

Customizing human genome: SNPs and their editing

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Abstract

Single nucleotide polymorphism (SNP) is single nucleotide variations at specific locations between individuals. This polymorphism could both be crucial for determining both some personal features (as eye or skin color) and be linked to different diseases. In this study, we analyzed the SNPs from genome data obtained by 23andMe project. We detected that the data came from a male person with brown eyes, whose ancestors were from Western Europe or Caucasus. Among potential risks of diseases there were risks to diabetes, lung cancer, tobacco addiction, heart diseases and a few neural diseases (autism, schizophrenia, Alzheimer disease). However, we should highlight that presence of these SNPs is not always associated with these conditions. Here, we also provide brief information about SNPs correction due to CRISPR-Cas system. CRISPR-Cas is a promise system for diseases treatment and we recommend to make changes for SNPs related to Alzheimer diseases, cancer, tobacco addition and others.

Keywords: SNP analysis, human genome, 23andMe

Introduction

Single nucleotide polymorphisms (SNPs) are a type of genetic variation where a single nucleotide (A, T, C, or G) at a specific location in the genome differs between individuals (Brookes 1999; Wray *et al.* 2013; Page *et al.* 2016). SNPs can be associated with disease risk, drug response, and other traits of interest, making them an important area of study in genetics (Emahiazion *et al.* 2001; Voisey and Morris 2008; Ahsan *et al.* 2020). In some cases, SNPs may cause disease directly, while in other cases they may be linked to a disease-causing variant or alter the function of a gene (Ingram 1956; Xue *et al.* 2020).

Genotyping chips are a type of microarray that can be used to rapidly genotype large numbers of SNPs in a sample of DNA (Rapley *et al.* 2004). Genotyping chips contain thousands to millions of probes that bind to specific SNPs, allowing researchers to determine which SNPs are present in a given sample (Perkel 2008). By comparing the genotypes of large groups of individuals with and without a particular disease or trait, researchers can identify SNPs that are associated with that disease or trait (Prokunina and Alarcón-Riquelme 2004; Heidema *et al.* 2006).

CRISPR-Cas9 can also be used to potentially correct SNPs in the genome (Doudna and Charpentier 2014). When a SNP is associated with a disease or trait, researchers may want to correct the SNP in order to reduce or eliminate the associated risk. CRISPR-Cas9 can be used to precisely target and modify specific locations in the genome, including SNPs. By introducing a guide RNA that targets the location of the SNP and using the Cas9 enzyme to cut the DNA, researchers can potentially replace the altered nucleotide with the correct one, effectively "correcting" the SNP (Savic *et al.* 2018; Min *et al.* 2019).

Together, the use of genotyping chips and CRISPR-Cas9 can be a powerful tool for identifying and potentially correcting disease-associated SNPs in the human genome. By identify-

ing SNPs associated with disease, researchers can gain insights into the genetic basis of the disease and potentially develop new treatments. Additionally, by using CRISPR-Cas9 to correct disease-associated SNPs, researchers may be able to prevent or reverse the disease-causing effects of the SNP. However, it's important to note that the use of CRISPR-Cas9 for human gene editing is still a relatively new technology and there are many ethical and safety considerations that need to be carefully considered before any clinical applications can be made.

Material and methods

Raw 23andMe data obtained from Mike Rayko was used for the analysis, where you have a chromosome, position, and a unique identifier (rsid) for each detected SNP. Version GRCh37 was a reference genome following 23andMe recommendation.

Plink v. 1.9 was used to convert 23andMe's raw data into standard vcf format (Purcell *et al.* 2007) with -snps-only parameter.

James Lick's mtHap utility was used for identifying maternal (mtDNA) haplogroups, and YSEQ Clade Finder (version 1.0) - for identifying paternal haplogroups.

To make SNP annotation and identify some characteristics we have used IGV browser v. 2.16.0, selecting GRCh37/hg19 as the reference genome (Thorvaldsdóttir *et al.* 2013). Selection of clinically relevant SNPs was conducted with VEP (Variant Effect Predictor) (McLaren *et al.* 2016). The specific information about each SNP was checked with SNPedia (Cariaso and Lennon 2012) and ClinVar database (Landrum *et al.* 2016).

