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Selection in the dopamine receptor 2 gene: New candidate
SNPs for disease-related studies

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Abstract (English version):

Dopamine is a major neurotransmitter in the human brain and is associated with various diseases. Schizophrenia, for example, is treated by blocking the dopamine receptors type 2. In 2009, Shaner, Miller and Mintz stated that schizophrenia was the low fitness variant of a highly variable mental trait. We therefore explore whether the dopamine receptor 2 gene (*DRD2*) underwent any selection processes. We acquired genotype data of the 1000 Genomes project (phase I), which contains 1093 individuals from 14 populations. We included only single nucleotide polymorphisms (SNPs) with a minor allele frequency (MAF) of over 0.05 in the analysis. This is equivalent to 151 SNPs for *DRD2*. We used two different approaches (an outlier approach and a Bayesian approach) to detect loci under selection. The combined results of both approaches yielded nine candidate SNPs under balancing selection. While directional selection strongly favours one allele over all others, balancing selection favours more than one allele. All candidates are in the intronic region of the gene and only one (rs12574471) has been mentioned in the literature. Two of our candidate SNPs are located in specific regions of the gene: rs80215768 lies within a promoter flanking region and rs74751335 lies within a transcription factor binding site. We strongly encourage research on our candidate SNPs and their possible phenotypic effects.

Abstract (German version):

Dopamin ist einer der wichtigsten Neurotransmitter im menschlichen Gehirn und steht mit diversen Erkrankungen in Verbindung. Schizophrenie kann erfolgreich behandelt werden wenn die Dopamin-Rezeptoren vom Typ 2 blockiert werden. 2009 meinten Shaner, Miller und Mintz, dass Schizophrenie die wenig angepasste Variante eines hoch variablen psychischen Charakterzuges wäre. Dieser Aussage folgend untersuchen wir ob das Gen des Dopamin-Rezeptors 2 (*DRD2*) einen Selektionsprozess durchgemacht hat. Die Genotypen von 1093 Individuen aus 14 verschiedenen Populationen wurden aus dem „1000 Genomes project“ (Phase I) entnommen. Es wurden nur Einzelnukleotid-Polymorphismen, die eine Frequenz des seltenen Alleles von über 5% aufweisen, in die Analyse aufgenommen. In *DRD2* sind das 151 Einzelnukleotid-Polymorphismen. Um Selektion zu detektieren wurden zwei verschiedene Algorithmen angewandt: ein bayesscher und eine Ausreißer Analyse. Die kombinierten Resultate dieser zwei Methoden ergaben neun Kandidaten für einen balancierten Polymorphismus. Während bei einer gerichteten Selektion ein Allel stark bevorzugt wird, ist bei einer stabilisierenden Selektion mehr als ein Allel vorteilhaft. Jeder der neun Einzelnukleotid-Polymorphismen liegt in einer intronischen Region des Gens und nur einer (rs12574471) wurde bisher in der Literatur erwähnt. Zwei der Kandidaten liegen in speziellen Regionen des Gens: rs80215768 liegt in einer promotorflankierenden Region und rs74751335 liegt in einer Transkriptionsfaktor Bindungsstelle. Diese Arbeit soll weitere Forschung an den gefundenen Kandidaten für einen balancierten Polymorphismus beleben um ihre möglichen phänotypischen Effekte zu ergründen.

Introduction:

The catecholamine dopamine is a neurotransmitter in the human brain. Dopaminergic neurons can be divided into four major pathways: nigrostriatal, mesolimbic, mesocortical and tuberoinfundibular (Andén et al., 1964; Dahlstroem and Fuxe, 1964). These neurons play an important role in voluntary movement, feeding, reward and learning, as well as certain other functions. Outside of the brain, dopamine takes on a physiological role in cardiovascular functions, hormonal regulation, renal functions and other (Snyder et al., 1970; Missale et al., 1998; Sibley, 1999; Carlsson, 2001; Iversen and Iversen, 2007). Due to this involvement in many different processes and systems, dopamine is also related to a variety of diseases. Parkinson's disease, which is caused by a loss of dopaminergic innervations in the striatum, is a prominent example (Ehringer and Hornykiewicz, 1960). Additionally, the expected associations between the dopaminergic system and schizophrenia stem from the fact that various dopamine receptor 2 blockers are used as antipsychotics in treating that condition (Snyder et al., 1970; Creese et al., 1976; Seeman et al., 1976; Carlsson et al., 2001). Further relationships with dopamine dysregulation are expected in Tourette's syndrome and attention deficit hyperactivity disorder (ADHD) (Mink, 2006; Swanson et al., 2007; Gizer et al., 2009). The strong involvement of dopamine in the reward system suggests an association with drug abuse and addiction (Hyman et al., 2006; Di Chiara and Bassareo, 2007; Koob and Volkow, 2010). Many more diseases and conditions are expected to involve dopamine dysfunctions. (As reviewed by Beaulieu & Gainetdinov, 2011)

In humans, five different dopamine receptors exist. They are classified into two categories based on their structure and their pharmacological and biochemical properties. The D1-class includes the dopamine receptors 1 and 5, while the D2-class consists of the dopamine receptors 2, 3 and 4 (Andersen et al., 1990; Niznik and Van Tol, 1992; Sibley and Monsma, 1992; Sokoloff et al., 1992a; Civelli et al., 1993; Vallone et al., 2000). The focus of our study is on the dopamine receptor 2 and its gene *DRD2*. The dopamine receptor 2 gene lies on the long arm of chromosome 11 (11q23.1). It spans from 113,280,317 to 113,346,413 for a total of 66,096 base pairs (bp) (information accessed on NCBI in the GnRH37 assembly). For the gene card, see Figure 1 in Results. *DRD2* has six introns (Gingrich and Caron, 1993). Alternative splicing between intron 4 and 5 of an 87 bp exon generates two variants of the dopamine receptor 2. The difference between D2S (short) and D2L (long) is a 29-amino-acids-long chain in the third intercellular loop of the protein (Giros et al., 1989; Monsma et al., 1989). While the short form (D2S) is mainly

expressed at the presynapse, the long form (D2L) is expressed postsynaptically (Usiello et al., 2000; De Mei et al., 2009). The D2S are mainly autoreceptors, i.e. they reduce the expression of dopamine when activated. This leads to an important negative feedback mechanism (Wolf and Roth, 1990; Missale et al., 1998; Sibley, 1999). (Again, as reviewed by Beaulieu & Gainetdinov, 2011)

Among the many single nucleotide polymorphisms (SNPs) of *DRD2*, one prominent example is rs6277, also known as C957T. It has been associated with schizophrenia in Han Chinese in Taiwan (Glatt et al., 2009), in Russians (Monakhov et al. 2008) and in Bulgarians (Betcheva et al. 2009). Together with the -141C allele, the 957T allele is associated with the diagnosis of anorexia nervosa (Bergen et al., 2005). A meta-analysis showed that the Ser311Cys polymorphism (rs1801028) in *DRD2* is a risk factor for schizophrenia. The heterozygotes (Ser/Cys) and the homozygotes for Cys were both at elevated risk for schizophrenia when compared to the Ser/Ser genotypes (Glatt and Jönsson, 2006). In a study with alcoholic patients and controls, the A allele of rs1076560 was more frequent in alcoholic patients (Sasabe et al., 2007). In 2012, Mileva-Seitz et al. conducted a study with Caucasian mothers and their infants. They taped mother-infant behaviour and genotyped various SNPs of *DRD2* and also *DRD1*. Rs1799732 and the previously mentioned rs6277 were both associated with direct vocalization of the mother towards the infant. The body of literature on SNPs and their possible effects is growing rapidly. Considering the influences those SNPs could have on human behaviour, and bearing in mind the different ecological habitats of *Homo sapiens*, we aimed to explore if *DRD2* underwent any selection processes. In 2009 an interesting proposal by Shaner, Miller and Mintz stated that schizophrenia was the low fitness variant of a highly variable mental trait. Because of the connection between dopamine receptor 2 and schizophrenia, as stated above, we focused our analysis on *DRD2*.

To reduce false-positives, we used two selection detection algorithms to explore *DRD2*. This is an exploratory (“hypothesis-free”) approach in which we want to find candidate SNPs that were under selection. The data basis of our analysis are the 1000 Genomes Project samples.

Material and Methods:

We acquired data from the 1000 Genomes Project (phase I) through SPSmart engine v5.1.1 (<http://spsmart.cesga.es/engines.php>; Amigo et al., 2008), using the search term “DRD2”. We included all single nucleotide polymorphisms (SNPs) with a minor allele frequency (MAF) greater than 0.05. Over the span of the whole *DRD2* gene (113,280,317 – 113,346,413 in the Gnrh37.p13 primary assembly; gene card shown in Results, Figure 1), this amounts to 151 SNPs. In total we included the following populations in our analysis.

Superpopulation (Code)	Population Code	Population	Number of Individuals
Africa (AFR)	ASW	African ancestry in Southwest USA	61
	LWK	Luhya in Webuye, Kenya	97
	YRI	Yoruba in Ibadan, Nigeria	88
Europe (EUR)	CEU	Utah residents with Northern and Western European ancestry	87
	FIN	Finnish from Finland	93
	GBR	British from England and Scotland	88
	IBS	Iberian populations in Spain	14
	TSI	Toscani in Italy	98
East Asia (ASN)	CHB	Han Chinese in Beijing, China	97
	CHS	Han Chinese South	100
	JPT	Japanese in Tokyo, Japan	89
America (AMR)	CLM	Colombians from Medellin, Co- lombia	66
	MXL	Mexican ancestry from Los Ange- les USA	60
	PUR	Puerto Ricans from Puerto Rico	55
All populations =			1093

Table 1. Populations of the 1000 Genomes Project.

The data was converted by hand into the CONVERT format. All further format conversions were performed by PGD Spider 2.0.5.2 (Lischer and Excoffier, 2012).

Two different programs were used to detect selection. Both use F_{ST} approaches to detect outliers. The program LOSITAN calculates FDIST, which uses F_{ST} and the expected heterozygosity. It assumes an island model of migration with neutral markers. An expected distribution of Wright's inbreeding coefficient is calculated and then outliers are identified. A neutral mean F_{ST} was computed by the program before the 50,000 simulations were performed. The infinite alleles model was used. To avoid false positive detection we set the significance level to $p < 0.01$ ($P(\text{Simulation } F_{ST} < \text{sample } F_{ST})$). (Antao et al., 2008)

BayeScan is a Bayesian statistics program. Basically it calculates two simulations for every loci: one in which it assumes the locus is under selection and the other one in which this assumption is dropped. It splits the F_{ST} coefficient into two parts. The alpha value is a locus-specific component shared by all populations. The beta value is a population-specific component shared by all loci. This is achieved via logistic regression and provides insight into selection. The alpha value serves as an indicator for selection. Significant positive values of alpha indicate directional selection, whereas significant negative values indicate balancing selection. The posterior probabilities are estimated using a reversible-jump Markov Chain Monte Carlo (MCMC) approach. The posterior probabilities are gained by counting how many times alpha is included in the model. Before the Markov chains are computed, we calculate 20 pilot runs with 5000 iterations each. The initial burn-in is set to 50,000 steps and the chains are run with 5000 iterations and a thinning interval of 10. The program output consists of a posterior probability, the logarithm (base 10) of the posterior odds and a q value. These three values are all for the model with selection. Furthermore, the alpha value is reported and an F_{ST} coefficient average of all population per locus. In BayeScan the threshold of a posterior P of > 0.99 and a $\log_{10}(\text{PO})$ of 2 or higher is used. This threshold is labelled as "Decisive" by BayeScan (see the program manual at http://cmpg.unibe.ch/software/BayeScan/files/BayeScan2.1_manual.pdf). (Foll and Gaggiotti, 2008)

To compute linkage disequilibrium (LD) of the SNPs, we used the R “genetics package” (<http://cran.r-project.org/web/packages/genetics/genetics.pdf>; Warnes et al., 2013). We used D' as a measurement for LD. In most populations one or more SNPs had to be excluded to successfully run the computation. The population IBS was excluded entirely from this computation. IBS is a very small population ($n = 14$), and 30 SNPs caused the computation to fail. For a detailed view on all excluded SNPs see Table S1 in the supplementary material.

We accessed information on the gene via NCBI (<http://www.ncbi.nlm.nih.gov/>) and on the specific SNPs via Ensembl (<http://www.ensembl.org/>).

Results:

The combined results of LOSITAN and BayeScan yielded nine candidate SNPs under balancing selection:

Locus	Major Allele (Frequency)	Minor Allele (Frequency)	F_{ST} (Lositan)	F_{ST} (BayeScan)	Location
rs60599314	C (0.871)	T (0.129)	0.0110	0.0272	113,306,431 (Intronic region)
rs79549222	T (0.87)	G (0.13)	0.0106	0.0260	113,310,340 (Intronic region)
rs12574471	C (0.891)	T (0.109)	0.0172	0.0364	113,316,236 (Intronic region)
rs80215768	G (0.925)	A (0.075)	0.0304	0.0328	113,318,880 (Intronic region)
rs76581995	C (0.925)	A (0.075)	0.0304	0.0328	113,319,835 (Intronic region)
rs80014933	T (0.923)	C (0.077)	0.0304	0.0332	113,328,135 (Intronic region)
rs74751335	G (0.915)	C (0.085)	0.0266	0.0322	113,328,810 (Intronic region)
rs77264605	A (0.915)	G (0.085)	0.0266	0.0327	113,328,913 (Intronic region)
rs76499333	G (0.925)	A (0.075)	0.0299	0.0327	113,329,449 (Intronic region)

Table 2. The dopamine receptor 2 gene's nine candidate SNPs for balancing selection.

