	-	-	-	-	-	-	-	-
1515	Q8WYJ6	Septin-1 (LARP) (Serologically defined breast cancer a	-	-	-	-	-	-	3	X	-
1516	Q9NVA2	Septin-11	-	-	-	-	-	-	3	X	-
1517	Q15019	Septin-2 (Protein NEDD5)	-	-	4	-	2	1	3	X	-
1518	Q14141	Septin-6	-	-	1	-	4	-	6	X	-
1519	Q16181	Septin-7 (CDC10 protein homolog)	-	-	2	-	5	-	8	-	-
1520	Q9UHD8	Septin-9 (MLL septin-like fusion protein) (MLL septin-li	-	1	1	-	8	-	5	-	-
1521	P34897	Serine hydroxymethyltransferase, mitochondrial precu	-	-	-	-	1	3	-	-	-
1522	O15269	Serine palmitoyltransferase 1 (EC 2.3.1.50) (Long cha	-	-	-	-	-	2	-	-	-
1523	P62140	Serine/threonine protein phosphatase PP1-beta cataly	-	-	5	-	6	-	7	X	-
1524	O94804	Serine/threonine-protein kinase 10 (EC 2.7.1.37) (Lym	-	-	-	-	3	1	12	-	-
1525	Q9Y6E0	Serine/threonine-protein kinase 24 (EC 2.7.11.1) (STE	-	-	4	-	-	-	-	-	-
1526	O00506	Serine/threonine-protein kinase 25 (EC 2.7.11.1) (Ster	-	-	-	-	2	-	-	-	-
1527	Q13043	Serine/threonine-protein kinase 4 (EC 2.7.11.1) (STE2	-	-	-	1	-	-	2	X	-
1528	Q8TD19	Serine/threonine-protein kinase Nek9 (EC 2.7.11.1) (N	-	-	-	-	-	-	1	-	-
1529	O95747	Serine/threonine-protein kinase OSR1 (EC 2.7.1.37) (O	-	1	-	-	-	-	1	-	-
1530	Q13177	Serine/threonine-protein kinase PAK 2 (EC 2.7.1.37) (P	-	-	1	-	-	1	1	X	-
1531	Q96C45	Serine/threonine-protein kinase ULK4 (EC 2.7.11.1) (U	-	-	-	-	-	-	1	-	-
1532	P63151	Serine/threonine-protein phosphatase 2A 55 kDa regu	-	-	-	1	-	-	1	X	-
1533	P30153	Serine/threonine-protein phosphatase 2A 65 kDa regu	-	-	2	1	7	5	9	X	-
1534	P67775	Serine/threonine-protein phosphatase 2A catalytic sub	-	-	1	-	1	-	-	X	-
1535	Q15257	Serine/threonine-protein phosphatase 2A regulatory su	-	-	-	-	-	-	1	-	-
1536	P62136	Serine/threonine-protein phosphatase PP1-alpha cata	-	-	5	-	6	-	8	X	-
1537	P02787	Serotransferrin precursor (Transferrin) (Siderophilin) (E	35	-	5	-	-	-	29	X	-
1538	P48595	Serpin B10 (Bomapin) (Protease inhibitor 10) - Homo s	-	-	-	4	-	1	-	-	-
1539	P50452	Serpin B8 (Cytoplasmic antiproteinase 2) (CAP2) (CAI	-	-	-	-	-	5	2	X	-
1540	P02768	Serum albumin precursor	56	17	-	-	-	-	60	X	-
1541	P02735	Serum amyloid A protein precursor (SAA) [Contains: A	2	-	-	-	-	-	-	-	-
1542	P35542	Serum amyloid A-4 protein precursor (Constitutively ex	8	-	1	-	-	-	-	-	-
1543	P02743	Serum amyloid P-component precursor (SAP) (9.5S al	9	-	-	-	-	-	-	-	-
1544	O95810	Serum deprivation-response protein (Phosphatidylserin	-	-	9	-	1	-	2	-	-
1545	P27169	Serum paraoxonase/arylesterase 1 (EC 3.1.1.2) (EC 3	7	-	-	-	-	-	-	X	-
1546	Q15166	Serum paraoxonase/lactonase 3 (EC 3.1.1.-) - Homo s	1	-	-	-	-	-	-	-	-
1547	P49591	Seryl-tRNA synthetase (EC 6.1.1.11) (Serine--tRNA lig	-	-	-	-	4	-	5	X	-
1548	P04278	Sex hormone-binding globulin precursor (SHBG) (Sex	3	-	-	-	-	-	-	-	-
1549	O60880	SH2 domain protein 1A (Signaling lymphocyte activati	-	-	-	-	2	-	3	-	-
1550	O75368	SH3 domain-binding glutamic acid-rich-like protein	-	-	4	3	3	4	5	X	-
1551	Q9UJC5	SH3 domain-binding glutamic acid-rich-like protein 2 (f	-	-	2	-	-	-	1	-	-
1552	Q9H299	SH3 domain-binding glutamic acid-rich-like protein 3 (S	-	-	4	2	2	4	4	-	-
1553	Q9Y3L3	SH3 domain-binding protein 1 (3BP-1) - Homo sapiens	-	-	-	-	4	-	-	-	-
1554	O75995	SH3 protein expressed in lymphocytes homolog	-	-	-	-	1	-	-	-	-
1555	Q16836	Short chain 3-hydroxyacyl-CoA dehydrogenase, mitoc	-	-	8	-	9	1	8	-	-
1556	Q9Y3A5	Shwachman-Bodian-Diamond syndrome protein - Hom	-	-	1	-	1	-	-	-	-
1557	Q9NR45	Sialic acid synthase (N-acetylneuraminate synthase) (	-	-	-	1	1	1	1	X	-
1558	O15389	Sialic acid-binding Ig-like lectin 5 OS=Homo sapiens G	-	-	-	1	-	-	-	-	-
1559	Q9Y286	Sialic acid-binding Ig-like lectin 7 precursor (Siglec-7) (	-	-	-	-	-	1	-	-	-
1560	Q9Y336	Sialic acid-binding Ig-like lectin 9 precursor (Siglec-9) (	-	-	-	-	-	2	1	-	-
1561	Q9H9B4	Sideroflexin-1 (Tricarboxylate carrier protein) (TCC)	-	-	-	-	5	-	4	-	-
1562	Q9BWM7	Sideroflexin-3 - Homo sapiens (Human)	-	-	-	-	1	-	2	-	-

1563	Q15005	Signal peptidase complex subunit 2 (EC 3.4.-.) (Micro	-	-	-	-	-	1	-	-
1564	P61009	Signal peptidase complex subunit 3 (EC 3.4.-.) (Micro	-	-	-	-	-	1	-	-
1565	P37108	Signal recognition particle 14 kDa protein (SRP14) (18	-	-	-	-	3	1	2	-
1566	O76094	Signal recognition particle 72 kDa protein (SRP72) - H	-	-	-	-	1	-	-	-
1567	P49458	Signal recognition particle 9 kDa protein (SRP9)	-	-	-	-	1	2	2	-
1568	P42224	Signal transducer and activator of transcription 1-alpha	-	-	-	-	4	-	10	-
1569	P40763	Signal transducer and activator of transcription 3 (Acu	-	-	-	-	-	-	3	-
1570	P51692	Signal transducer and activator of transcription 5B - H	-	-	-	-	1	1	3	-
1571	Q9Y3P8	Signaling threshold-regulating transmembrane adapte	-	-	-	-	1	-	-	-
1572	Q04837	Single-stranded DNA-binding protein, mitochondrial pr	-	-	1	-	2	1	7	-
1573	Q9UIB8	SLAM family member 5 precursor (Signaling lymphocy	-	-	1	-	-	-	-	-
1574	O43765	Small glutamine-rich tetratricopeptide repeat-contain	-	-	1	-	-	-	-	-
1575	P62304	Small nuclear ribonucleoprotein E (snRNP-E) (Sm pro	-	-	-	-	1	-	1	-
1576	P62314	Small nuclear ribonucleoprotein Sm D1 (snRNP core p	-	-	-	-	-	-	1	-
1577	P62316	Small nuclear ribonucleoprotein Sm D2 (snRNP core p	-	-	-	-	1	-	-	-
1578	P62318	Small nuclear ribonucleoprotein Sm D3 (snRNP core p	-	-	-	-	2	-	-	-
1579	P61956	Small ubiquitin-related modifier 2 precursor (SUMO-2)	-	-	-	1	1	1	1	X
1580	P13501	Small-inducible cytokine A5 precursor - Homo sapiens	-	-	2	-	-	-	-	-
1581	Q13126	S-methyl-5-thioadenosine phosphorylase (EC 2.4.2.28	-	-	1	1	-	-	4	X
1582	O95295	SNARE-associated protein Snapin (Synaptosomal-ass	-	-	-	-	1	2	1	-
1583	P05023	Sodium/potassium-transporting ATPase alpha-1 chain	-	-	-	-	1	4	6	-
1584	P54709	Sodium/potassium-transporting ATPase beta-3 chain (	-	-	-	-	-	1	-	-
1585	P11166	Solute carrier family 2, facilitated glucose transporter r	-	1	-	-	3	-	-	-
1586	Q8TDB8	Solute carrier family 2, facilitated glucose transporter r	-	-	-	2	-	-	-	-
1587	P11169	Solute carrier family 2, facilitated glucose transporter r	-	-	1	3	-	-	3	-
1588	P01241	Somatotropin precursor - Homo sapiens (Human)	1	-	-	-	-	-	-	-
1589	P30626	Sorcin (22 kDa protein) (CP-22) (V19)	-	-	4	-	4	4	2	X
1590	Q99523	Sortilin precursor (Neurotensin receptor 3) (NTR3) (NT	-	-	-	-	-	1	-	-
1591	O60493	Sorting nexin-3 (SDP3 protein)	-	-	1	2	-	3	-	-
1592	P09486	SPARC precursor (Secreted protein acidic and rich in	2	-	4	-	-	-	-	-
1593	Q13813	Spectrin alpha chain, brain (Spectrin, non-erythroid alp	-	3	-	-	-	1	2	-
1594	P02549	Spectrin alpha chain, erythrocyte (Erythroid alpha-spe	-	57	8	-	-	-	-	-
1595	Q01082	Spectrin beta chain, brain 1 (Spectrin, non-erythroid be	1	-	1	-	-	-	-	-
1596	P11277	Spectrin beta chain, erythrocyte (Beta-I spectrin) - Hor	-	49	14	-	-	-	1	-
1597	P63208	S-phase kinase-associated protein 1A (Cyclin A/CDK2	-	2	-	-	4	2	2	-
1598	Q13838	Spliceosome RNA helicase BAT1 (EC 3.6.1.-) (DEAD	-	-	-	-	2	-	3	X
1599	P26368	Splicing factor U2AF 65 kDa subunit (U2 auxiliary facto	-	-	-	-	-	-	1	-
1600	P23246	Splicing factor, proline- and glutamine-rich (Polypyrimi	-	-	-	-	-	-	1	-
1601	Q15020	Squamous cell carcinoma antigen recognized by T-cell	-	-	-	-	-	-	3	-
1602	O75563	Src kinase-associated phosphoprotein 2 - Homo sapie	-	-	1	3	-	4	-	-
1603	Q14247	Src substrate cortactin (Amplaxin) (Oncogene EMS1)	-	-	4	-	-	-	-	X
1604	Q7KZF4	Staphylococcal nuclease domain-containing protein 1	-	2	1	-	1	-	2	-
1605	P16949	Stathmin (Phosphoprotein p19) (pp19) (Oncoprotein 1	-	-	-	-	4	5	4	X
1606	Q9UJZ1	Stomatin-like protein 2 (SLP-2) (EPB72-like 2)	-	-	-	-	-	-	1	X
1607	P38646	Stress-70 protein, mitochondrial precursor (75 kDa glu	-	-	-	-	4	4	9	X
1608	P31948	Stress-induced-phosphoprotein 1 (STI1) (Hsc70/Hsp90	-	2	2	-	2	4	4	X
1609	Q9NRL3	Striatin-4 (Zinedin) - Homo sapiens (Human)	-	-	1	-	-	-	-	-
1610	Q9HCN8	Stromal cell-derived factor 2-like protein 1 precursor (S	-	-	-	-	-	1	1	-
1611	Q13586	Stromal interaction molecule 1 precursor - Homo sapie	-	-	1	-	-	-	-	-
1612	Q8WU79	Stromal membrane-associated protein 2 OS=Homo sa	-	-	-	2	-	-	-	-
1613	P31040	Succinate dehydrogenase [ubiquinone] flavoprotein su	-	-	-	-	2	1	4	X
1614	P21912	Succinate dehydrogenase [ubiquinone] iron-sulfur prot	-	-	-	-	5	3	3	-
1615	Q9P2R7	Succinyl-CoA ligase [ADP-forming] beta-chain, mitoch	-	-	-	-	1	-	-	X
1616	Q96199	Succinyl-CoA ligase [GDP-forming] beta-chain, mitoch	-	-	-	-	2	-	-	X
1617	P53597	Succinyl-CoA ligase [GDP-forming] subunit alpha, mit	-	-	-	-	3	-	2	-
1618	P55809	Succinyl-CoA:3-ketoacid-coenzyme A transferase 1, m	-	-	3	-	2	-	-	X

1619	P14410	Sucrase-isomaltase, intestinal OS=Homo sapiens GN	-	-	-	1	-	-	-	-
1620	Q9Y6N5	Sulfide:quinone oxidoreductase, mitochondrial precurs	-	-	-	-	4	5	4	-
1621	P50225	Sulfotransferase 1A1 (EC 2.8.2.1) (Aryl sulfotransferas	-	-	4	1	-	2	-	X
1622	P63279	SUMO-conjugating enzyme UBC9 (EC 6.3.2.-) (SUMO	-	-	-	-	2	2	5	-
1623	P00441	Superoxide dismutase [Cu-Zn] (EC 1.15.1.1)	2	5	5	4	8	6	8	X
1624	P04179	Superoxide dismutase [Mn], mitochondrial precursor (E	-	-	10	5	8	6	9	X
1625	Q9Y2Z0	Suppressor of G2 allele of SKP1 homolog (Sgt1) (Put	-	-	1	-	-	-	1	X
1626	Q8TF42	Suppressor of T-cell receptor signaling 1 (Sts-1) (Cbl-i	-	-	2	-	-	-	-	-
1627	O15260	Surfeit locus protein 4	-	-	-	1	1	1	2	-
1628	Q99536	Synaptic vesicle membrane protein VAT-1 homolog (E	-	-	-	11	3	2	2	X
1629	O15056	Synaptojanin-2 (EC 3.1.3.36) (Synaptic inositol-1,4,5-t	-	1	-	-	1	-	-	-
1630	O00161	Synaptosomal-associated protein 23 (SNAP-23) (Vesi	-	-	3	-	-	-	1	-
1631	O95721	Synaptosomal-associated protein 29 (SNAP-29) (Vesi	-	-	2	-	-	-	-	X
1632	Q96C24	Synaptotagmin-like protein 4 (Exophilin-2) (Granuphilin	-	-	2	-	-	-	-	-
1633	Q9NX95	Syntabulin - Homo sapiens (Human)	-	-	-	-	1	-	-	-
1634	O75558	Syntaxin-11 - Homo sapiens (Human)	-	-	4	-	-	-	1	-
1635	Q12846	Syntaxin-4 (NY-REN-31 antigen) - Homo sapiens (Hur	-	-	1	-	-	-	-	-
1636	O15400	Syntaxin-7 - Homo sapiens (Human)	-	-	2	-	-	1	1	-
1637	Q15833	Syntaxin-binding protein 2 (Unc-18 homolog 2) (Unc-1	-	-	7	1	-	-	-	X
1638	O00560	Syntenin-1 (Syndecan-binding protein 1) (Melanoma d	-	-	-	2	-	1	-	-
1639	Q9Y490	Talin-1	-	17	135	42	75	53	136	X
1640	Q9Y4G6	Talin-2 - Homo sapiens (Human)	-	-	-	-	-	-	8	-
1641	O15533	Tapasin precursor - Homo sapiens (Human)	-	-	1	-	1	1	1	-
1642	Q13148	TAR DNA-binding protein 43 (TDP-43)	-	-	-	-	-	-	2	X
1643	O60784	Target of Myb protein 1 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1644	Q6SJ96	TATA box-binding protein-like protein 2 - Homo sapien	-	-	-	1	-	-	-	-
1645	Q66K14	TBC1 domain family member 9B - Homo sapiens (Hur	-	-	-	-	-	1	-	-
1646	P56279	T-cell leukemia/lymphoma protein 1A (P14 TCL1 prote	-	-	-	-	-	-	2	-
1647	P04234	T-cell surface glycoprotein CD3 delta chain precursor	-	-	-	-	2	-	1	-
1648	P07766	T-cell surface glycoprotein CD3 epsilon chain precurs	-	-	-	-	1	-	-	-
1649	P20963	T-cell surface glycoprotein CD3 zeta chain precursor	-	-	-	-	1	-	-	-
1650	P06127	T-cell surface glycoprotein CD5 precursor (Lymphocyt	-	-	-	-	1	-	1	-
1651	P17987	T-complex protein 1 subunit alpha (TCP-1-alpha) (CC	-	2	2	-	6	2	8	X
1652	P78371	T-complex protein 1 subunit beta (TCP-1-beta) (CCT-l	-	-	6	-	12	1	6	X
1653	P50991	T-complex protein 1 subunit delta (TCP-1-delta) (CCT	-	2	2	1	6	4	5	X
1654	P48643	T-complex protein 1 subunit epsilon (TCP-1-epsilon) (C	-	1	2	-	5	1	5	X
1655	Q99832	T-complex protein 1 subunit eta (TCP-1-eta) (CCT-eta	-	3	2	1	5	1	8	X
1656	P49368	T-complex protein 1 subunit gamma (TCP-1-gamma) (C	-	1	4	-	8	-	8	X
1657	P50990	T-complex protein 1 subunit theta (TCP-1-theta) (CCT	-	2	6	-	8	4	10	X
1658	P40227	T-complex protein 1 subunit zeta (TCP-1-zeta) (CCT-z	-	1	4	1	10	6	11	X
1659	Q92526	T-complex protein 1 subunit zeta-2 (TCP-1-zeta-2) (C	-	-	2	-	-	-	-	-
1660	Q9UGI8	Testin (TESS)	-	-	-	-	-	-	3	-
1661	P05452	Tetranectin precursor (TN) (C-type lectin domain famil	5	-	-	-	-	-	-	-
1662	Q8NG11	Tetraspanin-14 (Tspan-14) (Transmembrane 4 superfa	-	-	-	-	-	1	-	-
1663	Q9Y3D6	Tetratricopeptide repeat protein 11 (TPR repeat protei	-	-	-	-	1	2	2	-
1664	Q9BU02	Thiamine-triphosphatase (EC 3.6.1.28) (ThTPase) - H	-	-	-	-	1	-	-	-
1665	Q9NPJ3	Thioesterase superfamily member 2 - Homo sapiens (	-	-	-	-	2	-	-	-
1666	P10599	Thioredoxin (ATL-derived factor) (ADF) (Surface-assor	-	-	2	5	1	4	3	X
1667	Q9H3N1	Thioredoxin domain-containing protein 1 precursor (Tr	-	-	-	1	-	2	3	-
1668	O95881	Thioredoxin domain-containing protein 12 precursor (E	-	-	-	2	-	-	-	-
1669	Q9BS26	Thioredoxin domain-containing protein 4 precursor (Er	-	-	-	-	-	1	-	X
1670	Q8NBS9	Thioredoxin domain-containing protein 5 precursor (Th	-	-	-	-	1	-	-	X
1671	Q16881	Thioredoxin reductase 1, cytoplasmic precursor (EC 1	-	-	-	1	-	-	-	X
1672	Q9NNW7	Thioredoxin reductase 2, mitochondrial precursor (EC	-	-	-	-	1	-	-	-
1673	P30048	Thioredoxin-dependent peroxide reductase, mitochond	-	-	6	2	4	8	8	X
1674	O43396	Thioredoxin-like protein 1 (32 kDa thioredoxin-related	-	1	6	-	-	-	-	X

1675	Q9BRA2	Thioredoxin-like protein 5 (14 kDa thioredoxin-related	-	-	-	2	1	3	-	-
1676	Q16762	Thiosulfate sulfurtransferase (EC 2.8.1.1) (Rhodanese	-	-	3	-	-	-	-	X
1677	P26639	Threonyl-tRNA synthetase, cytoplasmic (EC 6.1.1.3) (	-	-	-	-	-	1	3	-
1678	P07996	Thrombospondin-1 precursor	7	-	30	-	-	-	27	-
1679	P35443	Thrombospondin-4 precursor - Homo sapiens (Human	3	-	-	-	-	-	-	-
1680	P24557	Thromboxane-A synthase (EC 5.3.99.5) (TXA synthas	-	-	-	-	-	4	-	-
1681	P19971	Thymidine phosphorylase precursor (EC 2.4.2.4) (TdR	-	-	5	2	5	5	7	X
1682	P23919	Thymidylate kinase (EC 2.7.4.9) (dTMP kinase)	-	-	-	-	2	-	-	-
1683	P63313	Thymosin beta-10	-	-	-	-	-	1	1	-
1684	P62328	Thymosin beta-4 (T beta 4) (Fx) [Contains: Hematopo	-	-	-	1	-	3	2	-
1685	P05543	Thyroxine-binding globulin precursor (T4-binding globu	3	-	-	-	-	-	-	-
1686	Q9BVW5	TIMELESS-interacting protein - Homo sapiens (Huma	-	-	-	2	-	-	-	-
1687	Q8WZ42	Titin (EC 2.7.11.1) (Connectin) (Rhabdomyosarcoma a	2	-	-	-	-	-	-	-
1688	Q9H0E2	Toll-interacting protein	-	-	1	-	-	3	-	X
1689	O60603	Toll-like receptor 2 precursor (Toll/interleukin 1 recept	-	-	-	-	-	4	-	-
1690	Q6ZVM7	TOM1-like protein 2 - Homo sapiens (Human)	-	-	1	-	-	-	-	-
1691	O14656	Torsin A precursor (Torsin family 1 member A) (Dystor	-	-	-	1	-	-	1	-
1692	Q5JTV8	Torsin-1A-interacting protein 1	-	-	-	1	-	1	2	X
1693	Q9Y3C4	TP53RK-binding protein - Homo sapiens (Human)	-	-	-	-	1	-	1	-
1694	Q9Y228	TRAF3-interacting JNK-activating modulator (TRAF3-i	-	-	-	-	1	-	3	-
1695	O43617	Trafficking protein particle complex subunit 3 (BET3 ho	-	-	1	-	4	2	3	-
1696	P37837	Transaldolase (EC 2.2.1.2)	-	-	9	16	17	17	15	X
1697	P20061	Transcobalamin-1 precursor (Transcobalamin I) (TCI)	-	-	-	2	-	-	-	-
1698	P23193	Transcription elongation factor A protein 1 (Transcripti	-	-	-	-	-	-	2	-
1699	Q15369	Transcription elongation factor B polypeptide 1 (RNA p	-	-	2	-	-	-	1	-
1700	Q15370	Transcription elongation factor B polypeptide 2 (RNA p	-	-	-	2	-	-	1	-
1701	Q00059	Transcription factor A, mitochondrial precursor (mtTFA	-	-	-	-	-	-	2	-
1702	P20290	Transcription factor BTF3 (RNA polymerase B transcri	-	-	-	-	3	3	3	X
1703	Q96K17	Transcription factor BTF3 homolog 4 (Basic transcripti	-	-	-	-	1	-	1	X
1704	P17947	Transcription factor PU.1 (31 kDa transforming protein	-	-	-	-	-	1	-	-
1705	P13984	Transcription initiation factor IIF subunit beta - Homo s	-	-	-	-	1	-	-	-
1706	Q13263	Transcription intermediary factor 1-beta (TIF1-beta) (T	-	-	-	-	1	-	3	X
1707	P11308	Transcriptional regulator ERG (Transforming protein E	-	-	-	-	-	1	1	-
1708	P02786	Transferrin receptor protein 1 (TfR1) (TR) (TfR) (Trfr) (	-	-	-	-	1	-	-	-
1709	Q9Y6A5	Transforming acidic coiled-coil-containing protein 3 (Ei	-	-	-	-	-	-	1	-
1710	P01137	Transforming growth factor beta-1 precursor (TGF-beta	1	-	6	-	-	-	-	-
1711	O43294	Transforming growth factor beta-1-induced transcript 1	-	-	4	-	-	-	-	-
1712	P61586	Transforming protein RhoA precursor (H12)	-	1	7	7	10	6	12	X
1713	Q01995	Transgelin (Smooth muscle protein 22-alpha) (SM22-a	-	-	-	-	-	-	4	-
1714	P37802	Transgelin-2 (SM22-alpha homolog)	1	-	22	9	16	15	19	-
1715	P55072	Transitional endoplasmic reticulum ATPase (TER ATP	-	13	14	-	20	14	23	X
1716	P29401	Transketolase (EC 2.2.1.1) (TK)	-	2	2	23	16	21	23	X
1717	P13693	Translationally-controlled tumor protein (TCTP) (p23) (	-	-	3	1	4	2	4	X
1718	Q15631	Translin - Homo sapiens (Human)	-	-	-	-	4	6	2	-
1719	Q99598	Translin-associated protein X (Translin-associated fac	-	-	-	1	3	1	3	X
1720	P51571	Translocon-associated protein delta subunit precursor	-	-	-	-	3	2	2	X
1721	Q9UM00	Transmembrane and coiled-coil domain-containing pro	-	-	-	-	-	-	1	-
1722	Q15363	Transmembrane emp24 domain trafficking protein 2 pr	-	-	-	-	3	1	2	-
1723	P49755	Transmembrane emp24 domain-containing protein 10	-	-	-	-	4	5	5	-
1724	Q9Y3B3	Transmembrane emp24 domain-containing protein 7 p	-	-	1	-	-	-	-	-
1725	Q9BVK6	Transmembrane emp24 domain-containing protein 9 p	-	-	3	-	1	3	4	-
1726	Q9BVC6	Transmembrane protein 109 precursor (Mitsugumin-23	-	-	-	-	-	1	-	-
1727	Q4KMQ2	Transmembrane protein 16F - Homo sapiens (Human)	-	-	-	-	-	-	1	-
1728	Q86WV6	Transmembrane protein 173 - Homo sapiens (Human)	-	-	-	-	-	5	-	-
1729	Q6UW68	Transmembrane protein 205 - Homo sapiens (Human)	-	-	-	-	-	1	1	-
1730	P57088	Transmembrane protein 33 (DB83 protein) - Homo sap	-	-	-	-	-	1	1	-

1731	Q9BTV4	Transmembrane protein 43 - Homo sapiens (Human)	-	-	-	-	-	1	1	-
1732	Q92973	Transportin-1 (Importin beta-2) (Karyopherin beta-2) (H	-	-	-	-	1	-	2	-
1733	P02766	Transthyretin precursor (Prealbumin) (TBPA) (TTR) (A	15	1	2	-	-	6	6	-
1734	Q86YW5	Trem-like transcript 1 protein precursor (TLT-1) (Trigge	-	-	5	-	1	-	1	-
1735	P40939	Trifunctional enzyme alpha subunit, mitochondrial prec	6	-	-	-	2	1	17	-
1736	P55084	Trifunctional enzyme subunit beta, mitochondrial precu	-	-	1	-	2	3	5	-
1737	P60174	Triosephosphate isomerase (EC 5.3.1.1) (TIM) (Triose	-	4	16	11	20	16	21	X
1738	P29144	Tripeptidyl-peptidase 2 (EC 3.4.14.10) (Tripeptidyl-pep	-	-	2	-	-	-	2	-
1739	O14773	Tripeptidyl-peptidase I precursor (EC 3.4.14.9) (TPP-I)	-	-	1	2	1	4	3	X
1740	Q9UI30	TRM112-like protein - Homo sapiens (Human)	-	-	-	-	1	-	1	X
1741	Q9NZR1	Tropomodulin-2 (Neuronal tropomodulin) (N-Tmod) - H	-	-	-	1	-	-	-	-
1742	Q9NYL9	Tropomodulin-3 (Ubiquitous tropomodulin) (U-Tmod) -	-	-	6	3	-	-	-	X
1743	P09493	Tropomyosin 1 alpha chain (Alpha-tropomyosin)	-	-	11	-	7	6	9	X
1744	P06753	Tropomyosin alpha-3 chain (Tropomyosin-3) (Tropomy	-	-	14	-	16	12	16	X
1745	P67936	Tropomyosin alpha-4 chain (Tropomyosin-4) (TM30p1	-	-	25	-	14	9	19	X
1746	P07951	Tropomyosin beta chain (Tropomyosin 2) (Beta-tropon	-	-	11	-	7	7	8	X
1747	P23381	Tryptophanyl-tRNA synthetase (EC 6.1.1.2) (Tryptoph	-	-	-	2	1	5	5	X
1748	Q9Y3Q8	TSC22 domain family protein 4 - Homo sapiens (Huma	-	-	1	-	-	-	-	-
1749	Q8TAP9	TTD non-photosensitive 1 protein - Homo sapiens (Hu	-	-	-	-	-	-	1	-
1750	P68366	Tubulin alpha-1 chain (Alpha-tubulin 1) (Testis-specific	-	-	-	-	-	7	16	-
1751	Q13748	Tubulin alpha-2 chain (Alpha-tubulin 2)	-	-	-	-	-	5	-	-
1752	Q71U36	Tubulin alpha-3 chain (Alpha-tubulin 3) (Tubulin B-alph	-	-	-	10	-	9	17	X
1753	Q9BQE3	Tubulin alpha-6 chain (Alpha-tubulin 6)	-	-	17	-	-	-	-	X
1754	Q9NY65	Tubulin alpha-8 chain (Alpha-tubulin 8)	-	-	-	-	-	-	10	-
1755	P68363	Tubulin alpha-ubiquitous chain (Alpha-tubulin ubiquito	-	-	-	-	15	12	17	X
1756	Q9H4B7	Tubulin beta-1 chain - Homo sapiens (Human)	-	-	29	-	-	-	16	-
1757	P07437	Tubulin beta-2 chain	-	2	27	-	22	16	24	X
1758	Q13885	Tubulin beta-2A chain - Homo sapiens (Human)	-	-	-	-	-	-	16	-
1759	P68371	Tubulin beta-2C chain (Tubulin beta-2 chain)	-	-	-	14	-	7	21	-
1760	P04350	Tubulin beta-4 chain (Tubulin 5 beta)	-	-	-	-	-	-	15	-
1761	Q9BUF5	Tubulin beta-6 chain - Homo sapiens (Human)	-	-	7	-	-	-	6	-
1762	O75347	Tubulin-specific chaperone A (Tubulin-folding cofactor	-	-	1	1	2	3	2	X
1763	Q99426	Tubulin-specific chaperone B (Tubulin folding cofactor	-	-	2	-	3	-	2	X
1764	Q14166	Tubulin--tyrosine ligase-like protein 12	-	-	-	-	-	-	2	X
1765	Q6EMB2	Tubulin--tyrosine ligase-like protein 5 (SRC1 and TIF2	-	-	-	-	-	1	-	-
1766	O95379	Tumor necrosis factor, alpha-induced protein 8 - Homo	-	-	-	-	1	-	3	-
1767	Q6P589	Tumor necrosis factor, alpha-induced protein 8-like pro	-	-	-	1	2	1	3	-
1768	O43399	Tumor protein D54 (hD54) (Tumor protein D52-like 2)	-	-	2	-	2	4	3	X
1769	Q6IBS0	Twinfilin-2 (Twinfilin-1-like protein) (A6-related protei	-	-	6	4	3	2	5	X
1770	O43914	TYRO protein tyrosine kinase-binding protein precursor	-	-	-	-	-	2	1	-
1771	P41240	Tyrosine-protein kinase CSK (EC 2.7.1.112) (C-SRC k	-	-	2	-	4	3	6	X
1772	P08631	Tyrosine-protein kinase HCK (EC 2.7.10.2) (p59-HCK/	-	-	-	-	-	1	-	-
1773	P43405	Tyrosine-protein kinase SYK (EC 2.7.10.2) (Spleen tyr	-	-	-	-	-	4	-	-
1774	P43403	Tyrosine-protein kinase ZAP-70 (EC 2.7.1.112) (70 kD	-	-	-	-	1	-	4	-
1775	P18031	Tyrosine-protein phosphatase non-receptor type 1 (EC	-	-	1	-	1	-	-	-
1776	P29350	Tyrosine-protein phosphatase non-receptor type 6 (EC	-	-	2	5	6	11	20	-
1777	P35236	Tyrosine-protein phosphatase non-receptor type 7 - Ho	-	-	-	-	1	-	-	-
1778	P78324	Tyrosine-protein phosphatase non-receptor type subst	-	-	-	1	-	-	-	-
1779	P54577	Tyrosyl-tRNA synthetase, cytoplasmic (EC 6.1.1.1) (Ty	-	-	1	-	-	-	1	X
1780	Q8WWY3	U4/U6 small nuclear ribonucleoprotein Prp31 - Homo s	-	-	-	-	1	-	-	-
1781	Q9Y333	U6 snRNA-associated Sm-like protein LSm2 (SnRNP	-	-	-	-	3	3	2	-
1782	Q9Y4Z0	U6 snRNA-associated Sm-like protein LSm4 (Glycine-	-	-	-	-	-	-	1	-
1783	P62312	U6 snRNA-associated Sm-like protein LSm6 (Sm prote	-	-	-	-	1	-	-	-
1784	O95777	U6 snRNA-associated Sm-like protein LSm8	-	-	-	-	-	-	1	-
1785	P14927	Ubiquinol-cytochrome c reductase complex 14 kDa pro	-	-	-	-	1	1	-	-
1786	P47985	Ubiquinol-cytochrome c reductase iron-sulfur subunit,	-	-	1	-	2	-	3	X

1787	P22695	Ubiquinol-cytochrome-c reductase complex core prote	-	-	1	-	2	1	6	-
1788	P31930	Ubiquinol-cytochrome-c reductase complex core prote	-	-	1	-	4	4	8	X
1789	P62988	Ubiquitin	-	1	3	5	6	7	6	X
1790	P54578	Ubiquitin carboxyl-terminal hydrolase 14 (EC 3.1.2.15)	-	1	2	-	3	1	5	X
1791	Q9Y4E8	Ubiquitin carboxyl-terminal hydrolase 15 (EC 3.1.2.15)	-	-	-	-	-	-	1	-
1792	P45974	Ubiquitin carboxyl-terminal hydrolase 5 (EC 3.1.2.15)	-	4	-	-	6	2	9	X
1793	Q93009	Ubiquitin carboxyl-terminal hydrolase 7 (EC 3.1.2.15)	-	-	-	-	2	3	5	-
1794	P15374	Ubiquitin carboxyl-terminal hydrolase isozyme L3 (EC	-	-	-	-	1	-	2	X
1795	Q96FW1	Ubiquitin thiolesterase protein OTUB1 (EC 3.4.-.-) (Otu	-	-	2	2	5	1	7	-
1796	P22314	Ubiquitin-activating enzyme E1 (A1S9 protein)	-	6	5	6	18	14	25	X
1797	P41226	Ubiquitin-activating enzyme E1 homolog (D8) - Homo	-	-	3	-	1	1	-	-
1798	P62837	Ubiquitin-conjugating enzyme E2 D2 (EC 6.3.2.19) (Ubi	-	-	-	-	1	-	3	-
1799	P62256	Ubiquitin-conjugating enzyme E2 H (EC 6.3.2.19) (Ubi	-	-	-	-	-	-	1	-
1800	P68036	Ubiquitin-conjugating enzyme E2 L3 (EC 6.3.2.19) (Ubi	-	-	2	4	4	5	4	-
1801	O14933	Ubiquitin-conjugating enzyme E2 L6 (EC 6.3.2.19) (Ubi	-	-	-	-	-	3	1	-
1802	P61088	Ubiquitin-conjugating enzyme E2 N (EC 6.3.2.19) (Ubi	-	1	3	2	6	7	9	X
1803	Q9C0C9	Ubiquitin-conjugating enzyme E2 O - Homo sapiens (H	-	-	1	-	2	1	1	-
1804	Q13404	Ubiquitin-conjugating enzyme E2 variant 1 (UEV-1) (C	-	3	5	-	5	6	6	X
1805	Q15819	Ubiquitin-conjugating enzyme E2 variant 2 (MMS2) (E	-	2	3	3	5	-	4	X
1806	P61086	Ubiquitin-conjugating enzyme E2-25 kDa (EC 6.3.2.19	-	-	2	-	2	-	3	X
1807	Q9UBE0	Ubiquitin-like 1-activating enzyme E1A (SUMO-activat	-	-	-	-	2	-	1	X
1808	Q9UBT2	Ubiquitin-like 1-activating enzyme E1B (SUMO-1-activ	-	-	-	-	3	2	2	-
1809	Q9NYU2	UDP-glucose:glycoprotein glucosyltransferase 1 precu	-	-	1	-	-	10	14	X
1810	Q9Y3C8	Ufm1-conjugating enzyme 1 (Ubiquitin-fold modifier-co	-	-	2	-	2	-	-	-
1811	P30085	UMP-CMP kinase (EC 2.7.4.14) (Cytidylate kinase) (D	-	-	6	2	5	-	5	X
1812	Q86UX7	Unc-112-related protein 2 (Kindlin-3) (MIG2-like)	-	-	25	1	6	9	21	X
1813	Q70J99	Unc-13 homolog D (Munc13-4)	-	-	2	-	2	1	2	-
1814	Q9H1C4	UNC93 homolog B1 (UNC-93B protein) (hUNC93B1)	-	-	-	-	-	1	1	-
1815	Q9BRF8	Uncharacterized metallophosphoesterase CSTP1 - Hc	-	-	-	1	-	-	-	-
1816	Q8IXM2	Uncharacterized potential DNA-binding protein C17orf	-	-	-	-	3	2	3	-
1817	Q53FT3	Uncharacterized protein C11orf73 - Homo sapiens (Hu	-	-	1	-	1	-	1	-
1818	Q9BQ61	Uncharacterized protein C19orf43 - Homo sapiens (Hu	-	-	-	-	1	3	2	-
1819	Q6PJW8	Uncharacterized protein C1orf71 - Homo sapiens (Hur	-	-	-	-	1	-	-	-
1820	Q96HY6	Uncharacterized protein C20orf116 precursor - Homo	-	-	-	-	-	-	1	-
1821	Q7Z570	Uncharacterized protein C2orf10 - Homo sapiens (Hur	-	-	-	1	-	1	-	-
1822	Q9GZY8	Uncharacterized protein C2orf33 - Homo sapiens (Hur	-	-	1	-	-	-	-	-
1823	Q9BU61	Uncharacterized protein C3orf60 - Homo sapiens (Hur	-	-	-	-	1	-	-	-
1824	Q5VWP3	Uncharacterized protein C6orf142 - Homo sapiens (Hu	-	1	-	-	-	-	-	-
1825	Q86YL5	Uncharacterized protein C8orf42 - Homo sapiens (Hur	-	-	2	-	-	-	-	-
1826	Q9BUH6	Uncharacterized protein C9orf142 - Homo sapiens (Hu	-	-	-	-	5	2	5	-
1827	Q9Y3I0	UPF0027 protein C22orf28 - Homo sapiens (Human)	-	-	-	-	2	-	-	-
1828	Q9NRG7	UPF0105 protein C14orf124 - Homo sapiens (Human)	-	-	-	-	1	-	1	-
1829	Q9BVM4	UPF0131 protein - Homo sapiens (Human)	-	-	1	-	-	-	-	-
1830	Q9H993	UPF0364 protein C6orf211 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1831	Q6IAA8	UPF0404 protein C11orf59 - Homo sapiens (Human)	-	-	3	-	2	3	2	-
1832	Q9GZP4	UPF0424 protein C1orf128 - Homo sapiens (Human)	-	1	-	-	4	-	3	-
1833	Q4G0N4	UPF0465 protein C5orf33 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1834	Q9H1C7	UPF0467 protein C5orf32 - Homo sapiens (Human)	-	-	-	1	-	-	-	-
1835	Q9NRP0	UPF0527 membrane protein - Homo sapiens (Human)	-	-	-	-	-	1	1	-
1836	P06132	Uroporphyrinogen decarboxylase (EC 4.1.1.37) (URO	-	-	-	-	2	-	1	X
1837	Q96QR1	Uteroglobin-related protein 2 precursor (Cytokine HIN	2	-	-	-	-	-	-	-
1838	Q16851	UTP--glucose-1-phosphate uridylyltransferase 2 (EC 2	-	-	1	5	4	1	2	X
1839	P54727	UV excision repair protein RAD23 homolog B (hHR23B	-	-	-	1	-	-	-	-
1840	Q9P2Y5	UV radiation resistance-associated gene protein - Hom	-	-	-	-	-	-	1	-
1841	Q9BZF9	Uveal autoantigen with coiled-coil domains and ankyrin	-	-	1	-	-	-	-	-
1842	P38606	Vacuolar ATP synthase catalytic subunit A, ubiquitous	-	-	1	-	-	3	6	X

1843	P21281	Vacuolar ATP synthase subunit B, brain isoform (EC 3.6.3.14) (V-ATPase)	-	-	1	-	1	2	2	X
1844	P36543	Vacuolar ATP synthase subunit E (EC 3.6.3.14) (V-ATPase)	-	-	1	-	-	2	2	X
1845	O75348	Vacuolar ATP synthase subunit G 1 (EC 3.6.3.14) (V-ATPase)	-	-	-	1	-	1	1	-
1846	Q9UBQ0	Vacuolar protein sorting 29 (Vesicle protein sorting 29)	-	-	1	-	-	4	3	X
1847	Q96QK1	Vacuolar protein sorting 35 (Vesicle protein sorting 35)	-	-	-	-	1	2	5	-
1848	Q9BRG1	Vacuolar protein sorting-associated protein 25 (hVps25)	-	-	-	-	-	2	-	-
1849	O75436	Vacuolar protein sorting-associated protein 26A (Vesicle protein sorting 26A)	-	-	-	-	-	-	1	-
1850	Q9UK41	Vacuolar protein sorting-associated protein 28 homolog (Vesicle protein sorting 28)	-	-	1	-	-	-	-	-
1851	O75351	Vacuolar protein sorting-associated protein 4B (Suppression of vacuolar protein sorting 4B)	-	-	1	-	2	2	2	-
1852	P26640	Valyl-tRNA synthetase (EC 6.1.1.9) (Valine--tRNA ligase)	-	-	-	-	1	2	7	-
1853	O95498	Vascular non-inflammatory molecule 2 precursor (Vascular non-inflammatory molecule 2)	-	-	-	1	-	-	-	-
1854	Q9NY84	Vascular non-inflammatory molecule 3 precursor - Homo sapiens	-	-	-	1	-	-	-	-
1855	P50552	Vasodilator-stimulated phosphoprotein (VASP) - Homo sapiens	-	-	5	6	1	1	-	-
1856	O75396	Vesicle trafficking protein SEC22b (SEC22 vesicle trafficking protein)	-	-	-	2	-	4	5	-
1857	P63027	Vesicle-associated membrane protein 2 (VAMP-2) (Synaptic vesicle-associated membrane protein 2)	-	-	2	-	-	-	-	-
1858	Q15836	Vesicle-associated membrane protein 3 (VAMP-3) (Synaptic vesicle-associated membrane protein 3)	-	-	3	-	-	-	-	-
1859	Q9BV40	Vesicle-associated membrane protein 8 (VAMP-8) (Endoplasmic reticulum-associated membrane protein 8)	-	-	1	-	-	2	3	-
1860	Q9POL0	Vesicle-associated membrane protein-associated protein 1 (VAMP-Associated Protein 1)	-	-	1	-	-	-	-	-
1861	P46459	Vesicle-fusing ATPase (EC 3.6.4.6) (Vesicular-fusion ATPase)	-	-	-	-	-	-	1	X
1862	Q12907	Vesicular integral-membrane protein VIP36 precursor	-	-	1	-	2	-	1	-
1863	Q00341	Vigilin (High density lipoprotein-binding protein) (HDL-binding protein)	-	1	-	-	-	-	-	-
1864	P08670	Vimentin	-	-	-	1	-	1	14	X
1865	P18206	Vinculin (Metavinculin)	-	8	51	7	12	18	37	X
1866	P02774	Vitamin D-binding protein precursor (DBP) (Group-specific component)	10	-	1	-	-	-	2	X
1867	P04070	Vitamin K-dependent protein C precursor (EC 3.4.21.6)	3	-	-	-	-	-	-	-
1868	P07225	Vitamin K-dependent protein S precursor - Homo sapiens	2	-	3	-	-	-	-	-
1869	P04004	Vitronectin precursor (Serum spreading factor) (S-protein)	5	-	1	-	-	-	6	X
1870	P21796	Voltage-dependent anion-selective channel protein 1 (VDAC1)	-	-	9	-	6	3	9	-
1871	P45880	Voltage-dependent anion-selective channel protein 2 (VDAC2)	-	-	5	-	4	2	5	X
1872	Q9Y277	Voltage-dependent anion-selective channel protein 3 (VDAC3)	-	-	11	2	-	4	6	-
1873	O00305	Voltage-dependent L-type calcium channel subunit beta 1 (L-type calcium channel subunit beta 1)	-	-	-	1	-	-	-	-
1874	P04275	Von Willebrand factor precursor (vWF) [Contains: Von Willebrand factor type A domain]	-	-	34	-	-	-	5	-
1875	Q5JSH3	WD repeat protein 44 (Rabphilin-11) - Homo sapiens	-	-	2	-	-	-	-	-
1876	Q9GZS3	WD repeat protein 61 (Meiotic recombination REC14 protein)	-	-	-	-	1	-	-	-
1877	O75083	WD-repeat protein 1 (Actin-interacting protein 1) (AIP1)	-	2	15	7	15	5	12	X
1878	P42768	Wiskott-Aldrich syndrome protein (WASp)	-	-	-	1	-	-	4	-
1879	Q92558	Wiskott-Aldrich syndrome protein family member 1 (WASF1)	-	-	-	1	-	-	-	-
1880	O43516	Wiskott-Aldrich syndrome protein-interacting protein (WIP1)	-	-	-	-	1	-	2	-
1881	Q969T9	WW domain-binding protein 2 (WBP-2) - Homo sapiens	-	1	1	-	1	1	-	X
1882	Q9NQW7	Xaa-Pro aminopeptidase 1 (EC 3.4.11.9) (X-Pro aminopeptidase)	-	-	-	-	-	-	1	-
1883	P12955	Xaa-Pro dipeptidase (EC 3.4.13.9) (X-Pro dipeptidase)	-	-	-	-	2	-	-	X
1884	O15231	Zinc finger protein 185 (LIM-domain protein ZNF185) (Zinc finger protein 185)	-	-	1	-	-	-	-	-
1885	Q5T4S7	Zinc finger UBR1-type protein 1 - Homo sapiens (Human)	-	-	-	1	-	2	-	-
1886	P25311	Zinc-alpha-2-glycoprotein precursor (Zn-alpha-2-glycoprotein)	11	-	-	-	-	-	-	X
1887	Q15942	Zyxin (Zyxin-2)	-	-	9	-	-	3	5	X