Results

Analyzing mtDNA have led to identifying a certain haplogroup, which is H2 haplogroup. Specifically, it can be

H2a2a1, H2a2a1d, H2a2a1a, H2a2a1h, H2a2a, H2a2a1f, H2a2a1e, H2a2a1b, H2a2a1g or H2a2a1c haplogroup. We cannot predict with absolute certainty the specific haplotype, this is a probabilistic prediction, as well as paternal haplotype prediction. According to YSEQ Clade Finder (version 1.0), the desired paternal haplotype is R-M417 or R-M198, but according to Y-SNP Subclade Predictor it is R1a1a (R-M420).

To figure out the eye color we searched for the related to this feature SNPs in IGV browser. It appeared to be: rs12203592 on 6 chromosome, rs12896399, 14 chr, rs12913832, 15 chr, rs16891982, and the 5 chr. rs6119471 (chr 20) was absent.

(Table 1).

Discussion

1. Ancestry

Haplogroup H is a human mitochondrial DNA (mtDNA) haplogroup. The clade is believed to have originated in Southwest Asia, near present day Syria, around 20,000 to 25,000 years ago (Achilli *et al.* 2004). Mitochondrial haplogroup H is today predominantly found in Europe, and is believed to have evolved before the Last Glacial Maximum (LGM) (Brotherton *et al.* 2013). It first expanded in the northern Near East and Southern Caucasus soon, and later migrations from Iberia suggest that the clade reached Europe before the Last Glacial Maximum (Roostalu *et al.* 2007; Hernández *et al.* 2017). The haplogroup has also spread to parts of Africa, Siberia and inner Asia (Ennafaa *et al.* 2009). Today, around 40% of all maternal lineages in Europe belong to haplogroup H.

The H2, H6 and H8 haplogroups are somewhat common in Eastern Europe and the Caucasus (Pereira *et al.* 2005). They may be the most common H subclades among Central Asians and have also been found in West Asia.

Paternal haplogroup of the analysed male person is R1a1a (Zupan *et al.* 2013). Highest frequencies of this haplogroup are present in Western Europe. According to Pamjav *et al.* (2012) and coauthors, R1a1a diversified in the Eurasian Steppes or the Middle East and Caucasus region. In other words, this human has maternal ancestors from **Central Asia or Caucasus**.

2. Eye colour

Single nucleotide polymorphisms, or SNPs, are variations in a single DNA nucleotide that occur within a population. These variations can be associated with differences in traits, including eye color (Sturm and Frudakis 2004). Eye color is a complex trait that is influenced by multiple genes, but some SNPs have been found to be strongly associated with eye color (Hart *et al.* 2013).



Figure 1 The owner of the analyzed genome

One of the most well-known SNPs associated with eye color is rs12913832, located on chromosome 15 (Meyer *et al.* 2020). This SNP is strongly associated with the presence of blue eyes, and individuals with the GG genotype at this locus are more likely to have blue eyes (Sturm *et al.* 2008). The frequency of the G allele is highest in populations of European ancestry, where blue eyes are most common.

Another SNP associated with eye color is rs12896399, located on chromosome 14 (Sulem *et al.* 2007). This

SNP is strongly associated with the presence of brown eyes, and individuals with the GG genotype at this locus are more likely to have brown eyes (Andersen *et al.* 2013). The frequency of the G allele is highest in populations of African and Asian ancestry, where brown eyes are most common.

rs12913832	A/G
rs12896399	G/G

Table 1 Two most significant eye color associated SNPs

In our samples there are A/G allele of rs12913832 SNP and G/G of rs12896399 that are not typical for non-blue eyes. In our analysis the owner of the genome has most likely **brown eyes** due to presence of G/G genotype in rs12896399 and absence of synonymous alleles in other SNPs associated with eye colour. Moreover, in addition to these two SNPs, there are many other genetic variations that have been found to be associated with eye color.

While SNPs can be used to predict the likelihood of certain eye colors, it's important to remember that eye color is a complex trait that is influenced by many genes and environmental factors.

3. Risk factor associated SNPs

There are appeared to be a lot of risk factor associated SNPs in this genome. The owner has susceptibility to diabetes, lung cancer, tobacco addiction, heart diseases (coronary artery disease, dystonia, three vessel coronary disease), a few neural diseases (memory impairment, neural tube defects, autism, schizophrenia, Alzheimer disease) (Table 2 in supplementary) (Wang *et al.* 2013; Morozova *et al.* 2019; Korytina *et al.* 2022).