For a detailed view on the results of LOSITAN and BayeScan for all SNPs, see Table S2 in the supplementary material. In Figure 1 a gene view of *DRD2* with labels for the candidate SNPs is provided.

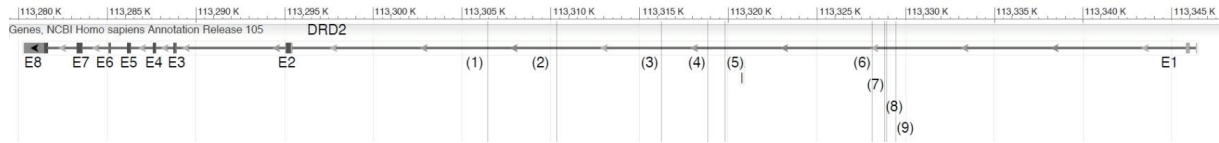


Figure 1. Location of candidate SNPs under balancing selection in *DRD2*.

E1-8 are exons 1 to 8. (1): rs60599314, (2): rs79549222, (3): rs12574471, (4): rs80215768, (5): rs76581995, (6): rs80014933, (7): rs74751335, (8): rs77264605, (9): rs76499333.

All nine SNPs are intron variants (Figure 1). Only rs12574471 (3) is mentioned in the literature because it is near a supposed recombination hotspot (Glatt et al, 2009). rs80215768 (4) lies within a promoter flanking region; rs74751335 (7) lies within a transcription factor binding site. However, we found no known associations for those two SNPs.

The F_{ST} values of these nine loci indicate an overall low genetic differentiation, as well as a low differentiation between populations (Table 2). This is in accordance with balancing selection acting on the gene. The differences in F_{ST} values stem from different algorithms used by the programs.

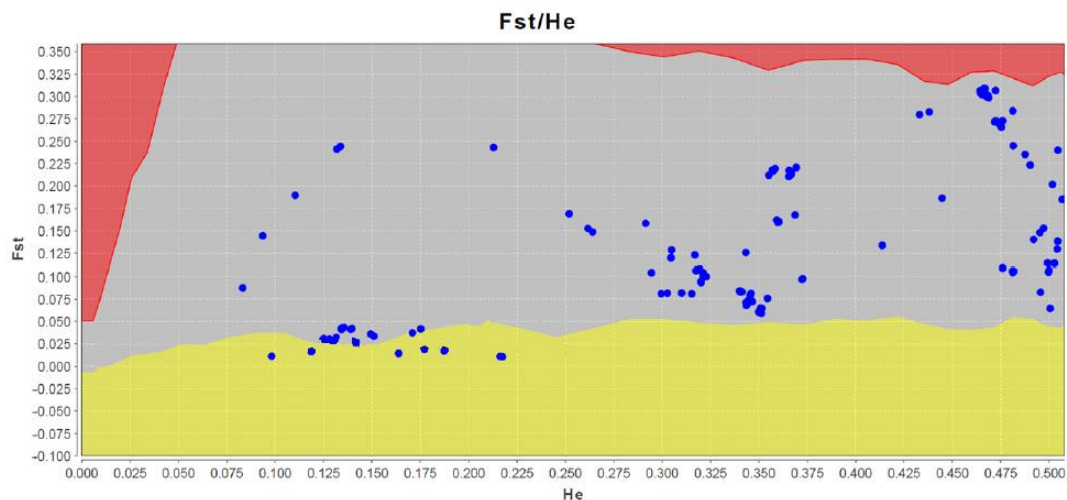


Figure 2. LOSITAN graphical output. Blue dots = SNPs. Yellow area = candidate loci for balancing selection. Grey area = neutral. Red area = candidate loci for positive selection. For the exact values see Table S2 in the supplementary material.

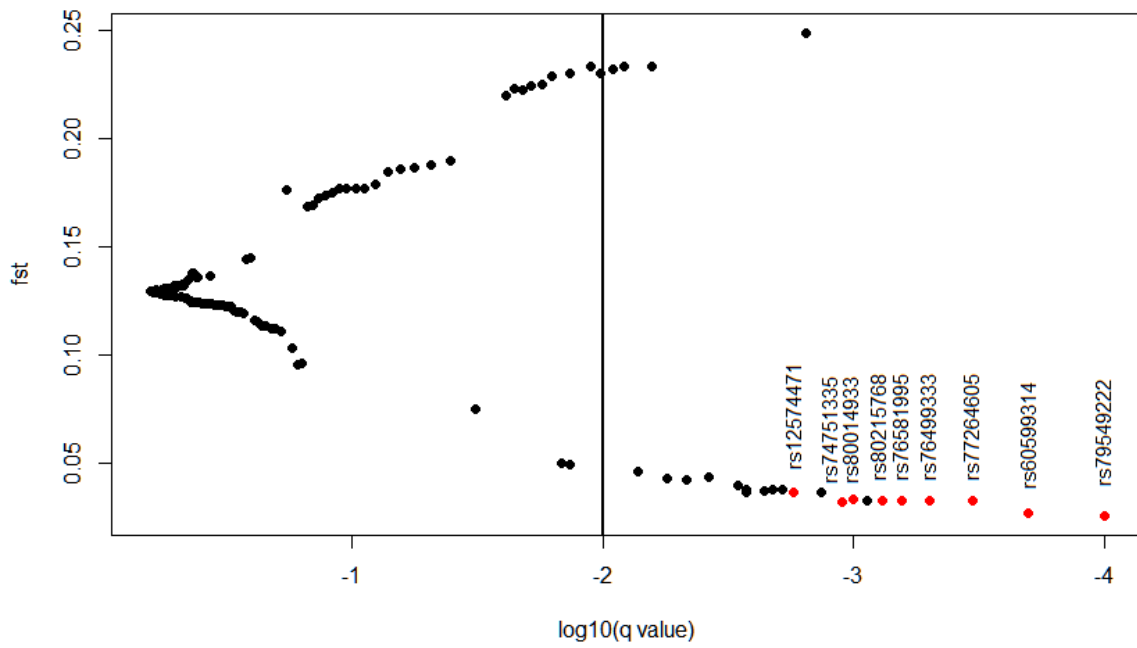


Figure 3. Graphical output of BayeScan. The red dots represent the overlapping SNPs with LOSITAN (Table 2). For the exact values see Table S2 in the supplementary material.

The Linkage Disequilibrium measurement D' was used. The heat maps for all nine populations are shown in the supplementary material (Figure S1 – S13). The relative position of the marked SNPs change because different populations had different SNPs excluded (see Table S1 for the list).

Discussion:

We found nine SNPs to be candidates for balancing selection and none for directional selection. Checking those SNPs with Genome Browser reveals that they are all intronic region variants. rs80215768 (4) lies within a promoter flanking region and rs74751335 (7) lies within a transcription factor binding site (TFBS). There have been many studies on the possible effects of mutations in such regions (Hayashi, Watanabe and Kawajiri, 1991; and In et al. 1997; or for a more general review on the topic, Jaenish & Bird, 2003). We strongly encourage further analysis of those two SNPs in order to analyse their possible effects. Nonetheless, the SNPs show low F_{ST} values, which is congruent with the finding of balancing selection. Sewall Wright's guidelines for interpreting F_{ST} values suggest little genetic differentiation in our populations (as cited by Jobling, 2013; Chapter 5, Box 5.2). As silent mutations in *DRD2* are known to alter the mRNA stability and even the synthesis of the receptor itself (Duan et al., 2003), we should be eager to explore the possible effects of these SNPs.

Additionally, the levels of the linkage disequilibrium measurement D' are typical for the respective populations: African populations show a dispersed pattern and no clear LD blocks (Figure S1, S9, and S13). While the LD blocks are visible in American populations (Figure S5, S10 and S11), they are not as clear as in Asian (Figure S3, S4 and S8) or European populations (Figure S2, S6, S7 and S12). Looking up the SNPs that are in high D' (> 0.8) with our nine candidate loci revealed no new information as to the nature of those loci.

All of our SNPs have a $MAF > 0.05$ and there are some individuals (0.8 – 2.3% per SNP, over all populations) that are homozygote for the minor allele. The finding of balancing selection suggests that in our sample the minor alleles bear some fitness disadvantage. Fitness is altered if survival or reproduction of an organism is affected. This raises the possibility of a connection between our candidate SNPs and diseases or malfunctions of dopamine receptor 2. In the list of diseases associated with dopamine (see Introduction) the most striking example is schizophrenia because dopamine receptor 2 blockers can successfully treat patients. Leaving the biochemical field, we can also find connections with diseases on a molecular level. Rs6277 is associated with schizophrenia in Han Chinese in Taiwan (Glatt et al., 2009), in Russians (Monakhov et al. 2008) and in Bulgarians (Betcheva et al. 2009). Rs1801028 was also described as a risk factor for schizophrenia (Glatt and Jönsson, 2006). Bergen et al. (2005) found an association between the alleles -141C and 957T and the diagnosis of anorexia nervosa. The A allele of rs1076560 was more frequent in alcoholic patients when compared with a control group (Sasabe et al., 2007). In

a meta-analysis, Le Foll et al. (2009) concluded that there are associations between variants of *DRD2* and alcohol dependency.

The question is whether these conditions could potentially affect fitness. Bassett et al. (1996) showed that reproductive fitness is reduced in groups of familial schizophrenia, which suggests a selection process. Puzzlingly enough, they also found some evidence for an increased fitness of a small subsample of sisters. Shaner, Miller and Mintz in 2009 proposed that schizophrenia is the low-fitness trait of a highly variable mental trait. They argue that the persistence of the illness at about 1% globally is too high for new mutations. Balancing selection would fit this hypothesis very well and our candidate SNPs could be viable indicators for this. Interestingly, rs6277 and rs1801028, which are both associated with schizophrenia (Glatt et al., 2009; Monakhov et al. 2008; Betcheva et al. 2009; Glatt and Jönsson, 2006), are candidates for neutral loci in our study. Note that also the other SNPs that are associated with alcohol dependency, anorexia nervosa or even the behaviour of mothers with their infants, are all candidates for neutral loci. This method does not allow us to make direct inferences about a phenotype (e.g. schizophrenia). We can only make assumptions about the phenotype based on our genotype data. This study is a potential precursor to future studies on the subject.

Lastly, what also should pique our interest is the fact that we only found candidates for balancing selection. We extended our analysis to the other 4 dopamine receptors and again only found candidates for balancing selection and none for directional selection (data not shown). Note that this applies only to SNPs. There has been evidence for directional selection in *DRD4*, by analysing a tandem repeat in the coding region (Ding et al. 2001). Recently, *DRD1* has been analysed as one of ten neurochemical genes that are responsible for the Social-Decision Making System (O'Connell & Hofmann, 2012). The study finds that the system underwent very little change during evolution. The authors wanted to include *DRD2* but too little data for different species were available. The fact that we find only balancing selection and no directional selection acting upon *DRD2* hints that it is a conserved region within the human genome.

To untangle the possible effects of our SNPs we propose a study in which our candidate SNPs are investigated in schizophrenic and non-schizophrenic persons. A simple comparison of the SNPs and the different haplotypes between the two groups should efficiently assess our findings. If this proposed study finds differences in those two groups, the mechanisms of those SNPs and their possible haplotypes must be investigated.

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References:

- Amigo, J., Salas, A., Phillips, C. & Carracedo, Á. (2008). SPSmart: adapting population based SNP genotype databases for fast and comprehensive web access. *BMC bioinformatics*, 9(1), 428.
- Andén, N. E., Carlsson, A., Dahlström, A., Fuxe, K., Hillarp, N. Å., & Larsson, K. (1964). Demonstration and mapping out of nigro-neostriatal dopamine neurons. *Life sciences*, 3(6), 523-530.
- Andersen, P. H., Gingrich, J. A., Bates, M. D., Dearry, A., Falardeau, P., Senogles, S. E., & Caron, M. G. (1990). Dopamine receptor subtypes: beyond the D 1/D 2 classification. *Trends in pharmacological sciences*, 11(6), 231-236.
- Antao, T., Lopes, A., Lopes, R. J., Beja-Pereira, A., & Luikart, G. (2008). LOSITAN: a workbench to detect molecular adaptation based on a Fst-outlier method. *BMC bioinformatics*, 9(1), 323.
- Bassett, A. S., Bury, A., Hodgkinson, K. A., & Honer, W. G. (1996). Reproductive fitness in familial schizophrenia. *Schizophrenia research*, 21(3), 151-160.
- Bertram, L. (2008). Genetic research in schizophrenia: new tools and future perspectives. *Schizophrenia bulletin*, 34(5), 806-812.
- Carlsson, A. (2001). A paradigm shift in brain research. *Science*, 294(5544), 1021-1024.
- Carlsson, A., Waters, N., Holm-Waters, S., Tedroff, J., Nilsson, M., & Carlsson, M. L. (2001). Interactions between monoamines, glutamate, and GABA in schizophrenia: new evidence. *Annual review of pharmacology and toxicology*, 41(1), 237-260.
- Civelli, O., Bunzow, J. R., & Grandy, D. K. (1993). Molecular diversity of the dopamine receptors. *Annual review of pharmacology and toxicology*, 33(1), 281-307.
- Creese, I., Burt, D. R., & Snyder, S. H. (1976). Dopamine receptor binding predicts clinical and pharmacological potencies of antischizophrenic drugs. *Science*, 192(4238), 481-483.
- Dahlström, A., & Fuxe, K. (1964). Evidence for the existence of monoamine-containing neurons in the central nervous system. I. Demonstration of monoamines in the cell bodies of brain stem neurons. *Acta Physiologica Scandinavica. Supplementum*, SUPPL-232.
- De Mei, C., Ramos, M., Iitaka, C., & Borrelli, E. (2009). Getting specialized: presynaptic and postsynaptic dopamine D2 receptors. *Current opinion in pharmacology*, 9(1), 53-58.
- Di Chiara, G., & Bassareo, V. (2007). Reward system and addiction: what dopamine does and doesn't do. *Current opinion in pharmacology*, 7(1), 69-76.