Supplementary Table 2

	AccNr	Protein	MW	pI	Distinct	C-PBMC	C-T cell	C-monocyte	C-platelet	C-neutrophil	C-erythrocyte	C-blood plasma
1	P61604	10 kDa heat shock protein, mitochondria	10800.5	8.91	3	X	X	X	X	X	-	-
2	P42704	130 kDa leucine-rich protein (LRP 130) (P42704)	145202.1	5.5	1	X	-	X	-	-	-	-
3	P31946	14-3-3 protein beta/alpha (Protein kinase C)	27951.3	4.76	5	X	X	X	X	X	-	-
4	P62258	14-3-3 protein epsilon (14-3-3E)	29174.1	4.63	6	X	X	X	X	X	X	-
5	Q04917	14-3-3 protein eta (Protein AS1)	28087.7	4.76	4	X	X	X	X	X	-	-
6	P61981	14-3-3 protein gamma (Protein kinase C)	28171.5	4.8	6	X	X	X	X	X	-	-
7	P27348	14-3-3 protein theta (14-3-3 protein tau) (P27348)	27764.4	4.68	8	X	X	X	X	X	-	-
8	P63104	14-3-3 protein zeta/delta (Protein kinase C)	27745.3	4.73	14	X	X	X	X	X	-	-
9	Q9Y4L1	150 kDa oxygen-regulated protein precursor	111335.9	5.16	1	X	X	-	-	-	-	-
10	P62191	26S protease regulatory subunit 4 (P26s)	49184.8	5.87	1	-	-	-	-	-	X	-
11	P17980	26S protease regulatory subunit 6A (TAP)	49203.8	5.13	1	X	X	-	-	-	-	-
12	P35998	26S protease regulatory subunit 7 (MSS)	48502.9	5.72	1	-	-	-	-	-	-	-
13	P62333	26S protease regulatory subunit S10B (P62333)	44173.2	7.09	2	X	X	X	-	-	X	-
14	O75832	26S proteasome non-ATPase regulatory subunit 1	24428	5.72	1	X	-	-	-	-	-	-
15	Q9UNM6	26S proteasome non-ATPase regulatory subunit 2	42918.7	5.53	1	X	X	X	X	-	-	-
16	Q13200	26S proteasome non-ATPase regulatory subunit 3	100200.3	5.08	1	X	X	X	-	-	X	-
17	O43242	26S proteasome non-ATPase regulatory subunit 4	60977.9	8.47	1	X	X	X	-	-	-	-
18	P51665	26S proteasome non-ATPase regulatory subunit 5	37025.6	6.29	1	X	X	X	-	-	-	-
19	Q02218	2-oxoglutarate dehydrogenase E1 component	113476.1	6.62	1	X	X	-	-	-	-	-
20	P42126	3,2-trans-enoyl-CoA isomerase, mitochondria	32816.2	8.8	2	-	X	X	-	X	-	-
21	Q9H9J2	39S ribosomal protein L44, mitochondria	37535.6	8.65	1	X	-	-	-	-	-	-
22	Q99714	3-hydroxyacyl-CoA dehydrogenase type 2	26792	7.87	2	X	X	X	X	X	-	-
23	P42765	3-ketoacyl-CoA thiolase, mitochondrial (P42765)	41924.4	8.32	6	X	X	-	-	-	-	-
24	P62263	40S ribosomal protein S14	16141.6	9.99	1	X	X	X	-	-	-	-
25	P62269	40S ribosomal protein S18 (Ke-3) (Ke3)	17718.8	9.99	2	X	X	X	-	-	-	-
26	P39019	40S ribosomal protein S19	15929.4	9.99	2	X	X	-	-	-	-	-
27	P15880	40S ribosomal protein S2 (S4) (LLRep3)	31324.6	9.99	3	X	X	X	-	-	-	-
28	P60866	40S ribosomal protein S20 - Homo sapiens	13372.8	9.95	4	X	X	-	-	-	-	-
29	P62854	40S ribosomal protein S26	12884.3	9.99	2	X	X	X	-	-	-	-
30	P62857	40S ribosomal protein S28	7841.1	9.99	1	X	X	X	-	-	-	-
31	P62701	40S ribosomal protein S4, X isoform (Sin)	29466.7	9.99	2	X	X	-	-	-	-	-
32	P46782	40S ribosomal protein S5	22745.3	9.73	1	X	X	X	-	-	-	-
33	P08865	40S ribosomal protein SA (p40) (34/67 kDa)	32723	4.79	3	X	X	X	-	X	-	-
34	P10809	60 kDa heat shock protein, mitochondria	61055	5.7	14	X	X	X	X	X	-	-
35	P05388	60S acidic ribosomal protein P0 (L10E)	34273.7	5.72	4	X	X	X	-	-	-	-
36	P05386	60S acidic ribosomal protein P1	11514	4.26	1	-	X	X	-	-	-	-
37	P05387	60S acidic ribosomal protein P2	11665	4.42	4	X	X	X	-	-	-	-
38	P62913	60S ribosomal protein L11 (CLL-associated)	20121.3	9.64	2	X	X	X	-	X	-	-
39	P30050	60S ribosomal protein L12	17818.7	9.48	3	X	X	X	-	-	-	-
40	P35268	60S ribosomal protein L22 (Epstein-Barr)	14655.9	9.22	1	X	X	X	-	-	-	-
41	P62888	60S ribosomal protein L30	12652.9	9.66	3	X	X	X	-	-	-	-
42	Q02878	60S ribosomal protein L6 (TAX-responsive)	32596.9	9.99	2	X	X	X	-	-	-	-
43	P52209	6-phosphogluconate dehydrogenase, de	53009.1	6.88	10	X	X	X	X	X	-	-
44	O95336	6-phosphogluconolactonase (EC 3.1.1.3)	27547	5.7	5	X	X	X	X	X	-	-
45	P11021	78 kDa glucose-regulated protein precursor	72333.3	5.07	6	X	X	X	X	X	-	-
46	Q9NUJ1	Abhydrolase domain-containing protein 1	33932.7	8.8	2	-	X	-	-	-	-	-
47	Q96IU4	Abhydrolase domain-containing protein 1	22345.8	5.94	3	X	X	X	X	X	-	-
48	P24752	Acetyl-CoA acetyltransferase, mitochondria	45199.8	8.98	1	X	X	X	-	X	-	-
49	P39687	Acidic leucine-rich nuclear phosphoprotein	28585.5	4	3	X	X	X	-	X	-	-

50	Q92688	Acidic leucine-rich nuclear phosphoprote	28787.9	3.94	3	X	X	X	-	X	-	-
51	Q9BTT0	Acidic leucine-rich nuclear phosphoprote	30692.6	3.77	2	X	X	X	-	X	-	-
52	Q99798	Aconitate hydratase, mitochondrial precu	85425.9	7.36	1	X	X	-	-	-	-	-
53	P60709	Actin, cytoplasmic 1 (Beta-actin)	41737	5.29	24	X	X	X	X	X	X	X
54	P63261	Actin, cytoplasmic 2 (Gamma-actin)	41793.1	5.31	24	X	X	X	X	X	X	X
55	P61160	Actin-like protein 2 (Actin-related protein	44761	6.29	9	X	X	X	X	X	X	-
56	P61158	Actin-like protein 3 (Actin-related protein	47371.4	5.61	9	X	X	X	X	X	-	-
57	O15143	Actin-related protein 2/3 complex subunit	40818.8	8.69	5	X	X	X	X	X	-	-
58	O15144	Actin-related protein 2/3 complex subunit	34333.2	6.84	4	X	X	X	X	X	X	-
59	O15145	Actin-related protein 2/3 complex subunit	20415.6	8.82	3	X	X	X	X	X	-	-
60	P59998	Actin-related protein 2/3 complex subunit	19535.9	8.53	2	X	X	X	X	X	-	-
61	O15511	Actin-related protein 2/3 complex subunit	16189.3	5.47	2	X	X	X	X	X	-	-
62	P53999	Activated RNA polymerase II transcriptio	14264.2	9.6	1	X	X	X	-	-	-	-
63	O95433	Activator of 90 kDa heat shock protein A	38274.5	5.41	1	-	-	X	X	-	-	-
64	P45954	Acyl-CoA dehydrogenase, short/branche	47485.7	6.53	1	-	X	-	-	-	-	-
65	P49748	Acyl-CoA dehydrogenase, very-long-cha	70390.5	8.92	4	X	-	X	-	-	-	-
66	P07741	Adenine phosphoribosyltransferase (EC	19476.7	5.79	4	X	X	X	X	X	X	-
67	P23526	Adenosylhomocysteinase (EC 3.3.1.1) (S	47585.2	5.92	4	X	X	X	-	X	X	-
68	P54819	Adenylate kinase isoenzyme 2, mitochon	26346.7	7.85	7	X	X	X	X	X	-	-
69	P30566	Adenylosuccinate lyase (EC 4.3.2.2) (Ad	54889.6	6.68	1	X	X	-	-	-	X	-
70	Q01518	Adenylyl cyclase-associated protein 1 (C	51542.1	8.13	15	X	X	X	X	X	-	-
71	Q9HDC9	Adipocyte plasma membrane-associated	46480.6	5.82	2	X	X	-	-	X	-	-
72	P05141	ADP/ATP translocase 2 (Adenine nucleo	32764.2	9.76	5	X	X	X	X	-	-	-
73	P84077	ADP-ribosylation factor 1	20565.7	6.36	5	X	X	X	X	X	X	-
74	P61204	ADP-ribosylation factor 3	20469.7	7.03	5	-	-	-	X	-	-	-
75	P84085	ADP-ribosylation factor 5	20398.6	6.36	3	-	X	X	-	-	-	-
76	Q12802	A-kinase anchor protein 13 - Homo sapie	307552	5.12	1	-	-	-	-	-	-	-
77	P14550	Alcohol dehydrogenase [NADP+] (EC 1.1	36442	6.35	1	X	X	-	-	X	-	-
78	P15121	Aldose reductase (EC 1.1.1.21) (AR) (Al	35722.4	6.56	2	X	X	X	X	-	X	-
79	P02763	Alpha-1-acid glycoprotein 1 precursor (A	23511.7	4.93	1	X	-	-	-	X	-	X
80	P02765	Alpha-2-HS-glycoprotein precursor (Fetu	39324.9	5.43	2	X	-	-	-	-	-	X
81	P01023	Alpha-2-macroglobulin precursor (Alpha-	163278.8	6	6	X	-	-	X	-	-	X
82	P12814	Alpha-actinin-1 (Alpha-actinin cytoskele	103058.1	5.25	2	X	X	X	X	X	X	-
83	P06733	Alpha-enolase (EC 4.2.1.11) (2-phospho	47038	6.99	22	X	X	X	X	X	X	-
84	P04083	Annexin A1 (Annexin I) (Lipocortin I) (Ca	38583.3	6.64	15	X	X	X	-	X	-	-
85	P50995	Annexin A11 (Annexin XI) (Calcyclin-ass	54390	7.53	4	X	X	X	X	X	-	-
86	P07355	Annexin A2 (Annexin II) (Lipocortin II) (C	38473.1	7.56	15	X	X	X	-	X	X	-
87	P09525	Annexin A4 (Annexin IV) (Lipocortin IV) (	35751.7	5.85	2	X	X	X	X	X	-	-
88	P08758	Annexin A5 (Annexin V) (Lipocortin V) (E	35805.7	4.94	8	X	X	X	X	X	-	-
89	P08133	Annexin A6 (Annexin VI) (Lipocortin VI) (	75742.5	5.42	20	X	X	X	X	X	-	-
90	P20073	Annexin A7 (Annexin VII) (Synexin)	52739.5	5.52	2	X	X	X	-	X	X	-
91	P02647	Apolipoprotein A-I precursor (Apo-AI) (Ap	30778	5.56	12	X	-	X	-	-	-	X
92	Q8NCW5	Apolipoprotein A-I-binding protein precu	31674.8	7.56	3	X	-	-	-	-	-	-
93	P06727	Apolipoprotein A-IV precursor (Apo-AIV)	45399.3	5.28	11	X	-	-	-	-	-	X
94	P02656	Apolipoprotein C-III precursor (Apo-CIII)	10852.4	5.23	2	X	-	X	-	-	-	X
95	P02649	Apolipoprotein E precursor (Apo-E) - Hor	36154.3	5.65	3	X	-	-	-	-	-	X
96	Q07812	Apoptosis regulator BAX, membrane isof	21184.5	5.08	2	X	X	X	-	X	-	-
97	P10415	Apoptosis regulator Bcl-2	26266	6.75	1	-	-	-	-	-	-	-
98	Q9ULZ3	Apoptosis-associated speck-like protein c	21626.9	5.95	2	X	X	X	-	X	-	-
99	P55145	ARMET protein precursor (Arginine-rich p	20256.7	8.69	1	X	X	X	X	X	-	-
100	P00505	Aspartate aminotransferase, mitochondrial	47475.8	9.13	6	X	X	X	X	X	-	-
101	P25705	ATP synthase alpha chain, mitochondrial	59750.9	9.16	21	X	X	X	X	X	-	-
102	P24539	ATP synthase B chain, mitochondrial pre	28908.8	9.37	4	X	X	X	X	X	-	-
103	P06576	ATP synthase beta chain, mitochondrial	56560.2	5.26	17	X	X	X	X	X	-	-
104	O75947	ATP synthase D chain, mitochondrial (EC	18360.1	5.22	2	X	X	X	X	X	-	-
105	P30049	ATP synthase delta chain, mitochondrial	17490	5.38	2	X	X	X	X	X	-	-

106	P56134	ATP synthase f chain, mitochondrial (EC	10786.7	9.7	2	X	X	X	-	-	-	-
107	P36542	ATP synthase gamma chain, mitochondr	32996.2	9.23	2	X	X	X	X	-	-	-
108	P48047	ATP synthase O subunit, mitochondrial p	23277.4	9.97	7	X	X	X	X	X	-	-
109	Q86UK0	ATP-binding cassette sub-family A mem	293252.3	7.89	1	-	-	-	-	-	-	-
110	P53396	ATP-citrate synthase (EC 2.3.3.8) (ATP-c	120825.9	6.95	1	X	X	X	-	X	X	-
111	P12956	ATP-dependent DNA helicase 2 subunit	69712.2	6.23	2	X	X	X	-	-	-	-
112	P13010	ATP-dependent DNA helicase 2 subunit	82573.8	5.55	1	X	X	X	-	-	-	-
113	P20160	Azurocidin precursor (Cationic antimicrob	26885.8	9.75	1	X	-	X	-	X	-	-
114	P51572	B-cell receptor-associated protein 31 (BC	27860.6	8.44	2	X	X	X	-	X	-	-
115	P61769	Beta-2-microglobulin precursor [Contains	13714.6	6.06	1	X	-	X	X	X	-	X
116	P13929	Beta-enolase (EC 4.2.1.11) (2-phospho-l	46855.9	7.73	4	X	-	-	X	X	X	-
117	P07686	Beta-hexosaminidase beta chain precurs	63111.7	6.29	1	X	-	X	-	-	-	-
118	P31939	Bifunctional purine biosynthesis protein F	64616.2	6.27	2	X	X	-	-	-	X	-
119	P53004	Biliverdin reductase A precursor (EC 1.3.	33428.7	6.06	2	X	X	X	X	X	-	-
120	P49593	Ca(2+)/calmodulin-dependent protein kin	49831.1	4.99	1	X	X	X	X	X	-	-
121	P31949	Calgizzarin (S100 calcium-binding protei	11740.5	6.56	1	X	X	X	-	X	-	X
122	P05109	Calgranulin A (Migration inhibitory factor-	10834.6	6.51	8	X	X	X	X	X	X	X
123	P06702	Calgranulin B (Migration inhibitory factor-	13242.1	5.71	7	X	X	X	-	X	-	X
124	P62158	Calmodulin (CaM)	16706.5	4.09	3	X	X	X	X	X	X	-
125	P27824	Calnexin precursor (Major histocompatib	67568.6	4.47	6	X	X	X	X	X	-	-
126	P04632	Calpain small subunit 1 (CSS1) (Calcium	28315.9	5.05	4	X	X	X	X	X	X	-
127	Q99439	Calponin-2 (Calponin H2, smooth muscle	33566.1	6.92	1	X	X	X	X	X	-	-
128	P27797	Calreticulin precursor (CRP55) (Calregul	48141.8	4.29	8	X	X	X	X	X	-	-
129	P10644	cAMP-dependent protein kinase type I- α	42981.9	5.27	1	X	X	X	X	X	-	-
130	P16152	Carbonyl reductase [NADPH] 1 (EC 1.1.1.	30243.9	8.55	4	X	X	X	X	X	X	-
131	O75828	Carbonyl reductase [NADPH] 3 (EC 1.1.1.	30719.2	5.82	2	X	-	-	-	-	-	-
132	P04040	Catalase (EC 1.11.1.6)	59625.3	6.95	6	X	X	X	X	X	X	-
133	P07339	Cathepsin D precursor (EC 3.4.23.5) [Co	44552.5	6.1	3	X	X	X	X	X	-	-
134	P25774	Cathepsin S precursor (EC 3.4.22.27)	37495.9	8.61	5	X	X	X	-	X	-	-
135	P60953	Cell division control protein 42 homolog p	21310.7	5.77	1	X	X	X	X	X	-	-
136	P62633	Cellular nucleic acid-binding protein (CNI	19462.9	8	1	X	X	X	-	-	-	-
137	O00299	Chloride intracellular channel protein 1 (N	26791.7	5.09	5	X	X	X	X	X	X	-
138	O75390	Citrate synthase, mitochondrial precursor	51712.7	8.45	5	X	X	X	X	X	-	-
139	Q00610	Clathrin heavy chain 1 (CLH-17)	191484.5	5.48	18	X	X	X	X	X	X	-
140	O43809	Cleavage and polyadenylation specificity	26227.4	8.85	1	X	X	-	-	-	-	-
141	P10909	Clusterin precursor (Complement-associ	52494.9	5.89	6	X	-	-	X	X	-	X
142	Q14019	Coactosin-like protein	15813.9	5.55	9	X	X	X	X	X	-	-
143	P23528	Cofilin-1 (Cofilin, non-muscle isoform) (1	18371.4	8.27	9	X	X	X	X	X	X	X
144	P01024	Complement C3 precursor [Contains: Co	187149.1	6.02	4	X	-	-	X	-	-	X
145	P31146	Coronin-1A (Coronin-like protein p57) (C	51026.6	6.25	11	X	X	X	X	X	-	-
146	P57737	Coronin-7 (70 kDa WD repeat tumor reje	100575.6	5.51	1	X	X	X	-	X	-	-
147	Q86VP6	Cullin-associated NEDD8-dissociated pro	136376.5	5.52	2	X	X	X	-	X	X	-
148	Q8ND76	Cyclin-Y - Homo sapiens (Human)	39336.9	6.76	1	-	-	-	-	-	-	-
149	P04080	Cystatin B (Liver thiol proteinase inhibitor	11139.6	6.96	1	X	X	X	-	X	-	-
150	P04839	Cytochrome b-245 heavy chain (p22 phag	65205.1	8.9	2	X	X	X	-	X	-	-
151	P13498	Cytochrome b-245 light chain (p22 phag	20827.3	9.61	1	-	-	X	-	X	-	-
152	P99999	Cytochrome c	11617.6	9.59	2	X	X	X	X	-	-	-
153	P00403	Cytochrome c oxidase subunit 2 (EC 1.9.	25565.2	4.67	5	X	X	X	-	-	-	-
154	P13073	Cytochrome c oxidase subunit IV isoform	19576.8	9.52	2	X	X	X	-	-	-	-
155	Q81UI8	Cytokine receptor-like factor 3 - Homo sa	49766.2	5.01	1	-	X	X	X	-	-	-
156	P50453	Cytoplasmic antiproteinase 3 (CAP3) (CA	42403.9	5.61	4	X	X	X	X	X	-	-
157	Q7L576	Cytoplasmic FMR1-interacting protein 1-	145183.3	6.46	1	X	-	X	-	-	-	-
158	P28838	Cytosol aminopeptidase (EC 3.4.11.1) (L	52640.4	6.28	1	X	X	X	X	-	-	-
159	Q96KP4	Cytosolic nonspecific dipeptidase (Glutar	52878.8	5.66	3	X	X	X	-	-	-	-
160	Q96EP5	DAZ-associated protein 1 (Deleted in azo	43383.6	8.73	2	X	X	-	-	-	-	-
161	P30046	D-dopachrome decarboxylase (EC 4.1.1.	12580.6	7.25	1	X	X	X	-	X	-	-

162	Q13011	Delta3,5-delta2,4-dienoyl-CoA isomerase	35816.4	8.16	5	X	X	X	X	X	-	-
163	P60981	Destrin (Actin-depolymerizing factor) (AD	18374.7	8.12	1	X	X	-	X	X	-	-
164	P09622	Dihydrolipoyl dehydrogenase, mitochond	54150.5	7.59	1	X	X	X	-	-	-	-
165	Q16555	Dihydropyrimidinase-related protein 2 (D	62294	5.95	1	X	X	X	X	X	-	-
166	P27695	DNA-(apurinic or apyrimidinic site) lyase	35423.5	8.42	6	X	X	X	-	X	-	-
167	O75937	DnaJ homolog subfamily C member 8 (S	29841.8	9.04	1	X	X	-	-	-	-	-
168	P39656	Dolichyl-diphosphooligosaccharide--prote	48809.7	5.43	1	X	-	X	-	X	-	-
169	P04844	Dolichyl-diphosphooligosaccharide--prote	69284.3	5.44	5	-	X	X	X	-	-	-
170	P04843	Dolichyl-diphosphooligosaccharide--prote	68569.7	5.96	4	X	X	X	-	X	-	-
171	Q9UJU6	Drebrin-like protein (SH3 domain-contain	48207.5	5.02	1	X	-	-	X	X	-	-
172	Q14203	Dynactin-1 (150 kDa dynein-associated p	141695.6	5.61	1	X	-	-	X	-	-	-
173	Q9HC35	Echinoderm microtubule-associated prot	108903.7	5.88	1	-	-	-	-	-	-	-
174	Q96C19	EF-hand domain-containing protein 2 (Sv	26697.4	5.15	1	X	X	X	X	X	-	-
175	Q9H4M9	EH-domain-containing protein 1 (Testilin)	60627.2	6.35	3	X	X	-	X	X	-	-
176	P13804	Electron transfer flavoprotein alpha-subu	35079.8	8.62	3	X	X	X	X	X	-	-
177	P38117	Electron transfer flavoprotein beta-subun	27843.8	8.25	3	X	X	X	X	-	-	-
178	P68104	Elongation factor 1-alpha 1 (EF-1-alpha-1	50141.1	9.1	13	X	X	X	X	X	X	-
179	P29692	Elongation factor 1-delta (EF-1-delta) (Ar	30990.8	4.9	3	X	X	X	X	-	-	-
180	P26641	Elongation factor 1-gamma (EF-1-gamma)	49987.9	6.27	3	X	X	X	X	X	-	-
181	P13639	Elongation factor 2 (EF-2)	95207.5	6.42	8	X	X	X	-	X	X	-
182	P49411	Elongation factor Tu, mitochondrial precu	49541.8	7.26	7	X	X	X	X	-	-	-
183	P30040	Endoplasmic reticulum protein ERp29 pr	28993.6	6.77	5	X	X	X	X	X	-	-
184	P14625	Endoplasmin precursor (94 kDa glucose-	92469.3	4.76	2	X	X	X	X	X	X	-
185	P10768	Esterase D (EC 3.1.1.1)	31463	6.54	2	X	X	X	X	X	X	-
186	P60842	Eukaryotic initiation factor 4A-I (EC 3.6.1	46154.2	5.32	2	X	X	X	X	X	X	-
187	Q14240	Eukaryotic initiation factor 4A-II (EC 3.6.1	46402.5	5.33	2	X	X	-	-	-	-	-
188	Q14152	Eukaryotic translation initiation factor 3 s	166570.2	6.38	4	X	X	-	-	-	-	-
189	Q15056	Eukaryotic translation initiation factor 4H	27254	6.92	1	X	X	X	X	-	-	-
190	P63241	Eukaryotic translation initiation factor 5A	16701.2	5.08	3	X	X	X	X	X	X	-
191	O14980	Exportin-1 (Chromosome region mainten	123386.6	5.71	1	X	-	X	-	-	-	-
192	P15311	Ezrin (p81) (Cytovillin) (Villin-2)	69267.9	5.95	8	X	X	X	-	X	-	-
193	O14745	Ezrin-radixin-moesin-binding phosphop	38737.4	5.55	2	X	X	X	X	X	-	-
194	P52907	F-actin capping protein alpha-1 subunit (f	32922.9	5.45	5	X	X	X	X	X	X	-
195	P47755	F-actin capping protein alpha-2 subunit (f	32818.1	5.58	1	X	X	X	X	X	X	-
196	P47756	F-actin capping protein beta subunit (Cap	31219.5	5.36	2	X	X	X	X	X	-	-
197	Q96AE4	Far upstream element-binding protein 1 (f	67473.6	7.18	1	X	X	X	-	-	-	-
198	Q01469	Fatty acid-binding protein, epidermal (E-f	15033.3	6.82	2	X	X	X	-	X	-	-
199	P02792	Ferritin light chain (Ferritin L subunit)	19888.6	5.51	4	X	X	X	-	X	-	-
200	P02671	Fibrinogen alpha chain precursor [Contai	94973.5	5.7	5	X	-	-	X	-	-	X
201	P02675	Fibrinogen beta chain precursor [Contain	55928.5	8.54	9	X	X	-	X	X	X	X
202	P02679	Fibrinogen gamma chain precursor	51511.9	5.37	6	X	-	-	X	-	-	X
203	P21333	Filamin-A (Alpha-filamin) (Filamin-1) (En	280631.3	5.73	47	X	X	X	X	X	X	-
204	P30043	Flavin reductase (EC 1.5.1.30) (FR) (NAI	21988.3	7.31	2	X	X	X	X	X	X	-
205	O95466	Formin-like 1 protein (Formin-like protein	121828.2	5.56	4	X	X	X	-	-	-	-
206	P09467	Fructose-1,6-bisphosphatase 1 (EC 3.1.3	36683.5	6.61	1	X	X	X	-	X	-	-
207	P04075	Fructose-bisphosphate aldolase A (EC 4	39289	8.39	10	X	X	X	X	X	X	-
208	P09972	Fructose-bisphosphate aldolase C (EC 4	39324.9	6.46	1	X	X	X	X	X	-	-
209	P09382	Galectin-1 (Beta-galactoside-binding lect	14584.6	5.34	4	X	X	X	-	-	-	-
210	P17931	Galectin-3 (Galactose-specific lectin 3) (N	26057.3	8.61	1	X	-	X	-	X	-	-
211	P09104	Gamma-enolase (EC 4.2.1.11) (2-phosph	47137.6	4.91	4	-	X	-	-	X	-	-
212	Q9P107	GEM-interacting protein (GMIP)	106733.5	5.5	1	X	-	X	-	-	-	-
213	P60983	Glia maturation factor beta (GMF-beta)	16582.1	5.19	1	X	X	X	X	-	-	-
214	O60234	Glia maturation factor gamma (GMF-gam	16801.4	5.18	3	X	X	X	X	X	-	-
215	P11413	Glucose-6-phosphate 1-dehydrogenase	59134.9	6.44	4	X	X	X	X	X	-	-
216	P06744	Glucose-6-phosphate isomerase (EC 5.3	63016.3	8.44	8	X	X	X	X	X	X	-
217	P00367	Glutamate dehydrogenase 1, mitochondr	61398.2	7.66	5	X	X	X	-	-	-	-

218	O94925	Glutaminase kidney isoform, mitochondri	73461.5	7.85	1	X	X	-	-	-	-	-
219	P07203	Glutathione peroxidase 1 (EC 1.11.1.9) (	21899.2	6.15	5	X	X	X	X	X	X	-
220	P00390	Glutathione reductase, mitochondrial pre	56257.4	8.74	5	X	X	X	X	X	X	-
221	Q9Y2Q3	Glutathione S-transferase kappa 1 (EC 2	25365.8	8.53	4	X	X	X	X	-	-	-
222	P09211	Glutathione S-transferase P (EC 2.5.1.18	23224.8	5.44	4	X	X	X	X	X	-	-
223	P78417	Glutathione transferase omega-1 (EC 2.5	27566	6.24	2	X	X	X	X	X	-	-
224	P04406	Glyceraldehyde-3-phosphate dehydrogen	35922.2	8.58	17	X	X	X	X	X	X	X
225	Q9HC38	Glyoxalase domain-containing protein 4	34793.7	5.4	3	X	X	-	X	X	-	-
226	Q9UBQ7	Glyoxylate reductase/hydroxypyruvate re	35668.5	7.01	1	X	-	-	-	-	-	-
227	Q9H4G4	Golgi-associated plant pathogenesis-rela	17087.2	9.44	2	X	X	X	X	X	-	X
228	P28676	Grancalcin	24010.2	5.02	2	X	X	X	X	X	-	-
229	P62993	Growth factor receptor-bound protein 2 (	25206.5	5.89	3	X	X	X	X	X	-	-
230	Q9NUV9	GTPase, IMAP family member 4 (Immun	37534	7.66	3	X	X	X	-	-	-	-
231	P62826	GTP-binding nuclear protein Ran (GTPas	24292	7.2	6	X	X	X	X	X	X	-
232	Q03113	Guanine nucleotide-binding protein alpha	44148.3	9.84	1	-	-	X	-	X	-	-
233	P63244	Guanine nucleotide-binding protein beta	35076.9	7.6	8	X	X	X	-	-	X	-
234	P04899	Guanine nucleotide-binding protein G(i),	40319.9	5.34	5	X	X	X	X	X	-	-
235	P62873	Guanine nucleotide-binding protein G(i)/G	37246	5.6	3	-	X	X	X	X	-	-
236	P62879	Guanine nucleotide-binding protein G(i)/G	37200.1	5.6	3	X	X	-	X	X	-	-
237	P08107	Heat shock 70 kDa protein 1 (HSP70.1) (	70052.6	5.48	6	X	X	X	X	X	X	-
238	P11142	Heat shock cognate 71 kDa protein (Hea	70898.4	5.38	12	X	X	X	X	X	X	-
239	Q12931	Heat shock protein 75 kDa, mitochondria	80110.4	8.3	1	X	X	X	X	X	-	-
240	P07900	Heat shock protein HSP 90-alpha (HSP 8	84543	4.94	11	X	X	X	X	X	X	-
241	P08238	Heat shock protein HSP 90-beta (HSP 8	83133.4	4.97	10	X	X	X	X	X	X	-
242	P14317	Hematopoietic lineage cell-specific prote	53998.3	4.74	1	X	X	X	-	-	X	-
243	Q9Y5Z4	Heme-binding protein 2 (Protein SOUL) (	22875.5	4.58	1	-	X	X	X	X	-	-
244	P69905	Hemoglobin subunit alpha (Hemoglobin a	15126.4	8.73	3	X	-	X	-	X	X	X
245	P68871	Hemoglobin subunit beta (Hemoglobin be	15867.3	6.81	9	X	-	X	-	X	X	X
246	P51858	Hepatoma-derived growth factor (HDGF)	26788.4	4.7	2	X	X	-	-	-	-	-
247	Q99729	Heterogeneous nuclear ribonucleoprotein	36612.7	9.04	1	-	-	-	-	-	-	-
248	P09651	Heterogeneous nuclear ribonucleoprotein	38714.8	9.26	6	X	X	X	-	X	-	-
249	Q14103	Heterogeneous nuclear ribonucleoprotein	38434.4	7.61	6	X	X	X	-	X	-	-
250	P52597	Heterogeneous nuclear ribonucleoprotein	45540.9	5.38	5	X	X	X	-	X	-	-
251	P31943	Heterogeneous nuclear ribonucleoprotein	49098.5	5.89	5	X	X	X	-	-	-	-
252	P55795	Heterogeneous nuclear ribonucleoprotein	49263.9	5.89	2	-	-	-	-	-	-	-
253	P61978	Heterogeneous nuclear ribonucleoprotein	50976.5	5.39	4	X	X	X	X	X	-	-
254	P22626	Heterogeneous nuclear ribonucleoprotein	37429.9	8.97	7	X	X	X	-	X	X	-
255	P07910	Heterogeneous nuclear ribonucleoprotein	33688.2	4.95	2	X	X	X	-	-	-	-
256	Q00839	Heterogenous nuclear ribonucleoprotein	90479.8	5.76	1	X	X	X	-	-	-	-
257	P09429	High mobility group protein 1 (HMG-1) (H	24762.7	5.62	7	X	X	X	-	-	-	-
258	P26583	High mobility group protein 2 (HMG-2)	23902.7	7.77	4	X	X	X	-	-	-	-
259	P49773	Histidine triad nucleotide-binding protein	13670.8	6.46	1	X	X	X	X	X	-	-
260	P0C0S8	Histone H2A type 1 (H2A.1) - Homo sapi	13960.3	9.99	3	-	-	-	-	-	-	-
261	P62805	Histone H4	11236.2	9.99	1	X	X	X	X	-	-	-
262	P13746	HLA class I histocompatibility antigen, A-	40937	5.77	3	-	-	-	X	-	-	-
263	P01892	HLA class I histocompatibility antigen, A-	40922.1	6.5	3	X	-	-	X	-	-	-
264	P01908	HLA class II histocompatibility antigen, D	28105.3	5.12	1	X	-	-	-	-	-	-
265	P50502	Hsc70-interacting protein (Hip) (Putative	41331.9	5.18	1	X	X	-	X	-	X	-
266	P00492	Hypoxanthine-guanine phosphoribosyltra	24448.3	6.24	2	X	X	X	X	X	X	-
267	P01876	Ig alpha-1 chain C region - Homo sapien	37654.9	6.08	4	X	X	-	-	-	-	X
268	P01857	Ig gamma-1 chain C region - Homo sapien	36106.1	8.46	6	X	-	-	-	-	X	X
269	P01859	Ig gamma-2 chain C region - Homo sapien	35884.8	7.66	5	X	-	-	-	-	-	X
270	P01834	Ig kappa chain C region - Homo sapiens	11608.9	5.58	3	X	-	-	-	X	X	X
271	P01842	Ig lambda chain C regions - Homo sapien	11236.6	6.91	2	X	X	-	-	X	-	X
272	Q9H2U2	Inorganic pyrophosphatase 2, mitochond	37962.5	7.06	2	X	X	-	X	X	-	-
273	P29218	Inositol monophosphatase (EC 3.1.3.25)	30189	5.16	1	X	X	X	X	X	-	-

274	Q16270	Insulin-like growth factor-binding protein	29130.5	8.25	2	-	-	-	-	-	-	-
275	P08514	Integrin alpha-IIb precursor (Platelet mem	113391.5	5.21	8	X	-	-	X	X	-	-
276	P20701	Integrin alpha-L precursor (Leukocyte ad	128770.3	5.4	3	X	X	X	-	-	-	-
277	P11215	Integrin alpha-M precursor (Cell surface	127179.2	6.88	12	X	X	X	-	X	-	-
278	P13164	Interferon-induced transmembrane prote	13938.5	7.78	1	X	X	-	-	X	-	-
279	Q2TAA2	Isoamyl acetate-hydrolyzing esterase 1 h	27598.9	5.13	1	-	-	-	-	-	-	-
280	P50213	Isocitrate dehydrogenase [NAD] subunit	39592	6.47	1	X	X	X	X	-	-	-
281	O43837	Isocitrate dehydrogenase [NAD] subunit	42212	8.64	1	X	-	-	-	-	-	-
282	O75874	Isocitrate dehydrogenase [NADP] cytopla	46659.6	6.53	2	X	-	X	X	X	-	-
283	P48735	Isocitrate dehydrogenase [NADP], mitocl	50909.6	8.88	10	X	X	X	X	X	-	-
284	Q86Y91	Kinesin-like protein LOC146909 - Homo	92195	8.73	1	-	-	-	-	-	-	-
285	Q04760	Lactoylglutathione lyase (EC 4.4.1.5) (Me	20588.6	5.25	3	X	X	X	X	X	-	-
286	P42166	Lamina-associated polypeptide 2 isoform	75361.2	7.8	1	-	-	-	-	-	-	-
287	P42167	Lamina-associated polypeptide 2, isoform	50539.3	9.39	1	X	-	-	-	-	-	-
288	Q32MZ4	Leucine-rich repeat flightless-interacting	89253.5	4.59	7	X	X	X	X	-	-	-
289	P08575	Leukocyte common antigen precursor (E	147255	5.77	16	X	X	X	-	X	-	-
290	P30740	Leukocyte elastase inhibitor (LEI) (Serp	42742	5.9	10	X	X	X	X	X	X	-
291	P09960	Leukotriene A-4 hydrolase (EC 3.3.2.6) (	69154.4	5.8	5	X	X	X	-	X	-	-
292	Q14847	LIM and SH3 domain protein 1 (LASP-1)	29717.3	6.61	3	X	X	X	X	X	-	-
293	P23141	Liver carboxylesterase 1 precursor (EC 3	62521.4	6.15	3	X	-	X	-	-	-	-
294	P00338	L-lactate dehydrogenase A chain (EC 1.1	36557.7	8.46	10	X	X	X	X	X	X	X
295	Q9BYZ2	L-lactate dehydrogenase A-like 6B (EC 1	41943.2	8.88	1	-	-	-	X	-	-	-
296	P07195	L-lactate dehydrogenase B chain (EC 1.1	36507.5	5.72	14	X	X	X	X	X	X	X
297	Q9NZR2	Low-density lipoprotein receptor-related	515501.7	5.09	1	-	-	-	-	-	-	-
298	P05455	Lupus La protein (Sjogren syndrome type	46837.3	6.68	6	X	X	-	-	-	-	-
299	Q7Z4W1	L-xylulose reductase (EC 1.1.1.10) (XR)	25913.2	8.33	1	X	X	-	X	X	-	-
300	Q13094	Lymphocyte cytosolic protein 2 (SH2 dom	60188.5	5.89	2	X	X	X	X	X	-	-
301	P42785	Lysosomal Pro-X carboxypeptidase prec	55800.1	6.76	2	-	-	X	-	X	-	-
302	P11279	Lysosome-associated membrane glycop	44773.3	9.22	2	X	X	X	-	X	-	-
303	P61626	Lysozyme C precursor (EC 3.2.1.17) (1,4	16537.1	9.38	3	X	X	X	-	X	-	X
304	P40121	Macrophage capping protein (Actin-regul	38517.8	5.89	4	X	X	X	-	X	X	-
305	P14174	Macrophage migration inhibitory factor (M	12345.2	8.24	1	X	X	X	X	X	-	-
306	P40925	Malate dehydrogenase, cytoplasmic (EC	36295.1	6.89	7	X	X	X	X	X	X	-
307	P40926	Malate dehydrogenase, mitochondrial pr	35531.5	8.92	11	X	X	X	X	X	-	-
308	Q5VYJ5	MAM and LDL-receptor class A domain-c	136444.6	5.7	1	-	-	-	-	-	-	-
309	Q96IJ6	Mannose-1-phosphate guanylttransferase	46291.4	6.74	1	-	-	-	-	-	-	-
310	Q96T17	MAP7 domain-containing protein 2 - Hom	81961.8	8.95	1	X	X	-	X	-	-	-
311	O15173	Membrane-associated progesterone rece	23818.6	4.76	1	-	X	-	-	-	-	-
312	Q15691	Microtubule-associated protein RP/EB fa	29868	5.02	1	X	X	X	X	X	-	-
313	Q02978	Mitochondrial 2-oxoglutarate/malate carri	33930.7	9.92	1	X	-	-	-	-	-	-
314	Q9NS69	Mitochondrial import receptor subunit TO	15390.5	4.27	1	X	X	X	X	-	-	-
315	P28482	Mitogen-activated protein kinase 1 (EC 2	41258.7	6.53	3	X	X	X	-	X	-	-
316	Q16539	Mitogen-activated protein kinase 14 (EC	41162.3	5.48	1	-	X	-	-	X	-	-
317	P26038	Moesin (Membrane-organizing extension	67689.2	6.09	17	X	X	X	X	X	X	-
318	Q7L9L4	Mps one binder kinase activator-like 1A (	24959.8	6.24	1	X	X	X	X	-	-	-
319	P22234	Multifunctional protein ADE2 [Includes: P	46948.3	7.09	2	X	X	-	X	-	-	-
320	O00499	Myc box-dependent-interacting protein 1	64699.7	4.97	1	X	X	-	-	-	-	-
321	P24158	Myeloblastin precursor (EC 3.4.21.76) (L	27807.2	8.71	1	X	X	X	-	X	-	-
322	P05164	Myeloperoxidase precursor (EC 1.11.1.7	83869.1	9.19	9	X	X	X	-	X	-	-
323	P60660	Myosin light polypeptide 6 (Myosin light c	16799	4.56	8	X	X	X	X	X	-	-
324	P19105	Myosin regulatory light chain 2, nonsarco	19663	4.67	2	X	X	X	X	X	-	-
325	Q7Z406	Myosin-14 (Myosin heavy chain, nonmus	228002.9	5.77	3	-	X	X	-	X	X	-
326	P35579	Myosin-9 (Myosin heavy chain, nonmusc	226402.2	5.5	53	X	X	X	X	X	X	-
327	P58546	Myotrophin (V-1 protein)	12763.7	5.28	1	X	X	X	X	X	-	-
328	P20933	N(4)-(beta-N-acetylglucosaminy)-L-aspa	37194.5	5.86	1	X	-	-	-	X	-	-
329	Q9UJ70	N-acetylglucosamine kinase (EC 2.7.1.5)	37244.7	5.82	4	X	X	X	-	X	X	-