It doesn't mean that this person might obtain such an impressive list of deseases. But these SNPs are associated with genes which make the risks. Some of them might be meaningful though. For example, rs763110 SNP, associated with lung cancer, is situated right in the centromere of chromosome 1. And centromeres are important for cell division (Zhou *et al.* 2015). Tobacco addiction related SNP rs2184026 is in the SHC3-202 gene, which is the signaling adapter that couples activated growth factor receptors to signaling pathway in neurons (Corradini *et al.* 2011; Yukseloglu *et al.* 2019).

The list goes on:

ID	RISK	GENE
rs763110	Lung cancer	centromere
rs6280	Schizophrenia	NECTIN3-211
rs1049296	Alzheimer disease	PIK3R4-201
rs13266634	Diabetes mellitus type 2	slc30a8
rs2184026	Tobacco addiction	SHC3-202

Table 2 Some genes that are close to the SNPs

Moreover, we have obtained the information about each SNP through ClinVar. It's important to note that the information in

ClinVar is not always 100% accurate or complete. ClinVar aggregates information from a variety of sources, including research studies, clinical laboratories, and other databases (Landrum *et al.* 2016). While the majority of the information in ClinVar is likely to be accurate, there may be errors, inconsistencies, or incomplete data that can affect the accuracy of the database.

In addition, the interpretation of genetic variations and their potential associations with diseases is a complex and evolving field. There may be different interpretations of the same genetic variation, and the potential clinical significance of a genetic variation may change over time as more research is conducted (Ward and Kellis 2012).

For these reasons, it's important to interpret the information in ClinVar with caution and to consult with a qualified healthcare professional or genetic counselor before making any medical decisions based on this information. These professionals can provide additional context and guidance to help individuals make informed decisions about their health and genetic testing.

4. Correcting risk factor associated SNPs

CRISPR enables researchers to correct a risk-associated SNP due to the ability to introduce the normal (wild-type) allele of the gene into the patient's genome. This would require careful design of the guide RNA to ensure that the Cas9 enzyme cuts the DNA at the correct location, and that the repair process introduces the correct changes to the DNA sequence (Lee *et al.* 2022).

One potential challenge in using CRISPR to correct disease-associated SNPs is the possibility of off-target effects. Off-target effects occur when the Cas9 enzyme cuts DNA at unintended locations in the genome, potentially introducing unintended changes to the DNA sequence (Zhang *et al.* 2015; Manghwar *et al.* 2020). To minimize the risk of off-target effects, researchers would need to carefully design the guide RNA and rigorously test the efficacy and specificity of the CRISPR system.

Another potential challenge is the delivery of the CRISPR system to the target cells (Glass *et al.* 2018; Tyumentseva *et al.* 2021). Depending on the type of cells being targeted, different delivery methods may be required, such as viral vectors or nanoparticles (Xu *et al.* 2019; Rahimi *et al.* 2020). Additionally, it may be necessary to ensure that the CRISPR system is delivered to a sufficient number of cells to achieve a therapeutic effect.

Despite these challenges, the use of CRISPR-Cas9 for correcting risk-associated SNPs holds great promise for the development of personalized medicine (Chen *et al.* 2020; Karimian *et al.* 2020). By correcting disease-associated SNPs in individual patients, it may be possible to reduce the risk of developing certain diseases and improve overall health outcomes. However, much more research is needed to fully understand the potential benefits and risks of using CRISPR-Cas9 for human genome editing (Chen *et al.* 2019).

In this case we would like to change SNPs that could influence the gene product, thus, SNPs that appeared to be inside coding sequences. For example, the SNPs from the Table 2.

Acknowledgments

This work exists thanks to Mikhail Rayko and his genome information :)

The template of this pdf document was given by Natalia Khotkina.

