Supplementary Information SI10

Retrieval of Modern Human and Ancient Hominin *AHR* mRNA Sequences

The sequence of the modern human aryl hydrocarbon receptor (*AHR*) reference gene transcript AHR-201 (ENST00000242057.8) was downloaded from the Ensembl website, version GRCh38/hg38, Release 95, January 2019:

http://jan2019.archive.ensembl.org/Homo_sapiens/Transcript/Idhistory?db=core;g=ENSG00000106546;r=7:17298622-17346150;t=ENST00000242057

The Altai- (Prüfer et al. 2014) and Vindija-Neanderthal (Prufer et al. 2017), and Denisovan (Meyer et al. 2012) *AHR* mRNA sequence were retrieved from the respective (chromosome 7) VCF file available online:

Altai: http://cdna.eva.mpg.de/neandertal/altai/AltaiNeandertal/VCF/

Vindija: http://cdna.eva.mpg.de/neandertal/Vindija/VCF/Vindija33.19/

Denisovan: https://bioinf.eva.mpg.de/jbrowse/data/ancient/

Using the Ensemble Data Slicer web tool (http://grch37.ensembl.org/Homo_sapiens/Tools/DataSlicer) the data subset for the *AHR* genomic region was extracted from these VCF files and loaded into Excel. Using the filtering functions of Excel, the positions where the VCF data (based on genome assembly GRCh37/hg19 as a reference) indicate that the ancient hominin sequences differ from the human *AHR* reference exon sequences were filtered out (Table SI10.1). Supplementary data SI1 shows an alignment of all *AHR* mRNA sequences studied here and by Hubbard et al. (2016).

The date accessed of all websites mentioned is April 21, 2020.

Table SI10.1. Differences observed between ancient hominin and modern human reference *AHR* mRNA sequences

GRCh38/hg38 Chromosome 7 Coordinate[1)]	GRCh37/hg19 Chromosome 7 Coordinate	dbSNP ID[2)]	Modern Human Reference (GRCh38/hg38)	Neanderthal		Denisovan	Functional Region	Evolutionary Details[3)]
				Altai	Vindija			
17298694	17338318	rs1382049002	C	C	T/C	C	5'-UTR	C = ancestral; chimpanzee/gorilla = C; in all primates, except bushbaby (= T) T = specific for Vindija-Neanderthal; probably newly derived
17298806	17338430	rs7796976	A	G	G	G	5'-UTR	A = derived; unique to modern humans G = ancestral; conserved in all other sequenced primates and far beyond
17335768	17375392	-	T	C	C	C	Coding variant Val381Ala	T = derived (= Val) and fixed in modern humans C = ancestral (= Ala); highly conserved, including all sequenced primates
17339486	17379110	rs2066853	G	A	A	A	Coding variant Arg554Lys	G = derived (= Arg); unique to modern humans A = ancestral (= Lys); conserved in all other sequenced primates
17343303	17382927	-	G	A	A	A	3'-UTR	G = derived; unique to modern humans A = ancestral; conserved in all other sequenced primates
17345312	17384936	rs77257221	CA	C-/CA	C-/CA	CA	3'-UTR	CA = ancestral? (gorilla = NA); in modern humans; C- = derived?; in chimpanzee; Altai-Neanderthal = C-/CA heterozygote Vindija-Neanderthal = C-/CA heterozygote Denisovan = CA but possibly C-/CA heterozygote since also 7 [C-] reads out of 41

1) GRCh37/hg19 coordinates were converted into GRCh38/hg38 coordinates using the UCSC Genome Browser LiftOver tool available from http://genome-euro.ucsc.edu/cgi-bin/hgLiftOver.
2) Based on dbSNP, build 153 (see: https://www.ncbi.nlm.nih.gov/SNP/index.html).
3) Data from the "Multiz Alignment of 100 Vertebrate Species" in the human UCSC Genome browser, assembly GRCh38/hg38.

References

Hubbard TD, Murray IA, Bisson WH, Sullivan AP, Sebastian A, Perry GH, Jablonski NG, Perdew GH. 2016. Divergent Ah Receptor Ligand Selectivity during Hominin Evolution. *Mol Biol Evol* 33(10):2648-58.

Meyer M, Kircher M, Gansauge MT, Li H, Racimo F, Mallick S, Schraiber JG, Jay F, Prufer K, de Filippo C et al. 2012. A high-coverage genome sequence from an archaic Denisovan individual. *Science* 338(6104):222-226.

Prufer K, de Filippo C, Grote S, Mafessoni F, Korlevic P, Hajdinjak M, Vernot B, Skov L, Hsieh P, Peyregne S et al. 2017. A high-coverage Neandertal genome from Vindija Cave in Croatia. *Science* 358(6363):655-658.

Prüfer K, Racimo F, Patterson N, Jay F, Sankararaman S, Sawyer S, Heinze A, Renaud G, Sudmant PH, de Filippo C et al. 2014. The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* 505(7481):43-49.