330	Q13423	NAD(P) transhydrogenase, mitochondria	113896.3	8.31	3	X	-	X	-	-	-	-
331	O95168	NADH dehydrogenase [ubiquinone] 1 be	15077.5	9.85	1	X	-	-	-	-	-	-
332	O00217	NADH-ubiquinone oxidoreductase 23 kD	23705.3	6	1	X	X	X	-	-	-	-
333	P19404	NADH-ubiquinone oxidoreductase 24 kD	27391.7	8.21	1	-	X	X	-	-	-	-
334	O75489	NADH-ubiquinone oxidoreductase 30 kD	30241.7	6.98	1	X	X	X	-	-	-	-
335	O95299	NADH-ubiquinone oxidoreductase 42 kD	40750.8	8.67	1	X	X	X	-	-	-	-
336	Q9P0J0	NADH-ubiquinone oxidoreductase B16.6	16567.2	8.24	1	X	-	X	-	-	-	-
337	Q13765	Nascent polypeptide-associated complex	23384	4.52	1	X	X	X	X	-	-	-
338	Q14697	Neutral alpha-glucosidase AB precursor	106874.5	5.73	3	X	X	X	X	X	X	-
339	P43490	Nicotinamide phosphoribosyltransferase	55521.4	6.69	1	-	X	-	-	X	-	-
340	P49321	Nuclear autoantigenic sperm protein (NA	85238.1	4.26	1	X	X	X	-	-	-	-
341	P19338	Nucleolin (Protein C23)	76483.5	4.6	1	X	X	-	-	X	-	-
342	P15531	Nucleoside diphosphate kinase A (EC 2.	17148.8	5.83	2	X	X	X	X	X	X	-
343	P22392	Nucleoside diphosphate kinase B (EC 2.	17298.1	8.52	5	X	X	X	X	X	-	-
344	Q56VL3	OCIA domain-containing protein 2 - Hom	16953.6	9.24	1	X	-	-	-	-	-	-
345	Q92882	Osteoclast-stimulating factor 1	23798.9	5.19	1	X	X	X	X	X	-	-
346	Q9UBV8	Peflin (PEF protein with a long N-termina	30381.1	6.1	1	X	-	-	-	X	-	-
347	Q9UJ68	Peptide methionine sulfoxide reductase (	26132.6	8.22	1	-	-	-	-	X	-	-
348	P62937	Peptidyl-prolyl cis-trans isomerase A (EC	17881.4	7.82	12	X	X	X	X	X	X	X
349	P23284	Peptidyl-prolyl cis-trans isomerase B pre	22742.5	9.33	5	X	X	X	X	X	-	X
350	Q9H2H8	Peptidyl-prolyl cis-trans isomerase-like 3	18154.6	6.29	1	X	X	X	-	X	-	-
351	Q06830	Peroxiredoxin-1 (EC 1.11.1.15) (Thioredd	22110.5	8.27	8	X	X	X	X	X	X	-
352	P32119	Peroxiredoxin-2 (EC 1.11.1.15) (Thioredd	21760.8	5.67	3	X	X	X	X	X	X	-
353	P30044	Peroxiredoxin-5, mitochondrial precursor	22026.5	8.85	2	X	X	X	X	X	-	-
354	P30041	Peroxiredoxin-6 (EC 1.11.1.15) (Antioxid	24903.9	6.03	6	X	X	X	X	X	X	-
355	Q00325	Phosphate carrier protein, mitochondrial	40095.1	9.45	2	X	X	X	-	-	-	-
356	O95674	Phosphatidate cytidyltransferase 2 (EC	51418.3	6.64	1	-	X	X	-	-	-	-
357	P30086	Phosphatidylethanolamine-binding protei	20925.7	7.43	5	X	X	X	X	X	X	-
358	P36871	Phosphoglucomutase-1 (EC 5.4.2.2) (Glu	61318.2	6.32	1	X	X	-	X	X	-	-
359	Q96G03	Phosphoglucomutase-2 (EC 5.4.2.2) (Glu	68210.6	6.18	1	X	X	X	-	X	-	-
360	P00558	Phosphoglycerate kinase 1 (EC 2.7.2.3)	44483.8	8.3	19	X	X	X	X	X	X	-
361	P18669	Phosphoglycerate mutase 1 (EC 5.4.2.1)	28672.9	6.75	10	X	X	X	X	X	-	-
362	P36969	Phospholipid hydroperoxide glutathione p	22128	8.65	1	X	X	X	X	-	-	-
363	Q9H008	Phospholysine phosphohistidine inorgani	29165.5	5.8	1	X	X	-	-	X	-	-
364	P35237	Placental thrombin inhibitor (Cytoplasmic	42590.1	5.19	1	X	X	X	X	X	-	-
365	Q14651	Plastin-1 (I-plastin) (Intestine-specific pla	70353	5.33	5	-	-	-	-	-	-	-
366	P13796	Plastin-2 (L-plastin) (Lymphocyte cytosol	70289.7	5.2	44	X	X	X	-	X	-	-
367	P02775	Platelet basic protein precursor (PBP) (S	13894.3	9.04	1	X	-	-	X	X	-	X
368	P68402	Platelet-activating factor acetylhydrolase	25569.4	5.57	2	X	X	X	X	-	-	-
369	Q15102	Platelet-activating factor acetylhydrolase	25734.4	6.33	2	X	X	X	-	-	-	-
370	P08567	Pleckstrin (Platelet p47 protein)	40097.1	8.5	3	X	X	-	X	X	-	-
371	Q9UUK3	Poly [ADP-ribose] polymerase 4 (EC 2.4.	192589.6	5.43	1	-	-	X	-	-	-	-
372	Q15365	Poly(rC)-binding protein 1 (Alpha-CP1) (I	37498	6.66	5	X	X	X	X	X	-	-
373	Q15366	Poly(rC)-binding protein 2 (Alpha-CP2) (I	38580.3	6.33	5	X	X	X	X	-	-	-
374	Q3KNV8	Polycomb group RING finger protein 3 - I	28115.7	8.53	1	-	-	-	-	-	-	-
375	Q96CX2	Potassium channel tetramerisation doma	35701	5.51	5	X	-	X	-	X	-	-
376	O75915	PRA1 family protein 3 (ARL-6-interacting	21614.8	9.77	3	X	X	X	-	X	-	-
377	O96008	Probable mitochondrial import receptor s	37893.3	6.79	1	X	X	-	-	-	-	-
378	P07737	Profilin-1 (Profilin I)	14923.1	8.47	11	X	X	X	X	X	-	X
379	P35232	Prohibitin.	29804.2	5.57	6	X	X	X	X	X	-	-
380	Q99623	Prohibitin-2 (B-cell receptor-associated p	33296.5	9.83	5	X	X	X	X	-	-	-
381	O94903	Proline synthetase co-transcribed bacteri	30344.1	7.09	1	X	X	X	X	-	-	-
382	Q15185	Prostaglandin E synthase 3 (EC 5.3.99.3)	18697.5	4.34	1	X	X	X	X	-	-	-
383	Q6S8J3	Prostate, ovary, testis-expressed protein	80753.2	5.64	10	-	-	-	-	X	-	-
384	Q06323	Proteasome activator complex subunit 1	28723.3	5.78	7	X	X	X	X	X	-	-
385	Q9UL46	Proteasome activator complex subunit 2	27230.6	5.44	8	X	X	X	X	X	X	-

386	P25786	Proteasome subunit alpha type 1 (EC 3.4.21.10)	29555.8	6.15	3	X	X	X	X	-	-	-
387	P25788	Proteasome subunit alpha type 3 (EC 3.4.21.10)	28302.2	5.19	4	X	X	X	X	X	X	-
388	P25789	Proteasome subunit alpha type 4 (EC 3.4.21.10)	29484	7.58	3	X	X	X	X	-	-	-
389	P28066	Proteasome subunit alpha type 5 (EC 3.4.21.10)	26411.2	4.74	3	X	X	X	X	-	-	-
390	P60900	Proteasome subunit alpha type 6 (EC 3.4.21.10)	27399.6	6.35	4	X	X	X	X	X	X	-
391	O14818	Proteasome subunit alpha type 7 (EC 3.4.21.10)	27887	8.6	8	X	X	X	X	X	-	-
392	P20618	Proteasome subunit beta type 1 (EC 3.4.21.10)	26489.5	8.27	5	X	X	X	X	X	-	-
393	P49721	Proteasome subunit beta type 2 (EC 3.4.21.10)	22836.4	6.52	3	X	X	X	X	X	-	-
394	P49720	Proteasome subunit beta type 3 (EC 3.4.21.10)	22949.1	6.14	2	X	X	X	X	X	-	-
395	P28062	Proteasome subunit beta type 8 precursor	30354.5	7.63	3	X	X	X	X	X	-	-
396	P28065	Proteasome subunit beta type 9 precursor	23264.4	4.93	3	X	X	X	X	-	-	-
397	Q969H8	Protein C19orf10 precursor (Stromal cell)	18795.3	6.2	3	X	X	X	-	X	-	-
398	Q9Y426	Protein C21orf25 precursor	75533.6	6.47	1	-	-	-	-	-	-	-
399	O75223	Protein C7orf24	21007.8	5.07	1	X	X	X	-	X	-	-
400	O60888	Protein CutA precursor (Brain acetylcholinesterase)	19116.4	5.42	1	X	X	X	-	-	-	-
401	O60610	Protein diaphanous homolog 1 (Diaphanous)	138979.4	5.31	18	X	X	X	X	X	-	-
402	P30101	Protein disulfide-isomerase A3 precursor	56782.7	5.99	11	X	X	X	X	X	-	-
403	Q15084	Protein disulfide-isomerase A6 precursor	48121.6	4.95	4	X	X	X	X	X	-	-
404	P07237	Protein disulfide-isomerase precursor (EC 1.8.1.7)	57116.6	4.76	9	X	X	X	X	X	-	-
405	Q99497	Protein DJ-1 (Oncogene DJ1)	19891.2	6.33	3	X	X	X	X	X	X	-
406	Q9H0Q0	Protein FAM49A	37313.1	5.71	2	X	X	-	-	-	-	-
407	Q9NUQ9	Protein FAM49B (L1)	36748.2	5.76	3	X	X	X	-	X	-	-
408	Q9BSJ8	Protein FAM62A (Membrane-bound C2 domain)	122857	5.57	7	X	X	X	X	-	X	-
409	Q8N163	Protein KIAA1967 (Deleted in breast cancer)	102902.1	5.14	2	X	-	-	-	-	-	-
410	P61326	Protein mago nashi homolog	17163.7	5.74	1	X	-	X	-	-	-	-
411	Q9UFN0	Protein NipSnap3A (NipSnap4) (Target for ubiquitination)	28466.8	9.21	4	X	X	X	X	X	-	-
412	Q15435	Protein phosphatase 1 regulatory subunit 1	41564.4	4.84	1	X	X	-	-	-	-	-
413	Q9P258	Protein RCC2 (Telophase disk protein of Drosophila)	56084.8	9.02	1	X	X	-	-	-	-	-
414	Q01105	Protein SET (Phosphatase 2A inhibitor 12)	33489	4.23	3	X	X	X	-	-	-	-
415	O94979	Protein transport protein Sec31A - Homo sapiens	133015.4	6.43	1	X	X	X	X	-	-	-
416	P61619	Protein transport protein Sec61 subunit alpha	52133.9	8.33	1	-	X	X	-	-	-	-
417	Q9ULC6	Protein-arginine deiminase type-1 (EC 3.5.1.15)	74666	6.07	1	X	X	X	X	-	-	-
418	P22061	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	24519.4	6.78	5	X	X	X	X	X	X	-
419	P00491	Purine nucleoside phosphorylase (EC 2.4.1.1)	32148.1	6.45	3	X	X	X	X	X	X	-
420	Q9NTK5	Putative GTP-binding protein PTD004	44743.8	7.64	1	X	X	X	X	-	-	-
421	Q9NTT1	Putative ubiquitin-conjugating enzyme E2	16905.5	8.81	1	X	-	X	X	-	-	-
422	Q6ZWB7	Putative uncharacterized protein FLJ413	23948.7	9.99	1	-	-	-	-	-	-	-
423	P08559	Pyruvate dehydrogenase E1 component	43295.9	8.35	1	X	-	-	-	-	-	-
424	P11177	Pyruvate dehydrogenase E1 component	39219.6	6.21	3	X	X	-	X	-	-	-
425	P14618	Pyruvate kinase isozymes M1/M2 (EC 2.7.1.40)	57806	7.95	30	X	X	X	X	X	X	-
426	Q08257	Quinone oxidoreductase (EC 1.6.5.5) (NADH dehydrogenase)	35206.8	8.56	3	X	X	-	-	-	X	-
427	P31150	Rab GDP dissociation inhibitor alpha (RabGDI)	50583	5	5	X	X	X	X	X	-	-
428	P50395	Rab GDP dissociation inhibitor beta (RabGDI2)	50663.5	6.11	14	X	X	X	X	X	X	-
429	P43487	Ran-specific GTPase-activating protein (RanGAP)	23310.2	5.19	1	X	X	X	X	X	-	-
430	Q15404	Ras suppressor protein 1 (Rsu-1) (RSP-1)	31409.3	8.57	3	X	X	-	X	X	-	-
431	P63000	Ras-related C3 botulinum toxin substrate 1	21450.2	8.77	4	X	X	X	X	X	-	-
432	P15153	Ras-related C3 botulinum toxin substrate 2	21428.9	7.52	8	X	X	X	X	X	-	-
433	P62491	Ras-related protein Rab-11A (Rab-11) (YPT1-related)	24262.4	6.14	2	X	X	X	X	X	-	-
434	P61106	Ras-related protein Rab-14	23765.9	5.86	5	X	X	X	X	X	-	-
435	P59190	Ras-related protein Rab-15	24390.8	5.53	2	X	X	X	X	X	-	-
436	P62820	Ras-related protein Rab-1A (YPT1-related)	22546.7	5.93	3	X	-	X	X	X	-	-
437	Q9H0U4	Ras-related protein Rab-1B	22171.3	5.55	4	X	X	X	X	X	-	-
438	Q9UL25	Ras-related protein Rab-21 - Homo sapiens	24216.5	8.16	2	X	X	X	-	X	-	-
439	P61019	Ras-related protein Rab-2A	23545.7	6.08	1	X	X	X	X	X	-	-
440	Q13637	Ras-related protein Rab-32 - Homo sapiens	24866.2	6.1	1	-	-	X	X	X	-	-
441	Q9H082	Ras-related protein Rab-33B	25717.7	6.71	1	X	X	X	X	-	-	-

442	Q15286	Ras-related protein Rab-35 (Rab-1C) (G	23025.3	8.53	2	X	X	X	X	X	-	-
443	P61018	Ras-related protein Rab-4B	23586.9	5.8	2	-	-	-	-	-	-	-
444	P61020	Ras-related protein Rab-5B	23706.9	8.29	2	-	X	-	X	X	-	-
445	P51148	Ras-related protein Rab-5C (RAB5L) (L1	23482.7	8.64	4	X	X	X	-	X	-	-
446	P20340	Ras-related protein Rab-6A (Rab-6)	23461.7	5.42	1	X	X	X	-	X	-	-
447	P51149	Ras-related protein Rab-7	23489.9	6.39	7	X	X	X	X	X	-	-
448	P62834	Ras-related protein Rap-1A precursor (G	20987.3	6.39	3	X	X	X	-	X	-	-
449	P61224	Ras-related protein Rap-1b precursor (G	20824.9	5.65	5	X	X	X	X	X	-	-
450	P52565	Rho GDP-dissociation inhibitor 1 (Rho G	23207.2	5.02	4	X	X	X	X	X	-	-
451	P52566	Rho GDP-dissociation inhibitor 2 (Rho G	22988.1	5.1	6	X	X	X	X	X	-	-
452	Q07960	Rho-GTPase-activating protein 1 (GTPas	50436	5.85	3	X	X	X	X	X	-	-
453	P13489	Ribonuclease inhibitor (Ribonuclease/an	49842.6	4.71	10	X	X	X	X	X	X	-
454	P49247	Ribose-5-phosphate isomerase (EC 5.3.	26091.2	6.97	1	X	X	-	X	X	-	-
455	P60891	Ribose-phosphate pyrophosphokinase I	34703.3	6.56	1	X	X	-	-	-	X	-
456	P35637	RNA-binding protein FUS (Oncogene FU	53426.1	9.4	1	X	-	-	-	-	-	-
457	P26447	S100 calcium-binding protein A4 (Metast	11728.6	5.85	4	X	X	X	-	X	-	-
458	P31153	S-adenosylmethionine synthetase isoform	43660.9	6.02	1	-	X	-	-	-	-	-
459	Q9Y3Z3	SAM domain and HD domain-containing	72200.9	6.7	19	X	X	X	-	-	-	-
460	Q93084	Sarcoplasmic/endoplasmic reticulum cal	113978.1	5.42	2	X	X	X	X	X	-	-
461	Q96C86	Scavenger mRNA decapping enzyme Dc	38681	5.84	1	-	X	X	-	-	-	-
462	Q15019	Septin-2 (Protein NEDD5)	41487.7	6.15	1	X	X	X	X	-	-	-
463	Q14141	Septin-6	49585.7	6.25	4	X	X	-	X	-	-	-
464	Q16181	Septin-7 (CDC10 protein homolog)	50680.2	8.77	4	X	X	-	X	-	-	-
465	Q9UHD8	Septin-9 (MLL septin-like fusion protein)	65369.7	9.05	3	X	X	-	X	-	X	-
466	O94804	Serine/threonine-protein kinase 10 (EC 2	112135.9	6.52	6	X	X	X	-	-	-	-
467	P63151	Serine/threonine-protein phosphatase 2A	51692.4	5.82	1	-	X	-	-	X	-	-
468	P30153	Serine/threonine-protein phosphatase 2A	65092.7	4.97	4	X	X	X	X	X	-	-
469	P62136	Serine/threonine-protein phosphatase PF	37512.3	5.94	3	X	X	-	X	X	-	-
470	P02768	Serum albumin precursor	69367.1	5.92	54	X	-	-	-	-	X	X
471	P49591	Seryl-tRNA synthetase (EC 6.1.1.11) (Se	58646.4	6.06	2	X	X	-	-	-	-	-
472	O60880	SH2 domain protein 1A (Signaling lymph	14187.3	8.74	1	X	X	-	-	-	-	-
473	O75368	SH3 domain-binding glutamic acid-rich-li	12774.3	5.22	3	X	X	X	X	X	-	-
474	Q9H299	SH3 domain-binding glutamic acid-rich-li	10437.8	4.82	1	X	X	X	X	X	-	-
475	Q16836	Short chain 3-hydroxyacyl-CoA dehydrog	34277.7	8.88	4	X	X	X	X	X	-	-
476	Q9H9B4	Sideroflexin-1 (Tricarboxylate carrier prot	35488.4	9.22	2	X	X	-	-	-	-	-
477	Q04837	Single-stranded DNA-binding protein, mi	17259.8	9.59	3	X	X	X	X	-	-	-
478	P62304	Small nuclear ribonucleoprotein E (snRN	10803.7	9.46	1	X	X	-	-	-	-	-
479	P62316	Small nuclear ribonucleoprotein Sm D2 (	13527	9.92	1	-	X	-	-	-	-	-
480	Q13126	S-methyl-5-thioadenosine phosphorylase	31250.3	6.75	1	X	-	-	X	X	-	-
481	Q4G0N8	Sodium/hydrogen exchanger 10 - Homo	135206.8	6.72	2	-	-	-	-	-	-	-
482	P30626	Sorcin (22 kDa protein) (CP-22) (V19)	21676.5	5.32	1	X	X	X	X	X	-	-
483	O60493	Sorting nexin-3 (SDP3 protein)	18631.2	8.73	1	-	-	X	X	X	-	-
484	Q13838	Spliceosome RNA helicase BAT1 (EC 3.	48991.6	5.44	3	X	X	-	-	-	-	-
485	P84103	Splicing factor, arginine/serine-rich 3 (Pre	19329.7	9.99	1	-	-	-	-	-	-	-
486	P31948	Stress-induced-phosphoprotein 1 (ST11)	62639.6	6.4	2	X	X	X	X	-	X	-
487	P21912	Succinate dehydrogenase [ubiquinone] in	31629.9	9.03	5	X	X	X	-	-	-	-
488	Q96I99	Succinyl-CoA ligase [GDP-forming] beta-	46510.9	6.15	1	-	X	-	-	-	-	-
489	Q9Y6N5	Sulfide:quinone oxidoreductase, mitoch	49961	9.18	1	X	X	X	-	X	-	-
490	P63279	SUMO-conjugating enzyme UBC9 (EC 6	18006.9	8.87	2	X	X	X	-	-	-	-
491	P00441	Superoxide dismutase [Cu-Zn] (EC 1.15.	15804.6	5.7	1	X	X	X	X	X	X	X
492	P04179	Superoxide dismutase [Mn], mitochondria	24722.2	8.34	2	X	X	X	X	X	-	-
493	O15260	Surfeit locus protein 4	30394.2	7.64	1	X	X	X	-	X	-	-
494	Q15833	Syntaxin-binding protein 2 (Unc-18 hom	66438.9	6.11	1	-	-	-	X	X	-	-
495	Q9Y490	Talin-1	269768.5	5.78	56	X	X	X	X	X	X	-
496	P78371	T-complex protein 1 subunit beta (TCP-1	57357.3	6.02	9	X	X	X	X	-	-	-
497	P50991	T-complex protein 1 subunit delta (TCP-1	57793.4	8.13	4	X	X	X	X	X	X	-

498	P48643	T-complex protein 1 subunit epsilon (TCP-1)	59671.4	5.45	2	X	X	X	X	X	X	-
499	Q99832	T-complex protein 1 subunit eta (TCP-1-epsilon)	59367	7.55	2	X	X	X	X	X	X	-
500	P49368	T-complex protein 1 subunit gamma (TCP-1-gamma)	60534.3	6.1	5	X	X	-	X	-	X	-
501	P50990	T-complex protein 1 subunit theta (TCP-1-theta)	59489.7	5.42	7	X	X	X	X	X	X	-
502	P40227	T-complex protein 1 subunit zeta (TCP-1-zeta)	57893.3	6.25	4	X	X	X	X	X	X	-
503	Q9UGI8	Testin (TESS)	47996.8	7.96	5	X	-	-	-	-	-	-
504	Q9Y3D6	Tetratricopeptide repeat protein 11 (TPR11)	16937.8	8.84	1	X	X	X	-	X	-	-
505	P10599	Thioredoxin (ATL-derived factor) (ADF) (ATL)	11606.4	4.82	1	X	X	X	X	X	-	-
506	Q9H3N1	Thioredoxin domain-containing protein 1	31791.4	4.92	1	X	-	X	-	-	-	-
507	Q8NBS9	Thioredoxin domain-containing protein 5	47629.1	5.63	2	-	X	-	-	-	-	-
508	P30048	Thioredoxin-dependent peroxide reductase (TRP)	27692.8	7.67	2	X	X	X	X	X	-	-
509	P19971	Thymidine phosphorylase precursor (EC 2.4.1.1)	49955.8	5.36	4	X	X	X	X	X	-	-
510	Q5JTV8	Torsin-1A-interacting protein 1	66248.7	8.21	1	X	-	X	-	X	-	-
511	P37837	Transaldolase (EC 2.2.1.2)	37540.3	6.36	12	X	X	X	X	X	-	-
512	P61586	Transforming protein RhoA precursor (H-Ras)	21768.3	5.83	5	X	X	X	X	X	X	-
513	P37802	Transgelin-2 (SM22-alpha homolog)	22260.4	8.45	8	X	X	X	X	X	-	X
514	P29401	Transketolase (EC 2.2.1.1) (TK)	67878	7.58	18	X	X	X	X	X	X	-
515	P13693	Translationally-controlled tumor protein (TCTP)	19595.5	4.84	2	X	X	X	X	X	-	-
516	P51571	Translocon-associated protein delta subunit	18998.7	5.76	2	X	X	X	-	X	-	-
517	P49755	Transmembrane emp24 domain-containing protein 1	24976.1	6.98	1	X	X	X	-	X	-	-
518	P55084	Trifunctional enzyme subunit beta, mitochondrial	51294.8	9.44	3	X	X	X	X	-	-	-
519	P60174	Triosephosphate isomerase (EC 5.3.1.1)	26538.4	6.51	13	X	X	X	X	X	X	-
520	P29144	Tripeptidyl-peptidase 2 (EC 3.4.14.10) (TPP2)	138219.4	5.9	2	X	-	-	X	-	-	-
521	O14773	Tripeptidyl-peptidase I precursor (EC 3.4.11.1)	61229.2	5.97	1	X	X	X	X	X	-	-
522	P06753	Tropomyosin alpha-3 chain (Tropomyosin 3)	32818.9	4.68	8	X	X	X	X	X	-	-
523	P67936	Tropomyosin alpha-4 chain (Tropomyosin 4)	28390.8	4.67	7	X	X	X	X	X	-	-
524	P07951	Tropomyosin beta chain (Tropomyosin 2)	32850.9	4.66	4	X	X	X	X	-	-	-
525	P23381	Tryptophanyl-tRNA synthetase (EC 6.1.1.1)	53165.7	5.83	3	X	X	X	-	X	-	-
526	P68366	Tubulin alpha-1 chain (Alpha-tubulin 1) (TUBA1A)	49924.7	4.95	13	X	-	-	X	-	-	-
527	P07437	Tubulin beta-2 chain	49671.1	4.78	19	X	X	X	X	X	X	-
528	P68371	Tubulin beta-2C chain (Tubulin beta-2 chain)	49831.3	4.79	17	X	-	-	-	X	-	-
529	P04350	Tubulin beta-4 chain (Tubulin 5 beta)	49631.2	4.81	15	X	-	-	-	-	-	-
530	O75347	Tubulin-specific chaperone A (Tubulin-fo	12723.7	5.25	1	X	X	X	X	X	-	-
531	Q6IBS0	Twinfilin-2 (Twinfilin-1-like protein) (A6-re	39548.2	6.37	4	X	X	X	X	X	-	-
532	P41240	Tyrosine-protein kinase CSK (EC 2.7.1.1)	50704.6	6.62	1	X	X	X	X	-	-	-
533	P29350	Tyrosine-protein phosphatase non-recep	67561.5	7.65	11	X	X	X	X	X	-	-
534	P22695	Ubiquinol-cytochrome-c reductase comp	48443.2	8.74	3	X	X	X	X	-	-	-
535	P62988	Ubiquitin	8564.9	6.56	5	X	X	X	X	X	X	-
536	Q93009	Ubiquitin carboxyl-terminal hydrolase 7 (U	128272.7	5.33	3	X	X	X	-	-	-	-
537	Q96FW1	Ubiquitin thiolesterase protein OTUB1 (E	31284.2	4.85	2	X	X	X	X	X	-	-
538	P22314	Ubiquitin-activating enzyme E1 (A1S9 pr	117849.6	5.49	1	X	X	X	X	X	X	-
539	P62837	Ubiquitin-conjugating enzyme E2 D2 (EC	16735.4	7.69	1	X	X	-	-	X	-	-
540	P68036	Ubiquitin-conjugating enzyme E2 L3 (EC	17861.7	8.68	2	X	X	X	X	X	-	-
541	P61088	Ubiquitin-conjugating enzyme E2 N (EC	17137.9	6.13	10	X	X	X	X	X	X	-
542	Q13404	Ubiquitin-conjugating enzyme E2 variant	25796.9	8.55	4	X	X	X	X	X	X	-
543	Q15819	Ubiquitin-conjugating enzyme E2 variant	16231.7	8.05	3	X	X	-	X	X	X	-
544	Q9UBE0	Ubiquitin-like 1-activating enzyme E1A (S	38450.1	5.17	1	X	X	-	-	-	-	-
545	Q9NYU2	UDP-glucose:glycoprotein glucosyltransf	174977.9	5.4	7	X	-	X	X	-	-	-
546	Q86UX7	Unc-112-related protein 2 (Kindlin-3) (M	75953.2	6.52	5	X	X	X	X	X	-	-
547	Q9BUH6	Uncharacterized protein C9orf142 - Homo	21639.7	5.39	1	X	X	X	-	-	-	-
548	Q6IAA8	UPF0404 protein C11orf59 - Homo sapie	17744.9	5.01	2	X	X	X	X	-	-	-
549	Q16851	UTP--glucose-1-phosphate uridylyltransf	56809.3	8.15	7	X	X	X	X	X	-	-
550	Q9UBQ0	Vacuolar protein sorting 29 (Vesicle prote	20505.8	6.28	2	X	-	X	X	-	-	-
551	O75396	Vesicle trafficking protein SEC22b (SEC2	24609.5	8.68	2	X	-	X	-	X	-	-
552	Q9BV40	Vesicle-associated membrane protein 8 (V	11438.3	6.73	2	X	-	X	X	-	-	-
553	P08670	Vimentin	53520.7	5.06	4	X	-	X	-	X	-	-

554	P18206	Vinculin (Metavinculin)	123668.8	5.51	4	X	X	X	X	X	X	-
555	P21796	Voltage-dependent anion-selective chan	30641.5	8.63	3	X	X	X	X	X	-	-
556	P45880	Voltage-dependent anion-selective chan	38092.9	6.32	3	X	X	X	X	-	-	-
557	Q9Y277	Voltage-dependent anion-selective chan	30658.8	8.84	5	X	-	X	X	X	-	-
558	Q6ZS11	VPS9 domain-containing protein FLJ459	50053.3	5.69	1	-	-	-	-	-	-	-
559	O75083	WD-repeat protein 1 (Actin-interacting pr	66062.7	6.18	9	X	X	X	X	X	X	-
560	P42768	Wiskott-Aldrich syndrome protein (WASp	52781.7	6.18	2	X	-	-	-	-	-	-
561	Q9H171	Z-DNA-binding protein 1 - Homo sapiens	46343.1	6.29	1	-	-	-	-	-	-	-
562	Q5T4S7	Zinc finger UBR1-type protein 1 - Homo s	573844.3	5.7	1	-	-	-	-	X	-	-
563	Q15942	Zyxin (Zyxin-2)	61277.7	6.22	3	X	-	X	X	X	-	-

Introducing a New Parameter for Quality Control of Proteome Profiles: Consideration of Commonly Expressed Proteins

Astrid Slany¹, Verena J. Haudek¹, Nina C. Gundacker¹, Johannes Griss¹, Thomas Mohr¹,
Helge Wimmer², Maria Eisenbauer¹, Leonilla Elbling¹, Christopher Gerner¹

¹Department of Medicine I, Institute of Cancer Research, Medical University of Vienna,
Austria

²Section Biomedical Laboratory Science, University of Applied Sciences, Vienna, Austria

Correspondence: Christopher Gerner, Department of Medicine I, Institute of Cancer
Research, Medical University of Vienna, Austria

Email: Christopher.gerner@meduniwien.ac.at

Phone: +43-1-4277-65230

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Abbreviations:

ACN: Acetonitrile

CPL/MUW: Clinical Proteomics Laboratories at the Medical University of Vienna

DC: Dendritic Cell

DMEM: Dulbecco's Modified Eagle Medium

HaCaT: Human keratinocyte cell line

HUVEC: Human Umbilical Vein Endothelial Cell

MEM: minimal essential medium

PRIDE: Proteomics Identifications Database (<http://www.ebi.ac.uk/pride>)

RuBPS: Ruthenium II tris (bathophenanthroline disulfonate)

SPI: Scored Peak Intensity

SQL: Structured Query Language

SW-480: human colon adenocarcinoma cell line

Reviewer account for PRIDE-submissions (<http://www.ebi.ac.uk/pride/plainLogin.do>):

A: dendritic cells and HUVEC:

Username: review35774

Password: DAs-RfzP

B: fibroblasts and HaCaT:

Username: review89790

Password: mDsGF\$cf

Abstract

Interpretation of proteome profiling experiments largely relies on comparative analyses. False positive identifications may cause fatal misinterpretation of data. On the other hand, proteome analysis may also suffer from false negatives, when proteins which are actually present are not detected. This circumstance may be as fatal as false positive identifications and was hardly considered until now. Appropriate positive controls would facilitate quality assessment of proteome profiling experiments. Based on cell biology knowledge, our aim was to generate a list of commonly expressed proteins which may serve as positive control. Following a pragmatic experimental strategy, we compared the cytoplasmic fractions of four largely differing kinds of cells, which were human dendritic cells, endothelial cells, fibroblasts and keratinocytes. Proteome profiling was performed by 2D-PAGE in addition to shotgun analysis. By shotgun analysis, 665 proteins were identified which occurred in each of the four cells types, 360 proteins of those were also detectable in the corresponding 2D gels. We consider these proteins as common proteins. All shotgun analysis data, including mass fragmentation spectra of the corresponding peptides, are accessible via the PRIDE database. As expected, most of the common proteins could be clearly assigned to at least one of the following functional categories: chaperones, cytoskeleton, energy metabolism, redox regulation, nucleic acid processing, protein turnover, membrane transport, protein synthesis and signaling. We suggest that the present data may prove helpful for data assessment, quality control and interpretation of a large variety of experiments based on proteome profiling.

Introduction

One important ambition of proteome research is the establishment of protein profiles of biological systems, providing insight in the protein expression pattern of the investigated cells or tissues. Comparative studies of protein profiles may support the understanding of biological processes as well as the identification of biomarkers and novel molecular drug targets [1-3].

The comparison of protein profiles for biomedical interpretation relies on the robustness and sensitivity of the applied methods. Current concepts for quality control focus on the reliability of protein identification and the elimination of false positive results [4, 5]. Here, we introduce a new parameter for an improved quality assessment of proteome profiles: the positive identification of proteins that are ubiquitous present in any human nucleated cell type. Even though cells arise from different origin and exert diverse functions, they comprise essential, ubiquitous cell organelles and beside cell- and function-specific proteins they consist of a standard set of proteins. Positive identification of these commonly expressed proteins may serve as validation of analytical quality. Missing of such proteins indicates inadequate or incomplete analysis which may, as well as false positive identifications, lead to fatal misinterpretation of data.

To generate a reference list of commonly expressed proteins the following strategy was used. Cells representative for human leukocytes, endothelial cells, epithelial cells and fibroblasts were chosen, comprising normal primary cells in addition to immortalized cultured cells, proliferating as well as non-proliferating cells. A protein list was generated selecting only proteins identified in each of the four different cell types.

Due to the large number of diverse molecules present in biological samples, protein analysis represents a big challenge. Many thousands of proteins, occurring at highly different concentrations spanning up to eight orders of magnitude [6] with very different chemical properties are mixed with a broad variety of non-protein molecules, such as lipids, polysaccharides and nucleic acids, which may impede analysis.

The most usual proteome analysis methods are based either on the separation of proteins, as two-dimensional polyacrylamide electrophoresis (2D-PAGE) [7], or on the separation of peptides by nano flow liquid chromatography (nano-LC) as employed for shotgun proteomics [8]. Proteins may then be identified by mass spectrometric analysis of peptides generated by most usually tryptic digest [9]. Using 2D-PAGE, proteins can be quantified by fluorescence detection according to integrated staining intensities [10]. Shotgun proteomics is based on the

identification of peptide sequences by fragmentation analysis via mass spectrometry [11] and enables the identification of a larger number of proteins compared to 2D-PAGE. We have achieved very high accordance combining the two techniques, 2D-PAGE and shotgun, supporting our concept of optimal data reliability.

In this study, we present proteome reference maps of dendritic cells as well as of human umbilical vein endothelial cells (HUVEC), fibroblasts and keratinocytes. These reference maps will be again presented elsewhere with focus on the identification of cell type-specific and cell function-associated proteins. Here, we used these reference maps with another objective, namely to find out ubiquitous rather than specific proteins. The consideration of these data allowed the implementation of a new parameter which may prove useful for quality control for proteome profiling: the introduction of commonly expressed proteins as a kind of internal standard.

Materials and Methods

Monocyte-derived DC preparation and maturation

Peripheral blood mononuclear cells were isolated from heparinized whole blood of four different healthy donors by standard density gradient centrifugation with Ficoll-Paque (GE Healthcare Bio-Sciences AB, Uppsala, Sweden). Subsequently, monocytes were separated by magnetic sorting using the MACS technique (Miltenyi Biotec, Bergisch Gladbach, Germany) as previously described [12]. Monocytes were enriched by using the biotinylated CD14 mAb VIM13 (purity 95%) as previously described [12]. Dendritic cells (DC) were generated by culturing purified blood monocytes for 7 days with a combination of granulocyte-macrophage colony-stimulating factor (GM-CSF) (50 ng/ml) and interleukin-4 (IL-4) (100 U/ml).

Isolation and culture of HUVECs

Human umbilical vein endothelial cells (HUVECs) were isolated as described by Jaffe *et al.* [13]. Obtained cells were seeded into tissue culture flasks (Corning, Corning NY) coated with 0.5 µg/cm² human fibronectin (HFN, Chemicon, Temecula, CA, USA) and cultivated in EBM-2(MV) (Cambrex) supplemented with growth factors according to the instructions of the manufacturer and additionally with 10% FCS and 10 µg/ml ECGS (EBM-2MV complete).

Isolation and cultivation of fibroblasts

Fibroblasts were cultured as described by Frazier *et al.* [14], except that cells were isolated from normal skin punches and were cultured in RPMI supplemented with 10% FCS at standard cell culture conditions.

Isolation and cultivation of HaCaT

HaCaT are a spontaneously transformed human epithelial cell line, which maintain full epidermal differentiation capacity, as described by Boukamp *et al.* [15]. Cells were cultured in DMEM supplemented with 10% FCS at standard cell culture conditions.

Sub-cellular fractionation

The isolation of cytoplasmic proteins was performed as described by Gundacker *et al.* [16]. Cells were lysed in hypotonic lysis buffer (10 mM HEPES/NaOH, pH 7.4, 0.25 M sucrose, 10 mM NaCl, 3 mM MgCl₂, 0.5% Triton X-100) supplemented with protease inhibitors and

pressed through a 26 g syringe to induce cell lysis. The cytoplasmic fraction was separated from nuclei by centrifugation and precipitated by the addition of ethanol. Afterwards, all protein samples were dissolved in sample buffer (7.5 M urea, 1.5 M thiourea, 4% CHAPS, 0.5% SDS, 100 mM DDT).

2D polyacrylamid gel electrophoresis (2D-PAGE)

Proteins were loaded by passive rehydration on IPG strips pH 5–8, 17 cm (BioRad, Hercules, CA) at room temperature. Alternatively, IPG Immobiline™ strips (GE) were used and applied at similar conditions, which gave similar results (not shown). IEF was performed in a stepwise fashion (1 h 0– 500 V linear; 5 h 500 V; 5 h 500–3500 V linear; 12 h 3500 V). After IEF, the strips were equilibrated with 100 mM DTT and 2.5% iodacetamide according to the instructions of the manufacturer (BioRad). Tube gels with free ampholytes were prepared as described previously [17]. For SDS-PAGE using the Protean II xi electrophoresis system (BioRad), the IPG strips were placed on top of 1.5 mm 12% polyacrylamide slab gels and overlaid with 0.5% low-melting agarose. The gels were stained with a 400 nM solution of Ruthenium II tris (bathophenanthroline disulfonate) (RuBPS) as described [18]. Fluorography scanning was performed with the FluorImager 595 (GE Healthcare, Fairfield, CT) at a resolution of 100 µm. [19]. All 2D gel data were independently reproduced two times. Gels were warped to a reference gel with the TT900 S2S software (version 2006.0.2389, Nonlinear dynamics, Carlsbad, CA) and evaluated with the Progenesis software PG200 (version 2006, Nonlinear) using the “same spot” algorithm. Spot assignment, background correction, normalization and statistical calculations (analysis of variance, ANOVA) were performed using this software package. The synthetic 2D image of common proteins (Figure 3) was generated with the aid of the ImageMaster 2D Platinum software (Amersham). The web-page accessible via <http://www.meduniwien.ac.at/proteomics/Bilder/common-PG200A/gel.html> was created using the Progenesis software PG200 (version 2006, Nonlinear).

1D-PAGE for subsequent shotgun analysis

Cytoplasmic protein fractions were loaded on 12% polyacrylamid gels, electrophoresis was performed until complete separation of a pre-stained molecular marker (Dual Color, Biorad, Hercules, CA) was visible. Gels were fixed with 50% methanol/10% acetic acid and subsequently silver stained as described below. Gel lanes were cut out of the gel and were digested with trypsin as described below.

MS-compatible silver staining procedure

2D gels were fixed with 50% methanol, washed and sensitized with 0.02% $\text{Na}_2\text{S}_2\text{O}_3$. The gels were stained with 0.1% AgNO_3 ice cold for 20 minutes, rinsed with bi-distilled water and subsequently developed with 3% Na_2CO_3 /0.05% formaldehyde as previously described [20].

Tryptic digest

Protein spots were cut out of the gel, the gel-pieces were de-stained with 15 mM $\text{K}_3\text{Fe}(\text{CN})_6$ /50 mM $\text{Na}_2\text{S}_2\text{O}_3$ and intensively washed with 50% methanol/10% acetic acid. The pH was adjusted with 50 mM NH_4HCO_3 , proteins were reduced with 10 mM DTT/50 mM NH_4HCO_3 for 30 minutes at 56°C and alkylated with 50 mM iodacetamide/50 mM NH_4HCO_3 20 minutes in the dark. Afterwards the gel-pieces were treated with acetonitril and dried in a speedvac. Between each step, the tubes were shaken 5-10 minutes (Eppendorf Thermomixer comfort). Dry gel-spots were treated with trypsin 0.1 mg/ml (Trypsin sequencing grade, Roche Diagnostics, Germany)/50 mM NH_4HCO_3 , in a ratio of 1:8 for 20 minutes on ice, afterwards covered with 50 mM NH_4HCO_3 and were subsequently incubated over night at 37°C. The digested peptides were eluted by adding 50 mM NH_4HCO_3 , the supernatant was transferred into silicon-coated tubes, and this procedure was repeated two times with 5% formic acid/50% acetonitril. Between each elution step the gel-spots were ultrasonicated for 10 minutes. Finally the peptide solution was concentrated in a speedvac to an appropriate volume.

Mass spectrometry analysis

For the identification of 2D spots, peptides were loaded on a Zorbax 300SB-C8 (5 μm , 0.3 mm, 5 mm) column and separated by nanoflow LC (1100 Series LC system, Agilent, Palo Alto, CA) with a Zorbax 300SB-C18 (5 μm , 75 mm, 150 mm) column at a flow rate of 250 nl/min using a gradient from 0.2% formic acid and 3% acetonitrile (ACN) to 0.2% formic acid and 45% ACN over 12 minutes. In case of shotgun analysis, peptides were separated by nano-flow LC (1100 Series LC system, Agilent, Palo Alto, CA) using the HPLC-Chip technology (Agilent) equipped with a 40 nl Zorbax 300SB-C18 trapping column and a 75 μm x 150 mm Zorbax 300SB-C18 separation column at a flow rate of 400 nl/min, using a gradient from 0.2% formic acid and 3% ACN to 0.2% formic acid and 50% ACN over 60 minutes. Peptide identification was accomplished by MS/MS fragmentation analysis with an iontrap mass spectrometer (XCT-Ultra, Agilent) equipped with an orthogonal nanospray ion source. The MS/MS data, including peak list-generation and search engine, were interpreted

by the Spectrum Mill MS Proteomics Workbench software (Version A.03.02, Agilent) allowing for two missed cleavages and searched against the SwissProt Database for human proteins (Version 20071025 containing 17 482 entries or alternatively Version 20080409 containing 19 038 entries) allowing for precursor mass deviation of 1.5 Da, a product mass tolerance of 0.7 Da and a minimum matched peak intensity (%SPI) of 70%. Due to previous chemical modification, carbamidomethylation of cysteine was set as fixed modification. No other modifications were considered here.

Construction of proteome reference maps

The following protein selection algorithm was applied for the generation of the final protein lists. Peptides scores were considered to select appropriate sequence assignments. To assess the reliability of the peptide scores, we performed searches against the corresponding reversed database. 5.9% positive hits were found with peptides scoring >9.0, while 0.21% positive hits were found with peptides scoring >13.0. Only peptides scoring higher than 9.0 were considered for protein identification. Identification details for each protein including all identified peptides, sequence coverage, peptide scores and MS² spectra are fully accessible via PRIDE database (<http://www.ebi.ac.uk/pride/>) [21, 22]. Dendritic cells: PRIDE accessions 3381-3884; HUVEC: PRIDE accessions 3718-3721, fibroblasts: PRIDE accessions 3860-3862; HaCat: PRIDE accessions 3863-3865. Each of the proteome reference maps listed in Tables S1 to S4 were generated by combining the corresponding independent shotgun experiments. These combinations list the sum of all peptides related to single proteins which were collected from all corresponding experiments. Proteins derived from obvious contaminants such as fetal calf serum were deleted. Proteins were selected based on the expression of specific peptides, identified in one protein only. Selection of protein isoforms was performed as described by Zhang *et al.* [23]. In case an unambiguous assignment was not possible due to sequence homologies, the biologically most plausible candidate based on gene expression data was selected.

Identification of common proteins

Final protein lists of dendritic cells and HUVEC, HaCaT and fibroblasts were compared and proteins present in each of these four cell types were determined using our own specially created SQL database (Clinical Proteomics Laboratories at the Medical University of Vienna, CPL/MUW-database, programmed by HW).

Results

Generation of proteome reference maps for human dendritic cells, endothelial cells, fibroblasts and keratinocytes

The use of sub-cellular fractions for protein profiling rather than whole cell lysates has been described previously to improve data reliability [16]. Therefore, the cytoplasmic protein fractions of four different kinds of human cells, namely dendritic cells, umbilical vein endothelial cells (HUVEC), cultured fibroblasts from skin punches and keratinocytes (HaCaT) were isolated and investigated by 2D-PAGE and shotgun analysis.

Immature DCs of four different donors were generated by *in vitro* cultivation and treatment of peripheral blood monocytes with GM-CSF and IL-4. Cytoplasmic proteins were isolated as described [16] and analyzed by shotgun proteomics and 2D-PAGE. The supplementary Table S1 lists all 1 347 distinct proteins assembled from the four independent shotgun experiments. The complete data generated by these experiments is accessible via PRIDE database (<http://www.ebi.ac.uk/pride/>) [21, 22], PRIDE accessions 3381-3384. 923 spots were reproducibly detected in 2D gels, cut out of silver-stained gels and subsequently analyzed by nano-LC-MS/MS. 768 spots were identified successfully, corresponding to 537 different proteins.

HUVEC were analyzed using the methods as described above. The supplementary Table S2 lists all 1 377 distinct proteins identified and assembled from four independent shotgun experiments, accessible via PRIDE accessions 3718-3721. 526 proteins were identified in 2D gels of these cells (Table S2).

Fibroblasts cultured from skin punches were analyzed similarly. The supplementary Table S3 lists all 1 262 distinct proteins identified and assembled from three independent shotgun experiments, accessible via PRIDE accessions 3860-3862. 715 spots were cut out of 2D gels from fibroblast cytoplasmic protein fractions, resulting in the identification of 512 different proteins.

1 460 different proteins were identified in three independent shotgun experiments with HaCaT keratinocyte cytoplasmic fractions (Table S4), accessible via PRIDE accessions 3381-3384. 745 spots were cut out of 2D gels derived from the same protein fractions, resulting in the identification of 539 different proteins.