Literature cited

- Achilli A, Rengo C, Magri C, Battaglia V, Olivieri A, Scozzari R, Torroni A. 2004. The molecular dissection of mtDNA haplogroup h confirms that the franco-cantabrian glacial refuge was a major source for the european gene pool. American journal of human genetics. 75:910–918.
- Ahsan T, Urmi NJ, Sajib AA. 2020. Heterogeneity in the distribution of 159 drug-response related snps in world populations and their genetic relatedness. PLoS One. 15:e0228000.
- Andersen JD, Johansen P, Harder S, Christoffersen SR, Delgado MC, Henriksen ST, Nielsen MM, Sørensen E, Ullum H, Hansen T *et al.* 2013. Genetic analyses of the human eye colours using a novel objective method for eye colour classification. Forensic Science International: Genetics. 7:508–515.
- Brookes AJ. 1999. The essence of snps. Gene. 234:177–186.
- Brotherton P, Haak W, Templeton J, Brandt G, Soubrier J, Jane Adler C, Richards SM, Sarkissian CD, Ganslmeier R, Friederich S *et al.* 2013. Neolithic mitochondrial haplogroup h genomes and the genetic origins of europeans. Nature communications. 4:1764.
- Cariaso M, Lennon G. 2012. Snpedia: a wiki supporting personal genome annotation, interpretation and analysis. Nucleic acids research. 40:D1308–D1312.
- Chen CL, Rodiger J, Chung V, Viswanatha R, Mohr SE, Hu Y, Perrimon N. 2020. Snp-crispr: a web tool for snp-specific genome editing. G3: Genes, Genomes, Genetics. 10:489–494.
- Chen M, Mao A, Xu M, Weng Q, Mao J, Ji J. 2019. Crispr-cas9 for cancer therapy: Opportunities and challenges. Cancer letters. 447:48–55.
- Corradini B, Sánchez-Diz P, Alu M, Estany-Gestal A, Carracedo A, Ferri G. 2011. Genetic variants related to nicotine dependence. Forensic Science International: Genetics Supplement Series. 3:e492–e493.
- Doudna JA, Charpentier E. 2014. The new frontier of genome engineering with crispr-cas9. Science. 346:1258096.
- Emahazion T, Feuk L, Jobs M, Sawyer SL, Fredman D, St Clair D, Prince JA, Brookes AJ. 2001. Snp association studies in alzheimer's disease highlight problems for complex disease analysis. TRENDS in Genetics. 17:407–413.
- Ennafaa H, Cabrera VM, Abu-Amero KK, González AM, Amor MB, Bouhaha R, Dzimir N, Elgaaied AB, Larruga JM. 2009. Mitochondrial dna haplogroup h structure in north africa. BMC genetics. 10:1–10.
- Glass Z, Lee M, Li Y, Xu Q. 2018. Engineering the delivery system for crispr-based genome editing. Trends in biotechnology. 36:173–185.
- Hart KL, Kimura SL, Mushailov V, Budimlija ZM, Prinz M, Wurmbach E. 2013. Improved eye-and skin-color prediction based on 8 snps. Croatian medical journal. 54:248–256.
- Heidema AG, Boer JM, Nagelkerke N, Mariman EC, van der A DL, Feskens EJ. 2006. The challenge for genetic epidemiologists: how to analyze large numbers of snps in relation to complex diseases. BMC genetics. 7:1–15.
- Hernández CL, Dugoujon JM, Novelletto A, Rodríguez JN, Cuesta P, Calderón R. 2017. The distribution of mitochondrial dna haplogroup h in southern iberia indicates ancient human genetic exchanges along the western edge of the mediterranean. BMC genetics. 18:1–14.
- Ingram VM. 1956. A specific chemical difference between the globins of normal human and sickle-cell anaemia haemoglobin. Nature. 178:792–794.
- Karimian A, Gorjizadeh N, Alemi F, Asemi Z, Azizian K,