- Ding, Y. C., Chi, H. C., Grady, D. L., Morishima, A., Kidd, J. R., Kidd, K. K., ... & Moyzis, R. K. (2002). Evidence of positive selection acting at the human dopamine receptor D4 gene locus. *Proceedings of the National Academy of Sciences*, 99(1), 309-314.
- Duan, J., Wainwright, M. S., Comeron, J. M., Saitou, N., Sanders, A. R., Gelernter, J., & Gejman, P. V. (2003). Synonymous mutations in the human dopamine receptor D2 (DRD2) affect mRNA stability and synthesis of the receptor. *Human molecular genetics*, 12(3), 205-216.
- Ehringer, H., & Hornykiewicz, O. (1960). Distribution of noradrenaline and dopamine (3-hydroxytyramine) in the human brain and their behavior in diseases of the extrapyramidal system. *Klinische Wochenschrift*, 38, 1236.
- Foll, M., & Gaggiotti, O. (2008). A genome-scan method to identify selected loci appropriate for both dominant and codominant markers: a Bayesian perspective. *Genetics*, 180(2), 977-993.
- Gingrich, J. A., & Caron, M. G. (1993). Recent advances in the molecular biology of dopamine receptors. *Annual review of neuroscience*, 16(1), 299-321.
- Giros, B., Sokoloff, P., Martres, M. P., Riou, J. F., Emorine, L. J., & Schwartz, J. C. (1989). Alternative splicing directs the expression of two D2 dopamine receptor isoforms. *Nature*, 342, 923 – 926.
- Gizer, I. R., Ficks, C., & Waldman, I. D. (2009). Candidate gene studies of ADHD: a meta-analytic review. *Human genetics*, 126(1), 51-90.
- Hayashi, S. I., Watanabe, J., & Kawajiri, K. (1991). Genetic polymorphisms in the 5'-flanking region change transcriptional regulation of the human cytochrome P450IIE1 gene. *Journal of biochemistry*, 110(4), 559-565.
- Hyman, S. E., Malenka, R. C., & Nestler, E. J. (2006). Neural mechanisms of addiction: the role of reward-related learning and memory. *Annual review of neuroscience*, 29, 565-598.
- In, K. H., Asano, K., Beier, D., Grobholz, J., Finn, P. W., Silverman, E. K., ... & Drazen, J. M. (1997). Naturally occurring mutations in the human 5-lipoxygenase gene promoter that modify transcription factor binding and reporter gene transcription. *Journal of clinical investigation*, 99(5), 1130.
- Iversen, S. D., & Iversen, L. L. (2007). Dopamine: 50 years in perspective. *Trends in neurosciences*, 30(5), 188-193.
- Jaenisch, R., & Bird, A. (2003). Epigenetic regulation of gene expression: how the genome integrates intrinsic and environmental signals. *Nature genetics*, 33, 245-254.
- Jobling, M., Hollox, E., Hurles, M., Kivisild, T. & Tyler-Smith, C. (2013). *Human evolutionary genetics*. New York and London: Garland Science.

- Koob, G. F., & Volkow, N. D. (2010). *Neurocircuitry of addiction. neuropsychopharmacology*, 35(1), 217-238.
- Le Foll, B., Gallo, A., Le Strat, Y., Lu, L., & Gorwood, P. (2009). Genetics of dopamine receptors and drug addiction: a comprehensive review. *Behavioural pharmacology*, 20(1), 1-17.
- Lischer, H. E. L., & Excoffier, L. (2012). PGDSpider: an automated data conversion tool for connecting population genetics and genomics programs. *Bioinformatics*, 28(2), 298-299.
- Mink, J. W. (2006). Neurobiology of basal ganglia and Tourette syndrome: basal ganglia circuits and thalamocortical outputs. *Advances in neurology*. New York: Raven Press, 99, 89.
- Missale, C., Nash, S. R., Robinson, S. W., Jaber, M., & Caron, M. G. (1998). Dopamine receptors: from structure to function. *Physiological reviews*, 78(1), 189-225.
- Monsma, F. J., McVittie, L. D., Gerfen, C. R., Mahan, L. C., & Sibley, D. R. (1989). Multiple D2 dopamine receptors produced by alternative RNA splicing. *Nature*, 342, 926 – 929.
- Niznik, H. B., & Van Tol, H. H. (1992). Dopamine receptor genes: new tools for molecular psychiatry. *Journal of psychiatry and neuroscience*, 17(4), 158.
- O'Connell, L. A., & Hofmann, H. A. (2012). Evolution of a vertebrate social decision-making network. *Science*, 336(6085), 1154-1157.
- Seeman, P., Lee, T., Chau-Wong, M., & Wong, K. (1976). Antipsychotic drug doses and neuroleptic/dopamine receptors. *Nature*, 261(5562), 717-719.
- Shaner, A., Miller, G., & Mintz, J. (2004). Schizophrenia as one extreme of a sexually selected fitness indicator. *Schizophrenia research*, 70(1), 101-109.
- Sibley, D. R. (1999). New insights into dopaminergic receptor function using antisense and genetically altered animals 1. *Annual review of pharmacology and toxicology*, 39(1), 313-341.
- Sibley, D. R., & Monsma, F. J. (1992). Molecular biology of dopamine receptors. *Trends in pharmacological sciences*, 13, 61-69.
- Snyder, S. H., Taylor, K. M., Coyle, J. T., & Meyerhoff, J. L. (1970). The role of brain dopamine in behavioral regulation and the actions of psychotropic drugs. *American journal of psychiatry*, 127(2), 199-207.
- Sokoloff, P., Andrieux, M., Besançon, R., Pilon, C., Martres, M. P., Giros, B., & Schwartz, J. C. (1992). Pharmacology of human dopamine D 3 receptor expressed in a mammalian cell line: comparison with D 2 receptor. *European journal of pharmacology: molecular pharmacology*, 225(4), 331-337.
- Swanson, J. M., Kinsbourne, M., Nigg, J., Lanphear, B., Stefanatos, G. A., Volkow, N., ... & Wadhwa, P. D. (2007). Etiologic subtypes of attention-deficit/hyperactivity disorder: brain imag-

ing, molecular genetic and environmental factors and the dopamine hypothesis. *Neuropsychology review*, 17(1), 39-59.

Usiello, A., Baik, J. H., Rougé-Pont, F., Picetti, R., Dierich, A., LeMeur, M., ... & Borrelli, E. (2000). Distinct functions of the two isoforms of dopamine D2 receptors. *Nature*, 408(6809), 199-203.

Vallone, D., Picetti, R., & Borrelli, E. (2000). Structure and function of dopamine receptors. *Neuroscience & biobehavioral reviews*, 24(1), 125-132.

Warnes, G., Leisch, F., Man, M., & Warnes, M. G. Package 'genetics' (2013).

Wolf, M. E., & Roth, R. H. (1990). Autoreceptor regulation of dopamine synthesis. *Annals of the New York academy of sciences*, 604(1), 323-343.

Supplementary Material:

Africa	ASW	rs75924850
	LWK	rs75924850
	YRI	rs2242591, rs6278, rs1124491, rs2075654, rs75349786, rs72999670, rs77541954, rs4322431, rs72999677, rs11214614, rs75924850
Europe	CEU	rs7126289
	FIN	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
	GBR	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
	IBS	rs2075652, rs7126289, rs7934416, rs4245145, rs4648319, rs4379875, rs4379875, rs80215768, rs76581995, chr11:113325866, rs80014933, rs74751335, rs77264605, rs76499333, rs74355206, rs75824731, rs10891553, rs77655590, rs12421616, rs73557296, rs4245149, rs60253148, rs7102650, rs55887984, rs75924850, rs117720003, rs79872790, rs79092434, rs7116768, rs1799978
	TSI	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
	CHB	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
East Asia	CHS	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
	JPT	rs7126289, rs7934416, rs4245145, rs4648319, rs4379875
America	CLM	none
	MXL	none
	PUR	rs75924850

Table S1. SNPs that caused the LD calculation of R to fail and thus were excluded from the LD calculation. IBS was excluded entirely because 30 SNPs were flawed (which is nearly 20% of all SNPs).

Locus	P	H _E	F _{ST}	P	log10(PO)	q-value	α_i	F _{ST}
rs2242591	0.3390	0.3045	0.1200	0.0454	-1.3227	0.5726	-0.0101	0.1283
rs11214603	0.9743	0.4330	0.2798	0.9964	2.4420	0.0015	0.9561	0.2485
rs2734842	0.6401	0.5069	0.1851	0.0556	-1.2300	0.5206	0.0205	0.1314
rs6278	0.3390	0.3045	0.1200	0.0454	-1.3227	0.5726	-0.0098	0.1283
rs6279	0.1893	0.4997	0.1049	0.0396	-1.3847	0.6041	-0.0046	0.1288
rs6276	0.6401	0.5069	0.1851	0.0610	-1.1872	0.5003	0.0197	0.1313
rs2734841	0.0767	0.4956	0.0826	0.0568	-1.2202	0.5167	-0.0175	0.1277
rs1124491	0.3390	0.3045	0.1200	0.0428	-1.3495	0.5817	-0.0098	0.1283
rs1124492	0.3826	0.4137	0.1338	0.0410	-1.3689	0.5932	-0.0001	0.1292
rs1124493	0.2013	0.4999	0.1068	0.0514	-1.2660	0.5393	-0.0062	0.1287
rs1079595	0.1418	0.3201	0.0948	0.1202	-0.8644	0.3432	-0.0753	0.1233
rs1079594	0.1418	0.3201	0.0948	0.1238	-0.8498	0.3285	-0.0793	0.1230
rs6277	0.9770	0.4381	0.2829	0.9622	1.4057	0.0112	0.8430	0.2329
rs6275	0.2530	0.4992	0.1145	0.0384	-1.3986	0.6193	-0.0033	0.1289
rs1076560	0.1342	0.3201	0.0934	0.1282	-0.8324	0.3209	-0.0843	0.1226
rs2511521	0.8009	0.5017	0.2018	0.0524	-1.2572	0.5320	0.0177	0.1311
rs2283265	0.1820	0.3216	0.1016	0.0970	-0.9688	0.4444	-0.0592	0.1245
rs12363125	0.9853	0.4678	0.2997	0.9238	1.0835	0.0209	0.7663	0.2226
rs2734839	0.8818	0.4902	0.2234	0.1060	-0.9259	0.4182	0.0580	0.1359
rs2734838	0.9683	0.4745	0.2695	0.5099	0.0172	0.1281	0.3776	0.1739
rs2734837	0.8818	0.4902	0.2234	0.1062	-0.9250	0.4127	0.0584	0.1359
rs2440390	< 0.0001	0.1772	0.0188	0.9800	1.6901	0.0038	-1.3782	0.0439
rs1107162	0.9681	0.4742	0.2692	0.5489	0.0852	0.0806	0.4156	0.1787
rs2075654	0.3957	0.3048	0.1287	0.0462	-1.3147	0.5664	-0.0076	0.1285
rs1079727	0.1969	0.3213	0.1040	0.1162	-0.8811	0.3769	-0.0679	0.1238
rs2002453	0.1608	0.4816	0.1060	0.0514	-1.2660	0.5393	-0.0142	0.1280
rs2005313	0.1520	0.4812	0.1045	0.0476	-1.3011	0.5599	-0.0151	0.1279
rs2245805	0.1551	0.4814	0.1051	0.0496	-1.2823	0.5499	-0.0136	0.1280
rs2734836	0.1792	0.3213	0.1012	0.1108	-0.9044	0.4013	-0.0648	0.1240
rs2734835	0.9859	0.4684	0.3011	0.9306	1.1273	0.0176	0.7844	0.2250
rs1800498	0.9696	0.4751	0.2707	0.5397	0.0691	0.0974	0.4032	0.1770
rs2234690	0.9696	0.4751	0.2707	0.5311	0.0541	0.1131	0.4008	0.1768