Identification of common proteins

The analysis of the four reference proteome maps revealed 665 proteins to occur in all of these cell types (Figure 1). We designated these proteins as common proteins. 360 of those were also detectable in 2D gels in at least one of the four investigated cell types. 230 spots were detectable in each of the 2D gels of the four investigated cell types (Figure 2A-D). A synthetic 2D gel was created consisting only of those 230 spots, extracted from the 2D gels of dendritic cells. This fully annotated gel was made publicly available via <http://www.meduniwien.ac.at/proteomics/Bilder/common-PG200A/gel.html>. The identified spots are listed in alphabetical order at <http://www.meduniwien.ac.at/proteomics/Bilder/common-PG200A/summary.html>. Clicking on a spot displays the corresponding 2D gel sections of the four different kinds of cells to enable direct comparison of the spot environments. In addition to the presently applied IPG strips from BioRad we tested Immobiline™ strips from Pharmacia and tube gel-based isoelectric focusing with free ampholytes [17], which resulted in similar spot patterns at corresponding pI ranges including the presently described common spots (data not shown). The common protein pattern may thus prove useful for the fast assignment of commonly expressed proteins in a broad variety of cells.

In Figure 3 we demonstrate the feasibility of this strategy with a 2D gel generated from the cytoplasmic fraction of human colon carcinoma SW40 cells. The main part of the common proteins was clearly assigned. To verify these results, identification of each protein has been confirmed independently by mass-spectrometry as well (data not shown).

Characterization of common proteins

Many common proteins are represented as highly abundant spots on 2D gels, most obvious in case of several chaperons and cytoskeletal proteins. On average, the sum of integrated intensities of the spots comprising the common proteins exceeds more than 50% of the total integrated spot intensities of the analyzed 2D gels. We classified the identified common proteins into nine categories, namely: 1) chaperones 2) cytoskeleton 3) energy metabolism 4) redox regulation 5) nucleic acid processing 6) protein synthesis 7) protein turnover 8) membrane transport and 9) signaling (Table 1).

Discussion

Numerous studies rely on the analysis of proteins derived from clinical samples [1]. Classical assessment of the applicability as well as of the sensitivity of analytical methods is based on the primary analysis of samples of known composition. Such an approach is not conceivable in case of proteome profiling because the nature of the analyzed samples is thus complex that it could not be adequately represented by an artificial mixture. Therefore, alternative strategies are required for quality assessment.

Somatic cells comprise several organelles in common as for example mitochondria, ribosomes or proteasomes. The protein composition of organelles may vary to some extent but certain proteins are essential and must be present in all cell types [24]. In this study we chose a pragmatic approach in order to perform systematic evaluation of these proteins, which has not been realized in this way until now. We compared cells of quite different origin and function and identified their common proteins. Indeed, according to our primary concept, most of them could be clearly related to basic cellular functions. To systematically structure the data, we defined nine different functional categories. Table 1 lists all common proteins including the assignment to functional categories as well as the information whether these proteins were identified in 2D gels. More than 93% of all common proteins were assigned to at least one of these functional categories. The remaining 7% are related to basic cell functions too, but are more heterogeneous regarding potential classifications.

The common proteins can therefore be regarded as a set of internal standard proteins as they are expected to occur in any kind of cell. It is obvious, however, that common proteins may still be expressed at quite different concentrations, depending on cell type and functional state. We analyzed the cytoplasmic fraction of a variety of other human cells by shotgun proteomics as well as by 2D-PAGE. Considering our shotgun experiments, results of considerable quality typically list 1 200 to 1 500 proteins per cell type. Such lists of proteins usually comprise about 95% of the common proteins (data not shown).

In addition to the shotgun data, common proteins were identified on 2D gels. As the protein amounts vary considerably depending on the cell type, some spots were not detected in all 2D gels. Based on the common proteins detectable in all 2D gels, a synthetic spot pattern was generated. Remarkably, the total spot intensity of these common proteins was found to sum up to more than 50% of the total integrated spot intensity of all 2D gels analyzed. This finding suggested that the identification of this spot pattern may facilitate quick and reliable assignment of a large number of protein spots in 2D gels of cytoplasmic fractions of nearly

any kind of human cells. Presuming optimal protein solubilization and separation [16], the common spot pattern was detectable independent of the conditions applied for iso-electric focusing. The feasibility of this approach is demonstrated for human colon carcinoma SW-480 cells in Figure 3. In 2D gels of cytoplasmic fractions of different human cells, we typically detected about 90% of the protein spots classified as common (data not shown). The fully annotated synthetic gel was made publicly available via www.meduniwien.ac.at/proteomics. Clicking on a spot on the synthetic gel provides the spot identification and the local spot environment of the four different cell types including normalized spot volumes. The same information is accessible via clicking proteins from an alphabetic protein list.

As a conclusion, the detection of common proteins, whose existence is biologically evident, can be used in proteomic experiments as positive control. The application of two different proteome profiling methods supported the validity of the protein list which we generated by the comparison of highly differing cell types. The knowledge of identity, spot position and relative intensity of commonly expressed proteins will prove useful for data interpretation within proteome profiling experiments.

Acknowledgments

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Legend to Figures:

Figure 1: Schematic presentation of the number of proteins identified by shotgun and 2D-PAGE. Results obtained from dendritic cells, HUVEC, HaCaT and fibroblasts were compared, the number of proteins shared by two different cells respectively are indicated in the intersection areas. 672 proteins were common to all four cell types. 364 of those were also identified in each of the 2D gels.

Figure 2: Proteome profiling of human dendritic cells (A), HUVEC (B), HaCaT (C) and fibroblasts (D). Corresponding 2D gel sections of the four different cell types are shown. Protein detection was performed by fluorescence staining with RuBPS. Proteins were identified by mass spectrometric analysis of tryptic digests. Annotation: Swiss Prot accession numbers.

Figure 3: Application of a synthetic 2D gel of commonly expressed proteins for the assignment of spot identities. Based on a 2D gel of dendritic cells a synthetic gel was generated including only common protein spots (common). A 2D gel of the cytoplasmic fraction of human colon carcinoma SW-480 cells was warped to the synthetic gel for easy and quick assignment of common proteins (common on SW-480).

Legend to Tables:

Table 1: List of common proteins identified by shotgun analysis. Proteins were classified into nine categories according to their specific function. AccNo, Swiss Prot accession number. 2D, proteins as well identified in 2D gels (X).

Supplementary Tables:

Table S1: Proteome reference map of human dendritic cells. Proteins were identified by shotgun analysis from four independent samples. Proteins are sorted according to protein names and identified by their SwissProt accession numbers. Molecular weight, pI value, the number of distinct peptides identified per protein and the consequent sequence coverage are indicated. Furthermore, protein identifications which contain at least one peptide not identified in any other protein (row: SP; specific peptide) and proteins which were independently identified in 2D gels as well (row: 2D) are marked (X).

Table S2: Proteome reference map of HUVEC. Annotation as in Table S1.

Table S3: Proteome reference map of human fibroblasts. Annotation as in Table S1.

Table S4: Proteome reference map of human HaCaT cells. Annotation as in Table S1.

These lists will be available at <http://www3.interscience.wiley.com/journal/10008330/home>.

References

- [1] Celis, J. E., Gromov, P., *Cancer Cell* 2003, 3, 9-15.
- [2] Nishimura, T., Ogiwara, A., Fujii, K., Kawakami, T., Kawamura, T., Anyouji, H., Kato, H., *Journal of gastroenterology* 2005, 40 Suppl 16, 7-13.
- [3] Stoughton, R. B., Friend, S. H., *Nature reviews* 2005, 4, 345-350.
- [4] Listgarten, J., Emili, A., *Mol Cell Proteomics* 2005, 4, 419-434.
- [5] Zhang, J., Li, J., Liu, X., Xie, H., Zhu, Y., He, F., *BMC Bioinformatics* 2008, 9, 29.
- [6] Shen, Y., Jacobs, J. M., Camp, D. G., 2nd, Fang, R., Moore, R. J., Smith, R. D., Xiao, W., Davis, R. W., Tompkins, R. G., *Analytical chemistry* 2004, 76, 1134-1144.
- [7] Hanash, S. M., *Electrophoresis* 2000, 21, 1202-1209.
- [8] Link, A. J., Eng, J., Schieltz, D. M., Carmack, E., Mize, G. J., Morris, D. R., Garvik, B. M., Yates, J. R., 3rd, *Nat Biotechnol* 1999, 17, 676-682.
- [9] Celis, J. E., Ostergaard, M., Jensen, N. A., Gromova, I., Rasmussen, H. H., Gromov, P., *FEBS letters* 1998, 430, 64-72.
- [10] Gerner, C., Vejda, S., Gelbmann, D., Bayer, E., Gotzmann, J., Schulte-Hermann, R., Mikulits, W., *Mol Cell Proteomics* 2002, 1, 528-537.
- [11] Chen, E. I., Hewel, J., Felding-Habermann, B., Yates, J. R., 3rd, *Mol Cell Proteomics* 2006, 5, 53-56.
- [12] Pickl, W. F., Majdic, O., Kohl, P., Stockl, J., Riedl, E., Scheinecker, C., Bello-Fernandez, C., Knapp, W., *J Immunol* 1996, 157, 3850-3859.
- [13] Jaffe, E. A., Nachman, R. L., Becker, C. G., Minick, C. R., *J Clin Invest* 1973, 52, 2745-2756.
- [14] Frazier, M. L., Pathak, S., Wang, Z. W., Cleary, K., Singletary, S. E., Olive, M., Mackay, B., Steck, P. A., Levin, B., *Pancreas* 1990, 5, 8-16.
- [15] Boukamp, P., Petrussevska, R. T., Breitkreutz, D., Hornung, J., Markham, A., Fusenig, N. E., *J Cell Biol* 1988, 106, 761-771.
- [16] Gundacker, N., Bayer, E., Traxler, E., Zwickl, H., Kubicek, M., Stockl, J., Gerner, C., *Electrophoresis* 2006, 27, 2712-2721.
- [17] Gerner, C., Frohwein, U., Gotzmann, J., Bayer, E., Gelbmann, D., Bursch, W., Schulte-Hermann, R., *J Biol Chem* 2000, 275, 39018-39026.
- [18] Rabilloud, T., Strub, J. M., Luche, S., van Dorsselaer, A., Lunardi, J., *Proteomics* 2001, 1, 699-704.
- [19] Zwickl, H., Traxler, E., Staettner, S., Parzefall, W., Grasl-Kraupp, B., Karner, J., Schulte-Hermann, R., Gerner, C., *Electrophoresis* 2005, 26, 2779-2785.
- [20] Mortz, E., Krogh, T. N., Vorum, H., Gorg, A., *Proteomics* 2001, 1, 1359-1363.
- [21] Jones, P., Cote, R. G., Cho, S. Y., Klie, S., Martens, L., Quinn, A. F., Thorncroft, D., Hermjakob, H., *Nucleic Acids Res* 2008, 36, D878-883.
- [22] Jones, P., Cote, R. G., Martens, L., Quinn, A. F., Taylor, C. F., Derache, W., Hermjakob, H., Apweiler, R., *Nucleic Acids Res* 2006, 34, D659-663.
- [23] Zhang, B., Chambers, M. C., Tabb, D. L., *J Proteome Res* 2007, 6, 3549-3557.
- [24] Gerner, C., Holzmann, K., Grimm, R., Sauermann, G., *J Cell Biochem* 1998, 71, 363-374.

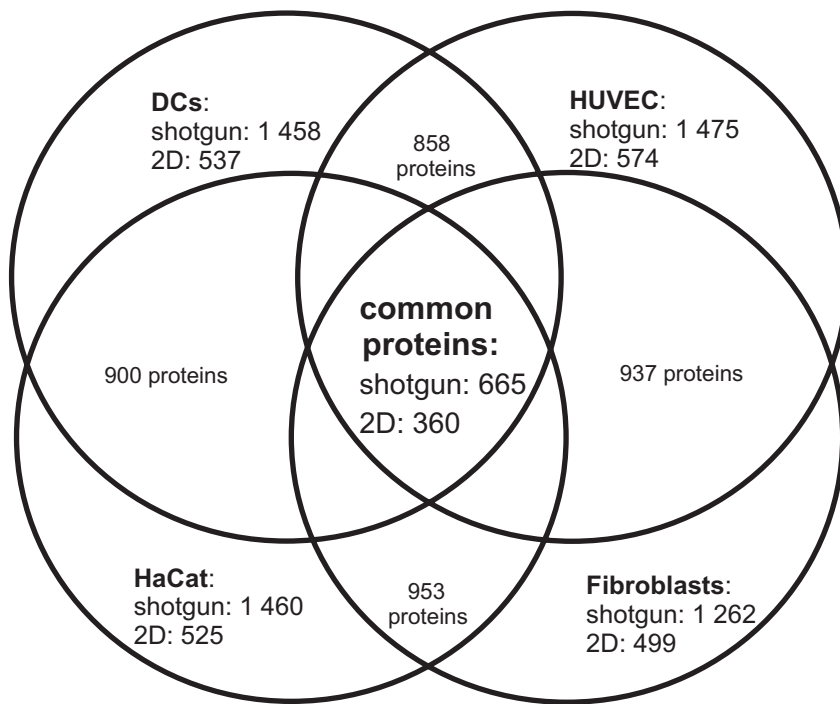


Figure 1

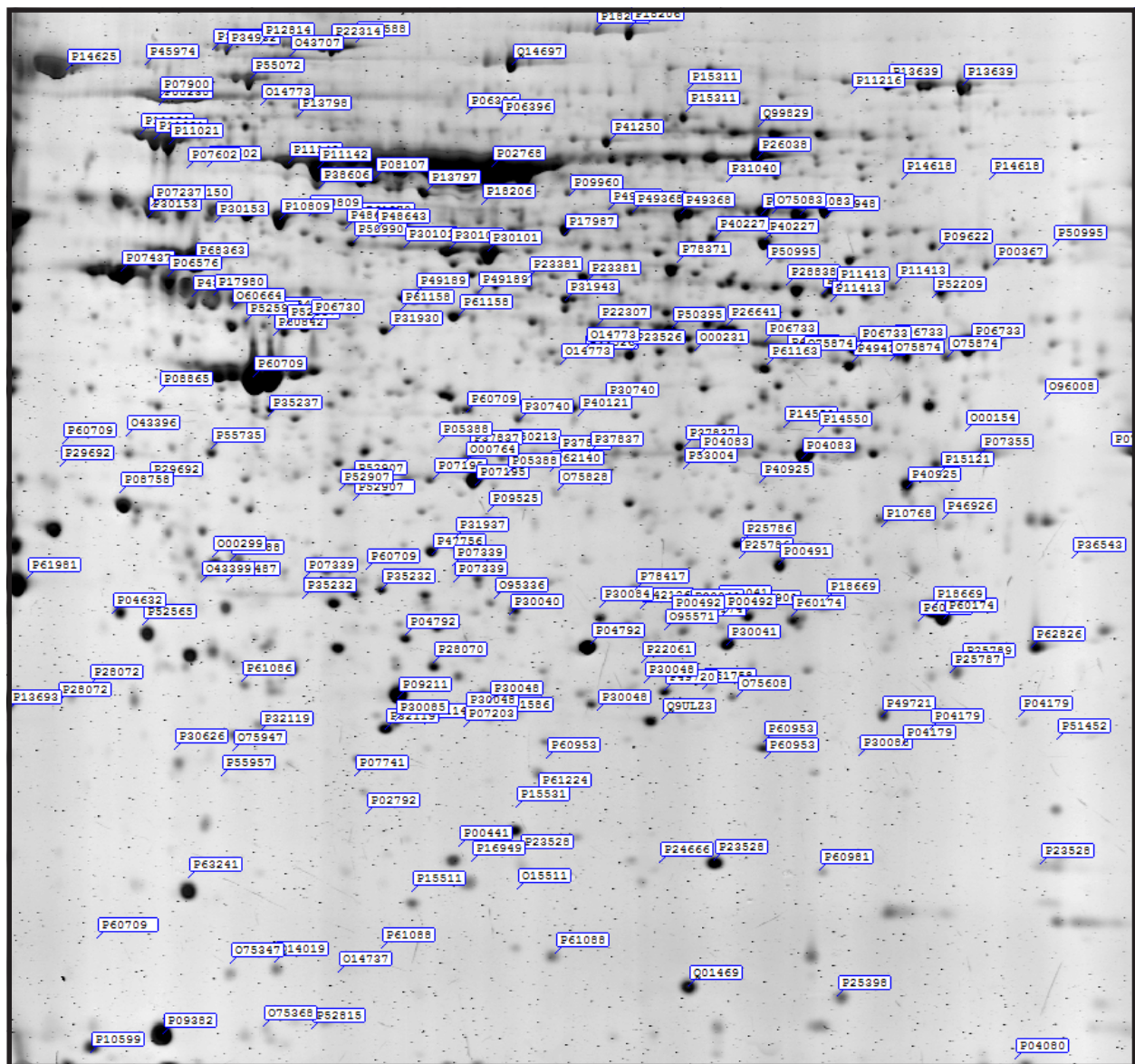
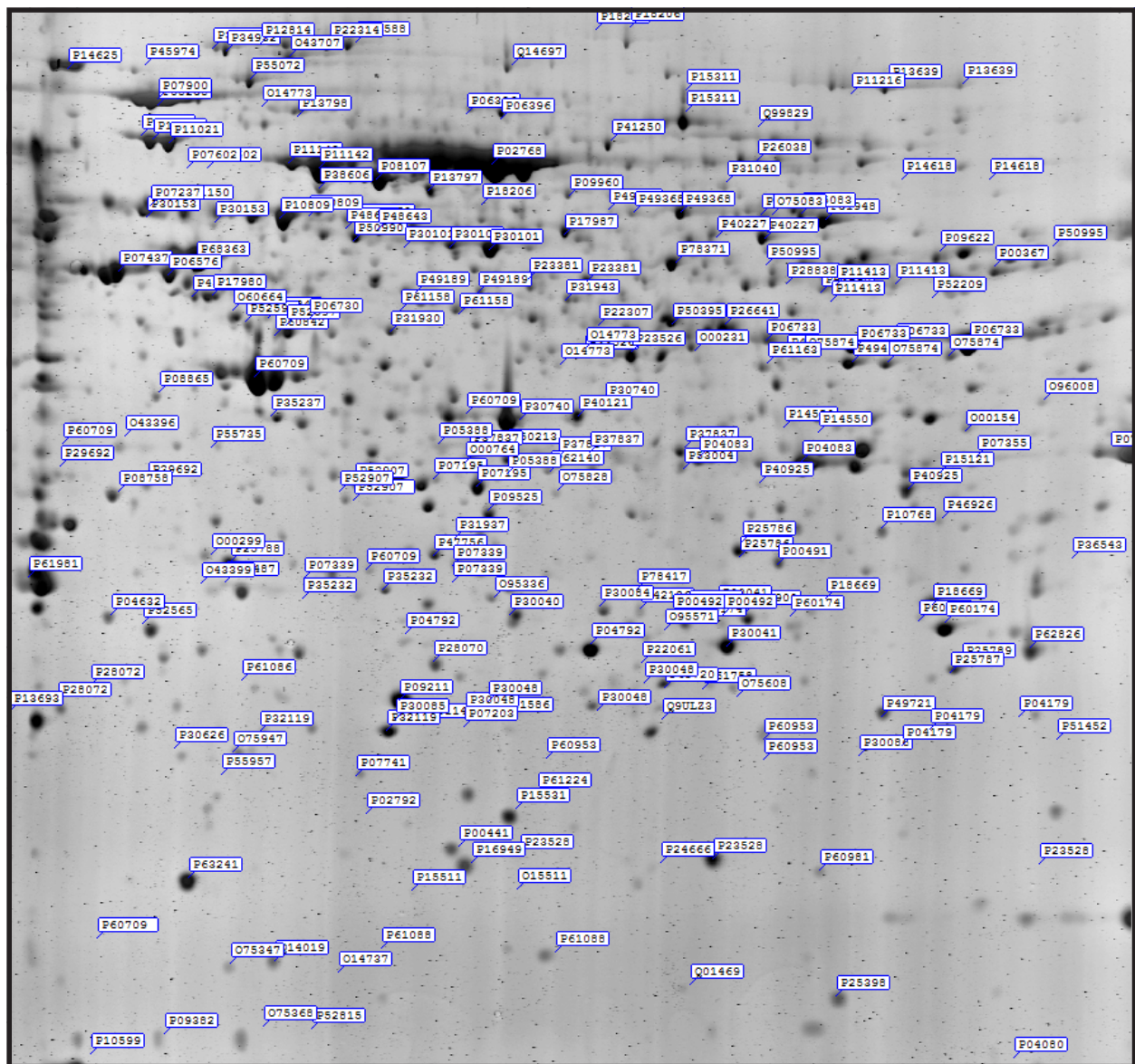


Figure 2b



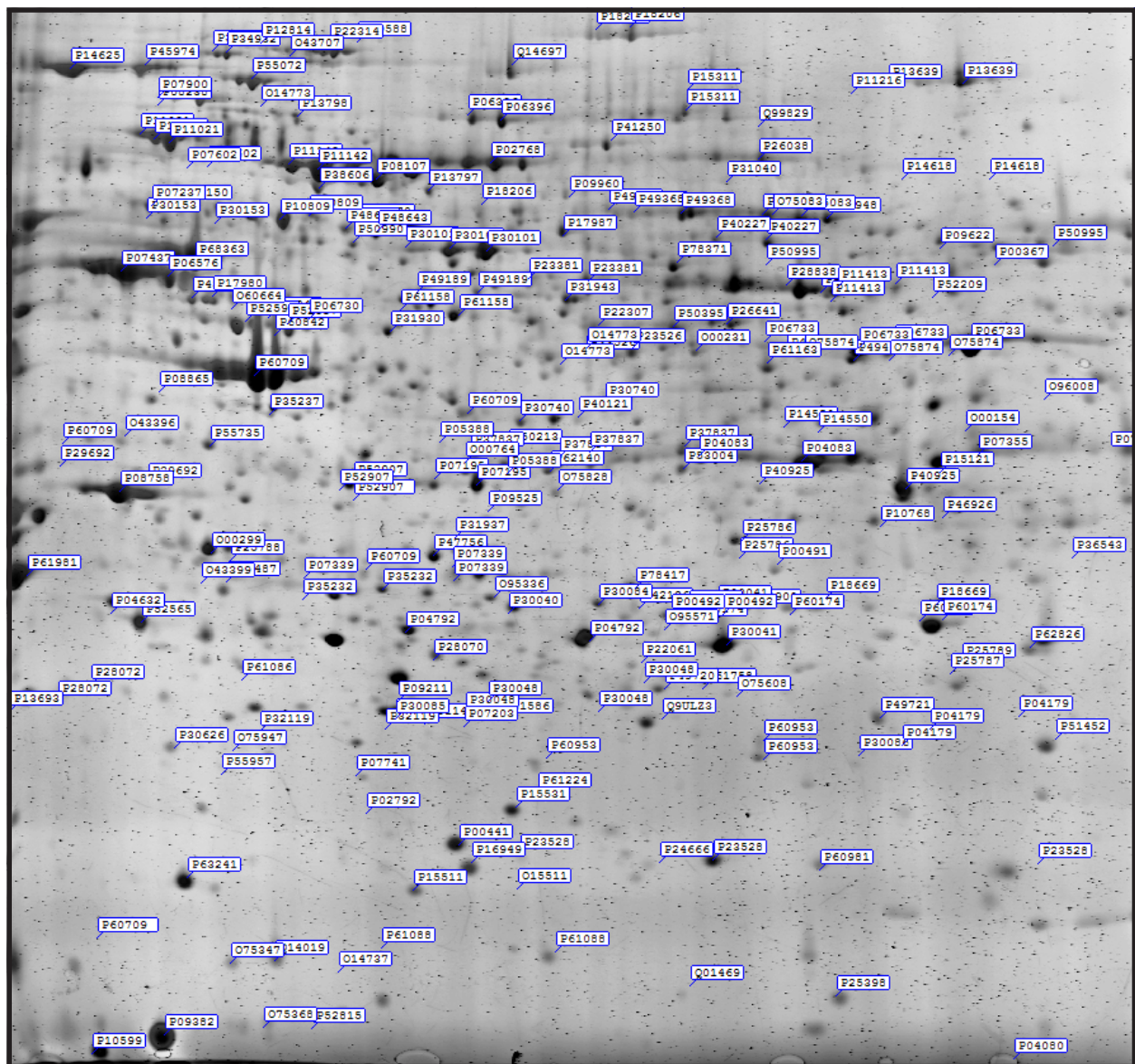


Figure 2d

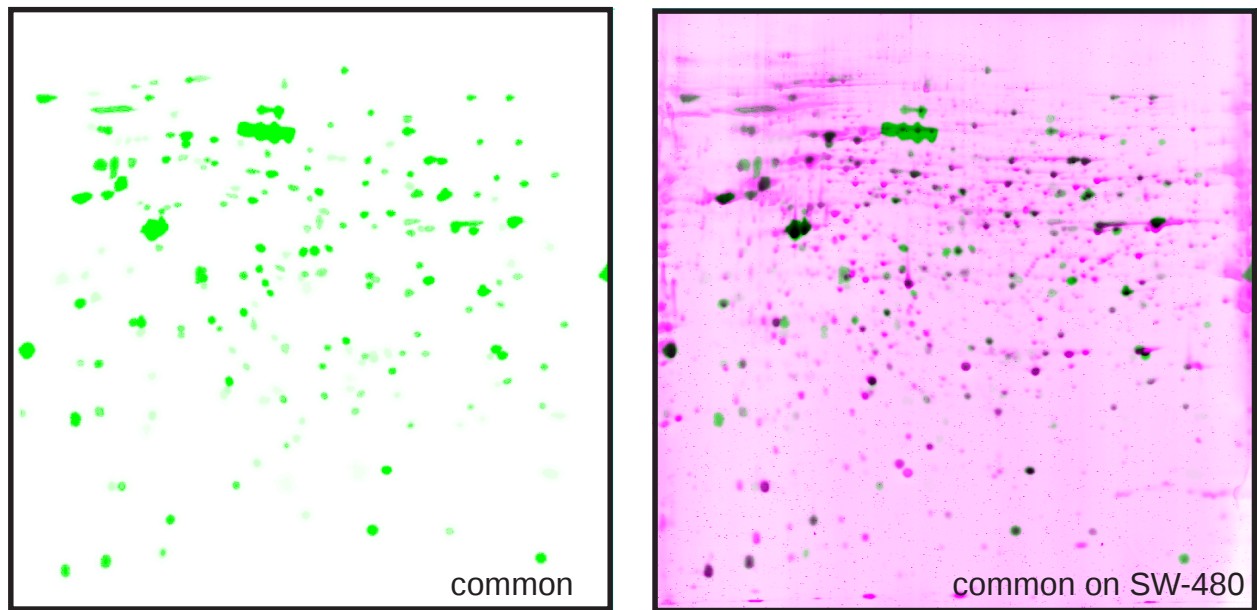


Figure 3

AccNr	Protein	Chaperone	Energy metabolism	Membrane Transport	Nucleic acid processing	Protein turnover	Signal transduction	Cytoskeleton	Protein synthesis	Redox regulation	2D
P61604	10 kDa heat shock protein, mitochondrial (Hsp10) (10 kDa chaperon	X	-	-	-	-	-	-	-	-	-
P42704	130 kDa leucine-rich protein (LRP 130) (GP130) (Leucine-rich PPR	-	X	-	-	-	-	-	-	-	X
Q9NRX4	14 kDa phosphohistidine phosphatase (EC 3.1.3,-) (Phosphohistidin	-	-	-	-	-	X	-	-	-	-
P31946	14-3-3 protein beta/alpha (Protein kinase C inhibitor protein 1) (KCIF	-	-	X	-	-	-	-	-	-	-
P62258	14-3-3 protein epsilon (14-3-3E)	-	-	X	-	-	-	-	-	-	-
Q04917	14-3-3 protein eta (Protein AS1)	-	-	X	-	-	-	-	-	-	-
P61981	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1,	-	-	X	-	-	-	-	-	-	X
P27348	14-3-3 protein theta (14-3-3 protein tau) (14-3-3 protein T-cell) (HS1	-	-	X	-	-	-	-	-	-	-
P63104	14-3-3 protein zeta/delta (Protein kinase C inhibitor protein 1) (KCIP	-	-	X	-	-	-	-	-	-	X
Q9Y4L1	150 kDa oxygen-regulated protein precursor (Orp150) (Hypoxia up-r	-	-	-	-	-	-	-	-	X	X
P17980	26S protease regulatory subunit 6A (TAT-binding protein 1) (TBP-1)	-	-	-	-	X	-	-	-	-	X
P43686	26S protease regulatory subunit 6B (MIP224) (MB67-interacting pro	-	-	-	-	X	-	-	-	-	X
P62195	26S protease regulatory subunit 8 (Proteasome subunit p45) (p45/S	-	-	-	-	X	-	-	-	-	X
P62333	26S protease regulatory subunit S10B (Proteasome subunit p42) (P	-	-	-	-	X	-	-	-	-	X
O00231	26S proteasome non-ATPase regulatory subunit 11 (26S proteasom	-	-	-	-	X	-	-	-	-	X
O00232	26S proteasome non-ATPase regulatory subunit 12 (26S proteasom	-	-	-	-	X	-	-	-	-	-
Q9UNM6	26S proteasome non-ATPase regulatory subunit 13 (26S proteasom	-	-	-	-	X	-	-	-	-	X
O00487	26S proteasome non-ATPase regulatory subunit 14 (26S proteasom	-	-	-	-	X	-	-	-	-	X
Q13200	26S proteasome non-ATPase regulatory subunit 2 (26S proteasome	-	-	-	-	X	-	-	-	-	-
P51665	26S proteasome non-ATPase regulatory subunit 7 (26S proteasome	-	-	-	-	X	-	-	-	-	X
P48556	26S proteasome non-ATPase regulatory subunit 8 (26S proteasome	-	-	-	-	X	-	-	-	-	X
P42126	3,2-trans-enoyl-CoA isomerase, mitochondrial precursor (EC 5.3.3.8	-	X	-	-	-	-	-	-	-	X
P52815	39S ribosomal protein L12, mitochondrial precursor (L12mt) (MRP-L	-	X	-	-	-	-	-	-	-	X
Q96EL3	39S ribosomal protein L53, mitochondrial precursor (L53mt) (MRP-L	-	X	-	-	-	-	-	-	-	-
Q99714	3-hydroxyacyl-CoA dehydrogenase type II (EC 1.1.1.35) (Type II HA	-	X	-	-	-	-	-	-	-	X
P31937	3-hydroxyisobutyrate dehydrogenase, mitochondrial precursor (EC 1	-	X	-	-	-	-	-	-	-	X
P09110	3-ketoacyl-CoA thiolase, peroxisomal precursor (EC 2.3.1.16) (Beta-	-	X	-	-	-	-	-	-	-	-
P46783	40S ribosomal protein S10	-	-	-	-	-	-	-	X	-	-
P62280	40S ribosomal protein S11 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P25398	40S ribosomal protein S12 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	X
P62277	40S ribosomal protein S13	-	-	-	-	-	-	-	X	-	-
P62263	40S ribosomal protein S14	-	-	-	-	-	-	-	X	-	-
P62244	40S ribosomal protein S15a	-	-	-	-	-	-	-	X	-	-
P62249	40S ribosomal protein S16	-	-	-	-	-	-	-	X	-	-
P08708	40S ribosomal protein S17 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P62269	40S ribosomal protein S18 (Ke-3) (Ke3)	-	-	-	-	-	-	-	X	-	-
P39019	40S ribosomal protein S19	-	-	-	-	-	-	-	X	-	-
P15880	40S ribosomal protein S2 (S4) (LLRep3 protein) - Homo sapiens (H	-	-	-	-	-	-	-	X	-	-
P60866	40S ribosomal protein S20 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P63220	40S ribosomal protein S21	-	-	-	-	-	-	-	X	-	-
P62266	40S ribosomal protein S23 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P62847	40S ribosomal protein S24 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P62851	40S ribosomal protein S25	-	-	-	-	-	-	-	X	-	-
P62854	40S ribosomal protein S26	-	-	-	-	-	-	-	X	-	-
P62857	40S ribosomal protein S28	-	-	-	-	-	-	-	X	-	-
P23396	40S ribosomal protein S3 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P61247	40S ribosomal protein S3a - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P62701	40S ribosomal protein S4, X isoform (Single copy abundant mRNA f	-	-	-	-	-	-	-	X	-	-
P46782	40S ribosomal protein S5	-	-	-	-	-	-	-	X	-	-
P62753	40S ribosomal protein S6 (Phosphoprotein NP33)	-	-	-	-	-	-	-	X	-	-
P62081	40S ribosomal protein S7	-	-	-	-	-	-	-	X	-	-
P62241	40S ribosomal protein S8	-	-	-	-	-	-	-	X	-	-
P46781	40S ribosomal protein S9 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P08865	40S ribosomal protein SA (p40) (34/67 kDa laminin receptor) (Colon	-	-	-	-	-	-	-	X	-	X
P49189	4-trimethylaminobutyraldehyde dehydrogenase (EC 1.2.1.47) (TMAI	-	-	-	-	-	-	-	-	X	X

P10809	60 kDa heat shock protein, mitochondrial precursor (Hsp60) (60 kDa	X	X	-	-	-	-	-	-	-	X
P10155	60 kDa SS-A/Ro ribonucleoprotein (60 kDa Ro protein) (60 kDa ribo	-	-	-	X	-	-	-	-	-	-
P05388	60S acidic ribosomal protein P0 (L10E)	-	-	-	-	-	-	-	X	-	X
P05387	60S acidic ribosomal protein P2	-	-	-	-	-	-	-	X	-	-
P27635	60S ribosomal protein L10 (QM protein) (Tumor suppressor QM) (L	-	-	-	-	-	-	-	X	-	-
P62913	60S ribosomal protein L11 (CLL-associated antigen KW-12)	-	-	-	-	-	-	-	X	-	-
P30050	60S ribosomal protein L12	-	-	-	-	-	-	-	X	-	-
P26373	60S ribosomal protein L13 (Breast basic conserved protein 1) - Horr	-	-	-	-	-	-	-	X	-	-
P50914	60S ribosomal protein L14 (CAG-ISL 7) - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P61313	60S ribosomal protein L15 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P18621	60S ribosomal protein L17 (L23) - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
Q07020	60S ribosomal protein L18	-	-	-	-	-	-	-	X	-	-
Q02543	60S ribosomal protein L18a - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P46778	60S ribosomal protein L21 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P35268	60S ribosomal protein L22 (Epstein-Barr virus small RNA-associated	-	-	-	-	-	-	-	X	-	-
P62829	60S ribosomal protein L23 (Ribosomal protein L17)	-	-	-	-	-	-	-	X	-	-
P62750	60S ribosomal protein L23a - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P83731	60S ribosomal protein L24 (Ribosomal protein L30) - Homo sapiens	-	-	-	-	-	-	-	X	-	-
P61353	60S ribosomal protein L27 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P46776	60S ribosomal protein L27a - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P47914	60S ribosomal protein L29 (Cell surface heparin-binding protein HIP	-	-	-	-	-	-	-	X	-	-
P62888	60S ribosomal protein L30	-	-	-	-	-	-	-	X	-	-
P42766	60S ribosomal protein L35 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P61513	60S ribosomal protein L37a - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P63173	60S ribosomal protein L38 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
Q02878	60S ribosomal protein L6 (TAX-responsive enhancer element-bindin	-	-	-	-	-	-	-	X	-	-
P18124	60S ribosomal protein L7 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P62424	60S ribosomal protein L7a (Surfeit locus protein 3) (PLA-X polypepti	-	-	-	-	-	-	-	X	-	-
P62917	60S ribosomal protein L8 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P32969	60S ribosomal protein L9 - Homo sapiens (Human)	-	-	-	-	-	-	-	X	-	-
P52209	6-phosphogluconate dehydrogenase, decarboxylating (EC 1,1,1,44)	-	-	-	-	-	-	-	-	X	X
O95336	6-phosphogluconolactonase (EC 3,1,1,31) (6PGL)	-	X	-	-	-	-	-	-	-	X
P11021	78 kDa glucose-regulated protein precursor (GRP 78) (Immunoglobuli	X	-	-	-	-	-	-	-	-	X
Q96IU4	Abhydrolase domain-containing protein 14B (CCG1-interacting facto	-	-	-	-	-	-	-	-	-	X
P24752	Acetyl-CoA acetyltransferase, mitochondrial precursor (EC 2,3,1,9) (	-	X	-	-	-	-	-	-	-	X
Q13510	Acid ceramidase precursor (EC 3,5,1,23) (Acylsphingosine deacylas	-	-	X	-	-	-	-	-	-	X
Q92688	Acidic leucine-rich nuclear phosphoprotein 32 family member B (PH	-	-	-	X	-	-	-	-	-	-
Q99798	Aconitate hydratase, mitochondrial precursor (EC 4,2,1,3) (Citrate h	-	X	-	-	-	-	-	-	-	X
P60709	Actin, cytoplasmic 1 (Beta-actin)	-	-	-	-	-	-	X	-	-	X
P61160	Actin-like protein 2 (Actin-related protein 2)	-	-	-	-	-	-	X	-	-	X
P61158	Actin-like protein 3 (Actin-related protein 3)	-	-	-	-	-	-	X	-	-	X
O15143	Actin-related protein 2/3 complex subunit 1B (ARP2/3 complex 41 kD	-	-	-	-	-	-	X	-	-	-
O15144	Actin-related protein 2/3 complex subunit 2 (ARP2/3 complex 34 kD	-	-	-	-	-	-	X	-	-	X
O15145	Actin-related protein 2/3 complex subunit 3 (ARP2/3 complex 21 kD	-	-	-	-	-	-	X	-	-	-
P59998	Actin-related protein 2/3 complex subunit 4 (ARP2/3 complex 20 kD	-	-	-	-	-	-	X	-	-	-
O15511	Actin-related protein 2/3 complex subunit 5 (ARP2/3 complex 16 kD	-	-	-	-	-	-	X	-	-	X
P53999	Activated RNA polymerase II transcriptional coactivator p15 (SUB1 I	-	-	-	X	-	-	-	-	-	-
O95433	Activator of 90 kDa heat shock protein ATPase homolog 1 (AHA1) (I	X	-	-	-	-	-	-	-	-	X
P07108	Acyl-CoA-binding protein (ACBP) (Diazepam-binding inhibitor) (DBI)	-	X	-	-	-	-	-	-	-	-
P07311	Acylphosphatase-1 (EC 3,6,1,7) (Acylphosphate phosphohydrolase	-	-	-	-	-	-	-	-	-	-
O75608	Acyl-protein thioesterase 1 (EC 3,1,2,-) (Lysophospholipase I)	-	-	-	-	-	-	-	-	-	X
O95372	Acyl-protein thioesterase 2 (EC 3,1,2,-) (Lysophospholipase II) (LPL	-	-	-	-	-	-	-	-	-	X
P07741	Adenine phosphoribosyltransferase (EC 2,4,2,7) (APRT)	-	-	-	X	-	-	-	-	-	X
P55263	Adenosine kinase (EC 2,7,1,20) (AK) (Adenosine 5'-phosphotransfe	-	-	-	X	-	-	-	-	-	X
P23526	Adenosylhomocysteinase (EC 3,3,1,1) (S-adenosyl-L-homocysteine	-	-	-	X	-	-	-	-	-	X
P54819	Adenylate kinase isoenzyme 2, mitochondrial (EC 2,7,4,3) (ATP-AM	-	-	-	X	-	-	-	-	-	X
Q01518	Adenylyl cyclase-associated protein 1 (CAP 1)	-	-	-	X	-	-	-	-	-	X
P05141	ADP/ATP translocase 2 (Adenine nucleotide translocator 2) (ANT 2)	-	-	-	X	-	-	-	-	-	-
P84077	ADP-ribosylation factor 1	-	-	-	X	-	-	-	-	-	-
P18085	ADP-ribosylation factor 4	-	-	-	X	-	-	-	-	-	-
P84085	ADP-ribosylation factor 5	-	-	-	X	-	-	-	-	-	-
P62330	ADP-ribosylation factor 6 - Homo sapiens (Human)	-	-	-	X	-	-	-	-	-	-
P36405	ADP-ribosylation factor-like protein 3 - Homo sapiens (Human)	-	-	-	X	-	-	-	-	-	-

Q9UUK9	ADP-sugar pyrophosphatase (EC 3,6,1,13) (EC 3,6,1,-) (Nucleoside	-	-	-	X	-	-	-	-	-	X
P49588	Alanyl-tRNA synthetase (EC 6,1,1,7) (Alanine--tRNA ligase) (AlaRS)	-	-	-	-	-	-	-	X	-	X
P14550	Alcohol dehydrogenase [NADP+] (EC 1,1,1,2) (Aldehyde reductase)	-	-	-	-	-	-	-	-	X	X
P15121	Aldose reductase (EC 1,1,1,21) (AR) (Aldehyde reductase)	-	-	-	-	-	-	-	-	X	X
P35221	Alpha-1 catenin (Cadherin-associated protein) (Alpha E-catenin)	-	-	-	-	-	-	X	-	-	-
P12814	Alpha-actinin-1 (Alpha-actinin cytoskeletal isoform) (Non-muscle alp	-	-	-	-	-	-	X	-	-	X
O43707	Alpha-actinin-4 (Non-muscle alpha-actinin 4) (F-actin cross linking p	-	-	-	-	-	-	X	-	-	X
P61163	Alpha-centractin (Centractin) (Centrosome-associated actin homolo	-	-	-	-	-	-	X	-	-	X
P06733	Alpha-enolase (EC 4,2,1,11) (2-phospho-D-glycerate hydro-lyase) (f	-	X	-	-	-	-	-	-	-	X
P04083	Annexin A1 (Annexin I) (Lipocortin I) (Calpactin II) (Chromobindin-9)	-	-	X	-	-	X	-	-	-	X
P50995	Annexin A11 (Annexin XI) (Calcyclin-associated annexin 50) (CAP-5	-	-	X	-	-	-	-	-	-	X
P07355	Annexin A2 (Annexin II) (Lipocortin II) (Calpactin I heavy chain) (Chr	-	-	X	-	-	-	-	-	-	X
P09525	Annexin A4 (Annexin IV) (Lipocortin IV) (Endonexin	-	-	X	-	-	-	-	-	-	X
P08758	Annexin A5 (Annexin V) (Lipocortin V) (Endonexin II) (Calphobindin	-	-	X	-	-	-	-	-	-	X
P20073	Annexin A7 (Annexin VII) (Synexin)	-	-	X	-	-	-	-	-	-	X
Q10567	AP-1 complex subunit beta-1 (Adapter-related protein complex 1 bet	-	-	-	-	-	-	-	-	-	-
Q9ULZ3	Apoptosis-associated speck-like protein containing a CARD (hASC)	-	-	-	-	-	X	-	-	-	X
P55145	ARMET protein precursor (Arginine-rich protein) - Homo sapiens (H	-	-	-	-	-	-	-	-	-	-
O43681	Arsenical pump-driving ATPase (EC 3,6,3,16) (Arsenite-translocatin	-	-	X	-	-	-	-	-	-	X
P00505	Aspartate aminotransferase, mitochondrial precursor (EC 2,6,1,1) (T	-	X	-	-	-	-	-	-	-	-
Q15121	Astrocytic phosphoprotein PEA-15 (Phosphoprotein enriched in diat	-	-	-	-	-	X	-	-	-	X
P25705	ATP synthase alpha chain, mitochondrial precursor (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	X
P24539	ATP synthase B chain, mitochondrial precursor (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	-
P06576	ATP synthase beta chain, mitochondrial precursor (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	X
O75947	ATP synthase D chain, mitochondrial (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	X
P30049	ATP synthase delta chain, mitochondrial precursor (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	X
P56385	ATP synthase e chain, mitochondrial (EC 3,6,3,14) - Homo sapiens	-	X	-	-	-	-	-	-	-	-
P56134	ATP synthase f chain, mitochondrial (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	-
P36542	ATP synthase gamma chain, mitochondrial precursor (EC 3,6,3,14)	-	X	-	-	-	-	-	-	-	-
P48047	ATP synthase O subunit, mitochondrial precursor (EC 3,6,3,14) (Oli	-	X	-	-	-	-	-	-	-	-
O75964	ATP synthase subunit g, mitochondrial (EC 3,6,3,14) (ATPase subu	-	X	-	-	-	-	-	-	-	-
P53396	ATP-citrate synthase (EC 2,3,3,8) (ATP-citrate (pro-S-)-lyase) (Citra	-	X	-	-	-	-	-	-	-	-
P12956	ATP-dependent DNA helicase 2 subunit 1 (EC 3,6,1,-) (ATP-depend	-	-	-	X	-	-	-	-	-	X
P13010	ATP-dependent DNA helicase 2 subunit 2 (EC 3,6,1,-) (ATP-depend	-	-	-	X	-	-	-	-	-	-
O00571	ATP-dependent RNA helicase DDX3X (EC 3,6,1,-) (DEAD box prote	-	-	-	X	-	-	-	-	-	X
O75531	Barrier-to-autointegration factor (Breakpoint cluster region protein 1)	-	-	-	X	-	-	-	-	-	-
P61769	Beta-2-microglobulin precursor [Contains: Beta-2-microglobulin vari	-	-	X	-	-	-	-	-	-	X
P07686	Beta-hexosaminidase beta chain precursor (EC 3,2,1,52) (N-acetyl-l	-	-	-	-	-	-	-	-	-	X
P55957	BH3 interacting domain death agonist (BID)	-	-	-	-	-	X	-	-	-	X
P31939	Bifunctional purine biosynthesis protein PURH [Includes: Phosphoril	-	-	-	X	-	-	-	-	-	X
P53004	Biliverdin reductase A precursor (EC 1,3,1,24) (Biliverdin-IX alpha-r	-	-	-	-	-	-	-	-	X	X
P78537	Biogenesis of lysosome-related organelles complex-1 subunit 1 (BL	-	-	-	-	X	-	-	-	-	-
P50583	Bis(5*-nucleosyl)-tetrphosphatase [asymmetrical] (EC 3,6,1,17) (Di	-	-	-	-	-	X	-	-	-	-
Q9H3K6	BolA-like protein 2	-	-	-	-	-	-	-	-	-	X
P11586	C-1-tetrahydrofolate synthase, cytoplasmic (C1-THF synthase) [Incl	-	X	-	-	-	-	-	-	-	-
P49593	Ca(2+)/calmodulin-dependent protein kinase phosphatase (EC 3,1,3	-	-	-	-	-	X	-	-	-	-
Q99653	Calcium-binding protein p22 (Calcium-binding protein CHP) (Calcine	-	-	X	-	-	-	-	-	-	-
P06703	Calcyclin (Prolactin receptor-associated protein) (PRA) (Growth fact	-	-	-	-	-	X	-	-	-	X
Q9HB71	Calcyclin-binding protein (CacyBP) (hCacyBP) (Siah-interacting prot	-	-	-	-	X	-	-	-	-	-
P31949	Calgizzarin (S100 calcium-binding protein A11) (S100C protein) (ML	-	-	-	-	-	X	-	-	-	-
P62158	Calmodulin (CaM)	-	-	-	-	-	X	-	-	-	-
P27824	Calnexin precursor (Major histocompatibility complex class I antigen	-	-	X	-	-	-	-	-	-	-
P60903	Calpactin I light chain (S100 calcium-binding protein A10) (p10 prote	-	-	X	-	-	-	-	-	-	X
P04632	Calpain small subunit 1 (CSS1) (Calcium-dependent protease small	-	-	-	-	X	-	-	-	-	X
P07384	Calpain-1 catalytic subunit (EC 3,4,22,52) (Calpain-1 large subunit)	-	-	-	-	X	-	-	-	-	-
P17655	Calpain-2 catalytic subunit precursor (EC 3,4,22,53) (Calpain-2 large	-	-	-	-	X	-	-	-	-	-
Q99439	Calponin-2 (Calponin H2, smooth muscle) (Neutral calponin)	-	-	-	-	-	-	X	-	-	X
P27797	Calreticulin precursor (CRP55) (Calregulin) (HACBP) (ERp60) (grp6	X	-	-	-	-	-	-	-	-	-
P16152	Carbonyl reductase [NADPH] 1 (EC 1,1,1,184) (NADPH-dependent	-	-	-	-	-	-	-	-	X	X
P42574	Caspase-3 precursor (EC 3,4,22,-) (CASP-3) (Apopain) (Cysteine pr	-	-	-	-	X	-	-	-	-	X
P21964	Catechol O-methyltransferase (EC 2,1,1,6)	-	-	X	-	-	-	-	-	-	X
P07858	Cathepsin B precursor (EC 3,4,22,1) (Cathepsin B1) (APP secretase	-	-	-	-	X	-	-	-	-	X
P07339	Cathepsin D precursor (EC 3,4,23,5) [Contains: Cathepsin D light ch	-	-	-	-	X	-	-	-	-	X