- Soleimanpour J, Malakouti F, Targhazeh N, Majidinia M, Yousefi B. 2020. Crispr/cas9 novel therapeutic road for the treatment of neurodegenerative diseases. *Life Sciences.* 259:118165.
- Korytina GF, Aznabaeva YG, Nasibullin TR, Kochetova OV, Khusnutdinova NN, Viktorova TV, Zagidullin NS. 2022. Gene-gene and gene-environment interactions of the inflammatory gene variants in the development of chronic obstructive pulmonary disease. *Global Translational Medicine.* 1:1–14.
- Landrum MJ, Lee JM, Benson M, Brown G, Chao C, Chitipiralla S, Gu B, Hart J, Hoffman D, Hoover J et al. 2016. Clinvar: public archive of interpretations of clinically relevant variants. *Nucleic acids research.* 44:D862–D868.
- Lee MH, Shin JI, Yang JW, Lee KH, Hyeon CD, Beom HJ, Park Y. 2022. Genome editing using crispr-cas9 and autoimmune diseases: A comprehensive review. *International Journal of Molecular Sciences.* 23:1337.
- Manghwar H, Li B, Ding X, Hussain A, Lindsey K, Zhang X, Jin S. 2020. Crispr/cas systems in genome editing: methodologies and tools for sgRNA design, off-target evaluation, and strategies to mitigate off-target effects. *Advanced science.* 7:1902312.
- McLaren W, Gil L, Hunt SE, Riat HS, Ritchie GR, Thormann A, Flicek P, Cunningham F. 2016. The ensembl variant effect predictor. *Genome biology.* 17:1–14.
- Meyer OS, Lunn MM, Garcia SL, Kjaerbye AB, Morling N, Børsting C, Andersen JD. 2020. Association between brown eye colour in rs12913832: Cg individuals and snps in tyr, tyrp1, and slc24a4. *PloS one.* 15:e0239131.
- Min YL, Li H, Rodriguez-Caycedo C, Mireault AA, Huang J, Shelton JM, McAnally JR, Amoasii L, Mammen PP, Bassel-Duby R et al. 2019. Crispr-cas9 corrects duchenne muscular dystrophy exon 44 deletion mutations in mice and human cells. *Science advances.* 5:eaav4324.
- Morozova A, Zorkina Y, Pavlov K, Pavlova O, Storozeva Z, Zubkov E, Zakharova N, Karpenko O, Reznik A, Chekhonin V et al. 2019. Association of rs4680 comt, rs6280 drd3, and rs7322347 5ht2a with clinical features of youth-onset schizophrenia. *Frontiers in Psychiatry.* 10:830.
- Page AJ, Taylor B, Delaney AJ, Soares J, Seemann T, Keane JA, Harris SR. 2016. Snp-sites: rapid efficient extraction of snps from multi-fasta alignments. *biorxiv.* p. 038190.
- Pamjav H, Fehér T, Németh E, Pádár Z. 2012. Brief communication: New y-chromosome binary markers improve phylogenetic resolution within haplogroup r1a1. *Genome research.* 149:611–615.
- Pereira L, Richards M, Goios A, Alonso A, Albarrán C, García O, Behar D, Görgé M, Hatina J, Al-Gazali L et al. 2005. High-resolution mtDNA evidence for the late-glacial resettlement of europe from an iberian refugium. *Genome research.* 15:910–918.
- Perkel J. 2008. Snp genotyping: six technologies that keyed a revolution. *Nature Methods.* 5:447–453.
- Prokunina L, Alarcón-Riquelme ME. 2004. Regulatory snps in complex diseases: their identification and functional validation. *Expert reviews in molecular medicine.* 6:1–15.
- Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, Maller J, Sklar P, De Bakker PI, Daly MJ et al. 2007. Plink: a tool set for whole-genome association and population-based linkage analyses. *The American journal of human genetics.* 81:559–575.
- Rahimi H, Salehiabar M, Charmi J, Barsbay M, Ghaffarouli M, Razlighi MR, Davaran S, Khalilov R, Sugiyama M, Nosrati H et al. 2020. Harnessing nanoparticles for the efficient delivery of the crispr/cas9 system. *Nano Today.* 34:100895.
- Rapley R, Harbron S et al. 2004. *Molecular analysis and genome discovery.* Wiley Online Library.
- Roostalu U, Kutuev I, Loogväli E, Metspalu E, Tambets K, Reidla M, Khusnutdinova E, Usanga E, Kivisild T, Villems R. 2007. Origin and expansion of haplogroup h, the dominant human mitochondrial dna lineage in west eurasia: the near eastern and caucasian perspective. *Molecular biology and evolution.* 24:436–448.
- Savic N, Ringnalda FC, Lindsay H, Berk C, Bargsten K, Li Y, Neri D, Robinson MD, Ciaudo C, Hall J et al. 2018. Covalent linkage of the dna repair template to the crispr-cas9 nuclease enhances homology-directed repair. *Elife.* 7:e33761.
- Sturm RA, Duffy DL, Zhao ZZ, Leite FP, Stark MS, Hayward NK, Martin NG, Montgomery GW. 2008. A single snp in an evolutionary conserved region within intron 86 of the herc2 gene determines human blue-brown eye color. *The American Journal of Human Genetics.* 82:424–431.
- Sturm RA, Frudakis TN. 2004. Eye colour: portals into pigmentation genes and ancestry. *TRENDS in Genetics.* 20:327–332.
- Sulem P, Gudbjartsson DF, Stacey SN, Helgason A, Rafnar T, Magnusson KP, Manolescu A, Karason A, Palsson A, Thorleifsson G et al. 2007. Genetic determinants of hair, eye and skin pigmentation in europeans. *Nature genetics.* 39:1443–1452.
- Thorvaldsdóttir H, Robinson JT, Mesirov JP. 2013. Integrative genomics viewer (igv): high-performance genomics data visualization and exploration. *Briefings in bioinformatics.* 14:178–192.
- Tyumentseva MA, Tyumentsev AI, Akimkin VG. 2021. Protocol for assessment of the efficiency of crispr/cas rnp delivery to different types of target cells. *Plos one.* 16:e0259812.
- Voicey J, Morris CP. 2008. Snp technologies for drug discovery: a current review. *Current Drug Discovery Technologies.* 5:230–235.
- Wang Y, Xu S, Liu Z, Lai C, Xie Z, Zhao C, Wei Y, Bi JZ. 2013. Meta-analysis on the association between the tf gene rs1049296 and ad. *Canadian journal of neurological sciences.* 40:691–697.
- Ward LD, Kellis M. 2012. Interpreting noncoding genetic variation in complex traits and human disease. *Nature biotechnology.* 30:1095–1106.
- Wray NR, Yang J, Hayes BJ, Price AL, Goddard ME, Visscher PM. 2013. Pitfalls of predicting complex traits from snps. *Nature Reviews Genetics.* 14:507–515.
- Xu CL, Ruan MZ, Mahajan VB, Tsang SH. 2019. Viral delivery systems for crispr. *Viruses.* 11:28.
- Xue LL, Wang F, Xiong LL, Du RL, Zhou HL, Zou Y, Wu MX, Yang MA, Dai J, He MX et al. 2020. A single-nucleotide polymorphism induced alternative splicing in tacr3 involves in hypoxic-ischemic brain damage. *Brain Research Bulletin.* 154:106–115.
- Yukseloglu EH, Ortug A, Rayimoglu G, Yonar FC, Erkan I, Kara U, Islek DS, Kolusayın Ozar MO, Dastan K, Karatas O. 2019. Association of 10 single nucleotide polymorphism loci with nicotine addiction in the anatolian population? *Biotechnology & Biotechnological Equipment.* 33:1011–1017.
- Zhang XH, Tee LY, Wang XG, Huang QS, Yang SH. 2015. Off-target effects in crispr/cas9-mediated genome engineering. *Molecular Therapy-Nucleic Acids.* 4:e264.
- Zhou L, Zhang G, Zhou X, Li J. 2015. The association between the snp rs763110 and the risk of gynecological cancer: a meta-analysis. *Biomedicine & Pharmacotherapy.* 69:208–213.