rs2587548	0.9696	0.4751	0.2707	0.5357	0.0621	0.1053	0.4010	0.1767
rs2734833	0.9347	0.4814	0.2451	0.2028	-0.5944	0.2554	0.1362	0.1451
rs67800399	0.9859	0.4684	0.3011	0.9274	1.1062	0.0193	0.7787	0.2243
rs2734831	0.9848	0.4688	0.2987	0.9204	1.0630	0.0226	0.7696	0.2231
rs1962262	0.1820	0.3216	0.1016	0.1008	-0.9503	0.4237	-0.0607	0.1243
rs2075652	0.8792	0.2128	0.2432	0.0444	-1.3328	0.5757	0.0106	0.1304
rs11608185	0.9646	0.4754	0.2658	0.4599	-0.0698	0.1512	0.3344	0.1687
rs12808482	0.9646	0.4754	0.2658	0.4645	-0.0618	0.1436	0.3382	0.1691
rs1076563	0.9686	0.4745	0.2697	0.5433	0.0754	0.0891	0.4005	0.1766
rs1076562	0.1607	0.4811	0.1060	0.0528	-1.2537	0.5283	-0.0157	0.1278
rs1116313	0.9659	0.4752	0.2670	0.4901	-0.0172	0.1357	0.3628	0.1721
rs1079598	0.1732	0.3227	0.1002	0.1086	-0.9142	0.4070	-0.0621	0.1243
rs1079597	0.0849	0.3402	0.0831	0.1176	-0.8752	0.3572	-0.0750	0.1233
rs1079596	0.0774	0.3459	0.0812	0.1174	-0.8760	0.3639	-0.0684	0.1238
rs1125394	0.0695	0.3454	0.0792	0.1206	-0.8627	0.3360	-0.0755	0.1233
rs1125393	0.2480	0.3175	0.1065	0.1114	-0.9017	0.3954	-0.0693	0.1237
rs2471857	0.0895	0.3401	0.0842	0.1184	-0.8718	0.3503	-0.0764	0.1233
rs12798900	0.9861	0.4656	0.3015	0.9450	1.2350	0.0159	0.8104	0.2285
rs2471856	0.4382	0.4919	0.1404	0.0388	-1.3939	0.6118	-0.0013	0.1291
rs75349786	< 0.0001	0.0982	0.0112	0.6817	0.3308	0.0323	-0.8099	0.0753
rs2471855	0.2213	0.3194	0.1077	0.0996	-0.9561	0.4394	-0.0541	0.1249
rs2471854	0.0853	0.3412	0.0832	0.1146	-0.8879	0.3832	-0.0704	0.1237
rs7131627	0.9705	0.4730	0.2717	0.6153	0.2040	0.0717	0.4673	0.1849
rs7131440	0.9714	0.4724	0.2728	0.6337	0.2381	0.0563	0.4826	0.1868
rs7131465	0.9705	0.4718	0.2717	0.6555	0.2794	0.0405	0.5037	0.1894
rs7131681	0.9714	0.4724	0.2728	0.6535	0.2756	0.0484	0.4915	0.1878
rs11214605	0.9870	0.4647	0.3037	0.9638	1.4252	0.0102	0.8217	0.2299
rs2471851	0.0904	0.3152	0.0809	0.1546	-0.7378	0.2970	-0.1121	0.1206
rs2471850	0.4891	0.4953	0.1481	0.0374	-1.4105	0.6264	0.0025	0.1295
rs12800853	0.9881	0.4644	0.3066	0.9678	1.4778	0.0092	0.8377	0.2321
rs11608109	0.9890	0.4664	0.3091	0.9702	1.5126	0.0082	0.8465	0.2334
rs7103679	0.0949	0.3101	0.0818	0.1666	-0.6991	0.2808	-0.1203	0.1200
rs4938017	0.9143	0.4877	0.2353	0.1964	-0.6118	0.2639	0.1314	0.1445
rs7122246	0.9889	0.4668	0.3088	0.9750	1.5910	0.0064	0.8481	0.2335

rs7350522	0.2318	0.2945	0.1041	0.0766	-1.0811	0.4641	-0.0360	0.1262
rs12364051	0.9716	0.4760	0.2729	0.6239	0.2199	0.0641	0.4752	0.1859
rs78022226	0.5596	0.2914	0.1583	0.0588	-1.2042	0.5086	-0.0236	0.1272
rs7126289	0.6176	0.0935	0.1444	0.3077	-0.3523	0.1834	0.3613	0.1764
rs60599314	< 0.0001	0.2162	0.0110	0.9996	3.3977	0.0002	-1.9167	0.0272
rs4436578	0.6978	0.4447	0.1865	0.0498	-1.2805	0.5429	0.0160	0.1309
rs4587762	0.9876	0.4665	0.3051	0.9552	1.3287	0.0135	0.8214	0.2300
rs4586205	0.5186	0.4971	0.1528	0.0368	-1.4178	0.6287	0.0039	0.1296
rs7934416	0.7497	0.1104	0.1896	0.0802	-1.0594	0.4544	0.0438	0.1347
rs17115583	0.1594	0.3726	0.0976	0.0544	-1.2400	0.5245	-0.0153	0.1279
rs4620755	0.1554	0.3722	0.0969	0.0496	-1.2823	0.5499	-0.0172	0.1278
rs79549222	< 0.0001	0.2174	0.0106	1.0000	1000 *	0.0000	-1.9641	0.0260
rs7125415	0.3607	0.3169	0.1233	0.0776	-1.0750	0.4593	-0.0384	0.1260
rs11214607	0.0942	0.3028	0.0816	0.1296	-0.8270	0.3132	-0.0904	0.1222
rs4648318	0.1803	0.4760	0.1090	0.0650	-1.1578	0.4829	-0.0231	0.1272
rs4245145	0.8714	0.1319	0.2412	0.1006	-0.9513	0.4290	0.0678	0.1376
rs4648319	0.0907	0.2995	0.0810	0.1306	-0.8232	0.3052	-0.0865	0.1225
rs4379875	0.8766	0.1337	0.2443	0.1004	-0.9522	0.4342	0.0704	0.1379
rs11214608	0.9903	0.4723	0.3068	0.9146	1.0297	0.0244	0.7472	0.2200
rs76208665	0.9798	0.4812	0.2840	0.5281	0.0489	0.1206	0.3886	0.1752
rs12574471	< 0.0001	0.1873	0.0172	0.9962	2.4185	0.0017	-1.5819	0.0364
rs17529477	0.3477	0.3433	0.1259	0.0392	-1.3893	0.6093	0.0076	0.1300
rs17601612	0.6175	0.3687	0.1676	0.0642	-1.1636	0.4873	0.0243	0.1319
rs4245146	0.4248	0.5044	0.1384	0.0356	-1.4327	0.6333	0.0011	0.1293
rs4245147	0.4248	0.5044	0.1384	0.0406	-1.3734	0.5960	-0.0005	0.1292
rs4936270	0.8616	0.3693	0.2207	0.0378	-1.4057	0.6241	0.0058	0.1298
rs4936271	0.2498	0.5028	0.1140	0.0422	-1.3559	0.5846	-0.0064	0.1286
rs80215768	0.0099	0.1249	0.0304	0.9986	2.8532	0.0008	-1.7050	0.0328
rs4936272	0.2515	0.5027	0.1143	0.0438	-1.3390	0.5787	-0.0055	0.1287
rs4274224	0.3622	0.5042	0.1297	0.0396	-1.3847	0.6041	-0.0003	0.1292
rs76581995	0.0099	0.1249	0.0304	0.9988	2.9202	0.0006	-1.7062	0.0328
rs77195172	0.0008	0.1186	0.0162	0.9772	1.6320	0.0055	-1.4064	0.0430
rs4245148	0.8362	0.3669	0.2130	0.0416	-1.3624	0.5904	0.0056	0.1297
rs55697087	0.9231	0.5045	0.2400	0.1166	-0.8794	0.3705	0.0650	0.1367

rs4460839	0.8432	0.3669	0.2150	0.0346	-1.4455	0.6399	0.0067	0.1298
rs72999670	0.0457	0.3450	0.0718	0.0468	-1.3088	0.5632	0.0124	0.1305
rs4581480	0.8514	0.3656	0.2175	0.0348	-1.4429	0.6377	0.0059	0.1298
chr11:113325866	0.0104	0.1251	0.0309	0.9984	2.7951	0.0009	-1.6918	0.0331
rs73557283	0.0014	0.1638	0.0144	0.9790	1.6685	0.0047	-1.4261	0.0427
rs77541954	0.0120	0.1316	0.0320	0.4525	-0.0828	0.1658	-0.4797	0.0958
rs7122454	0.0424	0.3447	0.0706	0.1686	-0.6929	0.2725	-0.1322	0.1193
rs80014933	0.0099	0.1280	0.0304	0.9982	2.7439	0.0010	-1.6935	0.0332
rs7948028	0.5684	0.3598	0.1594	0.0640	-1.1650	0.4917	0.0242	0.1319
rs10891550	0.0272	0.3511	0.0640	0.2423	-0.4953	0.2293	-0.2168	0.1133
rs74751335	0.0072	0.1417	0.0266	0.9980	2.6980	0.0011	-1.7267	0.0322
rs77264605	0.0072	0.1417	0.0266	0.9994	3.2215	0.0003	-1.7108	0.0327
rs76499333	0.0092	0.1251	0.0299	0.9990	2.9995	0.0005	-1.7042	0.0327
rs7131056	0.0276	0.5005	0.0646	0.1132	-0.8939	0.3894	-0.0656	0.1240
rs11214611	0.0289	0.3509	0.0648	0.2587	-0.4573	0.2114	-0.2297	0.1124
rs4936274	0.8579	0.3584	0.2195	0.0420	-1.3580	0.5875	0.0061	0.1298
rs4648317	0.0285	0.3515	0.0646	0.2449	-0.4891	0.2205	-0.2139	0.1134
rs10891551	0.0517	0.3446	0.0738	0.1662	-0.7003	0.2890	-0.1228	0.1199
rs74355206	0.0340	0.1342	0.0424	0.9944	2.2493	0.0027	-1.5322	0.0380
rs4322431	0.0577	0.3545	0.0758	0.0588	-1.2042	0.5086	0.0182	0.1312
rs7117915	0.0440	0.3433	0.0712	0.2144	-0.5639	0.2468	-0.1743	0.1162
rs10891552	0.5066	0.2641	0.1488	0.0394	-1.3870	0.6067	0.0011	0.1293
rs4337071	0.5780	0.3598	0.1610	0.0634	-1.1694	0.4961	0.0268	0.1322
rs4630328	0.5842	0.3592	0.1620	0.0662	-1.1493	0.4783	0.0296	0.1325
rs72999677	0.0469	0.3466	0.0722	0.0488	-1.2898	0.5533	0.0118	0.1304
rs11214612	0.8520	0.3568	0.2176	0.0360	-1.4277	0.6310	0.0049	0.1297
rs11214613	0.8485	0.3572	0.2166	0.0400	-1.3801	0.5987	0.0061	0.1298
rs11214614	0.0469	0.3466	0.0722	0.0484	-1.2935	0.5566	0.0119	0.1305
rs4350392	0.0415	0.3439	0.0703	0.2218	-0.5450	0.2381	-0.1893	0.1152
rs11601054	0.5722	0.3602	0.1600	0.0686	-1.1327	0.4736	0.0283	0.1324
rs61902787	0.5722	0.3602	0.1600	0.0700	-1.1233	0.4689	0.0298	0.1326
rs75824731	0.0370	0.1355	0.0435	0.9956	2.3545	0.0021	-1.5273	0.0381
rs10891553	0.8331	0.3552	0.2121	0.0352	-1.4378	0.6355	0.0037	0.1295
rs77655590	0.0297	0.1397	0.0421	0.9958	2.3748	0.0019	-1.5357	0.0379

rs12421616	0.6103	0.2519	0.1690	0.0386	-1.3962	0.6143	0.0002	0.1292
rs73557296	0.0033	0.1752	0.0417	0.9538	1.3147	0.0146	-1.2335	0.0498
rs4245149	0.0214	0.3498	0.0607	0.3739	-0.2239	0.1742	-0.3629	0.1030
rs60253148	0.0033	0.1752	0.0417	0.9552	1.3287	0.0135	-1.2386	0.0496
rs7102650	0.0182	0.1493	0.0360	0.9966	2.4670	0.0013	-1.5757	0.0367
rs55887984	0.5262	0.2616	0.1526	0.0378	-1.4057	0.6241	-0.0010	0.1291
rs75924850	0.3384	0.0832	0.0874	0.0954	-0.9768	0.4494	-0.0538	0.1251
rs117720003	0.0307	0.1342	0.0412	0.9952	2.3166	0.0023	-1.5471	0.0375
rs4938019	0.0363	0.3435	0.0682	0.2627	-0.4483	0.2023	-0.2321	0.1121
rs10891554	0.8473	0.3567	0.2162	0.0384	-1.3986	0.6193	0.0040	0.1296
rs61902807	0.5694	0.3597	0.1595	0.0572	-1.2169	0.5127	0.0258	0.1321
rs10789943	0.0363	0.3435	0.0682	0.2775	-0.4157	0.1929	-0.2458	0.1110
rs10789944	0.0188	0.3513	0.0591	0.4563	-0.0761	0.1586	-0.4585	0.0965
rs79872790	0.0282	0.1390	0.0414	0.9932	2.1644	0.0029	-1.4841	0.0397
rs79092434	0.0147	0.1511	0.0336	0.9944	2.2493	0.0027	-1.5862	0.0365
rs7116768	0.8284	0.3655	0.2108	0.0320	-1.4806	0.6421	0.0024	0.1294
rs1799978	0.0204	0.1709	0.0374	0.9740	1.5735	0.0073	-1.3142	0.0461

Table S2. Results for all 151 SNPs of *DRD2*. The left column shows the results of LOSITAN (see Figure 2 for the visual output). The right column the results of BayeScan (see Figure 3 for the visual output).