P16070	CD44 antigen precursor (Phagocytic glycoprotein I) (PGP-1) (HUTC	-	-	X	-	-	-	-	-	-	-
P13987	CD59 glycoprotein precursor (Membrane attack complex inhibition f	-	-	X	-	-	-	-	-	-	-
P60953	Cell division control protein 42 homolog precursor (G25K GTP-bindin	-	-	-	-	-	X	-	-	-	X
P62633	Cellular nucleic acid-binding protein (CNBP) (Zinc finger protein 9) -	-	-	-	X	-	-	-	-	-	-
O00299	Chloride intracellular channel protein 1 (Nuclear chloride ion channe	-	-	-	-	-	X	-	-	-	X
Q13185	Chromobox protein homolog 3 (Heterochromatin protein 1 homolog	-	-	-	X	-	-	-	-	-	X
O75390	Citrate synthase, mitochondrial precursor (EC 2,3,3,1)	-	X	-	-	-	-	-	-	-	-
Q00610	Clathrin heavy chain 1 (CLH-17)	-	-	-	-	-	-	X	-	-	-
P53675	Clathrin heavy chain 2 (CLH-22)	-	-	-	-	-	-	X	-	-	-
Q99417	C-Myc-binding protein (Associate of Myc 1) (AMY-1)	-	-	-	-	-	X	-	-	-	-
O43598	c-Myc-responsive protein Rcl	-	-	-	-	-	X	-	-	-	X
Q14019	Coactosin-like protein	-	-	-	-	-	-	X	-	-	X
P53618	Coatomer subunit beta (Beta-coat protein) (Beta-COP)	-	-	X	-	-	-	-	-	-	-
O14579	Coatomer subunit epsilon (Epsilon-coat protein) (Epsilon-COP)	-	-	X	-	-	-	-	-	-	X
Q9Y678	Coatomer subunit gamma (Gamma-coat protein) (Gamma-COP)	-	-	X	-	-	-	-	-	-	-
P61923	Coatomer subunit zeta-1 (Zeta-1 coat protein) (Zeta-1 COP) - Homo	-	-	X	-	-	-	-	-	-	-
P23528	Cofilin-1 (Cofilin, non-muscle isoform) (18 kDa phosphoprotein) (p18	-	-	-	-	-	-	X	-	-	X
Q9UBI1	COMM domain-containing protein 3 (Bup protein) (PIL protein)	-	-	-	-	-	-	-	-	-	X
Q9BT78	COP9 signalosome complex subunit 4 (Signalosome subunit 4) (SG	-	-	-	-	X	-	-	-	-	X
Q99627	COP9 signalosome complex subunit 8 (Signalosome subunit 8) (SG	-	-	-	-	X	-	-	-	-	X
Q99829	Copine-1 (Copine I)	-	-	X	-	-	-	-	-	-	X
Q86VP6	Cullin-associated NEDD8-dissociated protein 1 (Cullin-associated ar	-	-	-	-	X	-	-	-	-	-
P04080	Cystatin B (Liver thiol proteinase inhibitor) (CPI-B) (Stefin B)	-	-	-	-	-	-	-	-	-	X
P21291	Cysteine and glycine-rich protein 1 (Cysteine-rich protein 1) (CRP1)	-	-	-	-	-	-	-	-	-	X
P49589	Cysteinyl-tRNA synthetase, cytoplasmic (EC 6,1,1,16) (Cysteine--tR	-	-	-	-	-	-	-	X	-	-
O43169	Cytochrome b5 outer mitochondrial membrane isoform precursor	-	X	-	-	-	-	-	-	X	-
P99999	Cytochrome c	-	X	-	-	-	-	-	-	X	-
P20674	Cytochrome c oxidase polypeptide Va, mitochondrial precursor (EC	-	X	-	-	-	-	-	-	X	X
P00403	Cytochrome c oxidase subunit 2 (EC 1,9,3,1) (Cytochrome c oxidase	-	X	-	-	-	-	-	-	-	X
P28838	Cytosol aminopeptidase (EC 3,4,11,1) (Leucine aminopeptidase) (L	-	-	-	-	X	-	-	-	-	X
O00154	Cytosolic acyl coenzyme A thioester hydrolase (EC 3,1,2,2) (Long cl	-	X	-	-	-	-	-	-	-	X
Q96KP4	Cytosolic nonspecific dipeptidase (Glutamate carbo	-	-	-	-	X	-	-	-	-	X
P30046	D-dopachrome decarboxylase (EC 4,1,1,84) (D-dopachrome tautom	-	-	-	-	-	-	-	-	-	X
Q13011	Delta3,5-delta2,4-dienoyl-CoA isomerase, mitochondrial precursor (l	-	X	-	-	-	-	-	-	-	X
P60981	Destrin (Actin-depolymerizing factor) (ADF)	-	-	-	-	-	-	X	-	-	X
Q9NR28	Diablo homolog, mitochondrial precursor (Second mitochondria-deri	-	-	-	-	-	X	-	-	-	-
P09622	Dihydrolipoyl dehydrogenase, mitochondrial precursor (EC 1,8,1,4) (	-	X	-	-	-	-	-	-	-	X
Q16555	Dihydropyrimidinase-related protein 2 (DRP-2) (Collapsin response	-	-	-	-	-	X	-	-	-	X
P53634	Dipeptidyl-peptidase 1 precursor (EC 3,4,14,1) (Dipeptidyl-peptidase	-	-	-	-	X	-	-	-	-	-
P27695	DNA-(apurinic or apyrimidinic site) lyase (EC 4,2,99,18) (AP endonu	-	-	-	X	-	-	-	-	-	-
P04844	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 63 k	X	-	-	-	-	-	-	-	-	-
P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 67 k	X	-	-	-	-	-	-	-	-	-
Q9C005	Dpy-30-like protein - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	-
P51452	Dual specificity protein phosphatase 3 (EC 3,1,3,48) (EC 3,1,3,16) (l	-	-	-	-	-	X	-	-	-	X
Q13561	Dynactin subunit 2 (Dynactin complex 50 kDa subunit) (50 kDa dyne	-	-	-	-	-	-	X	-	-	X
O75935	Dynactin subunit 3 (Dynactin complex subunit 22 kDa subunit) (p22)	-	-	-	-	-	-	X	-	-	X
Q14203	Dynactin-1 (150 kDa dynein-associated polypeptide) (DP-150) (DAF	-	-	-	-	-	-	X	-	-	-
P63167	Dynein light chain 1, cytoplasmic (Dynein light chain LC8-type 1) (8	-	-	-	-	-	-	X	-	-	-
Q9NP97	Dynein light chain 2A, cytoplasmic (Dynein-associated protein Km25	-	-	-	-	-	-	X	-	-	-
Q15075	Early endosome antigen 1 (Endosome-associated protein p162) (Zir	-	-	X	-	-	-	-	-	-	-
Q96C19	EF-hand domain-containing protein 2 (Swiprosin-1)	-	-	-	-	-	X	-	-	-	X
Q9H4M9	EH-domain-containing protein 1 (Testilin) (hPAST1)	-	-	-	-	-	-	-	-	-	X
P13804	Electron transfer flavoprotein alpha-subunit, mitochondrial precursor	-	X	-	-	-	-	-	-	-	X
P38117	Electron transfer flavoprotein beta-subunit (Beta-ETF)	-	X	-	-	-	-	-	-	-	-
P68104	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor 1 A-1)	-	-	-	-	-	-	-	X	-	X
P24534	Elongation factor 1-beta (EF-1-beta)	-	-	-	-	-	-	-	X	-	-
P29692	Elongation factor 1-delta (EF-1-delta) (Antigen NY-CO-4)	-	-	-	-	-	-	-	X	-	X
P26641	Elongation factor 1-gamma (EF-1-gamma) (eEF-1B gamma)	-	-	-	-	-	-	-	X	-	X
P13639	Elongation factor 2 (EF-2)	-	-	-	-	-	-	-	X	-	X
P49411	Elongation factor Tu, mitochondrial precursor (EF-Tu) (P43)	-	-	-	-	-	-	-	X	-	X
P30040	Endoplasmic reticulum protein ERp29 precursor (ERp31) (ERp28)	X	-	-	-	-	-	-	-	-	X
P14625	Endoplasmic precursor (94 kDa glucose-regulated protein) (GRP94)	X	-	-	-	-	-	-	-	-	X
P30084	Enoyl-CoA hydratase, mitochondrial precursor (EC 4,2,1,17) (Short	-	X	-	-	-	-	-	-	-	X

P61916	Epididymal secretory protein E1 precursor (Niemann-Pick disease ty	-	-	X	-	-	-	-	-	-	X
Q96HE7	ERO1-like protein alpha precursor (EC 1,8,4,-) (ERO1-Lalpha) (Oxic	-	X	-	-	-	-	-	-	-	-
P10768	Esterase D (EC 3,1,1,1)	-	-	X	-	-	-	-	-	-	X
O95571	ETHE1 protein, mitochondrial precursor (EC 3,-,-,-) (Ethylmalonic er	-	X	-	-	-	-	-	-	-	X
P60842	Eukaryotic initiation factor 4A-I (EC 3,6,1,-) (ATP-dependent RNA h	-	-	-	-	-	-	-	X	-	X
Q14240	Eukaryotic initiation factor 4A-II (EC 3,6,1,-) (ATP-dependent RNA h	-	-	-	-	-	-	-	X	-	X
O43324	Eukaryotic translation elongation factor 1 epsilon-1 (Multisynthetase	-	-	-	-	-	-	-	X	-	-
P41567	Eukaryotic translation initiation factor 1 (eIF1) (Protein translation fa	-	-	-	-	-	-	-	X	-	X
P05198	Eukaryotic translation initiation factor 2 subunit 1 (Eukaryotic transla	-	-	-	-	-	-	-	X	-	X
O75822	Eukaryotic translation initiation factor 3 subunit 1 (eIF-3 alpha) (eIF3	-	-	-	-	-	-	-	X	-	-
Q14152	Eukaryotic translation initiation factor 3 subunit 10 (eIF-3 theta) (eIF	-	-	-	-	-	-	-	X	-	-
O00303	Eukaryotic translation initiation factor 3 subunit 5 (eIF-3 epsilon) (eIF	-	-	-	-	-	-	-	X	-	X
P55884	Eukaryotic translation initiation factor 3 subunit 9 (eIF-3 eta) (eIF3 p	-	-	-	-	-	-	-	X	-	-
Q04637	Eukaryotic translation initiation factor 4 gamma 1 (eIF-4-gamma 1) (	-	-	-	-	-	-	-	X	-	-
Q15056	Eukaryotic translation initiation factor 4H (eIF-4H) (Williams-Beuren	-	-	-	-	-	-	-	X	-	X
P55010	Eukaryotic translation initiation factor 5 (eIF-5)	-	-	-	-	-	-	-	X	-	X
P63241	Eukaryotic translation initiation factor 5A (eIF-5A) (eIF-4D) (Rev-bin	-	-	-	-	-	-	-	X	-	X
P56537	Eukaryotic translation initiation factor 6 (eIF-6) (B4 integrin interacto	-	-	-	-	-	-	-	X	-	-
P15311	Ezrin (p81) (Cytovillin) (Villin-2)	-	-	-	-	-	-	X	-	-	X
P52907	F-actin capping protein alpha-1 subunit (CapZ alpha-1)	-	-	-	-	-	-	X	-	-	X
P47756	F-actin capping protein beta subunit (CapZ beta),	-	-	-	-	-	-	X	-	-	X
Q92945	Far upstream element-binding protein 2 (FUSE-binding protein 2) (K	-	-	-	X	-	-	-	-	-	X
P14324	Farnesyl pyrophosphate synthetase (FPP synthetase) (FPS) (Farne	-	-	X	-	-	-	-	-	-	-
Q16658	Fascin (Singed-like protein) (55 kDa actin bundling protein) (p55)	-	-	-	-	-	-	X	-	-	X
P49327	Fatty acid synthase (EC 2,3,1,85) [Includes: [Acyl-carrier-protein] S-	-	X	-	-	-	-	-	-	-	-
Q01469	Fatty acid-binding protein, epidermal (E-FABP) (Psoriasis-associated	-	-	X	-	-	-	-	-	-	X
P02792	Ferritin light chain (Ferritin L subunit)	-	-	-	-	-	-	-	-	X	X
P21333	Filamin-A (Alpha-filamin) (Filamin-1) (Endothelial actin-binding prote	-	-	-	-	-	-	X	-	-	X
O75369	Filamin-B (FLN-B) (Beta-filamin) (Actin-binding-like protein) (Thyroid	-	-	-	-	-	-	X	-	-	-
P26885	FK506-binding protein 2 precursor (EC 5,2,1,8) (Peptidyl-prolyl cis-t	X	-	-	-	-	-	-	-	-	-
P30043	Flavin reductase (EC 1,5,1,30) (FR) (NADPH-dependent diaphorase	-	-	-	-	-	-	-	-	X	X
P04075	Fructose-bisphosphate aldolase A (EC 4,1,2,13) (Muscle-type aldol	-	X	-	-	-	-	-	-	-	X
P09972	Fructose-bisphosphate aldolase C (EC 4,1,2,13) (Brain-type aldolas	-	X	-	-	-	-	-	-	-	-
P07954	Fumarate hydratase, mitochondrial precursor (EC 4,2,1,2) (Fumaras	-	X	-	-	-	-	-	-	-	X
Q6P587	Fumarylacetoacetate hydrolase domain-containing protein 1 (EC 3,-	X	-	-	-	-	-	-	-	-	-
P09382	Galectin-1 (Beta-galactoside-binding lectin L-14-I) (Lactose-binding	-	-	-	-	-	X	-	-	-	X
P17931	Galectin-3 (Galactose-specific lectin 3) (Mac-2 antigen) (IgE-binding	-	-	-	-	-	X	-	-	-	-
P06396	Gelsolin precursor (Actin-depolymerizing factor) (ADF) (Brevin) (AGI	-	-	-	-	-	-	X	-	-	X
P60983	Glia maturation factor beta (GMF-beta)	-	-	-	-	-	X	-	-	-	X
P46926	Glucosamine-6-phosphate isomerase (EC 3,5,99,6) (Glucosamine-6	-	X	-	-	-	-	-	-	-	X
P11413	Glucose-6-phosphate 1-dehydrogenase (EC 1,1,1,49) (G6PD)	-	X	-	-	-	-	-	-	-	X
P06744	Glucose-6-phosphate isomerase (EC 5,3,1,9) (GPI) (Phosphoglucos	-	X	-	-	-	-	-	-	-	X
P14314	Glucosidase II beta subunit precursor (Protein kinase C substrate, 6	-	-	-	-	-	X	-	-	-	-
O94925	Glutaminase kidney isoform, mitochondrial precursor (EC 3,5,1,2) (C	-	X	-	-	-	-	-	-	-	X
P07203	Glutathione peroxidase 1 (EC 1,11,1,9) (GSHPx-1) (GPx-1) (Cellula	-	-	-	-	-	-	-	-	X	X
P00390	Glutathione reductase, mitochondrial precursor (EC 1,8,1,7) (GR) (C	-	-	-	-	-	-	-	-	X	-
Q9Y2Q3	Glutathione S-transferase kappa 1 (EC 2,5,1,18) (GST 13-13) (Gluta	-	-	-	-	-	-	-	-	X	-
P09211	Glutathione S-transferase P (EC 2,5,1,18) (GST class-pi) (GSTP1-1	-	-	-	-	-	-	-	-	X	X
P30711	Glutathione S-transferase theta-1 (EC 2,5,1,18) (GST class-theta-1)	-	-	-	-	-	-	-	-	X	-
P78417	Glutathione transferase omega-1 (EC 2,5,1,18) (GSTO 1-1)	-	-	-	-	-	-	-	-	X	X
P04406	Glyceraldehyde-3-phosphate dehydrogenase (EC 1,2,1,12) (GAPDH	-	X	-	-	-	-	-	-	-	X
P43304	Glycerol-3-phosphate dehydrogenase, mitochondrial precursor (EC	-	X	-	-	-	-	-	-	-	X
P11216	Glycogen phosphorylase, brain form (EC 2,4,1,1)	-	X	-	-	-	-	-	-	-	X
P41250	Glycyl-tRNA synthetase (EC 6,1,1,14) (Glycine--tRNA ligase) (GlyR	-	-	-	-	-	-	-	X	-	X
Q9HC38	Glyoxalase domain-containing protein 4 - Homo sapiens (Human)	-	X	-	-	-	-	-	-	-	-
Q9HAV7	GrpE protein homolog 1, mitochondrial precursor (Mt-GrpE#1) (HMC	-	X	-	-	-	-	-	-	-	X
Q9UIJ7	GTP:AMP phosphotransferase mitochondrial (EC 2,7,4,10) (Adenyl	-	X	-	-	-	-	-	-	-	-
P01112	GTPase HRas precursor (Transforming protein p21) (p21ras) (H-Ra	-	-	-	-	-	X	-	-	-	-
P01111	GTPase NRas precursor (Transforming protein N-Ras) - Homo sapi	-	-	-	-	-	X	-	-	-	-
P62826	GTP-binding nuclear protein Ran (GTPase Ran) (Ras-like protein T	-	-	-	X	-	-	-	-	-	X
Q9NR31	GTP-binding protein SAR1a (COPII-associated small GTPase)	-	-	-	X	-	-	-	-	-	X
Q9Y6B6	GTP-binding protein SAR1b (GTBPB)	-	-	-	X	-	-	-	-	-	X
P63244	Guanine nucleotide-binding protein beta subunit 2-like 1 (Guanine n	-	-	-	X	-	-	-	-	-	X

P62873	Guanine nucleotide-binding protein G(I)/G(S)/G(T) beta subunit 1 (T	-	X	-	X	-	-	-	-	-	X
P62879	Guanine nucleotide-binding protein G(I)/G(S)/G(T) beta subunit 2 (T	-	X	-	X	-	-	-	-	-	X
Q16774	Guanylate kinase (EC 2,7,4,8) (GMP kinase)	-	-	-	X	-	-	-	-	-	X
P08107	Heat shock 70 kDa protein 1 (HSP70,1) (HSP70-1/HSP70-2)	X	-	-	-	-	-	-	-	-	X
P34932	Heat shock 70 kDa protein 4 (Heat shock 70-related protein APG-2)	X	-	-	-	-	-	-	-	-	X
P11142	Heat shock cognate 71 kDa protein (Heat shock 70 kDa protein 8)	X	-	-	-	-	-	-	-	-	X
Q12931	Heat shock protein 75 kDa, mitochondrial precursor (HSP 75) (Tum	X	-	-	-	-	-	-	-	-	X
P07900	Heat shock protein HSP 90-alpha (HSP 86)	X	-	-	-	-	-	-	-	-	X
P08238	Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	X	-	-	-	-	-	-	-	-	X
Q92598	Heat-shock protein 105 kDa (Heat shock 110 kDa protein) (Antigen	X	-	-	-	-	-	-	-	-	X
P04792	Heat-shock protein beta-1 (HspB1) (Heat shock 27 kDa protein) (HS	X	-	-	-	-	-	-	-	-	X
Q9NRV9	Heme-binding protein 1 (p22HBP)	-	-	-	-	-	-	-	-	-	X
Q9Y5Z4	Heme-binding protein 2 (Protein SOUL) (Placental protein 23) (PP2	-	-	-	-	-	-	-	-	-	-
Q99729	Heterogeneous nuclear ribonucleoprotein A/B (hnRNP A/B) (APOBE	-	-	-	X	-	-	-	-	-	-
Q14103	Heterogeneous nuclear ribonucleoprotein D0 (hnRNP D0) (AU-rich e	-	-	-	X	-	-	-	-	-	X
P52597	Heterogeneous nuclear ribonucleoprotein F (hnRNP F) (Nucleolin-lil	-	-	-	X	-	-	-	-	-	X
P61978	Heterogeneous nuclear ribonucleoprotein K (hnRNP K) (Transforma	-	-	-	X	-	-	-	-	-	X
O60506	Heterogeneous nuclear ribonucleoprotein Q (hnRNP Q) (hnRNP-Q)	-	-	-	X	-	-	-	-	-	-
Q00839	Heterogeneous nuclear ribonucleoprotein U (hnRNP U) (Scaffold att	-	-	-	X	-	-	-	-	-	-
P19367	Hexokinase-1 (EC 2,7,1,1) (Hexokinase type I) (HK I) (Brain form he	-	X	-	-	-	-	-	-	-	-
P09429	High mobility group protein 1 (HMG-1) (High mobility group protein E	-	-	-	X	-	-	-	-	-	-
O15347	High mobility group protein B3 (High mobility group protein 4) (HMG	-	-	-	X	-	-	-	-	-	-
P49773	Histidine triad nucleotide-binding protein 1 (Adenosine 5'-monophos	-	-	-	X	-	-	-	-	-	X
Q9BX68	Histidine triad nucleotide-binding protein 2 (EC 3,-,-,-) (HINT-2) (HIN	-	-	-	X	-	-	-	-	-	X
P62805	Histone H4	-	-	-	X	-	-	-	-	-	-
P50502	Hsc70-interacting protein (Hip) (Putative tumor suppressor ST13) (P	X	-	-	-	-	-	-	-	-	X
P35914	Hydroxymethylglutaryl-CoA lyase, mitochondrial precursor (EC 4,1,3	-	X	-	-	-	-	-	-	-	-
P00492	Hypoxanthine-guanine phosphoribosyltransferase (EC 2,4,2,8) (HGI	-	-	-	X	-	-	-	-	-	X
O00629	Importin alpha-4 subunit (Karyopherin alpha-4 subunit) (Qip1 protei	-	-	-	X	-	-	-	-	-	-
Q14974	Importin beta-1 subunit (Karyopherin beta-1 subunit) (Nuclear factor	-	-	-	X	-	-	-	-	-	-
O00410	Importin beta-3 (Karyopherin beta-3) (Ran-binding protein 5) (RanB	-	-	-	X	-	-	-	-	-	-
O95373	Importin-7 (Imp7) (Ran-binding protein 7) (RanBP7) - Homo sapiens	-	-	-	X	-	-	-	-	-	-
P55060	Importin-alpha re-exporter (Chromosome segregation 1-like protein)	-	-	-	X	-	-	-	-	-	-
Q15181	Inorganic pyrophosphatase (EC 3,6,1,1) (Pyrophosphate phospho-h	-	-	-	-	-	X	-	-	-	X
Q9H2U2	Inorganic pyrophosphatase 2, mitochondrial precursor (EC 3,6,1,1) (	-	-	-	-	-	-	-	-	-	X
Q9BY32	Inosine triphosphate pyrophosphatase (EC 3,6,1,19) (ITPase) (Inosi	-	-	-	-	-	-	-	-	-	X
P05556	Integrin beta-1 precursor (Fibronectin receptor beta subunit) (Integri	-	-	X	-	-	-	-	-	-	-
P50213	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial precu	-	X	-	-	-	-	-	-	-	X
O75874	Isocitrate dehydrogenase [NADP] cytoplasmic (EC 1,1,1,42) (Oxalos	-	X	-	-	-	-	-	-	-	X
P33176	Kinesin heavy chain (Ubiquitous kinesin heavy chain) (UKHC)	-	-	-	-	-	-	X	-	-	-
Q04760	Lactoylglutathione lyase (EC 4,4,1,5) (Methylglyoxalase) (Aldoketom	-	-	-	-	-	-	-	-	-	X
P46379	Large proline-rich protein BAT3 (HLA-B-associated transcript 3) (Pro	X	-	-	-	-	-	-	-	-	-
P30740	Leukocyte elastase inhibitor (LEI) (Serp1 B1) (Monocyte/neutrophil	-	-	-	-	X	-	-	-	-	X
P09960	Leukotriene A-4 hydrolase (EC 3,3,2,6) (LTA-4 hydrolase) (Leukotrie	-	-	-	-	X	-	-	-	-	X
Q14847	LIM and SH3 domain protein 1 (LASP-1) (MLN 50)	-	-	-	-	-	-	X	-	-	X
P00338	L-lactate dehydrogenase A chain (EC 1,1,1,27) (LDH-A) (LDH musc	-	X	-	-	-	-	-	-	-	-
P07195	L-lactate dehydrogenase B chain (EC 1,1,1,27) (LDH-B) (LDH heart	-	X	-	-	-	-	-	-	-	X
P24666	Low molecular weight phosphotyrosine protein phosphatase (EC 3,1	-	-	-	-	-	-	-	-	-	X
P05455	Lupus La protein (Sjogren syndrome type B antigen) (SS-B) (La ribo	-	-	-	X	-	-	-	-	-	X
P10619	Lysosomal protective protein precursor (EC 3,4,16,5) (Cathepsin A)	-	-	-	-	X	-	-	-	-	-
P11279	Lysosome-associated membrane glycoprotein 1 precursor (LAMP-1	-	-	-	-	X	-	-	-	-	-
Q15046	Lysyl-tRNA synthetase (EC 6,1,1,6) (Lysine--tRNA ligase) (LysRS) -	-	-	-	-	-	-	X	-	-	-
P40121	Macrophage capping protein (Actin-regulatory protein CAP-G)	-	-	-	-	-	-	X	-	-	X
P14174	Macrophage migration inhibitory factor (MIF) (Phenylpyruvate taut	-	-	-	-	-	X	-	-	-	X
Q14764	Major vault protein (MVP) (Lung resistance-related protein)	X	-	-	-	-	-	-	-	-	X
P40925	Malate dehydrogenase, cytoplasmic (EC 1,1,1,37) (Cytosolic malate	-	X	-	-	-	-	-	-	-	X
P40926	Malate dehydrogenase, mitochondrial precursor (EC 1,1,1,37)	-	X	-	-	-	-	-	-	-	-
O60664	Mannose-6-phosphate receptor-binding protein 1 (Cargo selection p	-	-	X	-	-	-	-	-	-	X
O15173	Membrane-associated progesterone receptor component 2 (Progest	-	-	X	-	-	-	-	-	-	-
Q14696	Mesoderm development candidate 2 (NY-REN-61 antigen) - Homo s	-	-	-	-	-	-	-	-	-	-
Q9NZL9	Methionine adenosyltransferase 2 subunit beta - Homo sapiens (Hui	-	-	-	-	-	-	-	X	-	-
O14880	Microsomal glutathione S-transferase 3 (EC 2,5,1,18) (Microsomal C	-	-	-	-	-	-	-	-	X	-
P27816	Microtubule-associated protein 4 (MAP 4)	-	-	-	-	-	-	X	-	-	-

Q15691	Microtubule-associated protein RP/EB family member 1 (APC-binding)	-	-	-	-	-	-	X	-	-	X
Q9Y2B0	MIR-interacting saposin-like protein precursor (Transmembrane protein)	-	-	X	-	-	-	-	-	-	X
Q9NS69	Mitochondrial import receptor subunit TOM22 homolog (Translocase)	-	-	X	-	-	-	-	-	-	-
O94826	Mitochondrial precursor proteins import receptor (Translocase of outer membrane)	-	-	X	-	-	-	-	-	-	X
P28482	Mitogen-activated protein kinase 1 (EC 2,7,1,37) (Extracellular signal-regulated kinase 1)	-	-	-	-	-	X	-	-	-	X
P27361	Mitogen-activated protein kinase 3 (EC 2,7,1,37) (Extracellular signal-regulated kinase 3)	-	-	-	-	-	X	-	-	-	X
Q9UHA4	Mitogen-activated protein kinase kinase 1-interacting protein 1 (MEK1)	-	-	-	-	-	X	-	-	-	X
Q9Y2Q5	Mitogen-activated protein-binding protein-interacting protein (Late endosome)	-	-	-	-	-	X	-	-	-	-
P26038	Moesin (Membrane-organizing extension spike protein)	-	-	-	-	-	-	X	-	-	X
Q7L9L4	Mps one binder kinase activator-like 1A (Mob1 homolog 1A) (Mob1A)	-	-	-	-	-	X	-	-	-	X
P22234	Multifunctional protein ADE2 [Includes: Phosphoribosylaminoimidazole succinyl transferase]	-	-	-	X	-	-	-	-	-	X
Q9NZM1	Myoferlin (Fer-1-like protein 3) - Homo sapiens (Human)	-	-	X	-	-	-	-	-	-	-
O00159	Myosin Ic (Myosin I beta) (MMI-beta) (MMIb) - Homo sapiens (Human)	-	-	-	-	-	-	X	-	-	-
P60660	Myosin light polypeptide 6 (Myosin light chain alkali 3) (Myosin light chain 3)	-	-	-	-	-	-	X	-	-	-
P19105	Myosin regulatory light chain 2, nonsarcomeric (Myosin RLC)	-	-	-	-	-	-	X	-	-	X
P35580	Myosin-10 (Myosin heavy chain, nonmuscle IIb) (Nonmuscle myosin IIb)	-	-	-	-	-	-	X	-	-	-
Q7Z406	Myosin-14 (Myosin heavy chain, nonmuscle IIc) (Nonmuscle myosin IIc)	-	-	-	-	-	-	X	-	-	-
P35579	Myosin-9 (Myosin heavy chain, nonmuscle IIa) (Nonmuscle myosin IIa)	-	-	-	-	-	-	X	-	-	-
P58546	Myotrophin (V-1 protein)	-	-	-	-	-	-	-	X	-	X
Q9UJ70	N-acetylglucosamine kinase (EC 2,7,1,59) (GlcNAc kinase)	-	-	-	-	-	-	-	-	-	X
O43678	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2 (ND1)	-	X	-	-	-	-	-	-	X	-
O96000	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10 (ND10)	-	X	-	-	-	-	-	-	X	-
P00387	NADH-cytochrome b5 reductase (EC 1,6,2,2) (B5R) (Diaphorase-1)	-	X	-	-	-	-	-	-	X	-
Q16718	NADH-ubiquinone oxidoreductase 13 kDa-B subunit (EC 1,6,5,3) (E1)	-	X	-	-	-	-	-	-	X	X
O00217	NADH-ubiquinone oxidoreductase 23 kDa subunit, mitochondrial precursor	-	X	-	-	-	-	-	-	X	-
O75489	NADH-ubiquinone oxidoreductase 30 kDa subunit, mitochondrial precursor	-	X	-	-	-	-	-	-	X	X
P56556	NADH-ubiquinone oxidoreductase B14 subunit (EC 1,6,5,3) (EC 1,6,5,3)	-	X	-	-	-	-	-	-	X	-
Q13765	Nascent polypeptide-associated complex alpha subunit (NAC-alpha)	X	-	-	-	-	-	-	-	-	-
Q92597	NDRG1 protein (N-myc downstream-regulated gene 1 protein) (Differentiation)	X	-	-	-	-	-	-	-	-	X
Q15843	NEDD8 precursor (Ubiquitin-like protein Nedd8) (Neddylin) - Homo sapiens	-	-	-	-	X	-	-	-	-	-
P61081	NEDD8-conjugating enzyme Ubc12 (EC 6,3,2,-) (Ubiquitin-conjugating enzyme)	-	-	-	-	X	-	-	-	-	X
Q14697	Neutral alpha-glucosidase AB precursor (EC 3,2,1,84) (Glucosidase AB)	X	-	-	-	-	-	-	-	-	X
Q96TA1	Niban-like protein (Meg-3)	-	-	-	-	-	-	-	-	-	-
P43490	Nicotinamide phosphoribosyltransferase (EC 2,4,2,12) (NAMPTase)	-	-	-	X	-	-	-	-	-	X
Q86X76	Nitrilase homolog 1 (EC 3,5,-,-) - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	X
P22307	Nonspecific lipid-transfer protein, mitochondrial precursor (EC 2,3,1,1)	-	-	X	-	-	-	-	-	-	X
Q9UNZ2	NSFL1 cofactor p47 (p97 cofactor p47)	-	-	X	-	-	-	-	-	-	X
P61970	Nuclear transport factor 2 (NTF-2) (Placental protein 15) (PP15)	-	-	X	-	-	-	-	-	-	X
P15531	Nucleoside diphosphate kinase A (EC 2,7,4,6) (NDK A) (NDP kinase A)	-	-	-	X	-	-	-	-	-	X
P22392	Nucleoside diphosphate kinase B (EC 2,7,4,6) (NDK B) (NDP kinase B)	-	-	-	X	-	-	-	-	-	-
P55209	Nucleosome assembly protein 1-like 1 (NAP-1-related protein) (hNAP)	-	-	-	X	-	-	-	-	-	-
Q56VL3	OCIA domain-containing protein 2 - Homo sapiens (Human)	-	-	-	-	X	-	-	-	-	-
Q92882	Osteoclast-stimulating factor 1	-	-	-	-	-	X	-	-	-	X
P20962	Parathymosin - Homo sapiens (Human)	-	-	-	X	-	-	-	-	-	-
Q9UBV8	Peflin (PEF protein with a long N-terminal hydrophobic domain) (Peflin)	-	-	X	-	-	-	-	-	-	-
P62937	Peptidyl-prolyl cis-trans isomerase A (EC 5,2,1,8) (PPIase) (Rotamase)	X	-	-	-	-	-	-	-	-	X
P23284	Peptidyl-prolyl cis-trans isomerase B precursor (EC 5,2,1,8) (PPIase)	X	-	-	-	-	-	-	-	-	-
Q13526	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (EC 5,2,1,8) (PIN1)	X	-	-	-	-	-	-	-	-	-
Q9Y3E5	Peptidyl-tRNA hydrolase 2, mitochondrial precursor (EC 3,1,1,29) (F1)	X	-	-	-	-	-	-	-	-	-
Q06830	Peroxisome oxidoreductase 1 (EC 1,11,1,15) (Thioredoxin peroxidase 2) (Thioredoxin)	-	-	-	-	-	-	-	-	X	X
P32119	Peroxisome oxidoreductase 2 (EC 1,11,1,15) (Thioredoxin peroxidase 1) (Thioredoxin)	-	-	-	-	-	-	-	-	X	X
Q13162	Peroxisome oxidoreductase 4 (EC 1,11,1,15) (Prx-IV) (Thioredoxin peroxidase AC)	-	-	-	-	-	-	-	-	X	X
P30044	Peroxisome oxidoreductase 5, mitochondrial precursor (EC 1,11,1,15) (Prx-V) (Pe)	-	-	-	-	-	-	-	-	X	X
P30041	Peroxisome oxidoreductase 6 (EC 1,11,1,15) (Antioxidant protein 2) (1-Cys peroxi)	-	-	-	-	-	-	-	-	X	X
Q00325	Phosphate carrier protein, mitochondrial precursor (PTP) (Solute carrier)	-	-	X	-	-	-	-	-	-	-
P30086	Phosphatidylethanolamine-binding protein (PEBP) (Prostatic binding protein)	-	-	-	-	-	X	-	-	-	X
P36871	Phosphoglucosyltransferase-1 (EC 5,4,2,2) (Glucose phosphomutase 1) (F)	-	X	-	-	-	-	-	-	-	X
Q96G03	Phosphoglucosyltransferase-2 (EC 5,4,2,2) (Glucose phosphomutase 2) (F)	-	X	-	-	-	-	-	-	-	-
P00558	Phosphoglycerate kinase 1 (EC 2,7,2,3) (Primer recognition protein)	-	X	-	-	-	-	-	-	-	X
P18669	Phosphoglycerate mutase 1 (EC 5,4,2,1) (EC 5,4,2,4) (EC 3,1,3,13)	-	X	-	-	-	-	-	-	-	X
Q15126	Phosphomevalonate kinase (EC 2,7,4,2) (PMKase)	-	-	-	-	-	-	-	-	-	X
O00625	Pirin - Homo sapiens (Human)	-	-	-	X	-	-	-	-	-	-
P35237	Placental thrombin inhibitor (Cytoplasmic antiproteinase) (CAP) (Prc)	-	-	-	-	X	-	-	-	-	X

P13797	Plastin-3 (T-plastin)	-	-	-	-	-	-	X	-	-	X
P43034	Platelet-activating factor acetylhydrolase IB alpha subunit (PAF acet	-	-	-	-	-	X	X	-	-	-
P68402	Platelet-activating factor acetylhydrolase IB beta subunit (EC 3,1,1,4	-	-	-	-	-	X	X	-	-	X
Q15102	Platelet-activating factor acetylhydrolase IB gamma subunit (EC 3,1,	-	-	-	-	-	X	X	-	-	X
Q15365	Poly(rC)-binding protein 1 (Alpha-CP1) (hnRNP-E1) (Nucleic acid-bi	-	-	-	X	-	-	-	-	-	X
Q15366	Poly(rC)-binding protein 2 (Alpha-CP2) (hnRNP-E2)	-	-	-	X	-	-	-	-	-	X
P11940	Polyadenylate-binding protein 1 (Poly(A)-binding protein 1) (PABP 1	-	-	-	X	-	-	-	-	-	-
Q96CX2	Potassium channel tetramerisation domain-containing protein 12 (Pf	X	-	-	-	-	-	-	-	-	X
Q9UHV9	Prefoldin subunit 2	X	-	-	-	-	-	-	-	-	X
P61758	Prefoldin subunit 3 (Von Hippel-Lindau-binding protein 1) (VHL-bind	X	-	-	-	-	-	-	-	-	X
Q99471	Prefoldin subunit 5 (C-myc-binding protein Mm-1) (Myc modulator 1)	X	-	-	-	-	-	-	-	-	X
P07602	Proactivator polypeptide precursor [Contains: Saposin A (Protein A);	-	-	X	-	-	-	-	-	-	X
Q9HA77	Probable cysteinyl-tRNA synthetase, mitochondrial precursor (EC 6,	-	-	-	-	-	-	-	X	-	-
O96008	Probable mitochondrial import receptor subunit TOM40 homolog (Tr	-	X	-	-	-	-	-	-	-	X
P07737	Profilin-1 (Profilin I)	-	-	-	-	-	-	X	-	-	X
Q8WUM4	Programmed cell death 6-interacting protein (PDCD6-interacting pro	-	-	-	-	-	X	-	-	-	X
Q9BUL8	Programmed cell death protein 10 (TF-1 cell apoptosis-related prote	-	-	-	-	-	X	-	-	-	-
O14737	Programmed cell death protein 5 (Protein TFAR19) (TF-1 cell apopt	-	-	-	-	-	X	-	-	-	X
O75340	Programmed cell death protein 6 (Probable calcium-binding protein .	-	-	-	-	-	X	-	-	-	X
P35232	Prohibitin,	-	-	-	X	-	-	-	-	-	X
Q99623	Prohibitin-2 (B-cell receptor-associated protein BAP37) (Repressor c	-	-	-	X	-	-	-	-	-	-
Q9UQ80	Proliferation-associated protein 2G4 (Cell cycle protein p38-2G4 hor	-	-	-	-	-	X	-	-	-	X
O94903	Proline synthetase co-transcribed bacterial homolog protein	-	-	-	-	-	-	-	-	-	-
P48147	Prolyl endopeptidase (EC 3,4,21,26) (Post-proline cleaving enzyme)	-	-	-	-	X	-	-	-	-	X
Q9H7Z7	Prostaglandin E synthase 2 (EC 5,3,99,3) (Microsomal prostaglandi	-	-	-	-	-	X	-	-	-	X
Q15185	Prostaglandin E synthase 3 (EC 5,3,99,3) (Cytosolic prostaglandin E	X	-	-	-	-	-	-	-	-	X
Q06323	Proteasome activator complex subunit 1 (Proteasome	-	-	-	-	X	-	-	-	-	X
Q9UL46	Proteasome activator complex subunit 2 (Proteasome activator 28-b	-	-	-	-	X	-	-	-	-	X
P25786	Proteasome subunit alpha type 1 (EC 3,4,25,1) (Proteasome compo	-	-	-	-	X	-	-	-	-	X
P25787	Proteasome subunit alpha type 2 (EC 3,4,25,1) (Proteasome compo	-	-	-	-	X	-	-	-	-	X
P25788	Proteasome subunit alpha type 3 (EC 3,4,25,1) (Proteasome compo	-	-	-	-	X	-	-	-	-	X
P25789	Proteasome subunit alpha type 4 (EC 3,4,25,1) (Proteasome compo	-	-	-	-	X	-	-	-	-	X
P28066	Proteasome subunit alpha type 5 (EC 3,4,25,1) (Proteasome zeta cl	-	-	-	-	X	-	-	-	-	-
P60900	Proteasome subunit alpha type 6 (EC 3,4,25,1) (Proteasome iota ch	-	-	-	-	X	-	-	-	-	X
O14818	Proteasome subunit alpha type 7 (EC 3,4,25,1) (Proteasome subuni	-	-	-	-	X	-	-	-	-	X
P20618	Proteasome subunit beta type 1 (EC 3,4,25,1) (Proteasome compor	-	-	-	-	X	-	-	-	-	-
P49721	Proteasome subunit beta type 2 (EC 3,4,25,1) (Proteasome compor	-	-	-	-	X	-	-	-	-	X
P49720	Proteasome subunit beta type 3 (EC 3,4,25,1) (Proteasome theta ch	-	-	-	-	X	-	-	-	-	X
P28070	Proteasome subunit beta type 4 precursor (EC 3,4,25,1) (Proteasom	-	-	-	-	X	-	-	-	-	X
P28072	Proteasome subunit beta type 6 precursor (EC 3,4,25,1) (Proteasom	-	-	-	-	X	-	-	-	-	X
P28062	Proteasome subunit beta type 8 precursor (EC 3,4,25,1) (Proteasom	-	-	-	-	X	-	-	-	-	-
P28065	Proteasome subunit beta type 9 precursor (EC 3,4,25,1) (Proteasom	-	-	-	-	X	-	-	-	-	X
Q9NQ88	Protein C12orf5	-	-	-	-	-	-	-	-	-	-
Q9Y224	Protein C14orf166	-	-	-	-	-	-	-	-	-	X
Q969H8	Protein C19orf10 precursor (Stromal cell-derived growth factor SF2C	-	-	-	-	-	-	-	-	-	X
Q9P1F3	Protein C6orf115	-	-	-	-	-	-	-	-	-	X
O75223	Protein C7orf24	-	-	X	-	-	-	-	-	-	X
O60888	Protein CutA precursor (Brain acetylcholinesterase putative membra	-	-	-	-	-	-	-	-	-	-
O60610	Protein diaphanous homolog 1 (Diaphanous-related formin-1) (DRF:	-	-	-	-	-	-	-	-	-	-
P30101	Protein disulfide-isomerase A3 precursor (EC 5,3,4,1) (Disulfide isor	X	-	-	-	-	-	-	-	-	X
P13667	Protein disulfide-isomerase A4 precursor (EC 5,3,4,1) (Protein ERp	X	-	-	-	-	-	-	-	-	-
Q15084	Protein disulfide-isomerase A6 precursor (EC 5,3,4,1) (Protein disulf	X	-	-	-	-	-	-	-	-	X
P07237	Protein disulfide-isomerase precursor (EC 5,3,4,1) (PDI) (Prolyl 4-hy	X	-	-	-	-	-	-	-	-	X
Q99497	Protein DJ-1 (Oncogene DJ1)	X	-	-	-	-	-	-	-	X	X
Q9BSJ8	Protein FAM62A (Membrane-bound C2 domain-containing protein) -	-	-	X	-	-	-	-	-	-	-
Q9BPW8	Protein NipSnap1 - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	-
Q9UFN0	Protein NipSnap3A (NipSnap4) (Target for Salmonella secreted prot	-	-	-	-	-	-	-	-	-	-
O94979	Protein transport protein Sec31A - Homo sapiens (Human)	-	-	X	-	-	-	-	-	-	-
P22061	Protein-L-isoaspartate(D-aspartate) O-methyltransferase (EC 2,1,1,1,	X	-	-	-	-	-	-	-	-	X
Q04941	Proteolipid protein 2 (Intestinal membrane A4 protein) (Differentiatio	-	-	X	-	-	-	-	-	-	-
P61457	Pterin-4-alpha-carbinolamine dehydratase (EC 4,2,1,96) (PHS) (4-al	-	-	-	X	-	-	-	-	-	-
P00491	Purine nucleoside phosphorylase (EC 2,4,2,1) (Inosine phosphoryla	-	-	-	X	-	-	-	-	-	X
P55786	Puromycin-sensitive aminopeptidase (EC 3,4,11,-) (PSA)	-	-	-	-	X	-	-	-	-	-