Zupan A, Vrabec K, Glavač D. 2013. The paternal perspective of the slovenian population and its relationship with other populations. Annals of human biology. 40:515–526.

Supplementary

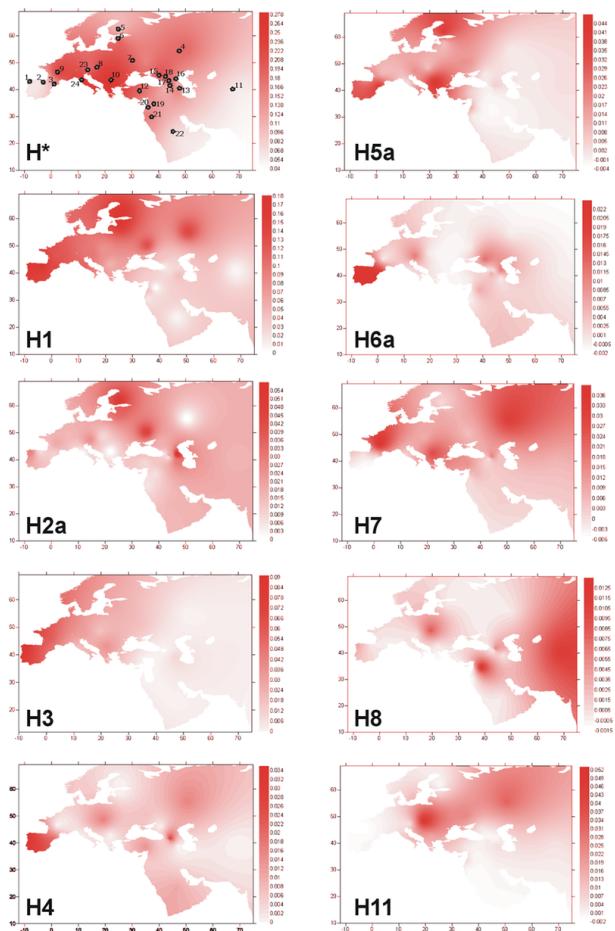


Figure 2 Projected spatial frequency distributions for haplogroups H*, H1, H2a, H3, H4, H5a, H6a, H7, H8 and H11