P = P (Simulation F_{ST} < sample F_{ST}); H_e = expected heterozygosity; F_{ST} = Fixation Indices subpopulation to total population.

P = posterior probability; $\log_{10}(PO)$ = logarithm (base 10) of the posterior odds; q-value = false discovery rate (FDR) analogue of the P value; α_i = locus-specific component (negative alpha suggests balancing selection, while positive alpha suggests directional selection); F_{ST} = Fixation Indices subpopulation to total population.

* - the value of 1000 means infinity (see BayeScan manual).

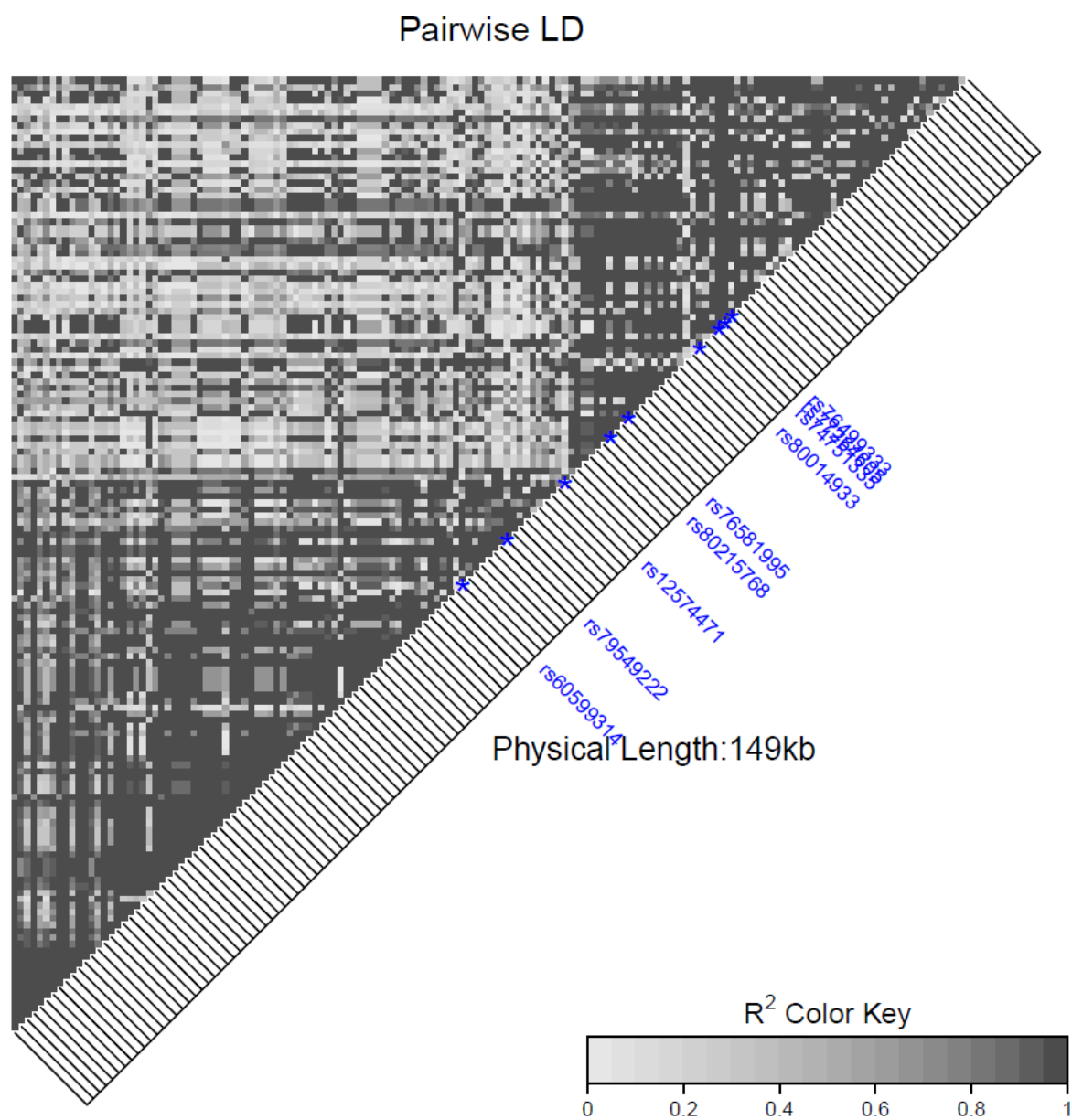


Figure S1. D' heat map of the ASW population.

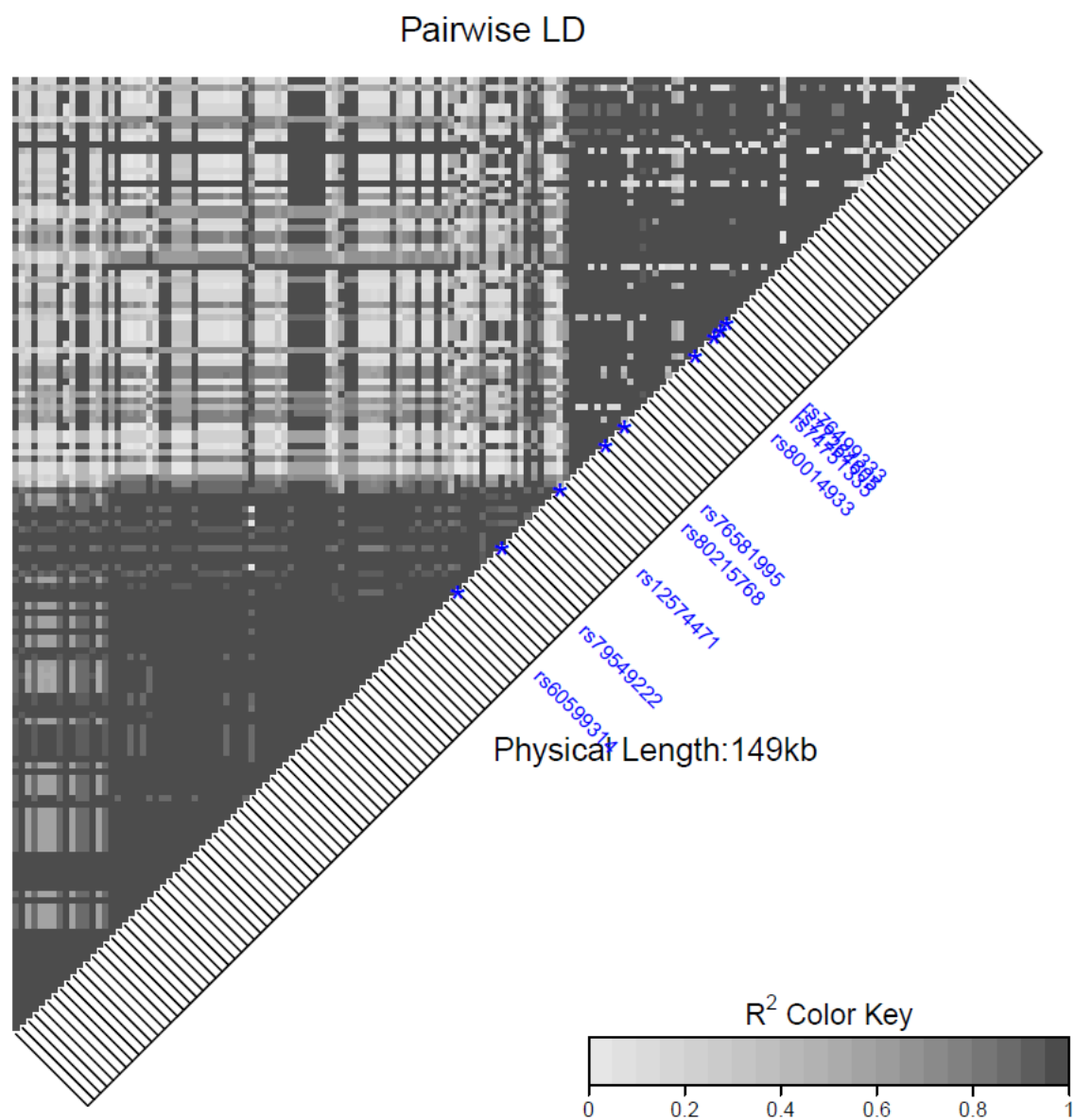


Figure S2. D' heat map of the CEU population.

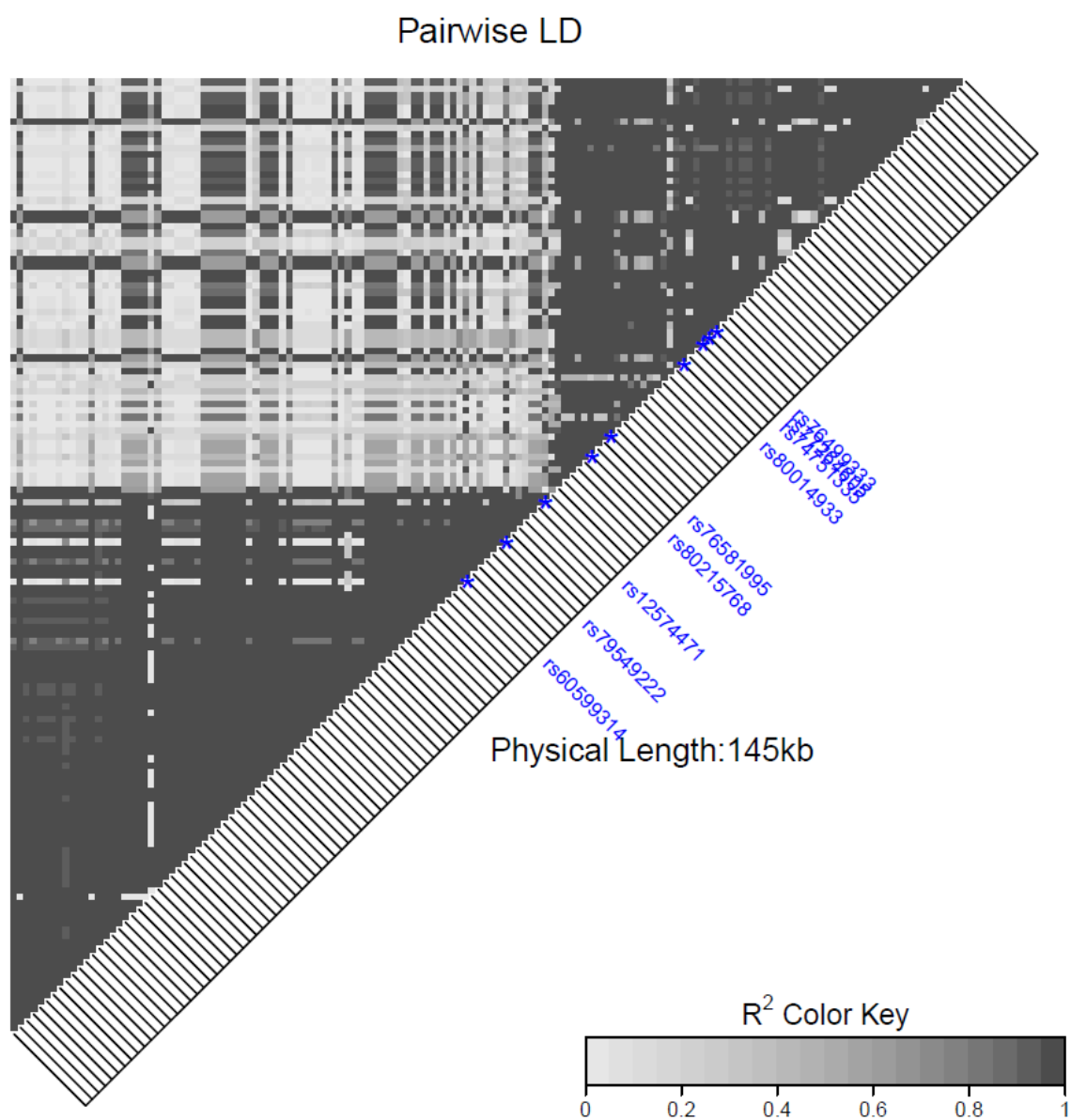


Figure S3. D' heat map of the CHB population.