Q9NTK5	Putative GTP-binding protein PTD004	-	-	-	X	-	-	-	-	-	-
P98179	Putative RNA-binding protein 3 (RNA-binding motif protein 3) (RNPL	-	-	-	X	-	-	-	-	-	-
O00764	Pyridoxal kinase (EC 2,7,1,35) (Pyridoxine kinase)	-	-	-	-	-	-	-	-	-	X
P14618	Pyruvate kinase isozymes M1/M2 (EC 2,7,1,40) (Pyruvate kinase m	-	X	-	-	-	-	-	-	-	X
P31150	Rab GDP dissociation inhibitor alpha (Rab GDI alpha) (Guanosine d	-	-	-	-	-	X	-	-	-	X
P50395	Rab GDP dissociation inhibitor beta (Rab GDI beta) (Guanosine dipl	-	-	-	-	-	X	-	-	-	X
O60518	Ran-binding protein 6 (RanBP6)	-	-	-	X	-	-	-	-	-	-
P43487	Ran-specific GTPase-activating protein (Ran-binding protein 1) (Rar	-	-	-	X	-	-	-	-	-	X
P46940	Ras GTPase-activating-like protein IQGAP1 (p195)	-	-	-	-	-	X	-	-	-	-
Q15404	Ras suppressor protein 1 (Rsu-1) (RSP-1)	-	-	-	-	-	X	-	-	-	-
P63000	Ras-related C3 botulinum toxin substrate 1 precursor (p21-Rac1) (R	-	-	-	-	-	X	-	-	-	-
P15153	Ras-related C3 botulinum toxin substrate 2 precursor (p21-Rac2) (S	-	-	-	-	-	X	-	-	-	X
P61026	Ras-related protein Rab-10	-	-	X	-	-	-	-	-	-	-
P62491	Ras-related protein Rab-11A (Rab-11) (YL8)	-	-	X	-	-	-	-	-	-	-
P61106	Ras-related protein Rab-14	-	-	X	-	-	-	-	-	-	-
P59190	Ras-related protein Rab-15	-	-	X	-	-	-	-	-	-	-
Q9NP72	Ras-related protein Rab-18 - Homo sapiens (Human)	-	-	X	-	-	-	-	-	-	-
P62820	Ras-related protein Rab-1A (YPT1-related protein)	-	-	X	-	-	-	-	-	-	X
Q9H0U4	Ras-related protein Rab-1B	-	-	X	-	-	-	-	-	-	-
Q9UL25	Ras-related protein Rab-21 - Homo sapiens (Human)	-	-	X	-	-	-	-	-	-	-
P61019	Ras-related protein Rab-2A	-	-	X	-	-	-	-	-	-	-
Q9H082	Ras-related protein Rab-33B	-	-	X	-	-	-	-	-	-	-
Q15286	Ras-related protein Rab-35 (Rab-1C) (GTP-binding protein RAY)	-	-	X	-	-	-	-	-	-	-
Q14964	Ras-related protein Rab-39A (Rab-39)	-	-	X	-	-	-	-	-	-	-
P20339	Ras-related protein Rab-5A	-	-	X	-	-	-	-	-	-	-
P61020	Ras-related protein Rab-5B	-	-	X	-	-	-	-	-	-	-
P51148	Ras-related protein Rab-5C (RAB5L) (L1880)	-	-	X	-	-	-	-	-	-	-
P20340	Ras-related protein Rab-6A (Rab-6)	-	-	X	-	-	-	-	-	-	-
P51149	Ras-related protein Rab-7	-	-	X	-	-	-	-	-	-	X
P61006	Ras-related protein Rab-8A (Oncogene c-mel)	-	-	X	-	-	-	-	-	-	-
P62834	Ras-related protein Rap-1A precursor (GTP-binding protein smg-p2:	-	-	X	-	-	-	-	-	-	-
P61224	Ras-related protein Rap-1b precursor (GTP-binding protein smg p21	-	-	X	-	-	-	-	-	-	X
P61225	Ras-related protein Rap-2b precursor	-	-	X	-	-	-	-	-	-	-
P35244	Replication protein A 14 kDa subunit (RP-A) (RF-A) (Replication fac	-	-	-	X	-	-	-	-	-	-
Q9NQC3	Reticulon-4 (Neurite outgrowth inhibitor) (Nogo protein) (Foocen) (N	-	-	-	-	-	-	-	-	-	-
P52565	Rho GDP-dissociation inhibitor 1 (Rho GDI 1) (Rho-GDI alpha)	-	-	-	-	-	-	X	-	-	X
P52566	Rho GDP-dissociation inhibitor 2 (Rho GDI 2) (Rho-GDI beta) (Ly-G	-	-	-	-	-	-	X	-	-	X
P08134	Rho-related GTP-binding protein RhoC precursor (H9)	-	-	-	-	-	-	X	-	-	-
P84095	Rho-related GTP-binding protein RhoG precursor	-	-	-	-	-	-	X	-	-	-
P13489	Ribonuclease inhibitor (Ribonuclease/angiogenin inhibitor 1) (RAI) (I	-	-	-	X	-	-	-	-	-	-
P52758	Ribonuclease UK114 (EC 3,1,-,-) (14,5 kDa translational inhibitor pr	-	-	-	X	-	-	-	-	-	-
P11908	Ribose-phosphate pyrophosphokinase II (EC 2,7,6,1) (Phosphoribo	-	-	-	X	-	-	-	-	-	X
Q96AT9	Ribulose-phosphate 3-epimerase (EC 5,1,3,1) (Ribulose-5-phospha	-	-	-	X	-	-	-	-	-	X
P35637	RNA-binding protein FUS (Oncogene FUS) (Oncogene TLS) (Trans	-	-	-	X	-	-	-	-	-	-
P55735	SEC13-related protein (SEC13-like protein 1)	-	-	X	-	-	-	-	-	-	X
P35270	Sepiapterin reductase (EC 1,1,1,153) (SPR) - Homo sapiens (Huma	-	-	-	-	-	-	-	-	X	-
Q15019	Septin-2 (Protein NEDD5)	-	-	-	-	-	-	X	-	-	X
P62140	Serine/threonine protein phosphatase PP1-beta catalytic subunit (E	-	-	-	-	-	X	-	-	-	X
P30153	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit	-	-	-	-	-	X	-	-	-	X
P62136	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit (E	-	-	-	-	-	X	-	-	-	X
Q9Y3F4	Serine-threonine kinase receptor-associated protein (UNR-interactin	-	-	-	-	-	X	-	-	-	X
P49591	Seryl-tRNA synthetase (EC 6,1,1,11) (Serine--tRNA ligase) (SerRS)	-	-	-	-	-	-	-	X	-	X
O75368	SH3 domain-binding glutamic acid-rich-like protein	-	-	-	-	-	-	-	-	-	X
Q9H299	SH3 domain-binding glutamic acid-rich-like protein 3 (SH3 domain-b	-	-	-	-	-	-	-	-	-	-
Q16836	Short chain 3-hydroxyacyl-CoA dehydrogenase, mitochondrial precu	-	X	-	-	-	-	-	-	-	-
Q9NR45	Sialic acid synthase (N-acetylneuraminase synthase) (EC 2,5,1,56) (	-	-	-	-	-	-	-	-	-	X
Q9BWM7	Sideroflexin-3 - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	-
P49458	Signal recognition particle 9 kDa protein (SRP9)	-	-	-	-	-	-	-	-	-	-
Q04837	Single-stranded DNA-binding protein, mitochondrial precursor (Mt-S	-	X	-	-	-	-	-	-	-	-
P62314	Small nuclear ribonucleoprotein Sm D1 (snRNP core protein D1) (S	-	-	-	X	-	-	-	-	-	-
Q13126	S-methyl-5-thioadenosine phosphorylase (EC 2,4,2,28) (5*-methylth	-	-	-	X	-	-	-	-	-	X
P05023	Sodium/potassium-transporting ATPase alpha-1 chain precursor (E	-	-	-	-	-	-	-	-	-	-
P30626	Sorcin (22 kDa protein) (CP-22) (V19)	-	-	-	-	-	X	-	-	-	X

O60493	Sorting nexin-3 (SDP3 protein)	-	-	X	-	-	-	-	-	-	-
Q7KZF4	Staphylococcal nuclease domain-containing protein 1 (p100 co-activator)	-	-	-	X	-	-	-	-	-	-
P16949	Stathmin (Phosphoprotein p19) (pp19) (Oncoprotein 18) (Op18) (Leukemia inhibitory factor)	-	-	-	-	-	-	X	-	-	X
Q9UJZ1	Stomatin-like protein 2 (SLP-2) (EPB72-like 2)	-	-	X	-	-	-	-	-	-	X
P38646	Stress-70 protein, mitochondrial precursor (75 kDa glucose-regulated protein)	X	-	-	-	-	-	-	-	-	X
P31948	Stress-induced-phosphoprotein 1 (STI1) (Hsc70/Hsp90-organizing protein)	X	-	-	-	-	-	-	-	-	X
P31040	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	-	X	-	-	-	-	-	-	X	X
Q9Y6N5	Sulfide:quinone oxidoreductase, mitochondrial precursor (EC 1,-,-,-)	-	X	-	-	-	-	-	-	X	-
P00441	Superoxide dismutase [Cu-Zn] (EC 1,15,1,1)	-	-	-	-	-	-	-	-	X	X
P04179	Superoxide dismutase [Mn], mitochondrial precursor (EC 1,15,1,1)	-	-	-	-	-	-	-	-	X	X
O15260	Surfeit locus protein 4	-	-	X	-	-	-	-	-	-	-
Q9UH65	Switch-associated protein 70 (SWAP-70) - Homo sapiens (Human)	-	-	X	-	-	-	-	-	-	-
Q99536	Synaptic vesicle membrane protein VAT-1 homolog (EC 1,-,-,-)	-	-	X	-	-	-	-	-	-	X
O95721	Synaptosomal-associated protein 29 (SNAP-29) (Vesicle-membrane-associated protein)	-	-	X	-	-	-	-	-	-	X
O00560	Syntenin-1 (Syndecan-binding protein 1) (Melanoma differentiation-associated protein)	-	-	-	-	-	-	X	-	-	-
Q9Y490	Talin-1	-	-	-	-	-	-	X	-	-	X
O14907	Tax1-binding protein 3 (Tax interaction protein 1) (TIP-1) (Glutaminase)	-	-	-	-	-	X	-	-	-	-
P17987	T-complex protein 1 subunit alpha (TCP-1-alpha) (CCT-alpha)	X	-	-	-	-	-	-	-	-	X
P78371	T-complex protein 1 subunit beta (TCP-1-beta) (CCT-beta)	X	-	-	-	-	-	-	-	-	X
P50991	T-complex protein 1 subunit delta (TCP-1-delta) (CCT-delta) (Stimulin)	X	-	-	-	-	-	-	-	-	-
P48643	T-complex protein 1 subunit epsilon (TCP-1-epsilon) (CCT-epsilon)	X	-	-	-	-	-	-	-	-	X
Q99832	T-complex protein 1 subunit eta (TCP-1-eta) (CCT-eta) (HIV-1 Nef-interacting protein)	X	-	-	-	-	-	-	-	-	-
P49368	T-complex protein 1 subunit gamma (TCP-1-gamma) (CCT-gamma)	X	-	-	-	-	-	-	-	-	X
P50990	T-complex protein 1 subunit theta (TCP-1-theta) (CCT-theta)	X	-	-	-	-	-	-	-	-	X
P40227	T-complex protein 1 subunit zeta (TCP-1-zeta) (CCT-zeta) (CCT-zeta)	X	-	-	-	-	-	-	-	-	X
Q9Y3D6	Tetratricopeptide repeat protein 11 (TPR repeat protein 11) (Fis1 homolog)	-	-	X	-	-	-	-	-	-	-
P10599	Thioredoxin (ATL-derived factor) (ADF) (Surface-associated sulphhydryl oxidase)	-	-	-	-	-	-	-	-	X	X
O95881	Thioredoxin domain-containing protein 12 precursor (EC 1,8,4,2) (Thioredoxin)	-	-	-	-	-	-	-	-	X	-
Q9BS26	Thioredoxin domain-containing protein 4 precursor (Endoplasmic reticulum)	-	-	-	-	-	-	-	-	X	X
P30048	Thioredoxin-dependent peroxide reductase, mitochondrial precursor	-	-	-	-	-	-	-	-	X	X
O43396	Thioredoxin-like protein 1 (32 kDa thioredoxin-related protein)	-	-	-	-	-	-	-	-	X	X
Q9BRA2	Thioredoxin-like protein 5 (14 kDa thioredoxin-related protein) (TRP)	-	-	-	-	-	-	-	-	X	-
P62328	Thymosin beta-4 (T beta 4) (Fx) [Contains: Hematopoietic system regulator]	-	-	-	-	-	-	X	-	-	-
Q9H0E2	Toll-interacting protein	-	-	-	-	-	X	-	-	-	X
O43617	Trafficking protein particle complex subunit 3 (BET3 homolog) - Homo sapiens	-	-	X	-	-	-	-	-	-	-
P37837	Transaldolase (EC 2,2,1,2)	-	X	-	-	-	-	-	-	-	X
Q15369	Transcription elongation factor B polypeptide 1 (RNA polymerase II associated)	-	-	-	X	-	-	-	X	-	-
P20290	Transcription factor BTF3 (RNA polymerase B transcription factor 3)	-	-	-	X	-	-	-	-	-	X
Q96K17	Transcription factor BTF3 homolog 4 (Basic transcription factor 3-like)	-	-	-	X	-	-	-	-	-	X
P61586	Transforming protein RhoA precursor (H12)	-	-	-	-	-	-	X	-	-	X
P37802	Transgelin-2 (SM22-alpha homolog)	-	-	-	-	-	-	X	-	-	-
P55072	Transitional endoplasmic reticulum ATPase (TER ATPase) (15S Mg ATPase)	X	-	-	-	-	-	-	-	-	X
P29401	Transketolase (EC 2,2,1,1) (TK)	-	X	-	-	-	-	-	-	-	X
P13693	Translationally-controlled tumor protein (TCTP) (p23) (Histamine-receptor)	-	-	-	-	-	X	-	-	-	X
Q99598	Translin-associated protein X (Translin-associated factor X)	-	-	-	X	-	-	-	-	-	X
P51571	Translocon-associated protein delta subunit precursor (TRAP-delta)	X	-	-	-	-	-	-	-	-	-
Q15363	Transmembrane emp24 domain trafficking protein 2 precursor (Membrane)	-	-	X	-	-	-	-	-	-	-
Q9BVK6	Transmembrane emp24 domain-containing protein 9 precursor (Glycophorin)	-	-	X	-	-	-	-	-	-	-
Q9BVC6	Transmembrane protein 109 precursor (Mitsugumin-23) (Mg23)	-	-	X	-	-	-	-	-	-	-
P40939	Trifunctional enzyme alpha subunit, mitochondrial precursor (TP-alpha)	-	X	-	-	-	-	-	-	-	-
P55084	Trifunctional enzyme subunit beta, mitochondrial precursor (TP-beta)	-	X	-	-	-	-	-	-	-	-
P22102	Trifunctional purine biosynthetic protein adenosine-3 [Includes: Phosphoribosyl transferase]	-	-	-	X	-	-	-	-	-	X
P60174	Triosephosphate isomerase (EC 5,3,1,1) (TIM) (Triose-phosphate isomerase)	-	X	-	-	-	-	-	-	-	X
O14773	Tripeptidyl-peptidase I precursor (EC 3,4,14,9) (TPP-I) (Tripeptidyl aminopeptidase)	-	-	-	-	X	-	-	-	-	X
Q9UI30	TRM112-like protein - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	X
Q9NYL9	Tropomodulin-3 (Ubiquitous tropomodulin) (U-Tmod) - Homo sapiens	-	-	-	-	-	-	X	-	-	X
P09493	Tropomyosin 1 alpha chain (Alpha-tropomyosin)	-	-	-	-	-	-	X	-	-	X
P06753	Tropomyosin alpha-3 chain (Tropomyosin-3) (Tropomyosin gamma)	-	-	-	-	-	-	X	-	-	X
P67936	Tropomyosin alpha-4 chain (Tropomyosin-4) (TM30p1)	-	-	-	-	-	-	X	-	-	X
P23381	Tryptophanyl-tRNA synthetase (EC 6,1,1,2) (Tryptophan--tRNA ligase)	-	-	-	-	-	-	-	X	-	X
P68363	Tubulin alpha-ubiquitous chain (Alpha-tubulin ubiquitous) (Tubulin K)	-	-	-	-	-	-	X	-	-	X
P07437	Tubulin beta-2 chain	-	-	-	-	-	-	X	-	-	X
Q9BUF5	Tubulin beta-6 chain - Homo sapiens (Human)	-	-	-	-	-	-	X	-	-	-

O75347	Tubulin-specific chaperone A (Tubulin-folding cofactor A) (CFA) (TC	X	-	-	-	-	-	X	-	-	X
Q99426	Tubulin-specific chaperone B (Tubulin folding cofactor B) (Cytoskele	X	-	-	-	-	-	X	-	-	X
O43399	Tumor protein D54 (hD54) (Tumor protein D52-like 2)	-	-	-	-	-	-	-	-	-	X
Q12792	Twinfilin-1 (Protein A6) (Protein tyrosine kinase 9) - Homo sapiens (I	-	-	-	-	-	-	X	-	-	-
Q6IBS0	Twinfilin-2 (Twinfilin-1-like protein) (A6-related protein) (hA6RP) (Pro	-	-	-	-	-	-	X	-	-	X
P54577	Tyrosyl-tRNA synthetase, cytoplasmic (EC 6,1,1,1) (Tyrosyl-tRNA li	-	-	-	-	-	-	-	X	-	X
Q9Y333	U6 snRNA-associated Sm-like protein LSm2 (SnRNP core Sm-like p	-	-	-	X	-	-	-	-	-	-
P47985	Ubiquinol-cytochrome c reductase iron-sulfur subunit, mitochondrial	-	X	-	-	-	-	-	-	-	X
P22695	Ubiquinol-cytochrome-c reductase complex core protein 2, mitochor	-	X	-	-	-	-	-	-	-	-
P62988	Ubiquitin	-	-	-	-	X	-	-	-	-	X
P54578	Ubiquitin carboxyl-terminal hydrolase 14 (EC 3,1,2,15) (Ubiquitin thio	-	-	-	-	X	-	-	-	-	X
P45974	Ubiquitin carboxyl-terminal hydrolase 5 (EC 3,1,2,15) (Ubiquitin thiol	-	-	-	-	X	-	-	-	-	X
P15374	Ubiquitin carboxyl-terminal hydrolase isozyme L3 (EC 3,4,19,12) (U	-	-	-	-	X	-	-	-	-	X
Q96FW1	Ubiquitin thiolesterase protein OTUB1 (EC 3,4,-,-) (Otubain 1) (OTU	-	-	-	-	X	-	-	-	-	-
P22314	Ubiquitin-activating enzyme E1 (A1S9 protein)	-	-	-	-	X	-	-	-	-	X
P62837	Ubiquitin-conjugating enzyme E2 D2 (EC 6,3,2,19) (Ubiquitin-protein	-	-	-	-	X	-	-	-	-	-
P68036	Ubiquitin-conjugating enzyme E2 L3 (EC 6,3,2,19) (Ubiquitin-protein	-	-	-	-	X	-	-	-	-	-
O14933	Ubiquitin-conjugating enzyme E2 L6 (EC 6,3,2,19) (Ubiquitin-protein	-	-	-	-	X	-	-	-	-	-
P61088	Ubiquitin-conjugating enzyme E2 N (EC 6,3,2,19) (Ubiquitin-protein	-	-	-	-	X	-	-	-	-	X
Q13404	Ubiquitin-conjugating enzyme E2 variant 1 (UEV-1) (CROC-1) (Ubiqui	-	-	-	-	X	-	-	-	-	X
Q15819	Ubiquitin-conjugating enzyme E2 variant 2 (MMS2) (Enterocyte diffe	-	-	-	-	X	-	-	-	-	X
P61086	Ubiquitin-conjugating enzyme E2-25 kDa (EC 6,3,2,19) (Ubiquitin-pr	-	-	-	-	X	-	-	-	-	X
P61960	Ubiquitin-fold modifier 1 precursor - Homo sapiens (Human)	-	-	-	-	X	-	-	-	-	X
Q9UBT2	Ubiquitin-like 1-activating enzyme E1B (SUMO-1-activating enzyme	-	-	-	-	X	-	-	-	-	-
Q9NYU2	UDP-glucose:glycoprotein glucosyltransferase 1 precursor (EC 2,4,1	X	-	-	-	-	-	-	-	-	-
P30085	UMP-CMP kinase (EC 2,7,4,14) (Cytidylate kinase) (Deoxycytidylate	-	-	-	X	-	-	-	-	-	X
Q6IAA8	UPF0404 protein C11orf59 - Homo sapiens (Human)	-	-	-	-	-	-	-	-	-	-
P54727	UV excision repair protein RAD23 homolog B (hHR23B) (XP-C repa	-	-	-	X	-	-	-	-	-	-
P38606	Vacuolar ATP synthase catalytic subunit A, ubiquitous isoform (EC 3	-	X	-	-	-	-	-	-	-	X
P36543	Vacuolar ATP synthase subunit E (EC 3,6,3,14) (V-ATPase E subur	-	X	-	-	-	-	-	-	-	X
O75348	Vacuolar ATP synthase subunit G 1 (EC 3,6,3,14) (V-ATPase G sub	-	X	-	-	-	-	-	-	-	-
Q9UBQ0	Vacuolar protein sorting 29 (Vesicle protein sorting 29) (hVPS29) (P	-	-	X	-	-	-	-	-	-	X
Q96QK1	Vacuolar protein sorting 35 (Vesicle protein sorting 35) (hVPS35) (M	-	-	X	-	-	-	-	-	-	-
Q9BRG1	Vacuolar protein sorting-associated protein 25 (hVps25) (ELL-assoc	-	-	X	-	-	-	-	-	-	-
P63027	Vesicle-associated membrane protein 2 (VAMP-2) (Synaptobrevin-2	-	-	X	-	-	-	-	-	-	-
P46459	Vesicle-fusing ATPase (EC 3,6,4,6) (Vesicular-fusion protein NSF) (	-	-	X	-	-	-	-	-	-	X
Q00341	Vigilin (High density lipoprotein-binding protein) (HDL-binding protei	-	-	X	-	-	-	-	-	-	-
P18206	Vinculin (Metavinculin)	-	-	-	-	-	-	X	-	-	X
P21796	Voltage-dependent anion-selective channel protein 1 (VDAC-1) (hVI	-	-	X	-	-	-	-	-	-	-
P45880	Voltage-dependent anion-selective channel protein 2 (VDAC-2) (hVI	-	-	X	-	-	-	-	-	-	X
Q9Y277	Voltage-dependent anion-selective channel protein 3 (VDAC-3) (hVI	-	-	X	-	-	-	-	-	-	-
O75083	WD-repeat protein 1 (Actin-interacting protein 1) (AIP1) (NORI-1)	-	-	-	-	-	-	X	-	-	X
Q92558	Wiskott-Aldrich syndrome protein family member 1 (WASP-family pr	-	-	-	-	-	-	X	-	-	-

Paper II

Author contribution: Verena Haudek helped with the concept design and performed 2D gels and 1D-PAGE.

Consequences of Acute and Chronic Oxidative Stress upon the Expression Pattern of Proteins in Peripheral Blood Mononuclear Cells

Verena J. Haudek,[†] Nina C. Gundacker,[†] Astrid Slany,[†] Helge Wimmer,[‡] Editha Bayer,[†]
Karoline Pablé,[§] and Christopher Gerner^{*,†}

Department of Medicine I, Institute of Cancer Research, Medical University of Vienna, Austria, Section
Biomedical Laboratory Science, University of Applied Science, Vienna, Austria, and Austrian Research Center
Seibersdorf, Vienna, Austria

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Oxidative stress accompanies various diseases associated with chronic inflammation, including cancer. We exposed human peripheral blood mononuclear cells (PBMCs) to hydrogen peroxide in autologous plasma imitating *in vivo* conditions. Proteome alterations of metabolically labeled cells were recorded by means of 2D gel electrophoresis in addition to shotgun analysis. Cells displayed a distinct stress response and down-regulated manganese superoxide dismutase, while a large number of other redox-regulating enzymes remained unaffected. In the second part of the experiment, we isolated PBMCs from cancer patients to analyze primary cells exposed to chronic oxidative stress. Plasma peroxidation levels of the patients were significantly higher than those of age and sex-matched controls. The corresponding cells displayed significant proteome alterations which appear to be related to inflammation and apoptosis regulation. The present data, fully accessible via PRIDE (accessions 3844–59), may be the first step in the design of a combined protein assay specifically indicating oxidative stress in human PBMCs.

Keywords: oxidative stress • 2D-PAGE • shotgun proteomics • lipid peroxidation

Introduction

In organisms, oxidative stress is generated when the concentration of free radicals and other reactive oxygen species (ROS) exceeds the capacity of the antioxidant defense system.¹ This may result in biological damage which is characteristic for arteriosclerosis and other diseases associated with chronic inflammation.² Many sources of ROS have been identified: endogenous sources via the respiratory-chain of mitochondria or peroxisomes and exogenous sources via exposure to xenobiotics, radiation, ultrasound, pollution, infections, drugs or smoke.^{3–5} High ROS generation and persistent oxidative stress have not only been associated with chronic inflammation, but have also been identified as characteristic features of carcinoma cells both *in vitro* and *in vivo*.^{2,6}

There is strong evidence that proteins are the main targets of oxidative stress and free radical action.^{7–9} These effects have been described regarding aging,¹⁰ Alzheimer's disease, asthma, atherosclerosis, diabetes mellitus and several other diseases.¹¹ Additionally, cell membranes containing unsaturated fatty acids are susceptible to oxidation when reacting with ROS. Free

radical chain reactions in the poly unsaturated lipid layer of cell membranes are characteristic of ROS-induced lipid peroxidation, promoting protein oxidation.^{2,12} Cells are equipped with a protein machinery to defend themselves against ROS. Particularly, superoxide dismutase (SOD) enzymes, glutathione peroxidases (GPX) and catalase enzymes serve as such defenses.

Proteome analysis is a very suitable method to investigate biological effects of oxidative stress.^{13,14} Comprehensive studies were performed on systems as diverse as rice,¹⁵ yeast¹⁶ and cultured human cells.^{17–20} Especially regarding neurodegenerative disorders, various proteome studies were performed with human clinical materials.²¹

Proteome studies focusing on oxidative stress may contribute to two important issues: First, comprehensive profiling might allow the identification of marker proteins specifically indicating and indirectly quantifying the extent of oxidative stress. Second, the investigation of the cellular response to oxidative stress may contribute to the understanding of the complex biochemistry of redox regulation in the context of diseases.

The present study was designed to account for both aspects. In contrast to many other proteome studies focusing on oxidative stress, we used primary human peripheral blood mononuclear cells (PBMCs). These cells are exposed to oxidative stress mediated via hydrogen peroxide *in vivo* and thus constitute an ideal model cell system for clinical research. The main disadvantage of these cells is the individual variation of protein expression and the limited time available to perform

* To whom correspondence should be addressed. Christopher Gerner, Department of Medicine I, Institute of Cancer Research, Medical University of Vienna, Austria. E-mail, Christopher.Gerner@meduniwien.ac.at; phone, 0043-1-4277-65230.

[†] Medical University of Vienna.

[‡] University of Applied Science.

[§] Austrian Research Center Seibersdorf.

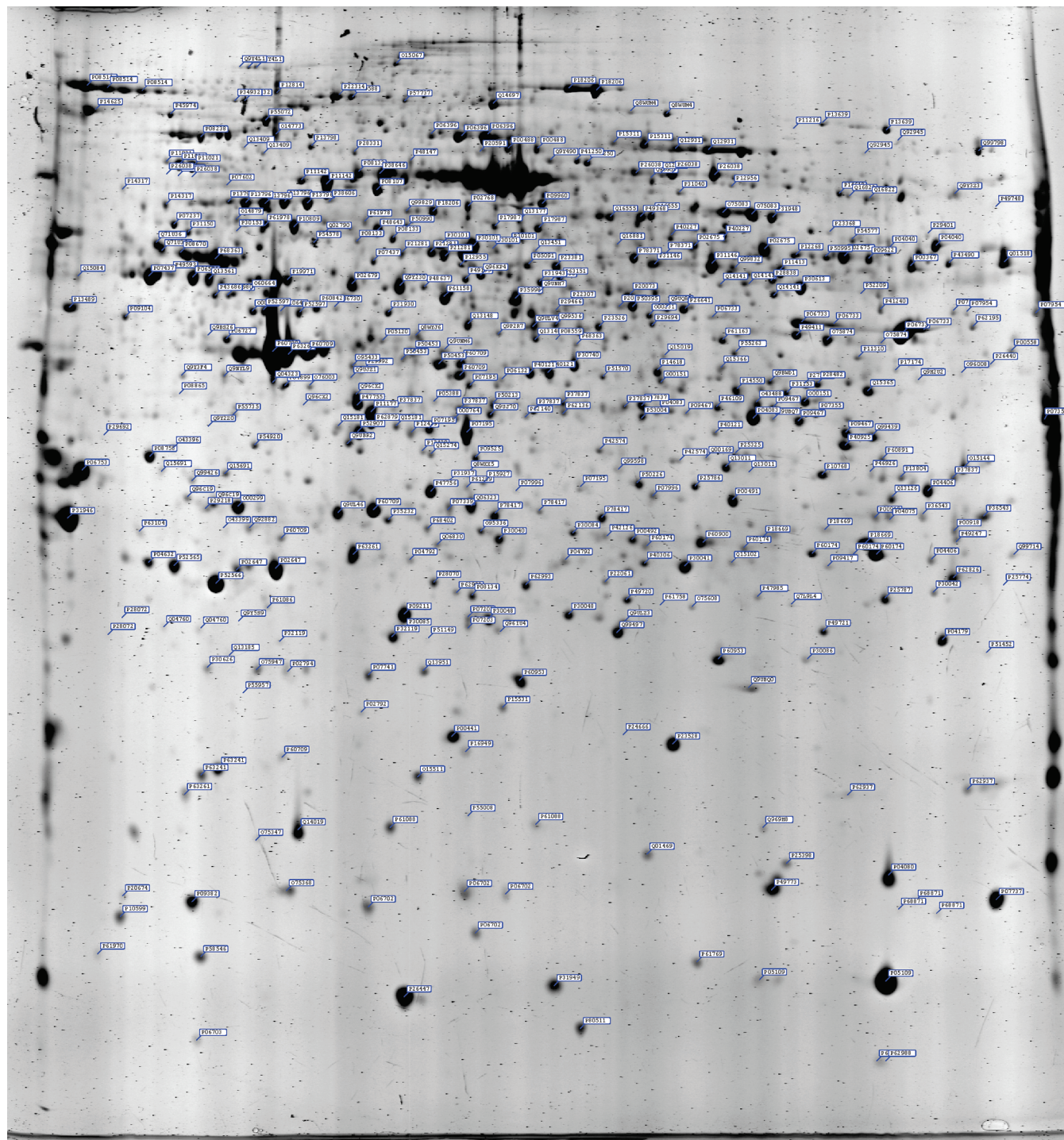


Figure 1. Fully annotated 2D-gel of the cytoplasmic protein fraction of human PBMCs. Proteins were detected by RuBPS fluorescence staining. Spots were cut out of the gel, digested with trypsin and subjected to LC-MS/MS analysis for identification of proteins. Swiss-Prot accession numbers are annotated.

in vitro experiments due to the fact that these cells cannot be maintained in culture.

We overcame some of these obstacles by designing a short-time experiment which was performed at conditions very much similar to *in vivo* conditions as the cells were kept in autologous plasma. The required sensitivity of the proteome profiling technique was achieved by metabolic labeling of the cells combined with autoradiographic detection of protein synthesis. To imitate physiologic conditions, we

VERENA HAUDEK PhD-thesis

resuspended cells in autologous plasma for treatment with hydrogen peroxide at concentrations which have been reported *in vivo*.²² Hydrogen peroxide was used for the *in vitro* approach due to its capacity to cross cell membranes and diffuse through mitochondria, thereby causing many types of cellular injuries.² By the use of metabolic labeling and subsequent two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) analysis, we investigated the immediate response of cells to the oxidative challenge *in vitro*. This

142

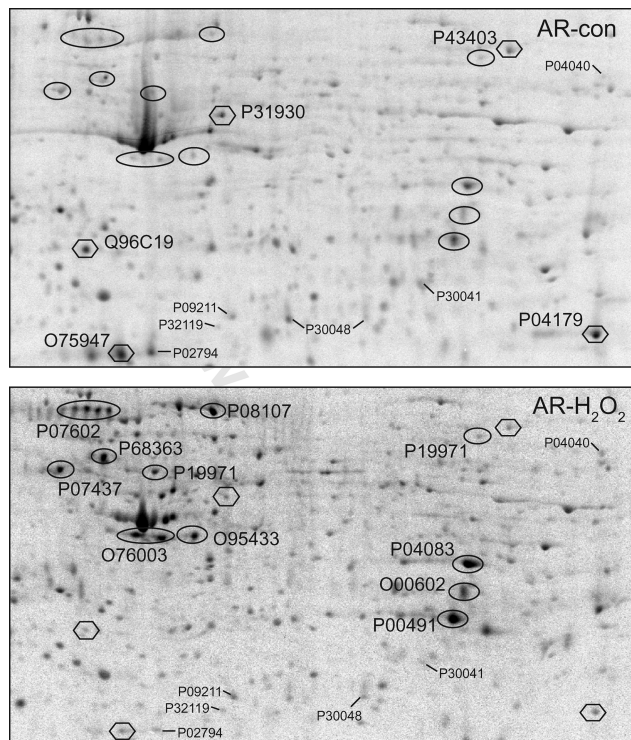


Figure 2. Differently expressed proteins caused by *in vitro* treatment of PBMCs with hydrogen peroxide. 2D-gel autoradiographs of untreated (AR-con) and hydrogen peroxide treated (AR-H₂O₂) PBMCs are shown. Proteins up-regulated by hydrogen peroxide are encircled and annotated in AR-H₂O₂, proteins down-regulated are marked by hexagons and annotated in AR-con. Several redox-regulating proteins which were not significantly regulated are annotated in both gel sections.

experimental strategy was combined with shotgun proteomics in order to achieve optimal reliability of data.

Furthermore, we hypothesized that some oxidative stress-induced proteins accumulate in cells and could therefore be useable as biomarkers. As indicated above, however, it is assumed that oxidative stress may occur in cancer patients *in vivo*. Cells from such patients, therefore, can serve as model for cells which were exposed to oxidative stress for a long period of time. To pursue this strategy, we determined the level of oxidative stress in plasma derived from tumor patients by standard lipid peroxidation assays. Higher levels of oxidative stress *in vivo* were successfully verified. These cells were also subjected to comprehensive proteome profiling and compared to cells from healthy age and sex-matched individuals.

Experimental Section

Sample Collection. Twenty milliliters of heparinized blood was collected per donor, aged between 50 and 80 years. A group of 10 cancer patients (6 with breast cancer, 2 with colon cancer and 2 with kidney cancer) was compared to 10 control persons, matched in sex and age. For the *in vitro* approach, four more healthy persons, aged between 28 and 40, were included. The study design was reviewed and approved by the "Forum Österreichischer Ethikkommissionen", EK-Nr. 360/2005. Two milliliters of the whole blood sample was used for plasma isolation by centrifugation for 10 min at room temperature at 8000g. The supernatant plasma was carefully isolated and stored at -80 °C. PBMCs were isolated by standard density

VERENA HAUDEK PhD-thesis

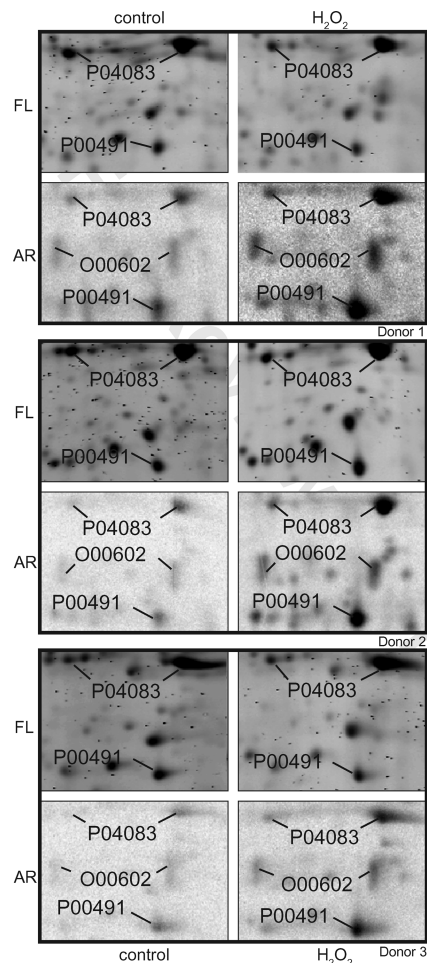


Figure 3. Up-regulation of proteins by hydrogen peroxide is highly reproducible with different donors. Corresponding 2D gel sections of three individual donors, untreated (control) and treated (H₂O₂). PBMC protein spots quantified by fluorescence detection (FL) and [³⁵S]-autoradiography (AR).

gradient centrifugation as described.^{23,24} The cells were subsequently washed with HBSS (Hanks' Buffered Salt Solution, 1:1).

In Vitro Treatment. Resuspended cells were treated *in vitro* for 6 h with hydrogen peroxide (H₂O₂, 100 μM) to simulate acute oxidative stress and the cell aliquots were labeled with 0.2 mCi/mL [³⁵S] methionine and cysteine (Trans35label, Biomedica, MP Biomedicals). Because of inherent catalase activity in plasma, the active concentration of hydrogen peroxide was immediately reduced. During the experiment, cell viability was assayed by Trypan blue staining and was found to be consistently higher than 95%. Cells were washed with HBSS and harvested after 6 h of incubation at 37 °C in a 5% humidified atmosphere.

Subcellular Fractionation. For isolation of cytoplasmic proteins, all buffers were supplemented with protease inhibitors: PMSF (1 mM), aprotinin, leupeptin and pepstatin A (each at 1 μg/mL). Cells were lysed in hypotonic buffer (10 mM HEPES/NaOH, pH 7.4, 0.25 M sucrose, 10 mM NaCl, 3 mM MgCl₂, 0.5% Triton X-100). Nuclei were separated from the cytoplasm by centrifugation at 1000g for 5 min at 4 °C. Cytoplasmic proteins were precipitated with ethanol and dissolved in sample buffer (7.5 M urea, 1.5 M thiourea, 4% CHAPS, 0.5% SDS, 100 mM DDT).

Table 1. Proteins Identified in the Present Study and Related to Oxidative Stress^a

	protein name	accession no.	[³⁵ S]	shotgun	published implications
		<i>1. In Vitro</i>			
cell stress	T-complex protein 1, beta subunit	P78371	2.3	up	up-regulated upon X-ray exposition ⁴¹
	Heat shock 70 kDa protein 1	P08107	12.3	n.a.	up-regulated by oxidative stress ¹⁶
	Activator of 90 kDa heat shock protein ATPase hom. 1	O95433	9.8	n.a.	down-regulated upon X-ray exposition ⁴¹
	Annexin A1	P04083	4.2	n.a.	up-regulated by oxidative stress, heat ⁴²
	Protein disulfide-isomerase A3 (ERp57)	P30101	2.5	n.a.	association with immunogenicity of cell death ⁴³
	Septin-6	Q14141	2.5	n.a.	DNA-damage response, ⁴⁴ melanoma ⁴⁵
	Stress-induced-phosphoprotein 1	P31948	2.1	n.a.	up-regulated by X-ray exposition ⁴¹
	Calreticulin precursor (Calregulin)	P27797	n.d.	up	association with immunogenicity of cell death ⁴³
	Heat shock protein HSP 90-alpha (HSP 86)	P07900	n.a.	down	down-regulated in cytoplasm during apoptosis ⁴⁶
	Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	P08238	n.a.	down	down-regulated in cytoplasm during apoptosis ⁴⁶
	Endoplasmic Stress-70 protein, mitochondrial precursor	P14625	n.a.	down	
		P38646	n.a.	down	
	Heat-shock protein beta-1 (HspB1) (Heat shock 27 kDa protein)	P04792	n.a.	n.a.	
	Coronin-1A	P31146	2.5	up	rearrangement of Actin cytoskeleton ⁴⁷
cytoskeletal	Tubulin alpha-1B chain	P68363	3.8	n.a.	
	Tubulin beta chain	P07437	2.9	n.a.	
	L-plastin (Lymphocyte cytosolic protein 1)	P13796	2.8	n.a.	rearrangement of actin cytoskeleton ⁴⁸
	Talin-1	Q9Y490	n.a.	down	adhesion to cell membrane 1 ⁴⁹
	Gelsolin precursor (Actin-depolymerizing factor) (ADF)	P06396	n.a.	down	
	Tubulin alpha-ubiquitous chain (Alpha-tubulin ubiquitous)	P68363	n.a.	n.a.	
redox-regulation	Superoxide dismutase [Mn], mitochondrial	P04179	-4,2	down	tumor-suppressor activity ³⁵⁻³⁷
	Cytochrome <i>b-c1</i> complex subunit 1	P31930	-3.5	n.a.	
	Glutaredoxin-3	O76003	6.5	n.d.	oxidative stress response ⁵⁰
	NADH-cytochrome b5 reductase	P00387	n.d.	up	
	Ferritin heavy chain (EC 1,16,3,1) (Ferritin H subunit)	P02794	n.a.	down	apoptosis resistance ⁵¹
	Ferritin light chain (Ferritin L subunit)	P02792	n.a.	down	
	Glutathione S-transferase kappa 1	Q9Y2Q3	n.d.	down	resistance to oxidative stress ⁵²
	Catalase	P04040	n.a.	n.a.	up-regulated by oxidative stress ^{15,16}
	Glutathione peroxidase 1	P07203	n.a.	n.a.	
	Glutathione reductase, mitochondrial precursor	P00390	n.d.	n.a.	

