

RESEARCH ARTICLE

A Draft Sequence of the Neandertal Genome

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Neandertals

First appear in the European fossil record about 400,000 years ago

Lived in Europe and Western Asia as far east as Southern Siberia and as far south as the Middle East

came into contact with modern humans from at least 80,000 years ago

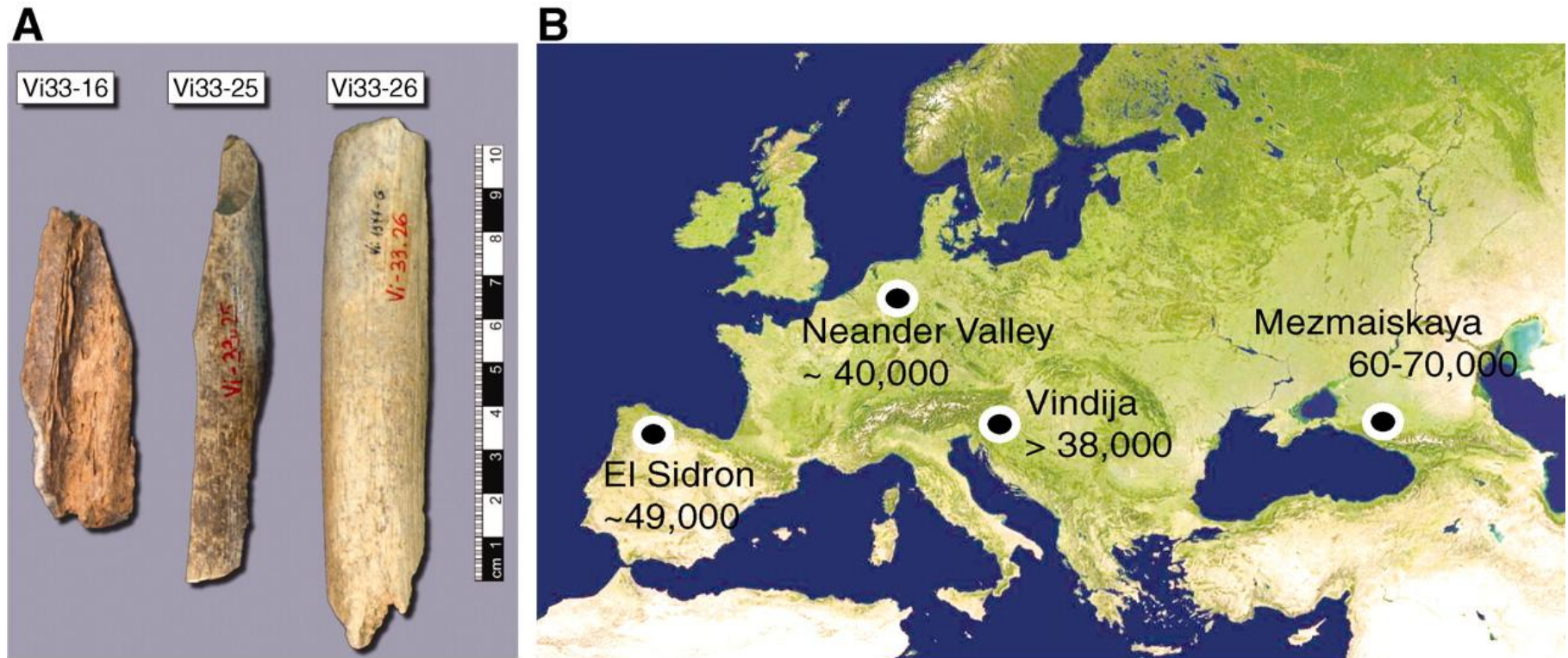
Neandertals

Neanderthal cranial capacity is thought to have been as large as babies or larger as adults than *Homo sapiens*