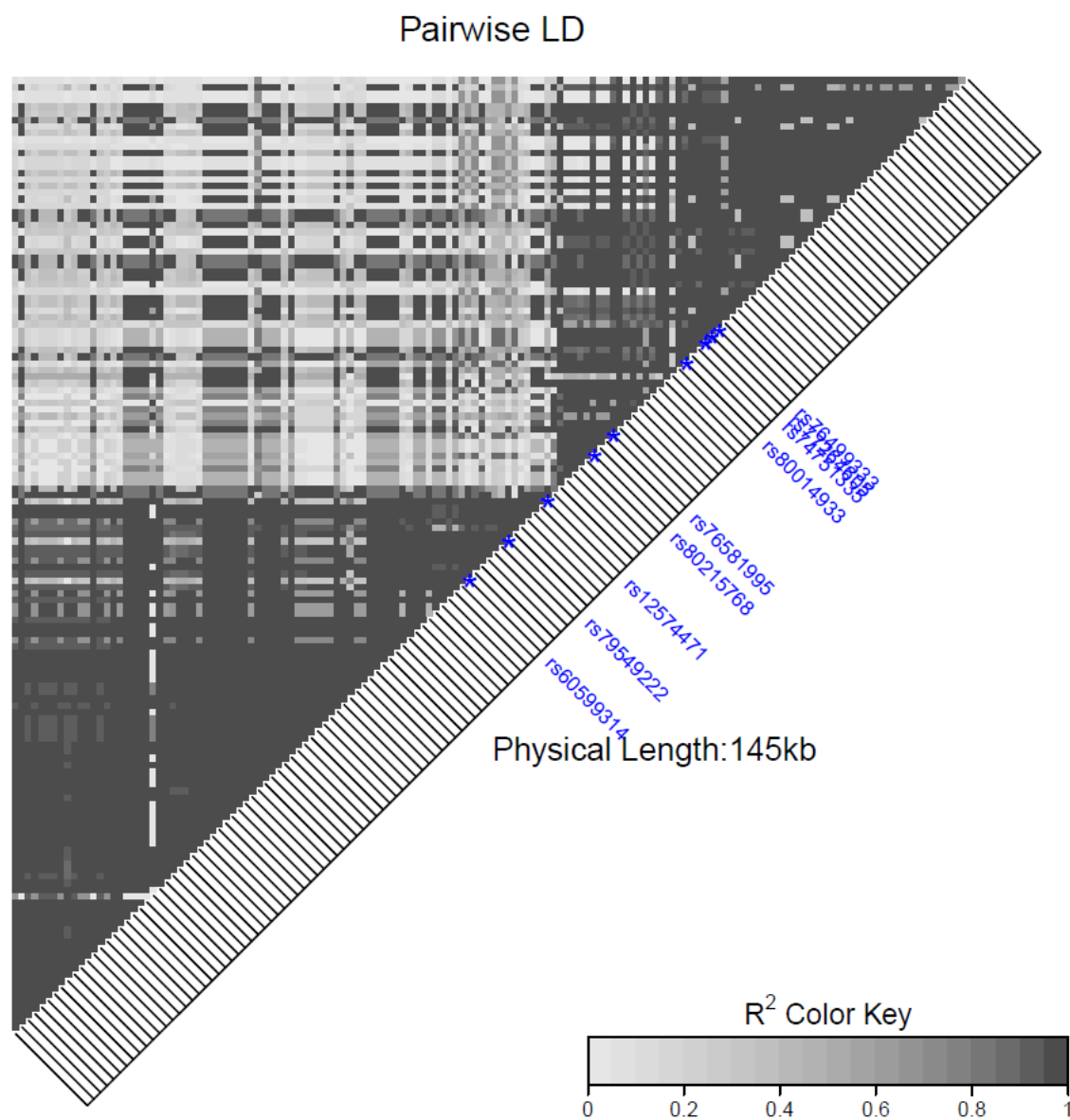


Figure S4. D' heat map of the CHS population.

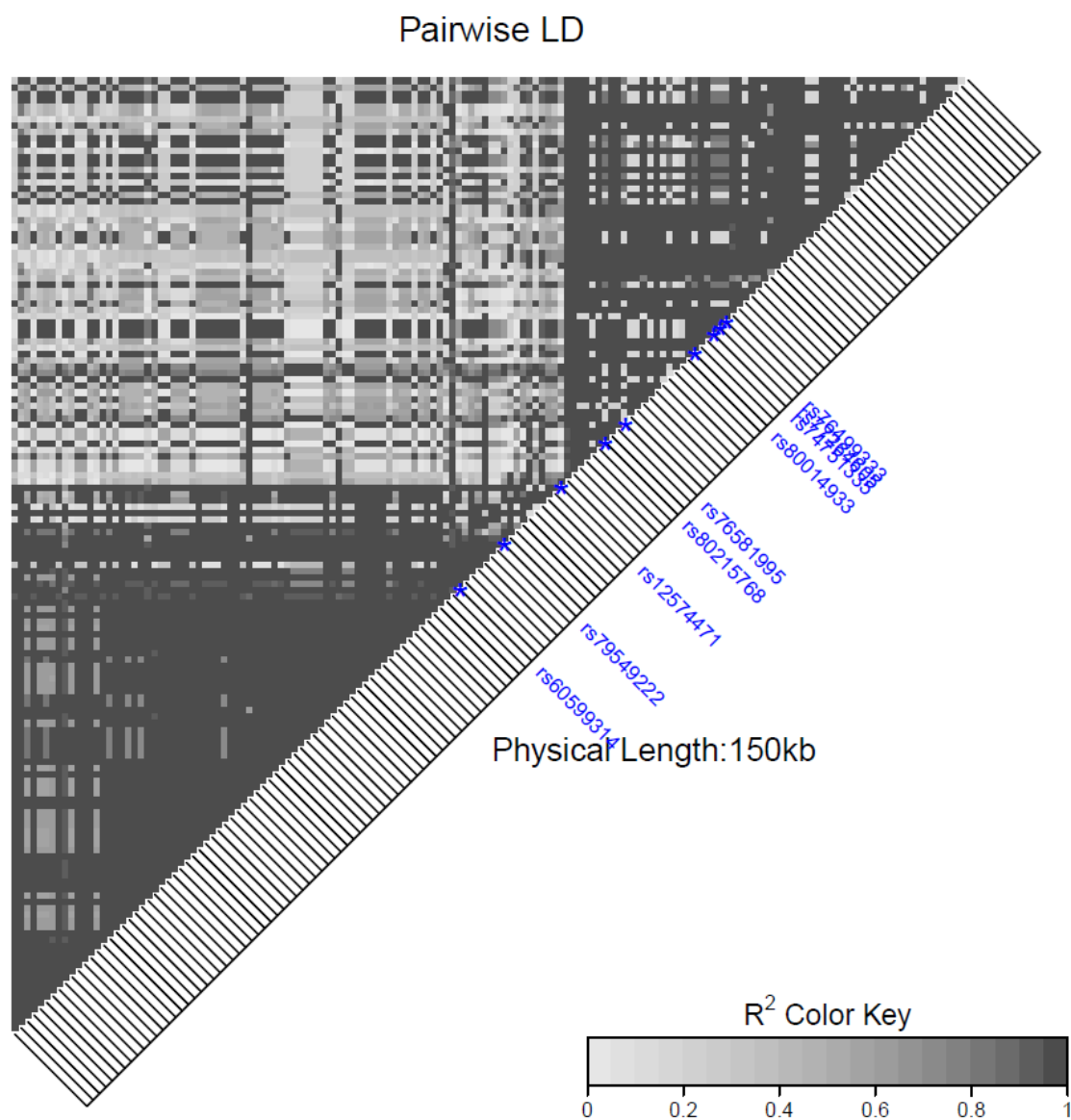


Figure S5. D' heat map of the CLM population.

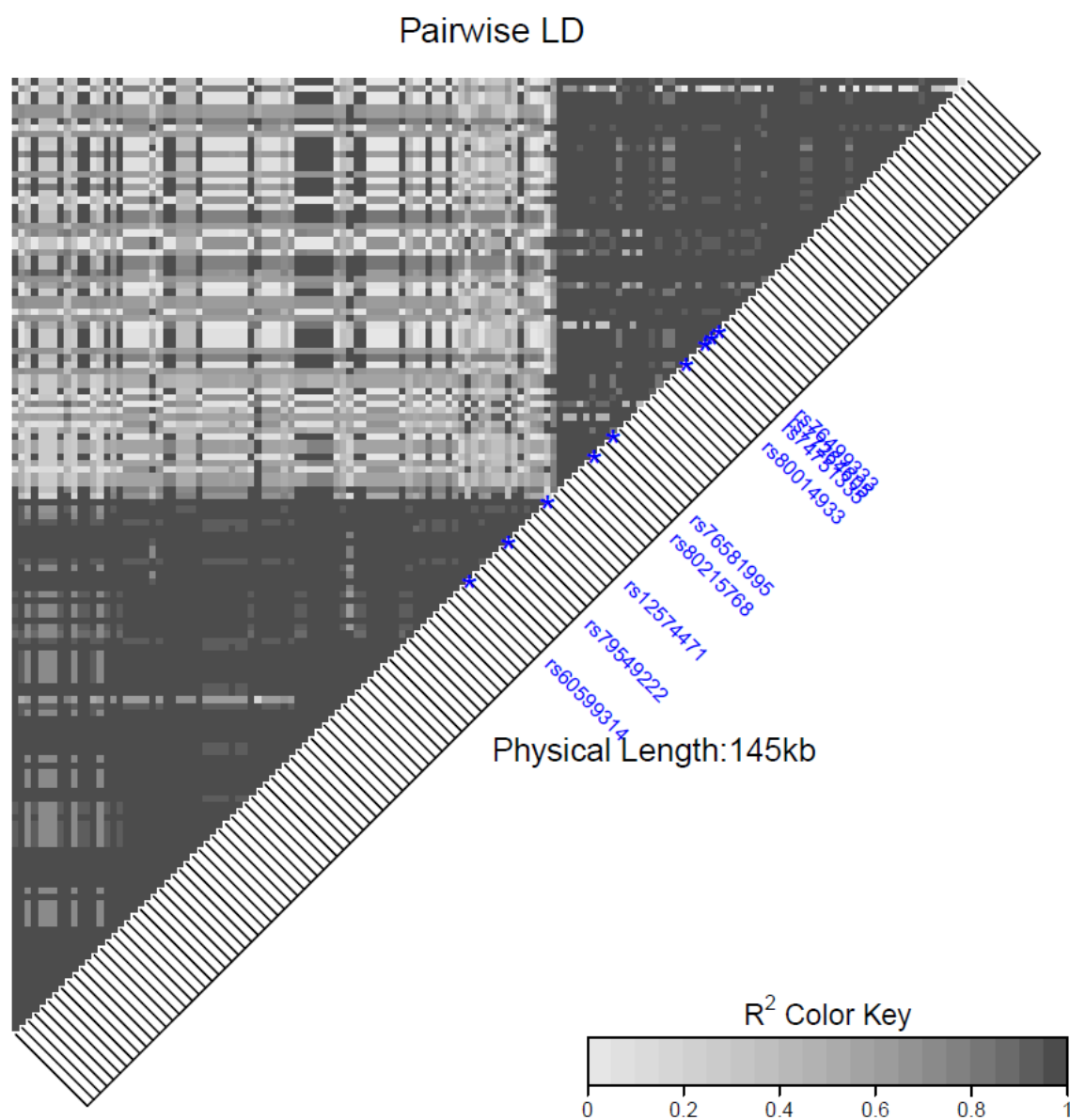


Figure S6. D' heat map of the FIN population.

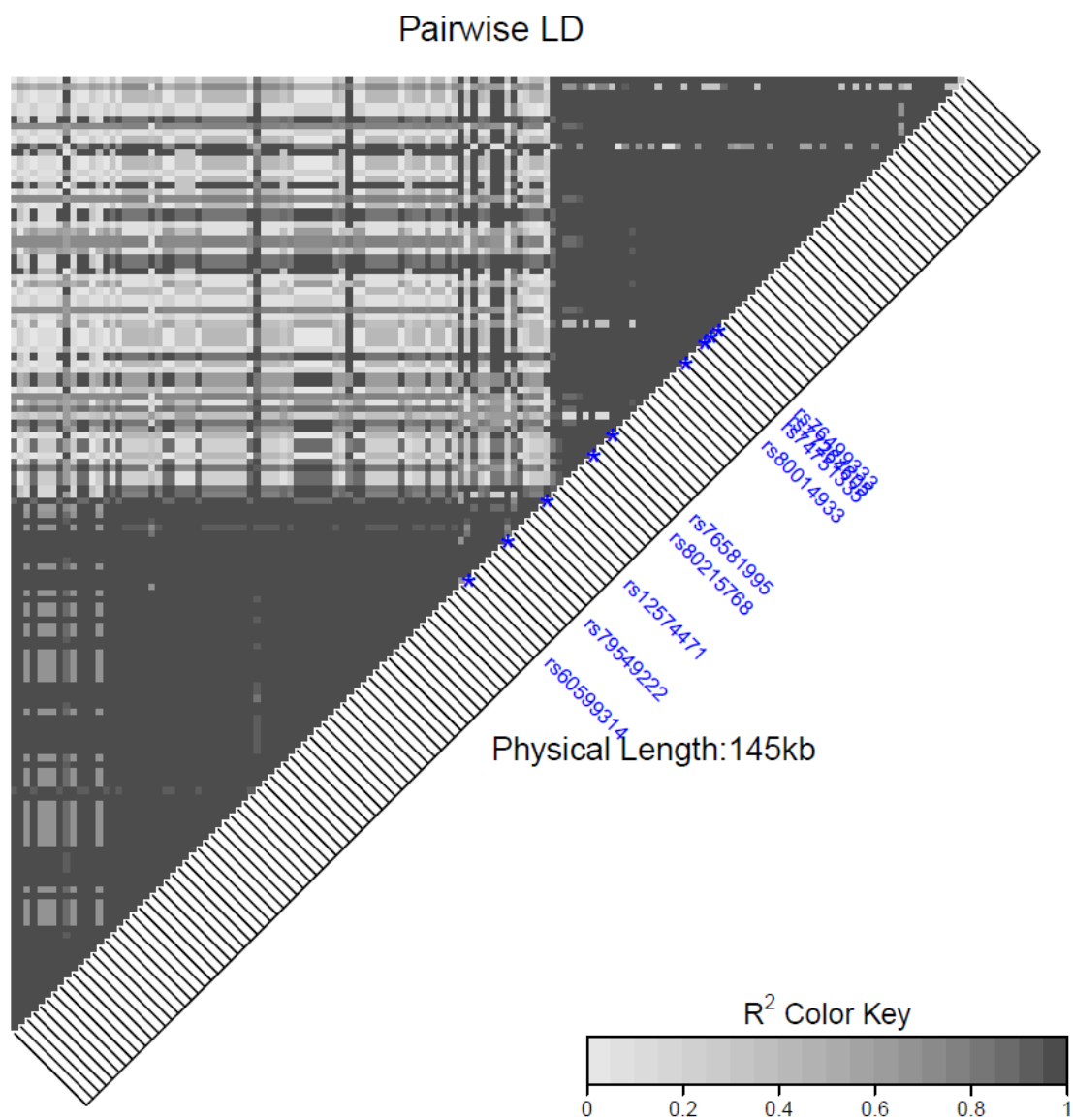


Figure S7. D' heat map of the GBR population.