Table 1. Continued

	protein name	accession no.	[³⁵ S]	shotgun	published implications
inflammation	Glutathione S-transferase Mu 1	P09488	n.d.	n.a.	
	Glutathione S-transferase Mu 3	P21266	n.a.	n.a.	
	Glutathione synthetase	P48637	n.a.	n.a.	
	Microsomal glutathione S-transferase 3	O14880	n.d.	n.a.	
	Peroxiredoxin-1 (Thioredoxin peroxidase 2)	Q06830	n.a.	n.a.	
	Peroxiredoxin-2 (Thioredoxin peroxidase 1)	P32119	n.a.	n.a.	
	Peroxiredoxin-4 (Thioredoxin peroxidase AO372)	Q13162	n.a.	n.a.	
	Peroxiredoxin-5, mitochondrial precursor	P30044	n.a.	n.a.	
	Peroxiredoxin-6 (Antioxidant protein 2)	P30041	n.a.	n.a.	
	Phospholipid hydroperoxide glutathione peroxidase, mitochondrial precursor	P36969	n.d.	n.a.	
	Superoxide dismutase [Cu–Zn]	P00441	n.a.	n.a.	
	Thioredoxin-dependent peroxide reductase (Peroxiredoxin-3)	P30048	n.a.	n.a.	
	Proactivator polypeptide	P07602	6.5	n.a.	
	Ficolin-1	O00602	3.5	n.d.	
	Thymidine phosphorylase	P19971	2.6	n.a.	
	Protein S100-A11 (Calgizzarin)	P31949	–4.3	down	
	Interleukin-1 beta precursor (IL-1 beta) (Catabolin)	P01584	n.d.	up	
	Mitogen-activated protein kinase 1	P28482	n.a.	up	
	Interleukin-16 precursor (IL-16) (Lymphocyte chemoattractant factor) (LCF)	Q14005	n.d.	down	
	Myeloperoxidase precursor (MPO)	P05164	n.d.	down	
Energy metabolism	Transaldolase	P37837	2.4	n.a.	regulate glutathione levels, ⁵³ up-regulated upon X-ray exposure ⁴¹
other	ATP synthase D chain. mitochondrial	O75947	–12.2	down	down-regulated during aging, ⁵⁴ X-ray exposure ⁴¹
	Histidine triad nucleotide-binding protein 1	P49773	–2.4	down	
	Tyrosine-protein kinase ZAP-70	P43403	–2.1	down	
	Purine nucleoside phosphorylase	P00491	3.7	n.a.	
	Ficolin-1	O00602	3.5	n.d.	
	Sorcin (22 kDa protein)	P30626	–6.2	n.a.	apoptosis ^{55,56}
	EF-hand domain-containing protein D2	Q96C19	–2.8	n.a.	
	Galectin-1	P09382	–2.2	n.a.	involved in cancer biology ⁵⁷
	UTP--glucose-1-phosphate uridylyltransferase 2	Q16851	n.d.	up	

Table 1. Continued

protein name	accession no.	[³⁵ S]	shotgun	published implications
ATP-dependent DNA helicase 2 subunit 1	P12956	n.a.	down	
ATP-dependent DNA helicase 2 subunit 2	P13010	n.d.	down	
Integrin alpha-M precursor (Cell surface glycoprotein MAC-1 alpha subunit)	P11215	n.d.	down	
Ras GTPase-activating-like protein IQGAP1 (p195)	P46940	n.d.	down	
Ras-related protein Rab-2A	P61019	n.d.	down	
Serine/threonine-protein kinase 10 (Lymphocyte-oriented kinase)	O94804	n.d.	down	
Ubiquinol-cytochrome-c reductase complex core protein I, mitochondrial precursor	P31930	n.a.	down	
2. <i>In Vivo</i>				
S100 calcium-binding protein A8 (Calgranulin A isoform 1)	P05109	6.8	n.a.	inflammation ^{58,59}
S100 calcium-binding protein A8 (Calgranulin A isoform 2)	P05109	6.4	n.a.	inflammation ^{58,59}
S100 calcium-binding protein A4 (Matastasin)	P26447	5.1	n.a.	inflammation, metastasis ^{60,61}
Myotrophin (V-1 protein)	P58546	1.9	n.a.	
Phosphoglycerate mutase 1	P18669	1.6	n.a.	glycolysis ⁶²
Serine/threonine protein phosphatase 2A, 65 kDa regulatory subunit	P30153	−1.8	n.a.	apoptosis ^{63,64}
Ezrin	P15311	−1.7	n.a.	
Caspase-3	P42574	−1.6	n.a.	Apoptosis ^{65,66}
Ubiquitin-activating enzyme E1	P22314	−1.6	n.a.	removal of damaged proteins ⁶⁷

^a *In vitro*, data derived from the *in vitro* treatment of PBMCs with hydrogen peroxide. Proteins are classified as indicated in the text. *In Vivo*, protein alterations observed when comparing PBMCs derived from cancer patients with age and sex-matched healthy controls. Proteins were assigned to functional groups. Accessions no., Swiss-Prot protein accessions. [³⁵S], difference factors determined from the comparison of normalized integrated autoradiography spot intensities of corresponding protein derived from treated cells divided by those of untreated cells. All ANOVA *p*-values derived from the four independent experiments are <0.05. Shotgun, alteration of protein amounts as determined by the spectral count method. Proteins reproducibly affected are marked by “up” or “down”, respectively. Related observations are indicated with references. n.a., not affected; n.d., not determined (not detectable with the corresponding technique).

Photometry. Lipid peroxide formation was measured using thiobarbituric assay (TBA-assay) and hydroperoxide assay with ferric xlenol orange (XO) complex. For the TBA-assay, 30 μ L of plasma was suspended in 1 mL of 0.37% TBA in 0.25 M HCl, heated for 45 min at 100 °C and afterward centrifuged for 10 min. Absorbance of the supernatant was read at 525 nm.⁷ For the XO assay, 30 μ L of plasma was suspended in a solution which contained 25 mM H₂SO₄, 100 μ M XO and 250 μ M ferrous ammonium sulfate in a volume of 1 mL. After 30 min in the dark, the absorbance was read at 560 nm with 100 μ M XO as blank.²⁵

2D Polyacrylamide Gel Electrophoresis (2D-PAGE). High resolution 2D-PAGE was carried out as described previously.²⁶ Proteins from PBMC were loaded on IPG strips pH 5–8, 17 cm (BioRad, Hercules, CA) by passive rehydration. IEF (isoelectric focusing) was performed in a stepwise fashion (1 h 0–500 V linear; 5 h 500 V; 5 h 500–3500 V linear; 12 h 3500 V). After IEF

and equilibration with 100 mM DTT and 2.5% iodacetamide, SDS-PAGE (19 cm $\times$ 18 cm $\times$ 1.5 mm, 12% polyacrylamide) was performed with the Protean II xi electrophoresis system (BioRad). The gels were stained with a 400 nM solution of Ruthenium II tris (bathophenanthroline disulfonate) (RuBPS) as described by Rabilloud et al.²⁷ Fluorography scanning was performed with the FluorImager 595 (GE Healthcare, Fairfield, CT) at a resolution of 100 μ m. Thereafter, gels of the radioactively labeled samples were dried and exposed to phosphor screens (Molecular Dynamics). Scanning was performed with the Phosphorimager SI (Molecular Dynamics) at a resolution of 100 μ m as previously described.²⁸ Comparative 2D gel analysis was performed with TT900 S2S software (Version 2006.0.2389, Nonlinear Dynamics, Carlsbad, CA) and Progenesis software PG200 (Version 2006, Nonlinear Dynamics) using the “same spot” algorithm. Spot assignment, background correction, normalization and statistical calculations (analysis of

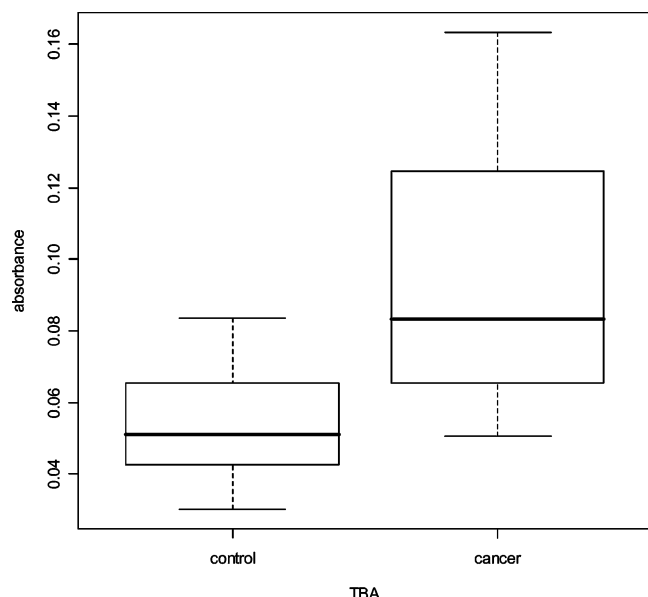


Figure 4. Comparison of lipid-peroxidation levels in plasma samples of "cancer" and "control" groups. The Kruskal–Wallis rank sum test showed a significant increase in the "cancer" group (p -value < 0.01).

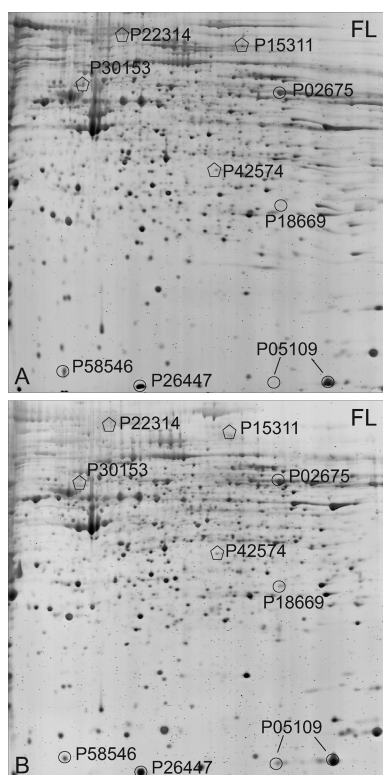


Figure 5. Differently expressed proteins detected in PBMCs of cancer patients displaying increased oxidative stress compared to healthy controls. 2D-gels of PBMCs of control (A) and cancer groups (B) are shown. Proteins were detected by RuBPS fluorescence staining. Proteins down-regulated in the "cancer" group are surrounded by pentagons, up-regulated proteins are encircled.

variance, ANOVA) were performed using this software package. Factors indicating up- and down-regulation of proteins in 2D gels were obtained using normalized integrated spot intensities.

VERENA HAUDEK PhD-thesis

1D-PAGE for Subsequent Shotgun analysis. The cytoplasmic protein fraction of the PBMC was loaded onto the slots of a 13% polyacrylamid gel; electrophoresis was performed until complete separation of the molecular marker (Dual Color, Bio-Rad) was achieved. Gels were fixed with 50% methanol/10% acidic acid and subsequently silver stained as described below. The different lanes were cut out of the gel with respect to the molecular weights shown by the molecular marker. The resulting thin gel-lanes were digested with trypsin as described below.

MS-Compatible Silver Staining Procedure for Proteolytic Digest. Gels were fixed with 50% methanol, washed and sensitized with 0.02% $\text{Na}_2\text{S}_2\text{O}_3$. They were stained with ice-cold 0.1% AgNO_3 for 20 min, rinsed with bidistilled water and subsequently developed with 3% Na_2CO_3 /0.05% formaldehyde as previously described.²⁹

Tryptic Digestion. Silver stained gel pieces were destained with 15 mM $\text{K}_3\text{Fe}(\text{CN})_6$ /50 mM $\text{Na}_2\text{S}_2\text{O}_3$ and intensively washed with 50% methanol/10% acetic acid. The pH was adjusted with 50 mM NH_4HCO_3 ; the proteins were reduced with 10 mM DTT/50 mM NH_4HCO_3 and alkylated with 50 mM iodoacetamide/50 mM NH_4HCO_3 for 20 min in the dark. After drying, the gel pieces were treated with 0.1 mg/mL trypsin (Trypsin sequencing grade, Roche Diagnostics, Germany)/50 mM NH_4HCO_3 overnight at 37 °C. Peptides were eluted with 5% formic acid/50% acetonitrile and concentrated in the Speed-Vac to an appropriate volume.

Mass Spectrometry Analysis. For the identification of 2D spots, peptides were loaded on a Zorbax 300SB-C8 (5 μm , 0.3 mm, 5 mm) column and separated by nanoflow LC (1100 Series LC system, Agilent, Palo Alto, CA) with a Zorbax 300SB-C18 (5 μm , 75 mm, 150 mm) column at a flow rate of 250 nL/min using a gradient from 0.2% formic acid and 3% acetonitrile (ACN) to 0.2% formic acid and 45% ACN over 12 min. In case of shotgun analysis, peptides were separated by nanoflow LC (1100 Series LC system, Agilent, Palo Alto, CA) using the HPLC-Chip technology (Agilent) equipped with a 40 nL Zorbax 300SB-C18 trapping column and a 75 μm × 150 mm Zorbax 300SB-C18 separation column at a flow rate of 400 nL/min, using a gradient from 0.2% formic acid and 3% ACN to 0.2% formic acid and 50% ACN over 60 min. Peptide identification was accomplished by MS/MS fragmentation analysis with an ion-trap mass spectrometer (XCT-Ultra, Agilent) equipped with an orthogonal nanospray ion source. The MS/MS data, including peak list-generation and search engine, were interpreted by the Spectrum Mill MS Proteomics Workbench software (Version A.03.02, Agilent). The software was set to allow two missed cleavages and searched against the Swiss-Prot Database for human proteins (Version 20080409 containing 19 038 entries) allowing for precursor mass deviation of 1.5 Da, a product mass tolerance of 0.7 Da and a minimum matched peak intensity (%SPI) of 70%. Because of previous chemical modification, carbamidomethylation of cysteines was set as fixed modification. No other modifications were considered here.

The following protein selection algorithm was applied for the generation of the final protein lists. Peptide scores were used to select appropriate sequence assignments. To assess the reliability of the peptide scores, we performed searches against the corresponding reversed database. A total of 5.9% positive hits were found with peptides scoring >9.0, while 0.21% positive hits were found with peptides scoring >13.0. Only peptides scoring higher than 9.0 were considered for protein identification. Identification details for each protein including

all identified peptides, sequence coverage, peptide scores and MS/MS spectra are fully accessible via PRIDE database (<http://www.ebi.ac.uk/pride/>),^{30,31} PRIDE accessions 3844–59. Table S1 in Supporting Information was generated by combining all independent shotgun experiments from the *in vitro* experiments. These combinations comprise all peptides related to single proteins which were collected from all individual experiments. Proteins were selected based on the expression of specific peptides (identified in one protein only, indicated in Table S1, row “Sg” in Supporting Information). Selection of protein isoforms was performed as described by Zhang et al.³²

Semiquantitative assessment was performed using the number of distinct peptides identified per protein. This approach is based on the fact that the number of peptides identified per protein increases with the concentration. For comparative analysis, we considered the difference of the number of distinct peptides per protein in the reference maps such as control versus treated. Furthermore, we introduced the matching factor. The matching factor shows the average difference between different sets of data. An increase of 6 peptides, for example, for a protein comparing the hydrogen peroxide-treated PBMCs to the untreated PBMCs with a matching factor of 0.33 translates to an average increase of two ($= 6 \times 0.33$) peptides observed in the four experiments. We considered proteins as up-regulated when the average increase in peptide number was more than one-third of the number of peptides of the corresponding control. Down-regulation was calculated vice versa.

Results and Discussion

In all 2D gels of the current study from cytoplasmic proteins isolated from PBMCs, 1034 spots were reproducibly detected. A total of 670 of these spots were successfully identified by mass spectrometry, corresponding to 519 different proteins (Figure 1). These 519 proteins were accessible to quantification via fluorescence detection as well as [³⁵S]-autoradiography. Furthermore, 1432 different proteins were independently identified by shotgun analysis. A total of 513 of the 519 proteins identified in the 2D gels were also independently identified by shotgun proteomics (Table S1 in Supporting Information).

Protein Expression Alterations of Primary White Blood Cells Induced by Oxidative Stress *in Vitro*. Treatment with hydrogen peroxide induced distinct proteome alterations as illustrated in Figure 2. We observed a general average increase of the [³⁵S]-incorporation of 42% ($\pm 29\%$). This was determined by summarizing the corresponding [³⁵S]-autoradiography spot intensities of all detected 2D gel spots. To elude this bias, quantitative assessment was corrected by normalization. Most importantly, the observed proteome alteration pattern was reproduced with cells derived from all donors as demonstrated in Figure 3. Seventeen proteins were found significantly (ANOVA $p < 0.05$) up-regulated and nine proteins were found significantly down-regulated (Table 1). By shotgun analysis of the corresponding protein samples, we found nine proteins markedly and reproducibly up-regulated and 23 down-regulated by hydrogen peroxide treatment (Table 1).

Somewhat unexpectedly, rather few redox-regulating proteins were found regulated. Table 1 lists some of these proteins which were successfully identified but did not show detectable alterations. Proteins presently found to be affected may be related to one of the following scenarios:

(1) Indication of Cell Stress. Up-regulation of several chaperones, cytoskeletal proteins, redox-regulating enzymes

and proteins related to DNA-repair was observed (Table 1) and was concordant with published data. Hydrogen peroxide may indirectly damage proteins by the introduction of oxidative modifications and thus functional inactivation, which may cause the observed cell stress response. These regulatory events may as well demonstrate the direct effort of the cells to cope with ROS. The observed down-regulation of ATP-dependent DNA helicase 2 subunits 1 and 2 (Ku antigens 70 and 80, Table 1) is consistent with cancelation of cell proliferation consequent to a general stress response.

(2) Indication of Distinct Survival Strategy. The cell stress response indicated above is a general survival strategy of cells. It is evoked in response to very different kinds of stressors. We also observed a distinct down-regulation of Mn-SOD which appears to be rather specific for oxidative-stress. One potential explanation might be the inactivation of this enzyme by hydrogen peroxide followed by proteasomal degradation as described for Cu/Zn-SOD (copper/zinc superoxide dismutase) in red blood cells by Salo et al.³³ Another explanation might be that this down-regulation is part of the cells' survival strategy. Mn-SOD decomposes superoxide to hydrogen peroxide, which is then processed to molecular oxygen and water by catalase, glutathione peroxidase and peroxiredoxin.^{2,10} If the capacity of the hydrogen peroxide processing enzymes such as catalase is insufficient, the catalysis of the reverse conversion of H₂O₂ to superoxide by Mn-SOD will predominate. Immediate down-regulating Mn-SOD synthesis may be a strategy to reduce superoxide production under acute oxidative stress. Quite notably, under conditions designed to reduce oxidative stress which were introduced in a controlled Brussels sprouts intervention study, Mn-SOD was found significantly up-regulated. This was accompanied by the down-regulation of hsp70.³⁴ In other studies, the down-regulation of Mn-SOD was also described in association with tumor-suppressor activity of this protein.^{35–37} We therefore suggest that down-regulation of Mn-SOD may be a specific response and thus an indicator for oxidative stress.

A similar interpretation applies to the observed down-regulation of proteins involved in energy metabolism (Table 1). As ROS formation invariably accompanies oxidative phosphorylation, it could make sense for cells to down-regulate the corresponding processes in order to increase the chance of survival.

(3) Indication of Compensatory Up-Regulation of Protein Synthesis. Several proteins, including hsp70, annexin A1, purine nucleoside phosphorylase and tubulin alpha displayed increased protein synthesis. However, shotgun analysis determined them to be decreased in protein amounts (Table 1). This apparent discrepancy may actually suggest a oxidative stress-induced loss of these proteins, accompanied by compensatory up-regulation of protein synthesis. This suggests that these proteins might be targets highly susceptible to irreversible oxidative damage.

(4) Inflammatory Activation of Monocytes. The increased expression of IL-1 β may indicate inflammatory activation of monocytes. Up-regulation of ficolin, an opsonin and thymidine phosphorylase (which is also known as platelet-derived endothelial cell growth factor) would be in line with this interpretation.

Assessment of Plasma Peroxidation Levels. Direct assessment of peroxidation was performed with plasma samples taken from 10 patients with cancer and 10 control persons matched in age and sex. Peroxidation of plasma samples was measured with the TBA assay.⁷ Figure 4 shows the significant

difference in the peroxidation level between the “control” and the “cancer” group. The calculated average malondialdehyde (MDA) value for the “control” group was 1.6 $\mu\text{mol/L}$ and for the “cancer” group 2.9 $\mu\text{mol/L}$. The absolute values obtained by this method may be somewhat inaccurate.³⁸ To investigate relative alterations of lipid peroxidation, this is a well-established method providing significant varieties.^{39,40} With the use of the hydroperoxide assay with ferric XO complex, the observed difference (although apparently more pronounced than that obtained with the TBA assay) was not significant.

Protein Expression Alterations of Primary White Blood Cells Related to Oxidative Stress *in Vivo*. PBMCs from blood of the donors described above were isolated. Comparative proteome analysis was performed focusing on the determination of protein amounts by 2D-PAGE for all 20 individual samples.

Compared to the group of PBMCs derived from healthy donors, the PBMCs isolated from cancer patients displayed eight significantly regulated proteins (ANOVA, $p < 0.05$, Figure 5, Table 1).

Shotgun analysis was performed with PBMCs from four members of each group. All proteins identified as altered by 2D-PAGE displayed a similar tendency of regulation with shotgun analysis. As exemplified in Figure 5, we observed some characteristic alterations. These alterations appear to be mainly related to chronic inflammation, metabolism and apoptosis regulation (Table 1). These data suggest that PBMCs of cancer patients may indeed display characteristic proteome alterations. None of these alterations, however, could be clearly related to oxidative stress.

Conclusion

In this study, a distinct proteome response of PBMCs to *in vitro* hydrogen peroxide treatment was observed. Besides classical indicators for stress response, the observed proteome alterations indicate cellular strategies to minimize superoxide production in order to increase the chances of survival. No potential single marker protein specifically induced by oxidative stress and up-regulated in PBMCs of cancer patients was identified. Down-regulation of Mn-SOD, however, may serve as characteristic marker to indicate oxidative stress. The present data suggest that the combined assessment of proteins related to survival, redox regulation and DNA damage repair in PBMCs may prove useful to specifically detect oxidative stress *in vivo*.

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Supporting Information Available: Table S1, list of proteins identified in PBMCs. Proteins are sorted according to protein names and identified by their Swiss-Prot Accession numbers. In addition, molecular weight, pI value, the number of distinct peptides identified per protein (Pep.) and the consequent sequence coverage (AA%) are indicated. Proteins, which contained at least one distinct peptide (row “Sg”) and which were independently identified as well in 2D gels (row “2D”) are marked (X). This material is available free of charge via the Internet at <http://pubs.acs.org>.

VERENA HAUDEK PhD-thesis

References

- (1) Abuja, P. M.; Albertini, R. Methods for monitoring oxidative stress, lipid peroxidation and oxidation resistance of lipoproteins. *Clin. Chim. Acta* **2001**, *306* (1–2), 1–17.
- (2) Karihtala, P.; Soini, Y. Reactive oxygen species and antioxidant mechanisms in human tissues and their relation to malignancies. *APMIS* **2007**, *115* (2), 81–103.
- (3) Pryor, W. A. Cancer and free radicals. *Basic Life Sci.* **1986**, *39*, 45–59.
- (4) Diplock, A. T. Defense against reactive oxygen species. *Free Radical Res.* **1998**, *29* (6), 463–7.
- (5) Klaunig, J. E.; Kamendulis, L. M. The role of oxidative stress in carcinogenesis. *Annu. Rev. Pharmacol. Toxicol.* **2004**, *44*, 239–67.
- (6) Brown, N. S.; Bicknell, R. Hypoxia and oxidative stress in breast cancer. Oxidative stress: its effects on the growth, metastatic potential and response to therapy of breast cancer. *Breast Cancer Res.* **2001**, *3* (5), 323–7.
- (7) Du, J.; Gebicki, J. M. Proteins are major initial cell targets of hydroxyl free radicals. *Int. J. Biochem. Cell Biol.* **2004**, *36* (11), 2334–43.
- (8) Gieseg, S.; Duggan, S.; Gebicki, J. M. Peroxidation of proteins before lipids in U937 cells exposed to peroxyl radicals. *Biochem. J.* **2000**, *350* Pt 1, 215–8.
- (9) Meyer, H. E.; Stuhler, K. High-performance proteomics as a tool in biomarker discovery. *Proteomics* **2007**, *7* (1), 18–26.
- (10) Giorgio, M.; Trinei, M.; Migliaccio, E.; Pelicci, P. G. Hydrogen peroxide: a metabolic by-product or a common mediator of ageing signals. *Nat. Rev. Mol. Cell Biol.* **2007**, *8* (9), 722–8.
- (11) Dalle-Donne, I.; Scaloni, A.; Giustarini, D.; Cavarra, E.; Tell, G.; Lungarella, G.; Colombo, R.; Rossi, R.; Milzani, A. Proteins as biomarkers of oxidative/nitrosative stress in diseases: the contribution of redox proteomics. *Mass Spectrom. Rev.* **2005**, *24* (1), 55–99.
- (12) Klaunig, J. E.; Xu, Y.; Isenberg, J. S.; Bachowski, S.; Kolaja, K. L.; Jiang, J.; Stevenson, D. E.; Walborg, E. F., Jr. The role of oxidative stress in chemical carcinogenesis. *Environ. Health Perspect.* **1998**, *106* (106), 289–95.
- (13) Rabilloud, T.; Chevallet, M.; Luche, S.; Leize-Wagner, E. Oxidative stress response: a proteomic view. *Expert Rev. Proteomics* **2005**, *2* (6), 949–56.
- (14) Sheehan, D. Detection of redox-based modification in two-dimensional electrophoresis proteomic separations. *Biochem. Biophys. Res. Commun.* **2006**, *349* (2), 455–62.
- (15) Wan, X. Y.; Liu, J. Y. Comparative proteomic analysis reveals an intimate protein network provoked by hydrogen peroxide stress in rice seedling leaves. *Mol. Cell. Proteomics* **2008**, *7*, 1469–88.
- (16) Kusch, H.; Engelmann, S.; Albrecht, D.; Morschhauser, J.; Hecker, M. Proteomic analysis of the oxidative stress response in *Candida albicans*. *Proteomics* **2007**, *7* (5), 686–97.
- (17) Lee, C. K.; Park, H. J.; So, H. H.; Kim, H. J.; Lee, K. S.; Choi, W. S.; Lee, H. M.; Won, K. J.; Yoon, T. J.; Park, T. K.; Kim, B. Proteomic profiling and identification of cofilin responding to oxidative stress in vascular smooth muscle. *Proteomics* **2006**, *6* (24), 6455–75.
- (18) Seong, J. K.; Kim, D. K.; Choi, K. H.; Oh, S. H.; Kim, K. S.; Lee, S. S.; Um, H. D. Proteomic analysis of the cellular proteins induced by adaptive concentrations of hydrogen peroxide in human U937 cells. *Exp. Mol. Med.* **2002**, *34* (5), 374–8.
- (19) Yamamoto, T.; Kikkawa, R.; Yamada, H.; Horii, I. Identification of oxidative stress-related proteins for predictive screening of hepatotoxicity using a proteomic approach. *J. Toxicol. Sci.* **2005**, *30* (3), 213–27.
- (20) Yan, Y.; Weaver, V. M.; Blair, I. A. Analysis of protein expression during oxidative stress in breast epithelial cells using a stable isotope labeled proteome internal standard. *J. Proteome Res.* **2005**, *4* (6), 2007–14.
- (21) Butterfield, D. A.; Sultana, R. Redox proteomics: understanding oxidative stress in the progression of age-related neurodegenerative disorders. *Expert Rev. Proteomics* **2008**, *5* (2), 157–60.
- (22) Stone, J. R. An assessment of proposed mechanisms for sensing hydrogen peroxide in mammalian systems. *Arch. Biochem. Biophys.* **2004**, *422* (2), 119–24.
- (23) Gerner, C.; Sauermann, G. Nuclear matrix proteins specific for subtypes of human hematopoietic cells. *J. Cell Biochem.* **1999**, *72* (4), 470–82.
- (24) Traxler, E.; Bayer, E.; Stockl, J.; Mohr, T.; Lenz, C.; Gerner, C. Towards a standardized human proteome database: quantitative proteome profiling of living cells. *Proteomics* **2004**, *4* (5), 1314–23.
- (25) Gay, C.; Collins, J.; Gebicki, J. M. Hydroperoxide assay with the ferric-xylenol orange complex. *Anal. Biochem.* **1999**, *273* (2), 149–55.

- (26) Gundacker, N.; Bayer, E.; Traxler, E.; Zwickl, H.; Kubicek, M.; Stockl, J.; Gerner, C. Knowledge-based proteome profiling: considering identified proteins to evaluate separation efficiency by 2-D PAGE. *Electrophoresis* **2006**, *27* (13), 2712–21.
- (27) Rabilloud, T.; Strub, J. M.; Luche, S.; van Dorsselaer, A.; Lunardi, J. A comparison between Sypro Ruby and ruthenium II tris (bathophenanthroline disulfonate) as fluorescent stains for protein detection in gels. *Proteomics* **2001**, *1* (5), 699–704.
- (28) Zwickl, H.; Traxler, E.; Staettner, S.; Parzefall, W.; Grasl-Kraupp, B.; Karner, J.; Schulte-Hermann, R.; Gerner, C. A novel technique to specifically analyze the secretome of cells and tissues. *Electrophoresis* **2005**, *26* (14), 2779–85.
- (29) Mortz, E.; Krogh, T. N.; Vorum, H.; Gorg, A. Improved silver staining protocols for high sensitivity protein identification using matrix-assisted laser desorption/ionization-time of flight analysis. *Proteomics* **2001**, *1* (11), 1359–63.
- (30) Jones, P.; Cote, R. G.; Cho, S. Y.; Klie, S.; Martens, L.; Quinn, A. F.; Thorneycroft, D.; Hermjakob, H. PRIDE: new developments and new datasets. *Nucleic Acids Res.* **2008**, *36* (Database issue), D878–83.
- (31) Jones, P.; Cote, R. G.; Martens, L.; Quinn, A. F.; Taylor, C. F.; Derache, W.; Hermjakob, H.; Apweiler, R. PRIDE: a public repository of protein and peptide identifications for the proteomics community. *Nucleic Acids Res.* **2006**, *34* (Database issue), D659–63.
- (32) Zhang, B.; Chambers, M. C.; Tabb, D. L. Proteomic parsimony through bipartite graph analysis improves accuracy and transparency. *J. Proteome Res.* **2007**, *6* (9), 3549–57.
- (33) Salo, D. C.; Pacifici, R. E.; Lin, S. W.; Giulivi, C.; Davies, K. J. Superoxide dismutase undergoes proteolysis and fragmentation following oxidative modification and inactivation. *J. Biol. Chem.* **1990**, *265* (20), 11919–27.
- (34) Hoelzl, C.; Lorenz, O.; Haudek, V.; Gundacker, N.; Knasmüller, S.; Gerner, C. Proteome alterations induced in human white blood cells by consumption of Brussel sprouts: Results of a pilot intervention study. *Proteomics Clin. Appl.* **2008**, *2* (1), 108–117.
- (35) Chuang, T. C.; Liu, J. Y.; Lin, C. T.; Tang, Y. T.; Yeh, M. H.; Chang, S. C.; Li, J. W.; Kao, M. C. Human manganese superoxide dismutase suppresses HER2/neu-mediated breast cancer malignancy. *FEBS Lett.* **2007**, *581* (23), 4443–9.
- (36) Oberley, L. W. Mechanism of the tumor suppressive effect of MnSOD overexpression. *Biomed. Pharmacother.* **2005**, *59* (4), 143–8.
- (37) Soini, Y.; Vakkala, M.; Kahlos, K.; Paakko, P.; Kinnula, V. MnSOD expression is less frequent in tumour cells of invasive breast carcinomas than in situ carcinomas or non-neoplastic breast epithelial cells. *J. Pathol.* **2001**, *195* (2), 156–62.
- (38) Halliwell, B.; Chirico, S. Lipid peroxidation: its mechanism, measurement, and significance. *Am. J. Clin. Nutr.* **1993**, *57* (5), 715S–724S, discussion 724S–725S.
- (39) Sitta, A.; Barschak, A. G.; Deon, M.; Terroso, T.; Pires, R.; Giugliani, R.; Dutra-Filho, C. S.; Wajner, M.; Vargas, C. R. Investigation of oxidative stress parameters in treated phenylketonuric patients. *Metab. Brain Dis.* **2006**, *21* (4), 287–96.
- (40) Nadeem, A.; Raj, H. G.; Chhabra, S. K. Increased oxidative stress and altered levels of antioxidants in chronic obstructive pulmonary disease. *Inflammation* **2005**, *29* (1), 23–32.
- (41) Eleuterio, E.; Di Giuseppe, F.; Sulpizio, M.; di Giacomo, V.; Rapino, M.; Cataldi, A.; Di Ilio, C.; Angelucci, S. Proteome analysis of X-ray irradiated human erythroleukemia cells. *Biochim. Biophys. Acta* **2008**, *1784* (4), 611–20.
- (42) Rhee, H. J.; Kim, G. Y.; Huh, J. W.; Kim, S. W.; Na, D. S. Annexin I is a stress protein induced by heat, oxidative stress and a sulfhydryl-reactive agent. *Eur. J. Biochem.* **2000**, *267* (11), 3220–5.
- (43) Panaretakis, T.; Joza, N.; Modjtahedi, N.; Tesniere, A.; Vitale, I.; Durchschlag, M.; Fimia, G. M.; Kepp, O.; Piacentini, M.; Froehlich, K. U.; van Endert, P.; Zitvogel, L.; Madeo, F.; Kroemer, G. The co-translocation of ERp57 and calreticulin determines the immunogenicity of cell death. *Cell Death Differ.* **2008**, *15*, 1499–509.
- (44) Matsuoka, S.; Ballif, B. A.; Smogorzewska, A.; McDonald, E. R., III; Hurov, K. E.; Luo, J.; Bakalarski, C. E.; Zhao, Z.; Solimini, N.; Lerenthal, Y.; Shiloh, Y.; Gygi, S. P.; Elledge, S. J. ATM and ATR substrate analysis reveals extensive protein networks responsive to DNA damage. *Science* **2007**, *316* (5828), 1160–6.
- (45) Jaeger, J.; Koczan, D.; Thiesen, H. J.; Ibrahim, S. M.; Gross, G.; Spang, R.; Kunz, M. Gene expression signatures for tumor progression, tumor subtype, and tumor thickness in laser-microdissected melanoma tissues. *Clin. Cancer Res.* **2007**, *13* (3), 806–15.
- (46) Gerner, C.; Gotzmann, J.; Frohwein, U.; Schamberger, C.; Ellinger, A.; Saueremann, G. Proteome analysis of nuclear matrix proteins during apoptotic chromatin condensation. *Cell Death Differ.* **2002**, *9* (6), 671–81.
- (47) Galkin, V. E.; Orlova, A.; Briehner, W.; Kueh, H. Y.; Mitchison, T. J.; Egelman, E. H. Coronin-1A stabilizes F-Actin by bridging adjacent Actin protomers and stabilizing opposite strands of the actin filament. *J. Mol. Biol.* **2008**, *376* (3), 607–13.
- (48) Delanote, V.; Vandekerckhove, J.; Gettemans, J. Plastins: versatile modulators of Actin organization in (patho)physiological cellular processes. *Acta Pharmacol. Sin.* **2005**, *26* (7), 769–79.
- (49) Manevich, E.; Grabovsky, V.; Feigelson, S. W.; Alon, R. Talin 1 and paxillin facilitate distinct steps in rapid VLA-4-mediated adhesion strengthening to vascular cell adhesion molecule 1. *J. Biol. Chem.* **2007**, *282* (35), 25338–48.
- (50) Xing, K. Y.; Lou, M. F. Effect of H(2)O(2) on human lens epithelial cells and the possible mechanism for oxidative damage repair by thioltransferase. *Exp. Eye Res.* **2002**, *74* (1), 113–22.
- (51) Aung, W.; Hasegawa, S.; Furukawa, T.; Saga, T. Potential role of ferritin heavy chain in oxidative stress and apoptosis in human mesothelial and mesothelioma cells: implications for asbestos-induced oncogenesis. *Carcinogenesis* **2007**, *28* (9), 2047–52.
- (52) Hayes, J. D.; Strange, R. C. Potential contribution of the glutathione S-transferase supergene family to resistance to oxidative stress. *Free Radical Res.* **1995**, *22* (3), 193–207.
- (53) Banki, K.; Hutter, E.; Colombo, E.; Gonchoroff, N. J.; Perl, A. Glutathione levels and sensitivity to apoptosis are regulated by changes in transaldolase expression. *J. Biol. Chem.* **1996**, *271* (51), 32994–3001.
- (54) Boraldi, F.; Bini, L.; Liberatori, S.; Armini, A.; Pallini, V.; Tiozzo, R.; Pasquali-Ronchetti, I.; Quagliano, D. Proteome analysis of dermal fibroblasts cultured in vitro from human healthy subjects of different ages. *Proteomics* **2003**, *3* (6), 917–29.
- (55) Qi, J.; Liu, N.; Zhou, Y.; Tan, Y.; Cheng, Y.; Yang, C.; Zhu, Z.; Xiong, D. Overexpression of sorcin in multidrug resistant human leukemia cells and its role in regulating cell apoptosis. *Biochem. Biophys. Res. Commun.* **2006**, *349* (1), 303–9.
- (56) Kawakami, M.; Nakamura, T.; Okamura, N.; Komoto, C.; Markova, S.; Kobayashi, H.; Hashimoto, N.; Okumura, K.; Sakaeda, T. Knock-down of sorcin induces up-regulation of MDR1 in HeLa cells. *Biol. Pharm. Bull.* **2007**, *30* (6), 1065–73.
- (57) Rabinovich, G. A. Galectin-1 as a potential cancer target. *Br. J. Cancer* **2005**, *92* (7), 1188–92.
- (58) Gebhardt, C.; Nemeth, J.; Angel, P.; Hess, J. S100A8 and S100A9 in inflammation and cancer. *Biochem. Pharmacol.* **2006**, *72* (11), 1622–31.
- (59) Yong, H. Y.; Moon, A. Roles of calcium-binding proteins, S100A8 and S100A9, in invasive phenotype of human gastric cancer cells. *Arch. Pharm. Res.* **2007**, *30* (1), 75–81.
- (60) Sherbet, G. V.; Lakshmi, M. S. S100A4 (MTS1) calcium binding protein in cancer growth, invasion and metastasis. *Anticancer Res.* **1998**, *18* (4A), 2415–21.
- (61) Tarabykina, S.; Griffiths, T. R.; Tulchinsky, E.; Mellon, J. K.; Bronstein, I. B.; Kriaievska, M. Metastasis-associated protein S100A4: spotlight on its role in cell migration. *Curr. Cancer Drug. Targets* **2007**, *7* (3), 217–28.
- (62) Kondoh, H.; Leonart, M. E.; Bernard, D.; Gil, J. Protection from oxidative stress by enhanced glycolysis; a possible mechanism of cellular immortalization. *Histol. Histopathol.* **2007**, *22* (1), 85–90.
- (63) Imai, A.; Sugiyama, M.; Furui, T.; Tamaya, T. Gi protein-mediated translocation of serine/threonine phosphatase to the plasma membrane and apoptosis of ovarian cancer cell in response to gonadotropin-releasing hormone antagonist cetrorelix. *J. Obstet. Gynaecol.* **2006**, *26* (1), 37–41.
- (64) Garcia, A.; Cayla, X.; Guernon, J.; Dessauge, F.; Hospital, V.; Rebollo, M. P.; Fleischer, A.; Rebollo, A. Serine/threonine protein phosphatases PP1 and PP2A are key players in apoptosis. *Biochimie* **2003**, *85* (8), 721–6.
- (65) Su, C. C.; Lin, J. G.; Li, T. M.; Chung, J. G.; Yang, J. S.; Ip, S. W.; Lin, W. C.; Chen, G. W. Curcumin-induced apoptosis of human colon cancer colo 205 cells through the production of ROS, Ca²⁺ and the activation of caspase-3. *Anticancer Res.* **2006**, *26* (6B), 4379–89.
- (66) Ubol, S.; Kramyu, J.; Masrinoul, P.; Kachangchaeng, C.; Pittayanurak, P.; Sophasan, S.; Reutrakul, V. A novel cycloheptapeptide exerts strong anticancer activity via stimulation of multiple apoptotic pathways in caspase-3 deficient cancer cells. *Anticancer Res.* **2007**, *27* (4B), 2473–9.
- (67) Shang, F.; Gong, X.; Taylor, A. Activity of ubiquitin-dependent pathway in response to oxidative stress. Ubiquitin-activating enzyme is transiently up-regulated. *J. Biol. Chem.* **1997**, *272* (37), 23086–93.

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RESEARCH ARTICLE

Proteome alterations induced in human white blood cells by consumption of Brussels sprouts: Results of a pilot intervention study

Christine Hoelzl, Olga Lorenz, Verena Haudek, Nina Gundacker, Siegfried Knasmüller and Christopher Gerner

Internal Medicine Clinic I, Institute of Cancer Research, Medical University of Vienna, Vienna, Austria

Epidemiological studies indicate a correlation of cruciferous vegetables consumption with reduced incidence of cancer. This study was designed to investigate molecular mechanisms, which may help to understand the beneficial effects of Brussels sprout consumption. In order to avoid the limitations of *in vitro* model systems, we performed a dietary intervention study with five participants. We investigated, whether sprout consumption affects the proteome profile of primary white blood cells. In order to achieve maximal sensitivity in detecting specific adaptive proteome alterations, we metabolically labelled freshly isolated cells in the presence of ³⁵S-methionine/cysteine and performed autoradiographic quantification of protein synthesis. Proteins were separated by 2-DE and spots of interest were cut out, digested and identified by MS. After the intervention, we found a significant up-regulation of the synthesis of manganese superoxide dismutase (1.56-fold) and significant down-regulation of the synthesis of heat shock 70 kDa protein (hsp70; 2.27-fold). Both proteins play a role in malignant transformation of cells. Hsp-70 is involved in the regulation of apoptosis, which leads to elimination of cancer cells, while SOD plays a key role in protection against reactive oxygen species mediated effects. Our findings indicate that the alteration of the synthesis of these proteins may be involved in the anti-carcinogenic effects of cruciferous vegetables, which was observed in earlier laboratory studies with animals.

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1 Introduction

Numerous epidemiological studies indicate that consumption of cruciferous vegetables is inversely related with the incidence of various form of cancer, in particular with colo-

rectal cancer; in some studies also inverse relations were observed with the incidences of lung, prostate and breast cancer [1–4]. Already in the 1970s, Wattenberg and co-workers [5, 6] reported that feeding of active compounds of these vegetables protects laboratory rodents against induction of cancer by polycyclic aromatic hydrocarbons; subsequent investigation confirmed these findings and showed that Brassicas are also protective against other dietary carcinogens such as nitrosamines and heterocyclic aromatic amines (for review see [7]). The chemoprotective properties of these plants were attributed to breakdown products (indoles, nitriles and isothiocyanates) of glucosinolates, which are constituents of cruciferous plants and were explained by modulation of the activities of drug metabolising enzymes (*e.g.*

Correspondence: Professor Christopher Gerner, Internal Medicine Clinic I, Institute of Cancer Research, Medical University of Vienna, Borschkegasse 8a, Vienna, Austria

E-mail: christopher.gerner@meduniwien.ac.at

Fax: +43-1-4277-9651

Abbreviations: hsp70, heat shock 70 kDa protein; Mn-SOD, manganese superoxide dismutase

GST, glucuronosyl transferase), which catalyse the activation and detoxification of these carcinogens [8]. Subsequent investigations showed that the glucosinolate metabolites activate transcription factors (*e.g.* Nrf2), which increase the transcription of phases I and II, as well as of antioxidant enzymes and of a number of proteins involved in cell signalling [1, 9, 10]. Apart from alterations of the activities of xenobiotic drug metabolising enzymes, also other mechanisms of cancer chemoprevention were identified. For example, potential protective effects towards breast cancer were explained on the basis of findings, which indicated that indoles inhibit the transcription of estrogen responsive genes (87R, 88R) and increase the excretion of 2-OHestrone (87R, 98R). Also induction of cell cycle arrest and apoptosis [1] as well as inhibition of tumour invasion and anti-inflammatory properties due to reduced binding of DNA to NF- κ B-a pro-inflammatory transcription factor may play a role in the cancer protective properties of Brassica vegetables [11].

In a recent intervention trial, we found in single cell gel electrophoresis assays that consumption of sprouts (300 g/P/day) over a period of 5 days causes a strong reduction of endogenous formation of oxidised DNA bases and reduces the sensitivity of the cells towards exogenous DNA damage by reactive oxygen species in peripheral lymphocytes [12].

The present article describes the results of a follow up study using an identical design and the same sprout cultivar as in the previous trial. Here, the impact of sprouts consumption on the protein expression profile of white blood cells was investigated. It has been emphasised repeatedly that proteomics is an important tool to improve our current knowledge of cancer prevention by dietary factors [13–17], but only few investigations have been published in which this technique was used to investigate the impact of dietary factors in animal models [18–20] or cell cultures [21–28].

2 Materials and methods

2.1 Brussels sprouts

The study was carried out with the cultivar 'Cyrus'. The glucosinolate contents of this variety have been analysed earlier by HPLC (for details see [21]).