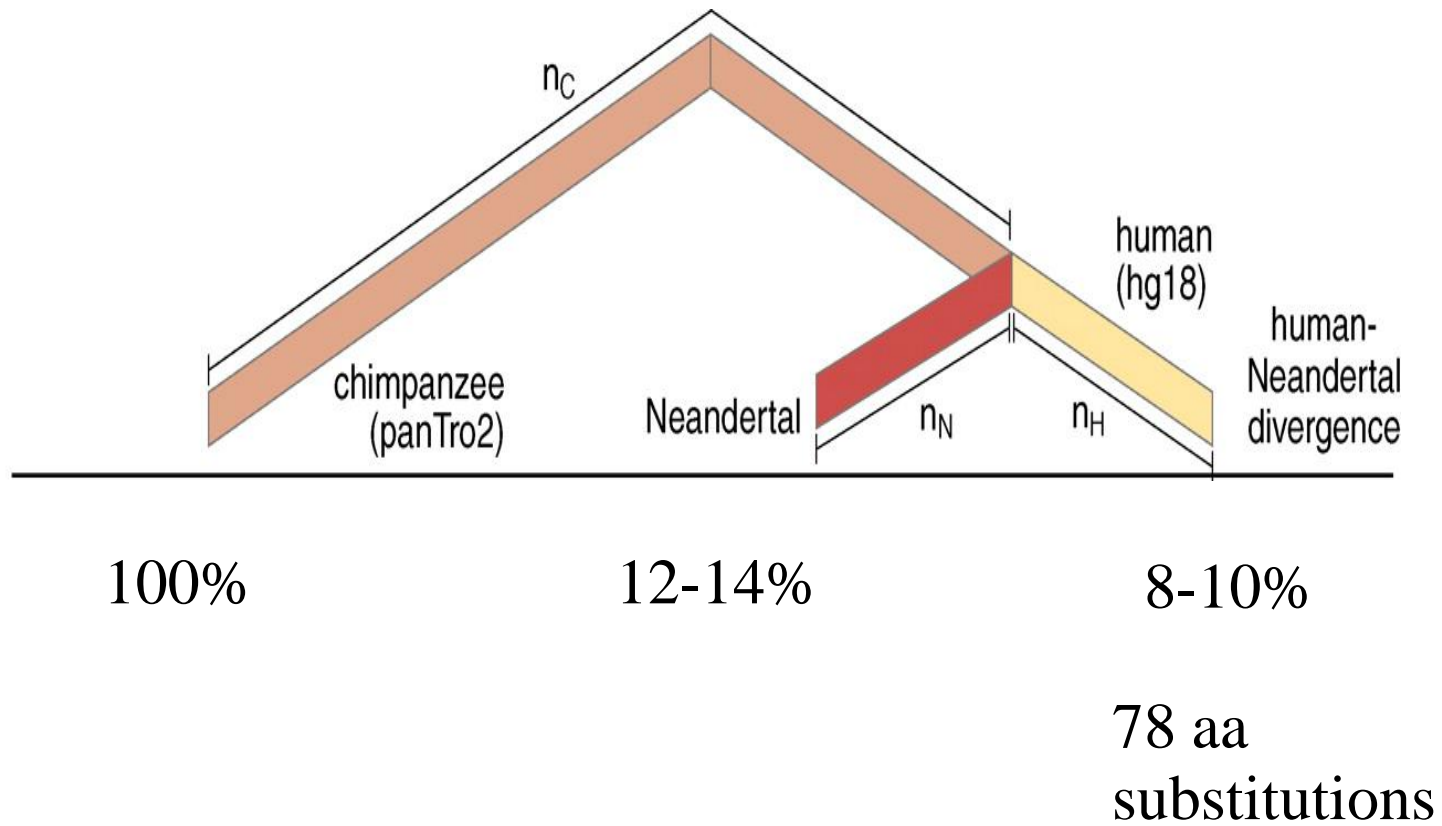
Neandertals were heavily built with robust bone structure.

They were much stronger than *Homo sapiens*, having particularly strong arms and hands

Samples and sites from which DNA was retrieved.