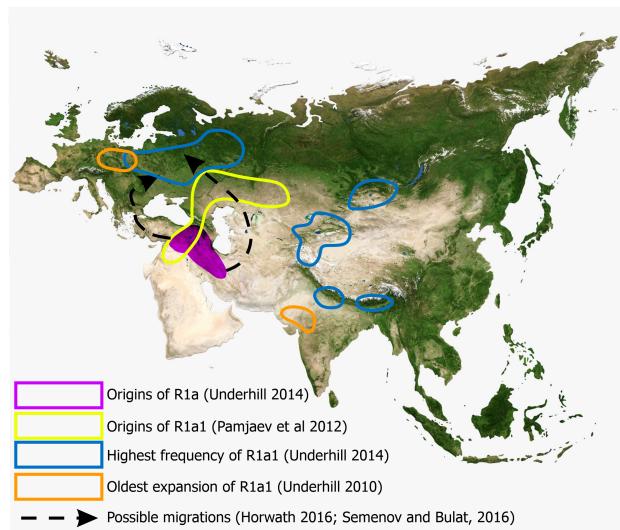


Figure 3 R1a origins (Underhill 2009; R1a1a origins (Pamjav et al. 2012); possible migration R1a to Baltic coast; and R1a1a oldest expansion and highest frequency (Underhill et al. 2014)

CHROMOSOME	POSITION	ID	RISK
11	27679916	rs6265	Memory impairment, susceptibility to
1	161010762	rs2073658	Hyperlipidemia, familial combined, susceptibility to
1	161479745	i6058143	*
1	161479745	rs1801274	Malaria, severe, susceptibility to
1	172627498	rs763110	LUNG CANCER, SUSCEPTIBILITY TO
1	196716319	rs460897	Hemolytic uremic syndrome, atypical, susceptibility to
1	201081943	rs2281845	Thyrotoxic periodic paralysis, susceptibility to
12	121416650	rs1169288	SERUM HDL CHOLESTEROL LEVEL, MODIFIER OF
1	230845794	rs699	renal failure
1	53712727	rs5174	Myocardial infarction 1
16	27374400	rs1801275	Atopy, susceptibility to
16	53720436	rs61747071	Retinitis pigmentosa in ciliopathies, modifier of
17	32579788	rs1024611	Coronary artery disease, modifier of
17	48437456	rs6504649	Pseudoxanthoma elasticum, modifier of severity of
17	5485367	rs12150220	Vitiligo-associated multiple autoimmune disease susceptibility 1
2	138759649	i3000469	*
2	204732714	rs231775	Diabetes mellitus type 2, susceptibility to
2	234183368	i6007787	*
2	234183368	rs2241880	Inflammatory bowel disease 10, susceptibility to
3	113890815	rs6280	Schizophrenia, susceptibility to
3	133494354	rs1049296	Alzheimer disease, susceptibility to
3	148459988	rs5186	Hypertension, essential, susceptibility to
3	185511687	rs4402960	Diabetes mellitus type 2, susceptibility to
4	2906707	rs4961	Hypertension, salt-sensitive essential, susceptibility to
5	7870973	rs1801394	Neural tube defects, folate-sensitive, susceptibility to
6	160113872	rs4880	superoxide dismutase 2 polymorphism, complications of diabetes
6	31540141	rs2239704	Leprosy, early-onset, susceptibility to
6	31540313	rs909253	Psoriatic arthritis, susceptibility to, Myocardial infarction
7	128578301	rs2004640	Systemic lupus erythematosus
7	146489606	rs7794745	Autism, susceptibility to
7	93055753	rs1801197	Bone mineral density quantitative trait locus 15
8	118184783	rs13266634	Diabetes mellitus type 2, susceptibility to
8	133909974	i6059141	*
9	101304348	rs2184026	Tobacco addiction, susceptibility to
9	132580901	rs1801968	Dystonia 1, torsion, modifier of
9	22096055	rs10757274	Three Vessel Coronary Disease
9	22098574	rs4977574	Three Vessel Coronary Disease

Table 3 Risk-associated SNPs