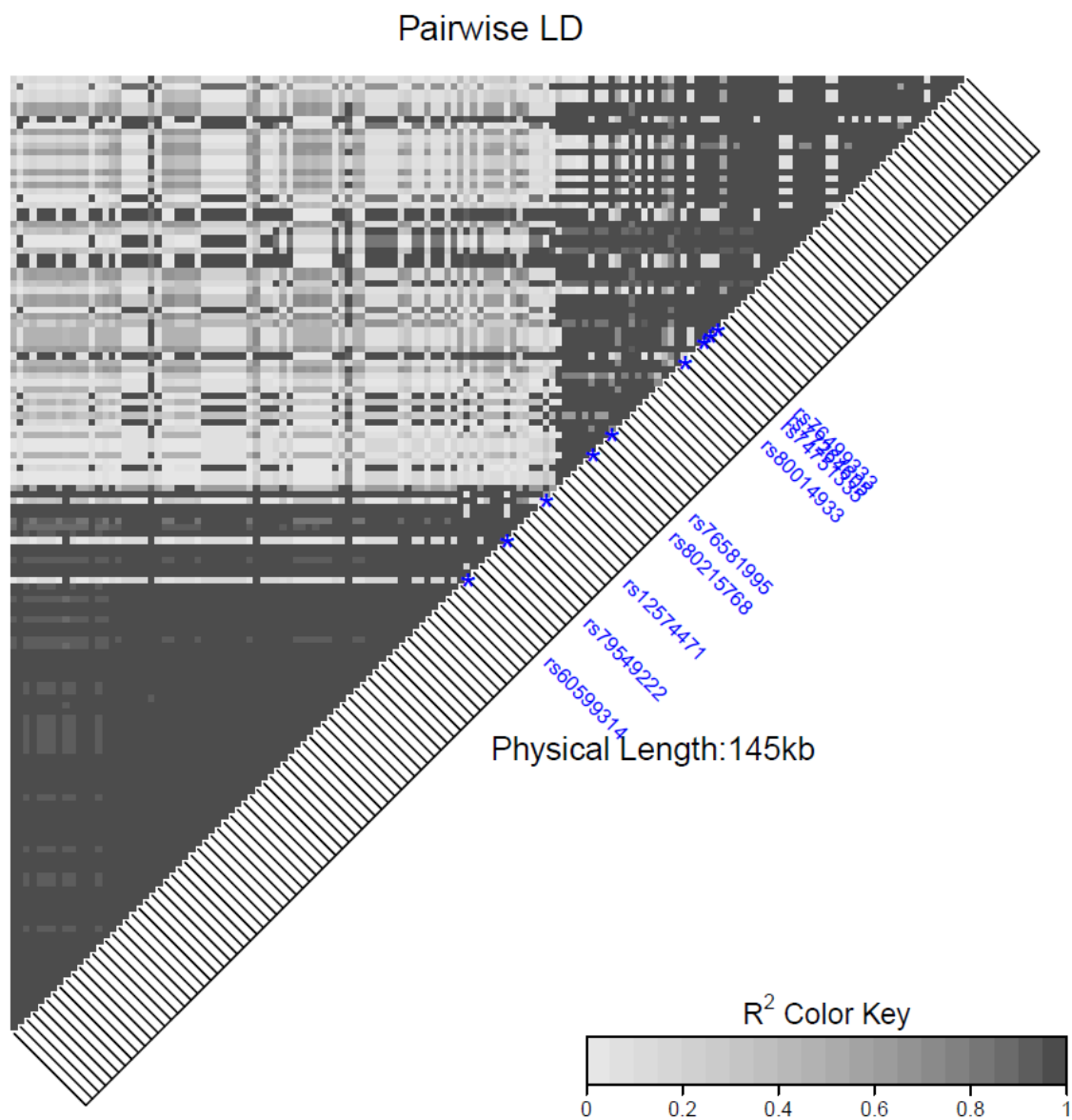


Figure S8. D' heat map of the JPT population.

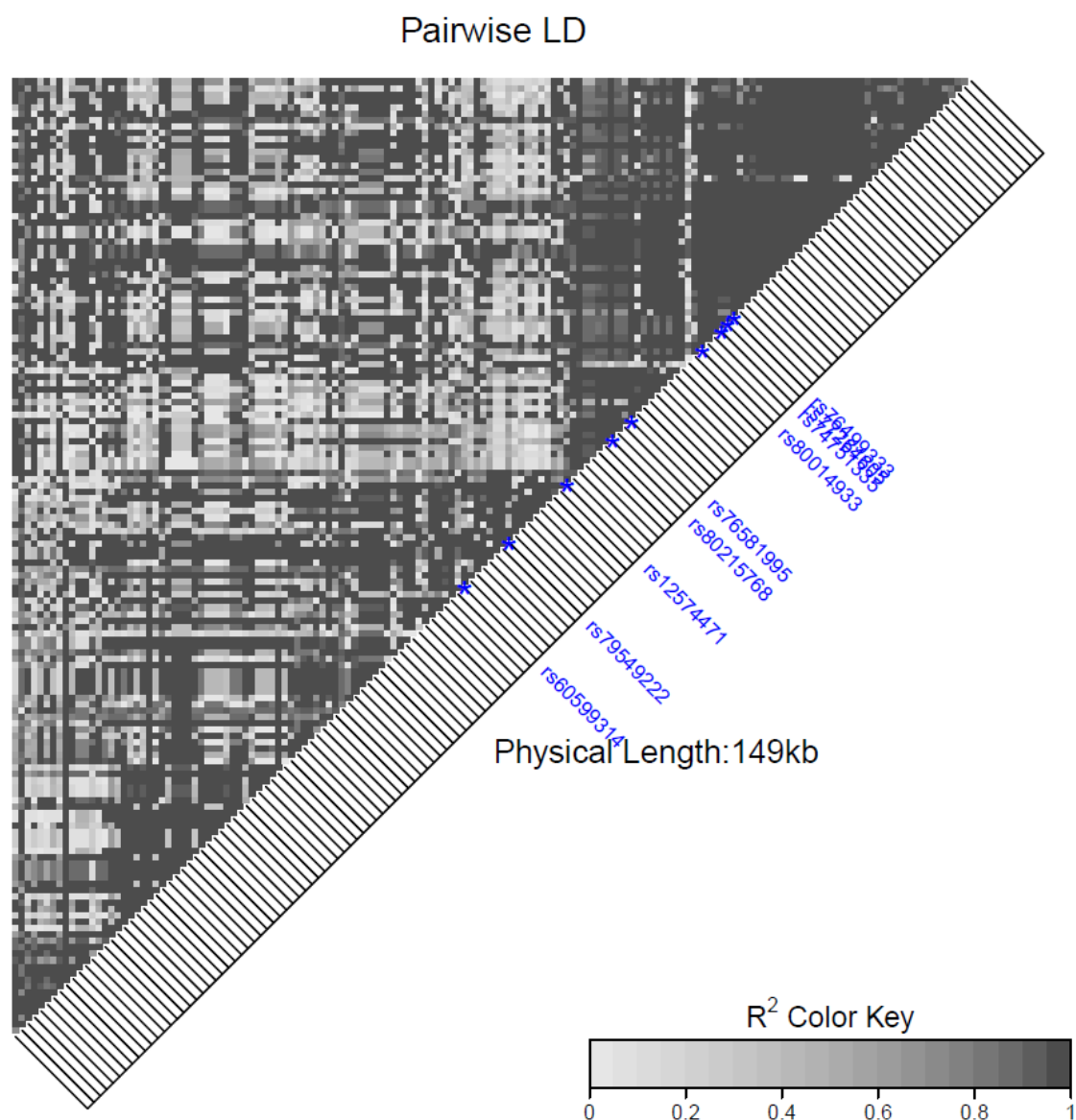


Figure S9. D' heat map of the LWK population.

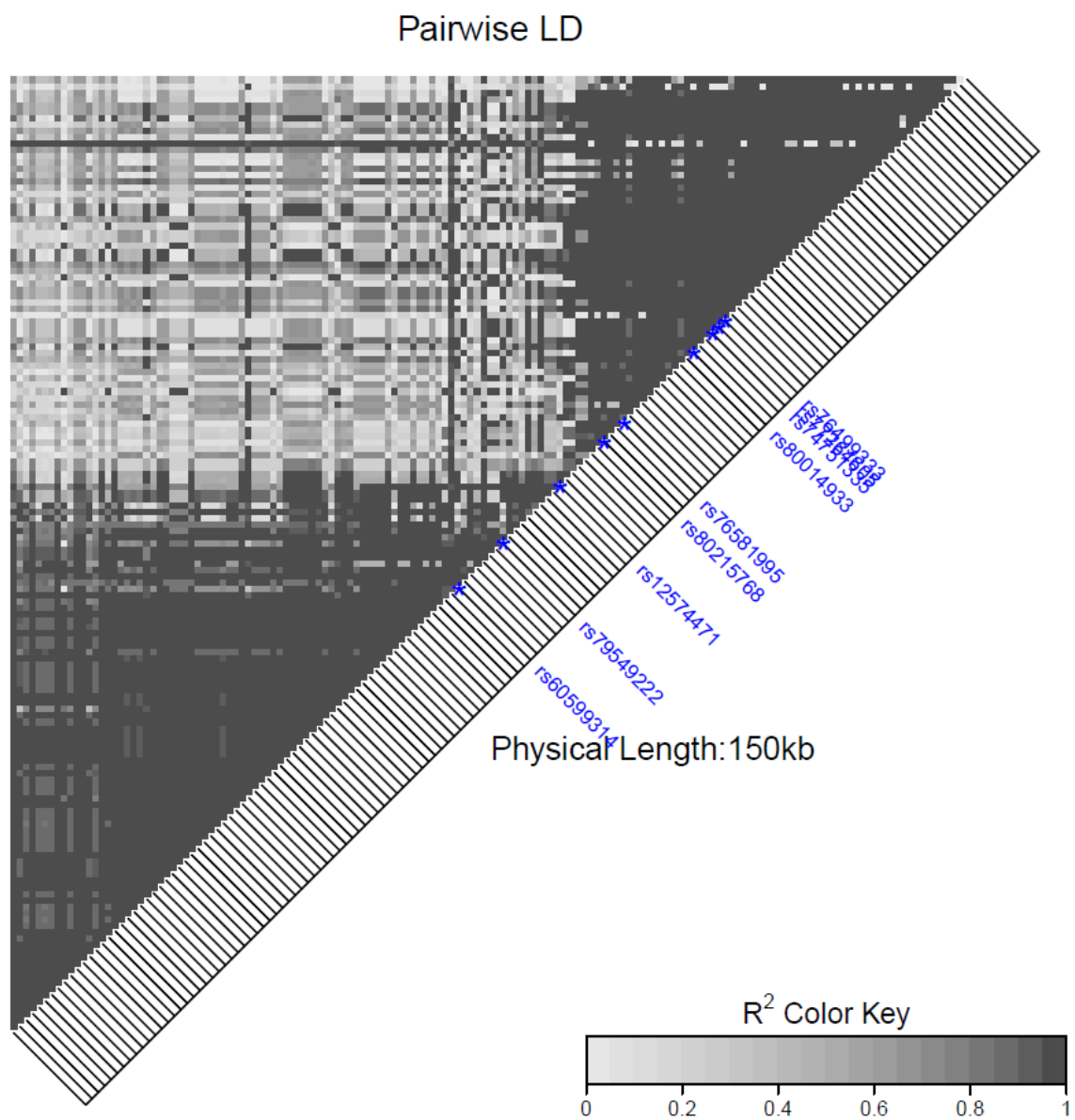


Figure S10. D' heat map of the MXL population.