R E Green et al. Science 2010;328:710-722



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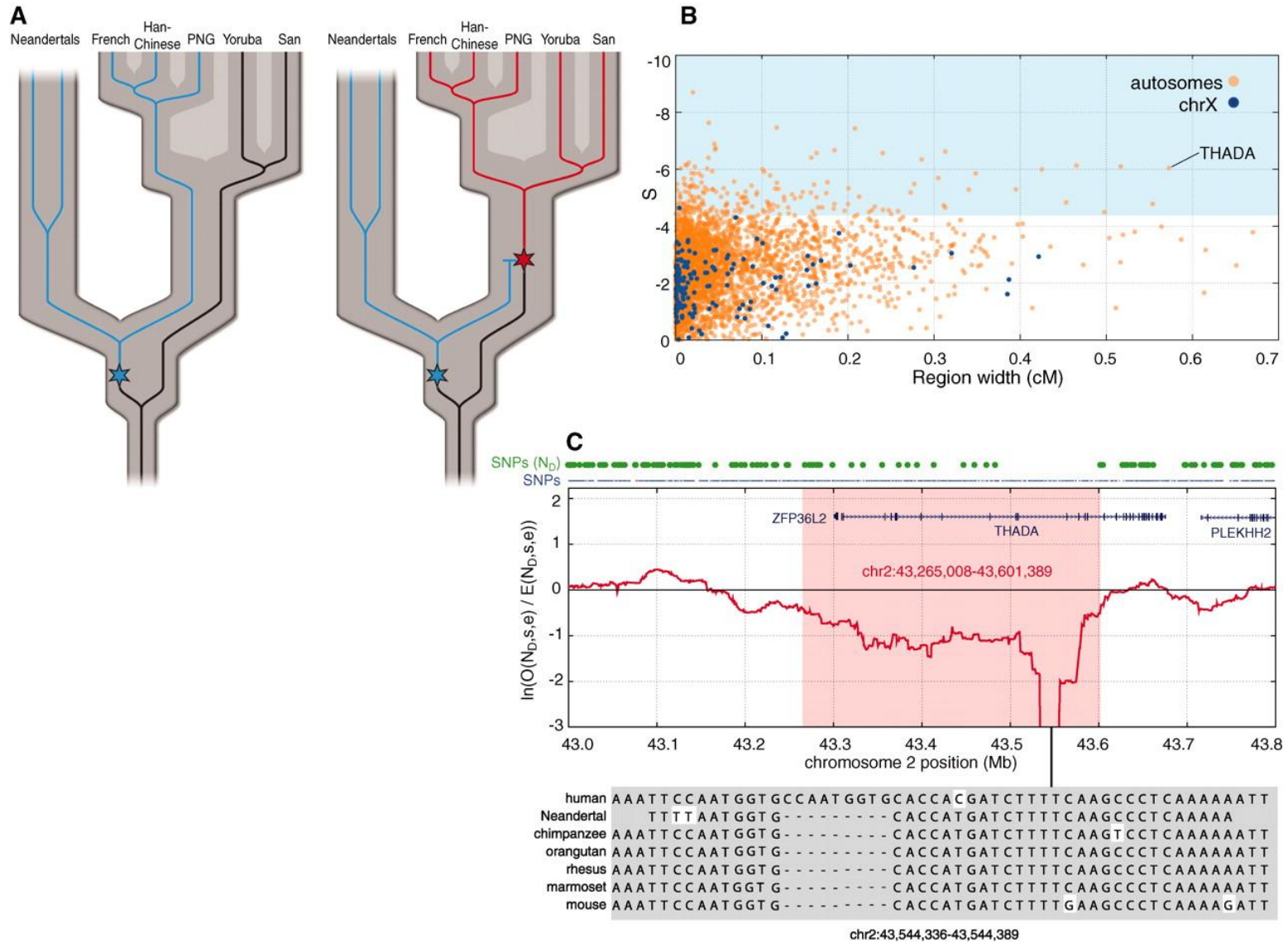


Table 2. Amino acid changes that are fixed in present-day humans but ancestral in Neandertals. The table is sorted by Grantham scores (GS). Based on the classification proposed by Li *et al.* in (87), 5 amino acid substitutions are radical (>150), 7 moderately radical (101 to 150), 33 moderately conservative (51 to

100) and 32 conservative (1 to 50). One substitution creates a stop codon. Genes showing multiple substitutions have bold SwissProt identifiers. (Table S15 shows the human and chimpanzee genome coordinates, additional database identifiers, and the respective bases.) Genes with two fixed amino acids are indicated in bold.