2.2 Design of the intervention study

Five healthy, nonsmoking participants (age: 33 ± 7 years, b.w.: 60 ± 7 kg, three males, two females) were included in the experiment. All of them were nonvegetarians and did not use pharmaceutical drugs 1 month before the study. Furthermore, they did not consume vitamin supplements or vitamin-enriched foods 5 days before ('run in'-phase) and during the intervention (5 days). The study design was identical to that of an earlier study in which the impact of Brussels sprouts consumption on DNA-stability in lymphocytes was studied [12], and similar run in-phase (5–7 days) have

been used in a number of earlier human intervention studies [22–24]. Five days before and during the intervention period (5 days), the volunteers were asked to consume a controlled diet to avoid inter individual differences, which may arise from different dietary habits. The usual food intake was recorded by use of a standardised questionnaire [25] and all of the participants consumed only low amounts of cruciferous vegetables (≤ 200 g/month). The evaluation also showed that all of them consumed a typical mixed (Austrian) diet (energy intake 2000–2540 kcal/day). All of them were provided with an information sheet in which the diet before and during the intervention was specified in detail, and were asked to record the approximate consumption of the controlled items on a daily base. The participants were not allowed to consume additional cruciferous vegetables and refrained from intake of more than 200 g/day of citrus fruits, fruit juices, onions and wholemeal products. It is known from earlier studies which were conducted with conventional techniques that these dietary factors cause antioxidant effects and/or induce detoxifying (phase II) enzymes [26–28]. Furthermore, it has also been shown for individual constituents such as resveratrol [18], quercetin [28], ascorbic acid [29] and genistein [30] that they affect the protein expression patterns. Therefore, additive or synergistic effects in combination of these items with consumption of Brussels sprouts cannot be excluded. Furthermore, the participants were also asked not to consume more than 200 mL wine, beer or coffee *per* day. During the intervention, the participants consumed one portion (300 g) of Brussels sprouts *per* day over a period of 5 days. At lunchtime, the deep frozen vegetables were cooked in a microwave (8 min, 950 W, Micromat 175Z, AEG Elektrolux, Stockholm) and were subsequently distributed to the participants who consumed them in 2–3 portions during the rest of the day (*i.e.* half of them during lunchtime and the second portion as dinner – between 6 and 8 pm). At the beginning and at the end of the study (after the last intervention day) 40 mL blood were collected in heparinised tubes (BN Vacutainer Systems, Plymouth, UK) in the morning (8 am). The rationale for the time schedule was designed on the basis of the results of earlier investigations [24]. Cruciferous vegetables (including Brussels sprouts) contain a specific group of chemoprotective compounds, so-called glucosinolates (for review see [4, 32, 33]). Their breakdown products and a number of metabolites are found transiently (up to 24 h) in the blood after consumption of Brassicas [24]. It is known from experiments with individual model compounds (*e.g.* sulphoraphane and phenethyl isothiocyanate) that they affect the transcription of numerous genes, in particular those controlled by the transcription factors Nrf2 and NF- κ B [9–11, 34–36].

2.3 Cell preparation

Peripheral blood mononuclear cells (PBMC) were isolated from heparinised whole blood of healthy donors (mixed with 2 vol. HBSS) by standard density gradient centrifugation

with Ficoll-Paque (Pharmacia Biotech). The interface cells (PBMF, here white blood cells, WBC) were resuspended in autologous plasma and supplemented with 0.2 mCi/mL ^{35}S Protein labelling Mix (Trans35label, Biomedica, MP Bio-medicals). After 6 h at 37°C in a humidified atmosphere containing 5% CO_2 , cells were washed and fractionated. Washing and fractionation was carried out at 4°C.

2.4 Subcellular fractionation

All buffers were supplemented with protease inhibitors PMSF (1 mM), aprotinin, leupeptin and pepstatin A (each at 1 mg/mL). Cells were lysed in 0.25 M sucrose, 3 mM MgCl_2 , 0.5% Triton X-100 in hypotonic buffer (10 mM HEPES/NaOH, pH 7.4, 10 mM NaCl, 3 mM MgCl_2). The cytoplasmatic fraction was separated from the nuclei by centrifugation through a 30% Sucrose gradient at 3500 rpm for 5 min at 4°C. After ethanol precipitation, the pelleted cytoplasmatic protein fraction was directly solubilised in sample buffer.

2.5 2-D PAGE

High resolution 2-DE was carried out as described previously [37] using a slightly modified method according to Hochstrasser *et al.* [38], using the Protean II xi electrophoresis system (BioRad, Hercules, CA). The protein samples were dissolved in sample buffer (7.5 M urea, 1.5 M thiourea, 4% CHAPS, 0.5% SDS, 100 mM DTT). To optimise solubilisation of proteins, we saturated the protein solution with urea by addition of solid urea. Solubilised protein (300 $\mu\text{g}/\text{gel}$) was diluted to 280 μL solution with sample buffer freshly adjusted to 0.2% resolutes pH 3.5–10 (BDH, Electran), and 0.1% Bromophenol blue. After 12 h rehydration of IPG strips pH 5–8, 17 cm (BioRad) at room temperature, IEF of protein samples was performed in a stepwise fashion (1 h, 0–500 V linear; 5 h, 500 V; 5 h, 500–3500 V linear; 12 h, 3500 V). After IEF the strips were equilibrated with 100 mM DTT and 2.5% iodoacetamide according to the manufacturer's instructions (BioRad). For SDS-PAGE, focussed and equilibrated IPG strips were placed on top of 1.5 mm 12% T polyacrylamide slab gels and overlaid with 0.5% low melting agarose. The gels were run at 15°C at 150 mA for about 4–5 h. The gels were stained with a 400 nM solution of Ruthenium II tris (bathophenanthroline disulphonate) (RuBPS) as described by Rabilloud *et al.* [39]. Fluorescence scanning was performed with the FluorImager 595 (Amersham Biosciences, Amersham, UK) at a resolution of 100 μm . After scanning, gels were laid on Whatman 3 MM chromatography paper, covered with cling film, and dried at 60°C using the slab gel dryer SE110 (Hoefer, San Francisco, CA, USA). Exposure of storage phosphor screens (Molecular Dynamics) occurred at room temperature for 24 h. Screens were subsequently scanned with the Phosphorimager SI (Molecular Dynamics) at a resolution of 100 μm .

Gels were warped to a reference gel with the TT900 S2S software (Version 2006.0.2389, Nonlinear dynamics, Carls-

bad, CA) and evaluated with the Progenesis software PG200 (Version 2006, Nonlinear, Newcastle upon Tyne, UK) using the 'same spot' algorithm. Spot assignment, background correction, normalisation and statistical calculations were performed with this software. Integrated intensities from fluorescence detection and autoradiography were normalised against the sum of all matched spots.

2.6 Tryptic digest

Protein spots were cut out of the gel, the gel-pieces were destained with 15 mM $\text{K}_3\text{Fe}(\text{CN})_6/50\text{ mM Na}_2\text{S}_2\text{O}_3$ and intensively washed with 50% methanol/10% acetic acid. The pH was adjusted with 50 mM NH_4HCO_3 , the proteins were reduced with 10 mM DTT/50 mM NH_4HCO_3 for 30 min at 56°C and finally alkylated with 50 mM iodoacetamide/50 mM NH_4HCO_3 20 min in the dark. Afterwards the gel-pieces were dried with ACN and accelerated dried in the SpeedVac. Between each step, the tubes were shaken 5–10 min (Eppendorf Thermomixer comfort).

The dried gel-spots were treated with trypsin 0.1 mg/mL (Trypsin sequencing grade, Roche Diagnostics, Germany)/50 mM NH_4HCO_3 , in a ration of 1:8 for 20 min on ice, covered with 50 mM NH_4HCO_3 and were subsequently stored over night at 37°C.

The digested peptides were eluted adding 50 mM NH_4HCO_3 to the gel spots, the supernatant was transferred into silicon-coated tubes, and the extraction procedure repeated for two times with 5% formic acid/50% ACN. Between each elution step the gel spots were sonicated. Finally the peptide solution was concentrated to an appropriate volume.

2.7 MS analysis

Proteins were identified by mass spectrometric analysis. Peptides were loaded on a Zorbax 300SB-C8 (5 μm , 0.3 mm $\times$ 5 mm) column and separated by nanoflow LC (1100 Series LC system, Agilent, Palo Alto, CA) with a Zorbax 300SB-C18 (5 μm , 75 μm $\times$ 150 mm) column at a flow-rate of 250 nL/min using a gradient from 0.2% formic acid and 3% ACN to 0.2% formic acid and 45% ACN over 12 min. Peptide identification was accomplished by MS/MS fragmentation analysis with an IT mass spectrometer (XCT-Ultra, Agilent) equipped with an orthogonal nanospray ion source. The MS/MS data were interpreted by the Spectrum Mill MS Proteomics Workbench software (Version A.03.02, Agilent) and searched against the Swiss-Prot Database version 20061207 allowing the initial search algorithm for precursor mass deviation of 2.5 Da, a product mass tolerance of 0.7 Da and a minimum matched peak intensity (%SPI) of 70%. Due to previous chemical modification, carbamidomethylation of cysteines was set as fixed modification. No other modifications were considered here. Peptide scores are essentially calculated from sequence tag lengths, but also consider mass deviations. To assess the reliability of the peptide scores, we performed searches against the corresponding reverse data-

of those were identified (Fig. 1) by peptide fragmentation analysis of tryptic digests.

The spots with the greatest difference ratios between the two groups and additionally several redox-regulating proteins are listed in Table 1. The reproducibility of the protein patterns was very high (Fig. 2). When a difference exceeding at least 50% of the control value was set as lowest threshold, no protein spot showed a significant difference in fluorescence intensity between the two groups (not shown). Applying the same criteria, two statistically significant alterations in ³⁵S-autoradiograph intensities were identified (Fig. 2). After 5 days of controlled diet with Brussels sprout consumption, the synthesis rate of manganese superoxide dismutase (Mn-SOD) was 1.56-fold up-regulated ($p < 0.001$) (Fig. 3, Table 1). On the other hand, heat shock 70 kDa protein 1 (hsp70) showed a 2.27-fold down-regulation (56% reduction of the control value, $p < 0.05$, Table 1). Other proteins such as 78 kDa glucose-regulated protein were up-regulated, and elongation factor 1-delta and epidermal fatty acid-binding protein were down-regulated, but to a lesser extent (Table 1), and may be thus of minor relevance. As we focus on redox regulation, all identified proteins potentially relevant in this context are listed as well in Table 1.

[illegible]

Figure 1. Fluorescence detection of a 2-D gel of cytoplasmic proteins isolated from white blood cells. Proteins were separated according to *pI* in the first dimension (linear from 5.0 at the left-hand side to 8.0 at the right-hand side) and molecular weight (about 250 kDa on top to 10 kDa at the bottom). For identification, spots of interest were excised, digested and forwarded to peptide fragmentation analysis by MS. Spot annotations are Swiss-Prot Accession numbers (see also Table 1).

Table 1. Protein alterations induced by a controlled dietary intervention with Brussels sprouts in human primary white blood cells

Protein	Accession no.	Norm. vol. (CV)	Difference ('norm. vol.' vs. 'AR before')	ANOVA (<i>p</i>)
26S protease regulatory subunit 6A	P17980	0.077 (18%)	−1.022	0.017
40S ribosomal protein SA	P08865	0.053 (25%)	1.026	0.006
78 kDa glucose-regulated protein	P11021	0.439 (34%)	1.504	0.286
Alcohol dehydrogenase [NADP+]	P14550	0.041 (26%)	−1.292	0.371
Aldehyde dehydrogenase	P05091	0.208 (22%)	−1.033	0.277
Catalase	P04040	0.096 (30%)	−1.370	0.005
Cofilin-1	P23528	0.156 (33%)	−1.553	1.547e-005
Core-binding factor, beta subunit	Q13951	0.060 (33%)	−1.271	0.013
Cytoplasmic antiproteinase 3	P50453	0.826 (38%)	1.497	0.026
Cytosol aminopeptidase	P28838	0.048 (35%)	−1.231	0.037
DJ-1 protein	Q99497	0.207 (30%)	−1.083	2.719e-007
Dynactin subunit 2	Q13561	0.052 (37%)	1.200	0.002
EF-hand domain-containing protein 2	Q96C19	0.427 (15%)	1.235	0.045
Elongation factor 1-delta	P29692	0.061 (10%)	−1.872	0.023
Fatty acid-binding protein, epidermal	Q01469	0.191 (40%)	−1.606	0.002
Ferritin heavy chain	P02794	0.062 (38%)	−1.233	0.023
Ferritin light chain	P02792	0.449 (32%)	−1.067	2.229e-006
Glucose-6-phosphate 1-dehydrogenase	P11413	0.175 (19%)	−1.158	0.179
Glutamate dehydrogenase 1, mitochondrial	P00367	0.032 (9%)	−1.534	0.803
Glutathione peroxidase 1	P07203	0.143 (35%)	−1.136	0.202
GST P	P09211	0.268 (30%)	−1.086	1.443e-007
Glutathione transferase omega 1	P78417	0.260 (22%)	−1.124	0.188
Glyoxylate reductase/hydroxypyruvate reductase	Q9UBQ7	0.067 (36%)	−1.342	0.475
Hsp70	P08107	0.142 (10%)	−2.277	0.039
Hematopoietic lineage cell-specific protein	P14317	0.249 (18%)	1.233	9.314e-005
NADH-ubiquinone oxidoreductase 75 kDa subunit	P28331	0.046 (12%)	−1.020	0.036
Peroxiredoxin 2	P32119	0.096 (37%)	−1.161	0.047
Peroxiredoxin 6	P30041	0.075 (30%)	−1.254	0.004
Peroxiredoxin-5, mitochondrial	Q9GLW9	0.050 (44%)	−1.396	0.056
Phosphoglycerate kinase 1	P00558	0.043 (22%)	−1.602	0.345
Proactivator polypeptide precursor	P07602	0.228 (21%)	1.453	1.662e-004
Protein disulphide-isomerase A3	P30101	0.332 (14%)	1.131	0.002
Superoxide dismutase [Cu–Zn] 1	P00441	0.065 (46%)	−1.393	7.126e-004
Superoxide dismutase [Mn], mitochondrial	P04179	1.083 (18%)	1.563	8.254e-007
Synaptic vesicle membrane protein VAT-1 homologue	Q99536	0.042 (16%)	−1.173	0.075
Thioredoxin	P10599	0.098 (44%)	−1.342	0.001
Thioredoxin domain containing protein 4 (ERp44)	Q9BS26	0.139 (21%)	1.037	0.161
Thioredoxin reductase 1, cytoplasmic	Q16881	0.037 (20%)	−1.319	0.062
Thioredoxin-dependent peroxide reductase, mitochondrial	P30048	0.067 (33%)	−1.355	1.135e-006
Thioredoxin-like protein 1	Q43396	0.134 (12%)	−1.075	1.578e-004
Thioredoxin-like protein 2	O76003	0.062 (18%)	−1.191	0.068
Thymidine phosphorylase	P19971	0.245 (21%)	−1.047	0.839
Transaldolase	P37837	0.098 (17%)	−1.250	0.555
Triosephosphate isomerase	P60174	0.257 (30%)	−1.120	0.155
Ubiquinol-cytochrome <i>c</i> reductase complex core protein I	P31930	0.478 (63%)	1.396	0.054

Spot volumes were calculated from ³⁵S-autoradiographs and normalised to total sum of spot volumes of the gels. Values are provided for the group of five individuals after consumption of Brussels sprouts with CV in relation to the values before consumption of Brussels sprouts (difference factors). Proteins were identified by mass analysis. Here, the most significant alterations of all spots accessible to quantification in the 2-D gels, in addition to redox-regulating proteins, are listed. Proteins were considered as relevant which showed alterations exceeding 50% of the control value with *p*-values below 0.05 (listed in bold font).

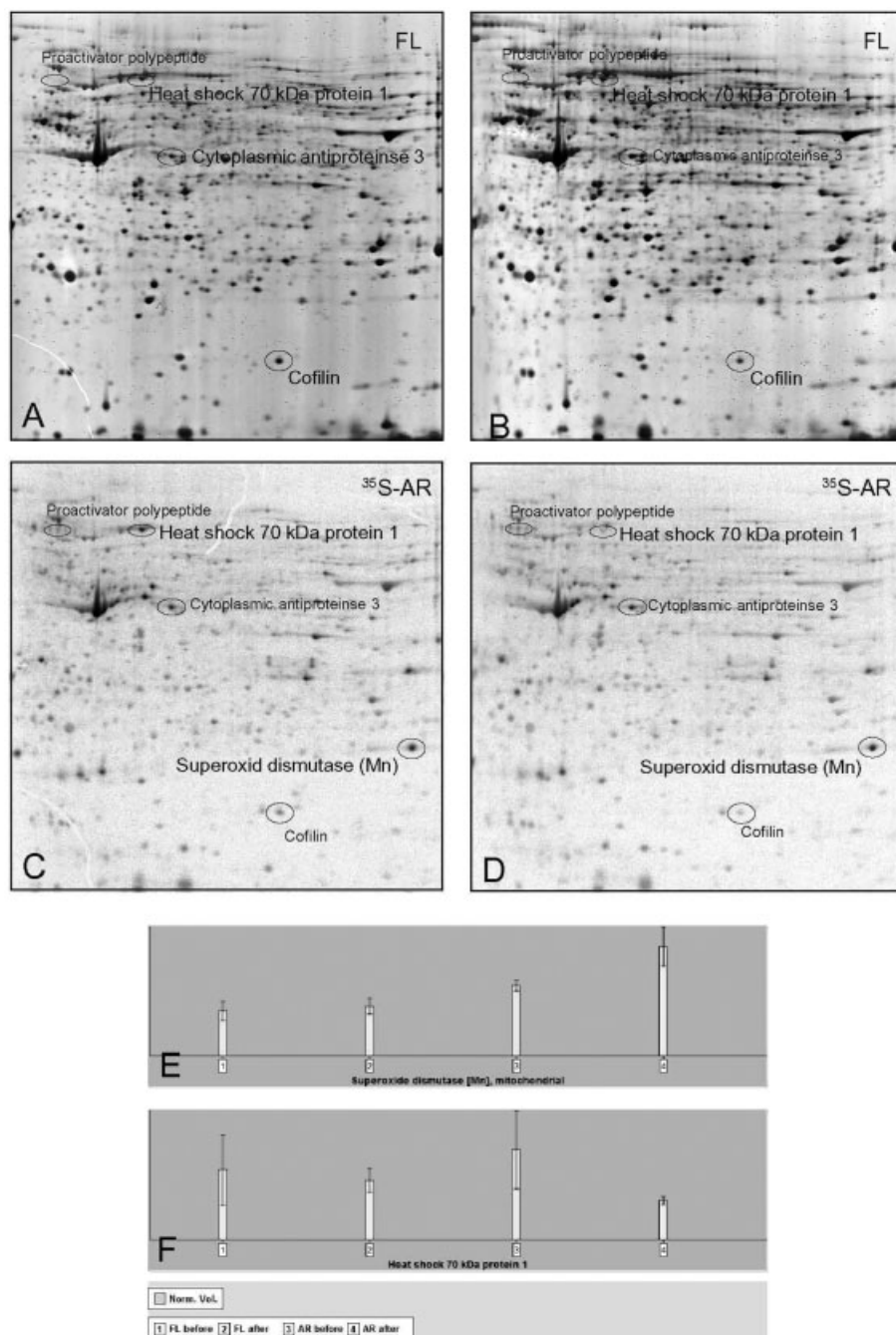


Figure 2. Proteome alteration induced by Brussels sprout consumption. 2-D gels of a donor before (A, C) and after (B, D) the dietary intervention. Fluorescence detection (A, B) did not reveal significant alterations after normalisation. In contrast, ³⁵S-autoradiography of the same gels (C, D) showed more pronounced differences. The two most significant effects are displayed below including error bars from five different individuals. While the amount of SOD was not altered (E, bar 2 compared to bar 1), the synthesis rate was significantly up-regulated (E, bar 4 compared to bar 3, see also Table 1). Similarly, the amount of hsp70 was only slightly down-regulated, while the autoradiograph showed a significant down-regulation of the synthesis rate (F). FL, fluorescence detection; AR, autoradiography.

The observed effects may seem to be subtle. Quantitative proteome analysis solely based on protein amounts is a quite daunting challenge which may provide limited reproducibility and thus poor statistical scores [40]. Therefore, we have applied in the present study more sensitive techniques which are based on the measurement of protein synthesis [37]. We demonstrated previously that the measurement of protein synthesis is a much more sensitive technique when compared to the measurement of protein amounts [37, 41].

Actually cells can only adjust protein amounts in two ways: they can synthesise new proteins or degrade existing ones. A new stimulus may elicit the need for a new protein, which would then result in *de novo* synthesis. The response of a cell to any challenge, however, can be much easier detected when protein synthesis is compared to protein amounts. Due to a generally low-level turn-over of proteins, the change of protein amounts can as well be considered as more inertial as the change of protein synthesis. To double the amount of a

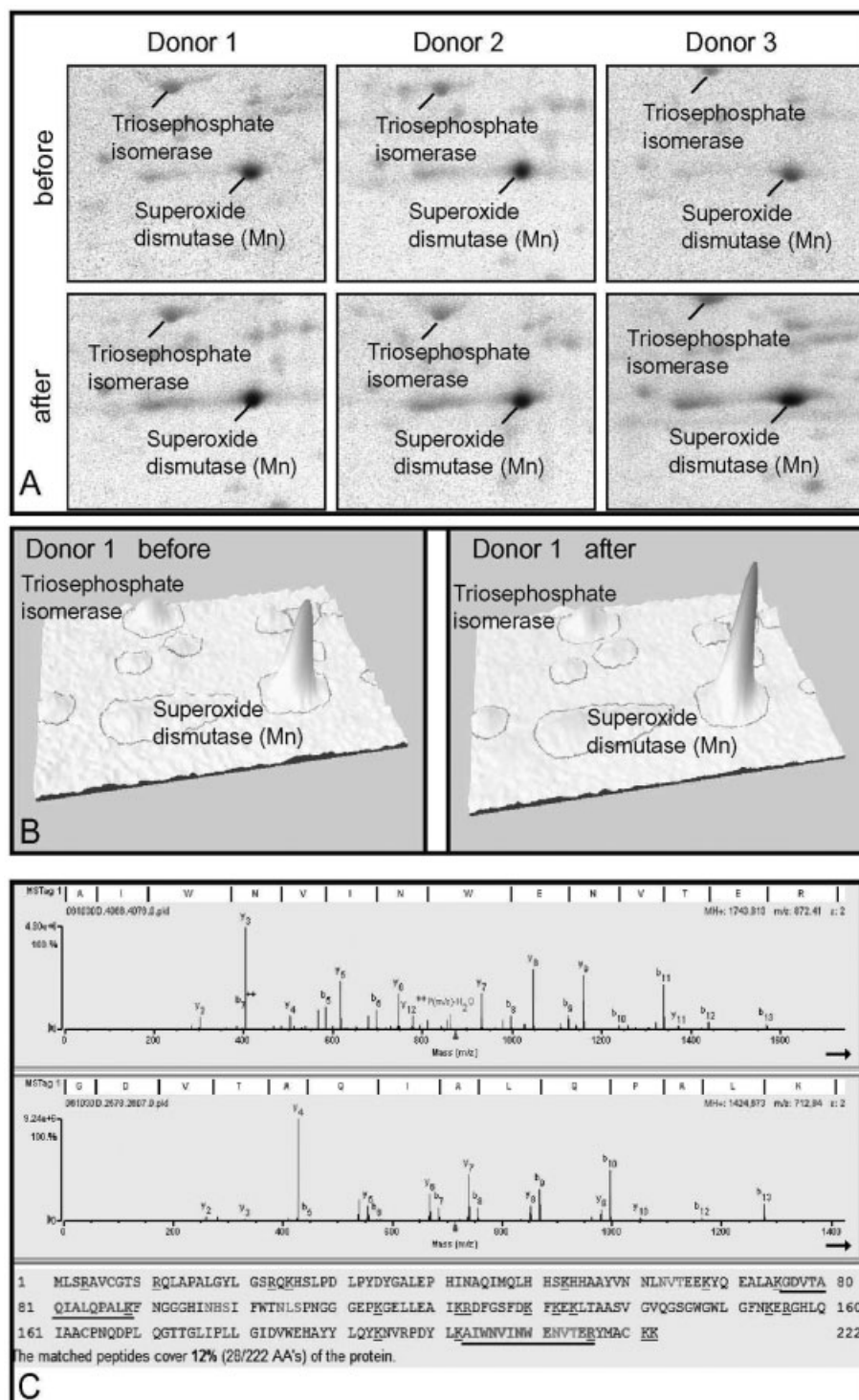


Figure 3. SOD (Mn) is significantly up-regulated upon Brussels sprout consumption. (A) 2-D gel sections of corresponding gel pairs from three different donors displaying ^{35}S autoradiograph intensities of superoxide dismutase (Mn) compared to the neighbouring protein triosephosphate isomerase before and after dietary intervention. (B) 3-D view of the 2-D gel section (^{35}S autoradiography) of donor 1 pointing out the specific up-regulation of superoxide dismutase (Mn). (C) Identification of SOD (Mn) by peptide fragmentation analysis. The peptide fragmentation (MS/MS) spectra of two peptides of the protein are shown. Note that almost complete *b*- and *y*-series were obtained, proving unequivocal identification. The shown peptides are underlined in the amino acid sequence of the total protein.

protein, it may be easily required to induce the synthesis rate more than ten-fold over a certain time period [37]. Comparative measurements detect a ten-fold increase in synthesis much easier than a two-fold increase in protein amount. This is why the quantification of synthesis rates is much more

sensitive in detecting specific adaptive proteome alterations than the quantification of protein amounts.

We cannot provide reliable conclusions whether or not other proteins are regulated by Brussels sprouts consumption. This may be due to small difference ratios or poor sta-

tistical significance (Table 1). These limitations may be overcome by an increase in the number of participants and by an optimisation of the intervention protocol or other parameters. However, the present results clearly indicate that consumption of the vegetables leads to a significant alteration of two proteins, which are known to play a crucial role in cancer prevention.

Mn-SOD, which was up-regulated more than 1.56-fold, is one of the most important antioxidant defence enzymes, and it is known that dysfunction are associated with a number of human pathologies (for review see [42]). It has been found that certain dietary factors associated with DNA and cancer protection such as EGCG ((-)-epigallocatechin-3-gallate, unpublished data), selenium, coffee consumption, as well as phenol-rich diet cause an induction of SOD [43–46]. Furthermore, in an earlier *in vivo* study with rats fed cruciferous vegetables an induction of hepatic SOD has been found [47]. SOD is controlled via the transcription factor Nrf2 [48] and there is clear evidence that glucosinolates activate the transcription factor Nrf2 [1, 9, 35]. These findings support the assumption that glucosinolates, which are contained in higher amounts in Brussels sprouts compared with other cruciferous vegetables [21], account for the effect we observed.

It is not known from earlier investigations with other dietary factors if continuous consumption of inducers is required to maintain higher enzyme levels, but it was found in a study with medicinal plants that daily uptake (over 120 days) led to a continuous increase of the activity [49]. It is also notable in this context that Mn-SOD has been credited tumour-suppressive activities, and such effects were observed, for example, with human melanoma cells [50, 51].

Our findings may also explain the strong antioxidative effects (prevention of endogenous formation of oxidised purines and pyrimidines in peripheral lymphocytes) of Brussels sprouts consumption, which we observed in a previous single cell gel electrophoresis study, in which an identical design was used [12].

Mn-SOD, however, is a double-edged sword and may, upon overexpression and decreased expression of catalase and peroxiredoxins, induce H_2O_2 formation and consequent cell damage [52]. The accompanying observation, the decrease in hsp70 expression (Fig. 2), contradicts such an interpretation. Hsp70 is an important chaperone and is strongly up-regulated upon cell-stress and protein damage [53]. If Mn-SOD was induced by stress caused by Brussels sprout consumption, we would expect strong up-regulation of hsp70. The present observation suggests that Mn-SOD was not induced by cell stress, but rather by another, yet unknown mechanism. Hsp70 may have oncogenic activity due to inhibition of apoptosis [54] and has been observed up-regulated in many forms of cancer such as hepatocellular carcinoma [55]. Furthermore, hsp70 was found down-regulated by TGF-beta-induced epithelial-mesenchymal transition [56]. Interestingly, we observed previously down-regulation of hsp70 upon silencing of the oncogenic TEL/AML1

fusion gene [57], which accounts for childhood acute lymphoblastic leukaemia. The suppression of an oncogene resulted in a similar down-regulation of hsp70 as observed in the present study.

Only few studies have been published in which the effects of cruciferous vegetables and their constituents (*i.e.* glucosinolates and their breakdown products) have been investigated with -omics technologies. Thimmulappa *et al.* [9] and also Hu *et al.* [58] conducted comparative experiments with normal and Nrf2 knockout mice with sulphoraphane and isothiocyanate formed from glucobrassica which is contained in Brussels sprouts in substantial amounts [21] and found up- and down-regulation of several hundreds of genes. Also in an experiment with rats in which the effects of two other glucosinolate metabolites (phenethyl isothiocyanate and indole 3-carbinol) were analysed by use of microarrays and proteome analyses, strong effects were observed [34]. On the contrary, Mitchell *et al.* [59] could identify only two significant protein alteration in a human trial (similar to ours) in the plasma of the participants; one of the peaks was identified as 2-HS-glycoprotein a serum glycoprotein involved in insulin resistance and immune functions. The lack of a strong effect on the proteasome after consumption of the sprouts in contrast to the strong alterations seen in the aforementioned animal studies may be due to the fact that in the rodents experiments relatively high concentrations of pure compounds were administered, also organ specific effects may play a important role. Our results did also not support the finding of Mitchell *et al.* [59], as we did not detect up-regulation of the 2-HS-glycoprotein; this difference will be due to the fact that they analysed plasma proteins, while we studied the effects in lymphocytes.

4 Concluding remarks

Taken together the results of our study show that consumption of sprouts leads to significant alteration of the levels of two proteins, which are associated with cancer formation/protection supporting the assumption that the vegetables may elicit chemopreventive properties in man.

As a result, the observed proteome alterations after consumption of Brussels sprouts may generate better protection against oxidative damage and its consequences.

The authors have declared no conflict of interest.

5 References

- [1] Lynn, A., Collins, A., Fuller, Z., Hillman, K., Ratcliffe, B., Cruciferous vegetables and colo-rectal cancer. *Proc. Nutr. Soc.* 2006, **65**, 135–144.

- [2] Steinmetz, K. A., Potter, J. D., Vegetables, fruit, and cancer prevention: a review. *J. Am. Diet. Assoc.* 1996, **96**, 1027–1039.
- [3] Talalay, P., Fahey, J. W., Phytochemicals from cruciferous plants protect against cancer by modulating carcinogen metabolism. *J. Nutr.* 2001, **131**, 3027S–3033S.
- [4] Higdon, J. V., Delage, B., Williams, D. E., Dashwood, R. H., Cruciferous vegetables and human cancer risk: epidemiologic evidence and mechanistic basis. *Pharmacol. Res.* 2007, **55**, 224–236.
- [5] Wattenberg, L. W., Effects of dietary constituents on the metabolism of chemical carcinogens. *Cancer Res.* 1975, **35**, 3326–3331.
- [6] Wattenberg, L. W., Loub, W. D., Inhibition of polycyclic aromatic hydrocarbon-induced neoplasia by naturally occurring indoles. *Cancer Res.* 1978, **38**, 1410–1413.
- [7] Kassie, F., Knasmüller, S., in: Remacle, C., Reusens, B. (Eds.), *Functional Foods, Ageing and Degenerative Disease*, Woodhead Publishing Cambridge, UK 2004, p771.
- [8] Verhoeven, D. T., Verhagen, H., Goldbohm, R. A., van den Brandt, P. A., van Poppel, G., A review of mechanisms underlying anticarcinogenicity by brassica vegetables. *Chem. Biol. Interact.* 1997, **103**, 79–129.
- [9] Thimmulappa, R. K., Mai, K. H., Srisuma, S., Kensler, T. W. et al., Identification of Nrf2-regulated genes induced by the chemopreventive agent sulforaphane by oligonucleotide microarray. *Cancer Res.* 2002, **62**, 5196–5203.
- [10] McWalter, G. K., Higgins, L. G., McLellan, L. I., Henderson, C. J. et al., Transcription factor Nrf2 is essential for induction of NAD(P)H:quinone oxidoreductase 1, glutathione S-transferases, and glutamate cysteine ligase by broccoli seeds and isothiocyanates. *J. Nutr.* 2004, **134**, 3499S–3506S.
- [11] Keum, Y. S., Jeong, W. S., Kong, A. N., Chemoprevention by isothiocyanates and their underlying molecular signaling mechanisms. *Mutat. Res.* 2004, **555**, 191–202.
- [12] Hoelzl, C., Glatt, H. R., Meinel, W., Sontag, G. et al., Consumption of brussels sprouts protects peripheral human lymphocytes against 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and oxidative DNA-damage: results of a controlled human intervention trial. *Mol. Nutr. Food Res.* 2007, DOI: 10.1002/mnfr.200700406.
- [13] Daniel, H., Genomics and proteomics: importance for the future of nutrition research. *Br. J. Nutr.* 2002, **87**, S305–S311.
- [14] Davis, C. D., Milner, J., Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention. *Mutat. Res.* 2004, **551**, 51–64.
- [15] Go, V. L., Butrum, R. R., Wong, D. A., Diet, nutrition, and cancer prevention: the postgenomic era. *J. Nutr.* 2003, **133**, 3830S–3836S.
- [16] Go, V. L., Wong, D. A., Wang, Y., Butrum, R. R., et al., Diet and cancer prevention: evidence-based medicine to genomic medicine. *J. Nutr.* 2004, **134**, 3513S–3516S.
- [17] Guengerich, F. P., Functional genomics and proteomics applied to the study of nutritional metabolism. *Nutr. Rev.* 2001, **59**, 259–263.
- [18] Breikers, G., van Breda, S. G., Bouwman, F. G., van Herwijnen, M. H., et al., Potential protein markers for nutritional health effects on colorectal cancer in the mouse as revealed by proteomics analysis. *Proteomics* 2006, **6**, 2844–2852.
- [19] Lee, S. C., Chan, J., Clement, M. V., Pervaiz, S., Functional proteomics of resveratrol-induced colon cancer cell apoptosis: caspase-6-mediated cleavage of lamin A is a major signaling loop. *Proteomics* 2006, **6**, 2386–2394.
- [20] Rowell, C., Carpenter, D. M., Lamartiniere, C. A., Chemoprevention of breast cancer, proteomic discovery of genistein action in the rat mammary gland. *J. Nutr.* 2005, **135**, 2953S–2959S.
- [21] Kassie, F., Uhl, M., Rabot, S., Grasl-Kraupp, B. et al., Chemoprevention of 2-amino-3-methylimidazo[4,5-f]quinoline (IQ)-induced colonic and hepatic preneoplastic lesions in the F344 rat by cruciferous vegetables administered simultaneously with the carcinogen. *Carcinogenesis* 2003, **24**, 255–261.
- [22] Wilms, L. C., Boots, A. W., de Boer, V. C., Maas, L. M. et al., Impact of multiple genetic polymorphisms on effects of a 4-week blueberry juice intervention on ex vivo induced lymphocytic DNA damage in human volunteers. *Carcinogenesis* 2007, **28**, 1800–1806.
- [23] Arendt, B. M., Ellinger, S., Kekic, K., Geus, L. et al., Single and repeated moderate consumption of native or dealcoholized red wine show different effects on antioxidant parameters in blood and DNA strand breaks in peripheral leukocytes in healthy volunteers: a randomized controlled trial (ISRCTN 68505294). *Nutr. J.* 2005, **4**, 33.
- [24] Gasper, A. V., Al-Janobi, A., Smith, J. A., Bacon, J. R. et al., Glutathione S-transferase M1 polymorphism and metabolism of sulforaphane from standard and high-glucosinolate broccoli. *Am. J. Clin. Nutr.* 2005, **82**, 1283–1291.
- [25] Wagner, K. H., Tomasch, R., Elmadfa, I., Impact of diets containing corn oil or olive/sunflower oil mixture on the human plasma and lipoprotein lipid metabolism. *Eur. J. Nutr.* 2001, **40**, 161–167.
- [26] Gerhäuser, C., Klimo, K., Heiss, E., Neumann, I. et al., Mechanism-based in vitro screening of potential cancer chemopreventive agents. *Mutat. Res.* 2003, **523–524**, 163–172.
- [27] Steinmetz, K. A., Potter, J. D., Vegetables, fruit, and cancer. II. Mechanisms. *Cancer Causes Control* 1991, **2**, 427–442.
- [28] Watzl, B., Leitzmann, C., *Bioaktive Substanzen in Lebensmitteln*, Hippokrates Verlag GmbH, Stuttgart 1999.
- [29] Wenzel, U., Herzog, A., Kuntz, S., Daniel, H., Protein expression profiling identifies molecular targets of quercetin as a major dietary flavonoid in human colon cancer cells. *Proteomics* 2004, **4**, 2160–2174.
- [30] Park, S., Lee, J., Yeom, C. H., A proteomic approach to the identification of early molecular targets changed by L-ascorbic acid in NB4 human leukemia cells. *J. Cell Biochem.* 2006, **99**, 1628–1641.
- [31] Fuchs, D., de Pascual-Teresa, S., Rimbach, G., Virgili, F. et al., Proteome analysis for identification of target proteins of genistein in primary human endothelial cells stressed with oxidized LDL or homocysteine. *Eur. J. Nutr.* 2005, **44**, 95–104.
- [32] Lund, E., Non-nutritive bioactive constituents of plants: dietary sources and health benefits of glucosinolates. *Int. J. Vitam. Nutr. Res.* 2003, **73**, 135–143.
- [33] Steinkellner, H., Rabot, S., Freywald, C., Nobis, E. et al., Effects of cruciferous vegetables and their constituents on drug metabolizing enzymes involved in the bioactivation of DNA-reactive dietary carcinogens. *Mutat. Res.* 2001, **480–481**, 285–297.

- [34] Izzotti, A., Bagnasco, M., Cartiglia, C., Longobardi, M. *et al.*, Modulation of multigene expression and proteome profiles by chemopreventive agents. *Mutat. Res.* 2005, **591**, 212–223.
- [35] Keum, Y. S., Owuor, E. D., Kim, B. R., Hu, R., Kong, A. N., Involvement of Nrf2 and JNK1 in the activation of antioxidant responsive element (ARE) by chemopreventive agent phenethyl isothiocyanate (PEITC). *Pharmaceut. Res.* 2003, **20**, 1351–1356.
- [36] Jakubikova, J., Sedlak, J., Bod'ó, J., Bao, Y., Effect of isothiocyanates on nuclear accumulation of NF-kappaB, Nrf2, and thioredoxin in caco-2 cells. *J. Agric. Food Chem.* 2006, **54**, 1656–1662.
- [37] Gerner, C., Vejda, S., Gelbmann, D., Bayer, E. *et al.*, Concomitant determination of absolute values of cellular protein amounts, synthesis rates, and turnover rates by quantitative proteome profiling. *Mol. Cell. Proteomics* 2002, **1**, 528–537.
- [38] Hochstrasser, D. F., Harrington, M. G., Hochstrasser, A. C., Miller, M. J., Merrill, C. R., Methods for increasing the resolution of two-dimensional protein electrophoresis. *Anal. Biochem.* 1988, **173**, 424–435.
- [39] Rabilloud, T., Strub, J. M., Luche, S., van Dorsselaer, A., Lunardi, J., A comparison between Sypro Ruby and ruthenium II tris (bathophenanthroline disulfonate) as fluorescent stains for protein detection in gels. *Proteomics* 2001, **1**, 699–704.
- [40] Righetti, P. G., Castagna, A., Antonucci, F., Piubelli, C., *et al.*, Critical survey of quantitative proteomics in two-dimensional electrophoretic approaches. *J. Chromatogr. A* 2004, **1051**, 3–17.
- [41] Traxler, E., Bayer, E., Stockl, J., Mohr, T. *et al.*, Towards a standardized human proteome database: quantitative proteome profiling of living cells. *Proteomics* 2004, **4**, 1314–1323.
- [42] Johnson, F., Giulivi, C., Superoxide dismutases and their impact upon human health. *Mol. Aspects Med.* 2005, **26**, 340–352.
- [43] Na, H. K. and Surh, Y. J., *The 5th International Conference on Environmental Mutagens in Human Populations*, European Environmental Mutagen Society, Antalya, Turkey 2007.
- [44] Kim, H. Y., Kim, O. H., Sung, M. K., Effects of phenol-depleted and phenol-rich diets on blood markers of oxidative stress, and urinary excretion of quercetin and kaempferol in healthy volunteers. *J. Am. Coll. Nutr.* 2003, **22**, 217–223.
- [45] El-Bayoumy, K., Sinha, R., Molecular chemoprevention by selenium: a genomic approach. *Mutat. Res.* 2005, **591**, 224–236.
- [46] Bichler, J., Cavin, C., Simic, T., Chakraborty, A. *et al.*, Coffee consumption protects human lymphocytes against oxidative and 3-amino-1-methyl-5H-pyrido[4,3-b]indole acetate (Trp-P-2) induced DNA-damage: results of an experimental study with human volunteers. *Food Chem. Toxicol.* 2007, **45**, 1428–1436.
- [47] Vang, O., Rasmussen, B. F., Sorensen, H., Clausen, J., Anderson, O., The effect of dietary broccoli on oxidative stress biomarkers. *Clin. Chem.* 1995, **41**, 1910–1911.
- [48] Zhu, H., Itoh, K., Yamamoto, M., Zweier, J. L., Li, Y., Role of Nrf2 signaling in regulation of antioxidants and phase 2 enzymes in cardiac fibroblasts: protection against reactive oxygen and nitrogen species-induced cell injury. *FEBS letters* 2005, **579**, 3029–3036.
- [49] Nelson, S. K., Bose, S. K., Grunwald, G. K., Myhill, P., McCord, J. M., The induction of human superoxide dismutase and catalase *in vivo*: a fundamentally new approach to antioxidant therapy. *Free Radic. Biol. Med.* 2006, **40**, 341–347.
- [50] Church, S. L., Grant, J. W., Ridnour, L. A., Oberley, L. W. *et al.*, Increased manganese superoxide dismutase expression suppresses the malignant phenotype of human melanoma cells. *Proc. Natl. Acad. Sci. USA* 1993, **90**, 3113–3117.
- [51] Ridnour, L. A., Oberley, T. D., Oberley, L. W., Tumor suppressive effects of MnSOD overexpression may involve imbalance in peroxide generation versus peroxide removal. *Antioxid. Redox Signal.* 2004, **6**, 501–512.
- [52] Kattan, Z., Minig, V., Leroy, P., Dauca, M., Becuwe, P., Role of manganese superoxide dismutase on growth and invasive properties of human estrogen-independent breast cancer cells. *Breast Cancer Res. Treat* 2007, DOI: 10.1007/s10549-007-9597-5.
- [53] Bukau, B., Horwich, A. L., The Hsp70 and Hsp60 chaperone machines. *Cell* 1998, **92**, 351–366.
- [54] Garrido, C., Schmitt, E., Cande, C., Vahsen, N. *et al.*, HSP27 and HSP70: potentially oncogenic apoptosis inhibitors. *Cell Cycle* 2003, **2**, 579–584.
- [55] Luk, J. M., Lam, C. T., Siu, A. F., Lam, B. Y. *et al.*, Proteomic profiling of hepatocellular carcinoma in Chinese cohort reveals heat-shock proteins (Hsp27, Hsp70, GRP78) up-regulation and their associated prognostic values. *Proteomics* 2006, **6**, 1049–1057.
- [56] Keshamouni, V. G., Michailidis, G., Grasso, C. S., Anthwal, S. *et al.*, Differential protein expression profiling by iTRAQ-2DLC-MS/MS of lung cancer cells undergoing epithelial-mesenchymal transition reveals a migratory/invasive phenotype. *J. Proteome Res.* 2006, **5**, 1143–1154.
- [57] Diakos, C., Krapf, G., Gerner, C., Inthl, A. *et al.*, RNAi-mediated silencing of TEL/AML1 reveals a heat-shock protein- and survivin-dependent mechanism for survival. *Blood* 2007, **109**, 2607–2610.
- [58] Hu, R., Xu, C., Shen, G., Jain, M. R. *et al.*, Gene expression profiles induced by cancer chemopreventive isothiocyanate sulforaphane in the liver of C57BL/6J mice and C57BL/6J/Nrf2 (-/-) mice. *Cancer Lett.* 2006, **243**, 170–192.
- [59] Mitchell, B. L., Yasui, Y., Lampe, J. W., Gafken, P. R., Lampe, P. D., Evaluation of matrix-assisted laser desorption/ionization-time of flight mass spectrometry proteomic profiling: identification of alpha 2-HS glycoprotein B-chain as a biomarker of diet. *Proteomics* 2005, **5**, 2238–2246.

Paper IV

Author contribution: Verena Haudek helped with the concept design, performed 2D gels and investigated the 2D gel analysis.

5. Curriculum Vitae

Personal Data

Name: Verena Johanna Haudek

Nationality: Austria

Date of Birth: 06.01.1980

Private Address: Oeynhausnerstraße 13, 2512 Tribuswinkel

Education

Primary School: VS Tribuswinkel; 1986-90

Secondary School: BG und BRG Frauengasse, Baden; 1990-98

School leaving examination: 26.06.1998

Study on the University of Vienna: Biology/Ecology 1998-2004

Diploma-thesis: “Waldreste des Wiener Beckens – aktuelle Vegetation und Veränderung seit 1820”, Department of Conservation Biology, Vegetation Ecology and Landscape Ecology, finished on 14.12.2004

Research Work:

- Austrian Research Centre Seibersdorf, 2004-05
- Institute of Cancer Research, Medical University of Vienna, since 2005

PhD-thesis: Institute of Cancer Research, since October 2005