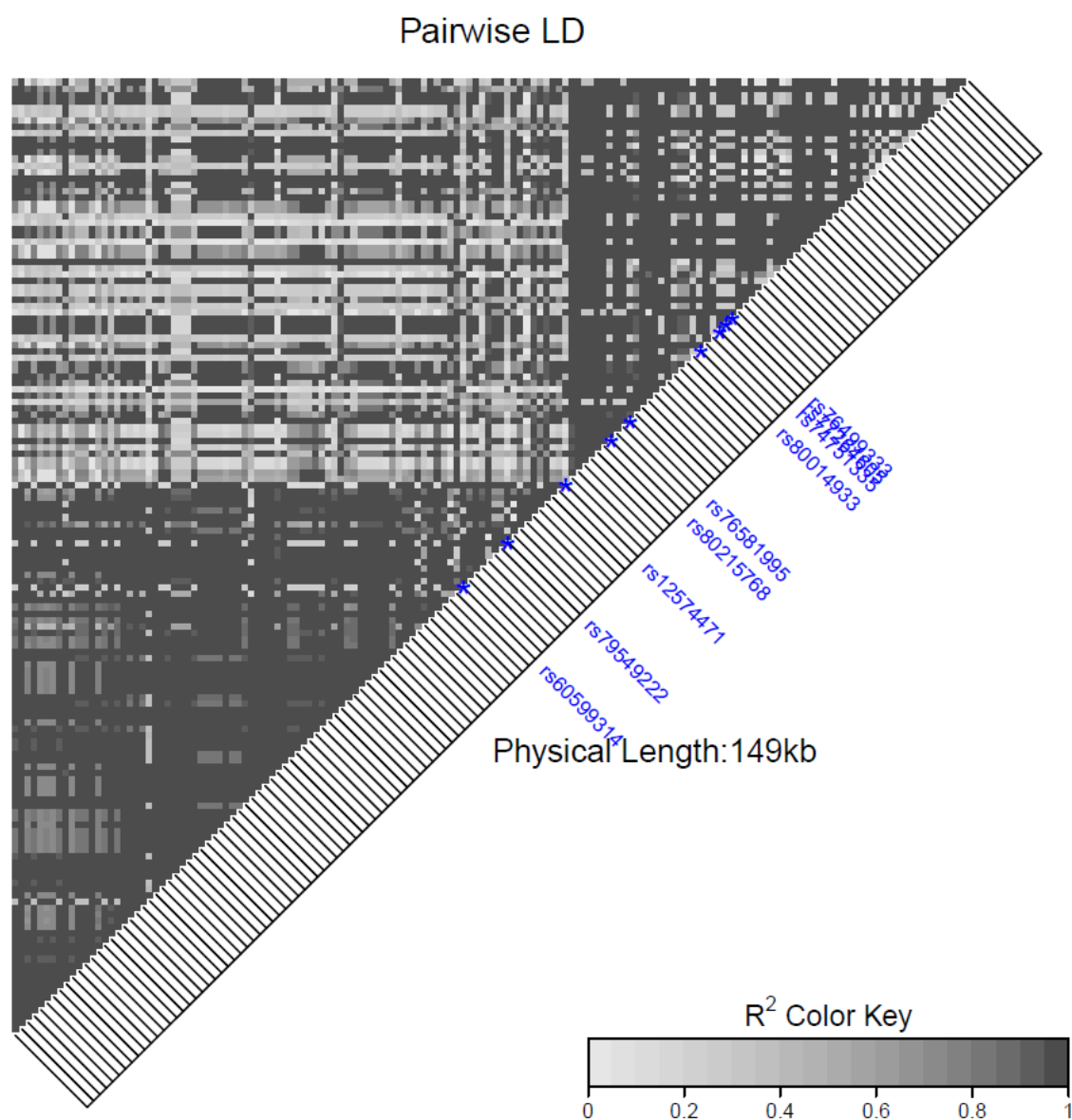


Figure S11. D' heat map of the PUR population.

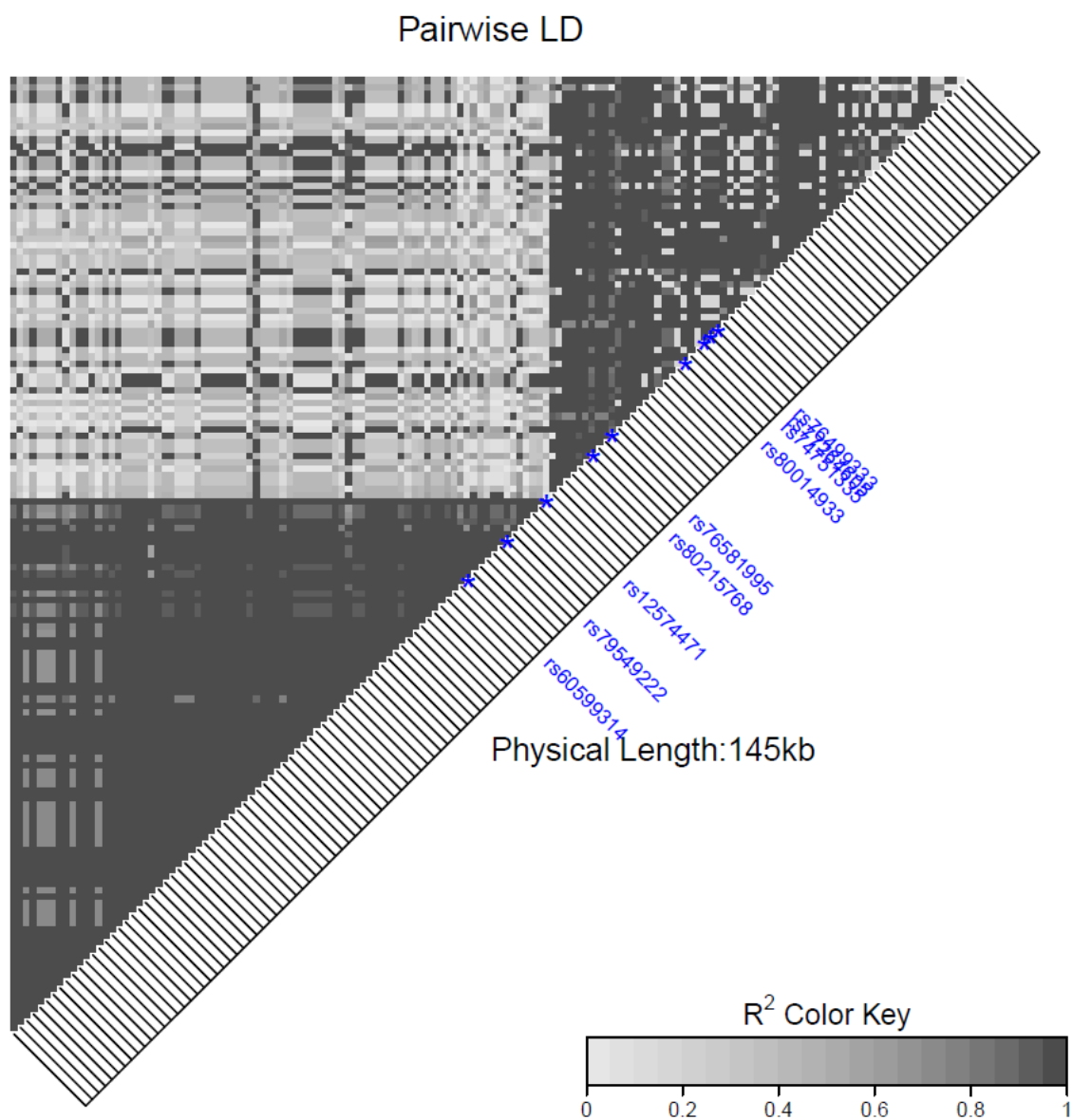


Figure S12. D' heat map of the TSI population.

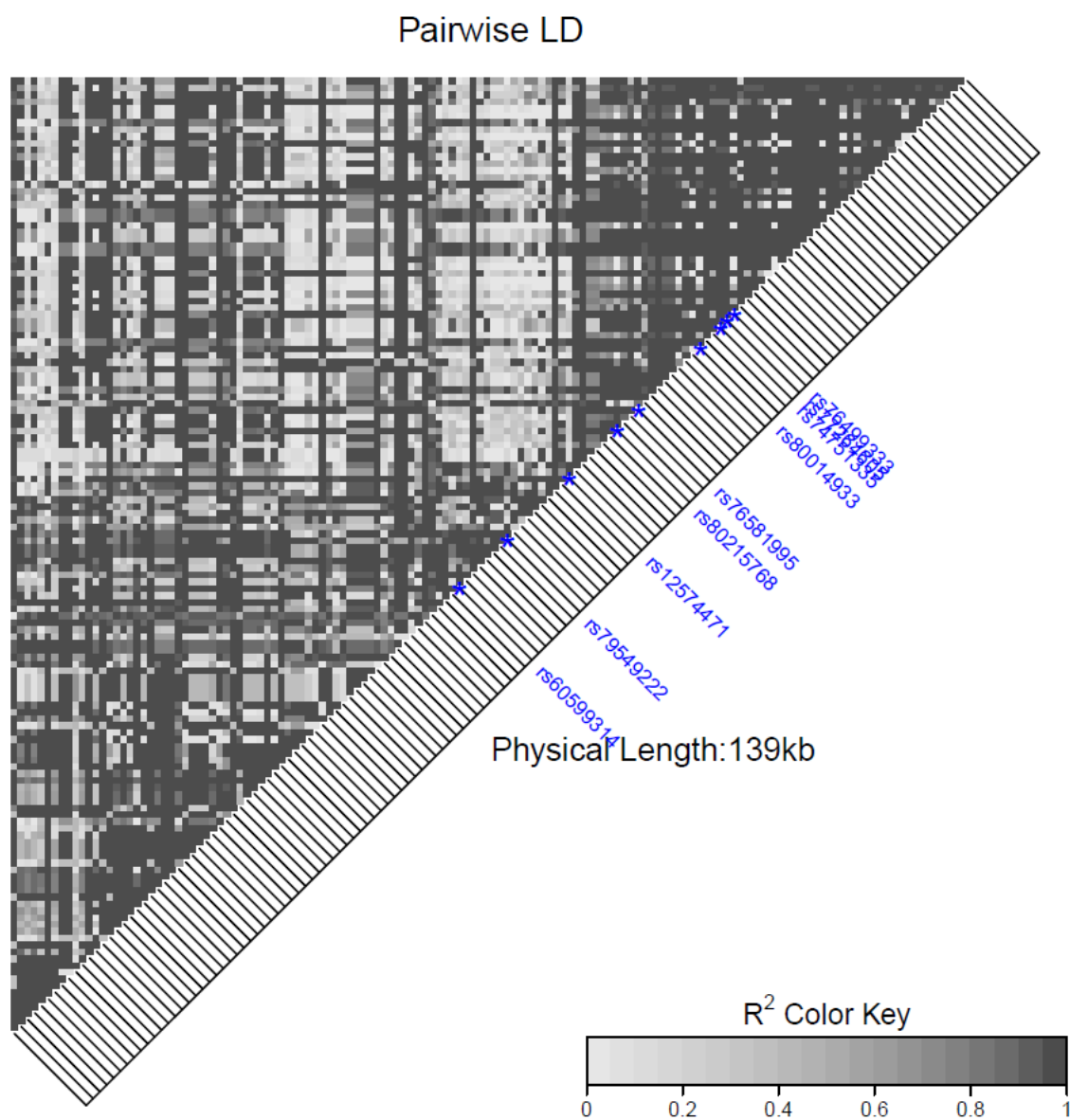


Figure S13. D' heat map of the YRI population.

Curriculum vitae:

EDUCATION

- 1996 – 2000 Primary school: VS 35 in Linz.
- 2000 – 2004 Secondary school: BRG Landwiedstraße.
Emphasis on Biology and Physics. (“Laborzweig”)
- 2004 – 2008 Secondary school (continued): BRG Landwiedstraße
Emphasis on Biology, Physics and Chemistry.
Additional courses in English language and Informatics.
Matura – “guter Erfolg” (pass with merit)
- 2009 – 2015 Anthropology at the University of Vienna.
Bachelor of Science (BSc) achieved on 6th of March, 2013.
My masters was a mix consisting of human ethology, human life history and genetics. The shift to human evolutionary genetics came gradually and I plan on advancing further in this field. Recently, I became acquainted with cultural and social anthropology. I strongly believe that an interdisciplinary cooperation with this field, will benefit both disciplines and deepen our understanding of humans.

UNIVERSITY-RELATED ACTIVITIES

- 15–16. May 2014 Presentation at the 9. Tage der KSA (15–16 May 2014).
“A Historical Glance at Anthropology in Vienna, Curricula and Numbers”
(part of Workshop B: Wiener Anthropologien).
- March – May 2015 NaturTalente 2015 (High Potential Program for Master- and PhD Students of Science and Informatics)
- Fall 2014 and ongoing Part of the Student Organizing Committee of the 11th Conference on Hunting and Gathering Societies (CHAGS 11, 7.–11. September 2015).

WORK EXPERIENCE

Aug. 2007	Internship at BuchPlus, a facility of ProMente Oberösterreich.
Sep. 2008	Internship at the hospital Barmherzigen Schwestern (Linz).
Nov. 2008 – Jul. 2009	Civil service at the Landes-Nervenklinik Wagner Jauregg.

PERSONAL SKILLS

Languages	German (mother tongue), English (proficient user), Spanish (basic user).
Driving licence	B
Computer skills	Office applications, SPSS, R. Worked with various genetic and population genetics programs.
Laboratory	Experienced in genetic laboratory work.

PERSONAL INTERESTS

Hobbies	Running, Strength training, Cooking.
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