ID	Pos	AA	GS	Description/function
RPTN	785	*/R	–	Multifunctional epidermal matrix protein
GREB1	1164	R/C	180	Response gene in estrogen receptor–regulated pathway
OR1K1	267	R/C	180	Olfactory receptor, family 1, subfamily K, member 1
SPAG17	431	Y/D	160	Involved in structural integrity of sperm central apparatus axoneme
NLRX1	330	Y/D	160	Modulator of innate immune response
NSUN3	78	S/F	155	Protein with potential SAM-dependent methyl-transferase activity
RGS16	197	D/A	126	Retinally abundant regulator of G-protein signaling
BOD1L	2684	G/R	125	Biorientation of chromosomes in cell division 1-like
CF170	505	S/C	112	<i>Uncharacterized protein: C6orf170</i>
STEAP1	336	C/S	112	Metalloreductase, six transmembrane epithelial antigen of prostate 1
F16A2	630	R/S	110	<i>Uncharacterized protein: family with sequence similarity 160, member A2</i>
LTK	569	R/S	110	Leukocyte receptor tyrosine kinase
BEND2	261	V/G	109	<i>Uncharacterized protein: BEN domain-containing protein 2</i>
O52W1	51	P/L	98	Olfactory receptor, family 52, subfamily W, member 1
CAN15	427	L/P	98	Small optic lobes homolog, linked to visual system development
SCAP	140	I/T	89	Escort protein required for cholesterol as well as lipid homeostasis
TTF1	474	I/T	89	RNA polymerase I termination factor
OR5K4	175	H/D	81	Olfactory receptor, family 5, subfamily K, member 4
SCML1	202	T/M	81	Putative polycomb group (PcG) protein

Fig. 4 Selective sweep screen.



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Table 3. Top 20 candidate selective sweep regions.

Region (hg18)	S	Width (cM)	
chr2:43265008-43601389	-6.04	0.5726	<i>ZFP36L2;TH</i>
chr11:95533088-95867597	-4.78	0.5538	<i>TRKL;CCDC8</i>
chr10:6234331			Changes in THADA (T2D gene) may have affected
chr21:3758012			
chr10:8333660			aspects of energy metabolism in early modern hum
chr14:100248111-100411124	-4.84	0.4555	
chr3:157244328-157597592	-6	0.425	<i>KCNAB1</i>
chr11:30601000-30992792	-5.29	0.3951	
chr2:176635412-176978762	-5.86	0.3481	<i>HOXD11;HO</i>
			<i>HOXD4;HO</i>
chr11:71572763-71914957	-5.28	0.3402	<i>CLPB;FOLR1</i>
chr7:41537742-41838097	-6.62	0.3129	<i>INHBA</i>
chr10:60015775-60262822	-4.66	0.3129	<i>BICC1</i>
chr6:45440283-45705503	-4.74	0.3112	<i>RUNX2;SUP</i>
chr1:149553200-149878507	-5.69	0.3047	<i>SELENBP1;P</i>
			<i>PSMB4</i>
chr7:121763417-122282663	-6.35	0.2855	<i>RNF148;RN</i>
chr7:93597127-93823574	-5.49	0.2769	
chr16:62369107-62675247	-5.18	0.2728	
chr14:48931401-49095338	-4.53	0.2582	
chr6:90762790-90903925	-4.43	0.2502	<i>BACH2</i>
chr10:8650088-8786054	-4.56	0.2475	

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chr10:62343313-62655667	-6.1	0.5167	<i>RHOBTB1</i>
chr21:37580123-37789088	-4.5	0.4977	<i>DYRK1A</i>
chr10:83336607-83714543	-6.13	0.4654	<i>NRG3</i>
chr14:10024817-10024817			
chr3:157244328-157244328			
chr11:30601000-30601000			
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DYRK1A is thought to underlie some of the cognitive impairment associated with having three copies of 21

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chr10:83336607-83714543	-6.13	0.4654	<i>NRG3</i>
chr14:100248177-100447777	-6.1	0.4555	<i>USP37;USP37</i>
chr3:157244321-157443821	-6.1	0.4555	<i>USP37;USP37</i>
chr11:30601000-30992792	-5.29	0.3951	
chr2:176635412-176978762	-5.86	0.3481	<i>HOXD11;HOXD11</i> <i>HOXD4;HOXD4</i>
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NRG3 is associated with schizophrenia

Supplementary Online Materials 17

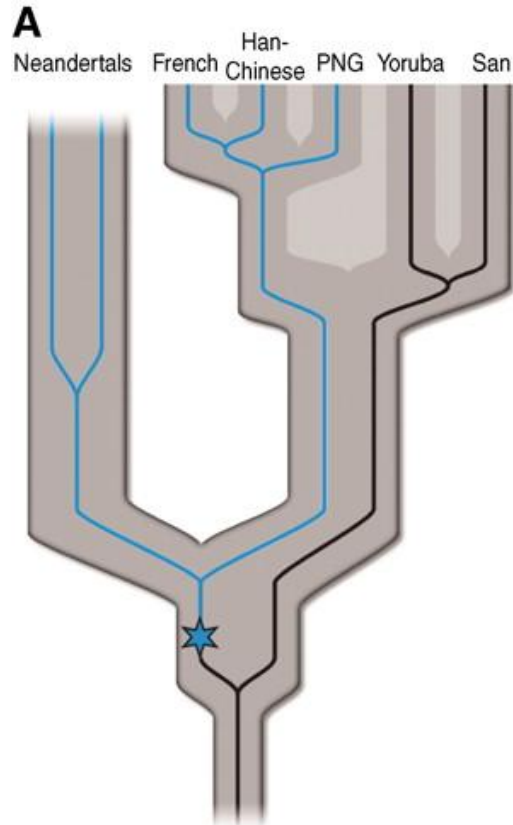
Non-African haplotypes match Neandertal at an unusual rate

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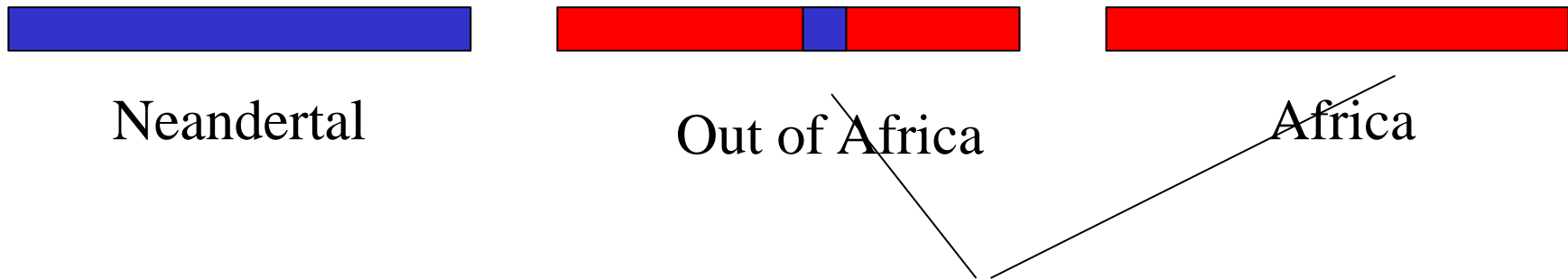
Scenario for Neandertal gene flow into OOA genomes.



The Neandertals are equally close to Europeans and East Asians. However, the Neandertals are significantly closer to non-Africans than to Africans

R E Green et al. *Science* 2010;328:710-722





Step 1: candidate region

In a 50 kb region, search for regions in which OOA is very different from Africa

Step 2: compare to Neandertal

Look for cases in which there is high match to the Neandertal sequence across many SNPs. The OOA/Neandertal allele should be derived, not ancestral

Neandertal Alleles

Use at your own risk.

[Compute my Neandertal Index](#)

Neandertal

Are you a neandertal?

You have **12** out of 82 Neandertal alleles. ————— Running total

dbSNP	Derived Allele	Ancestral Allele	Out of Africa Allele	Genotype	Count
10800485	C	T	C	CT	1
6670818	G	A	G	AA	0
10915846	A	G	A	GG	0
16845098	C	T	C	CT	1
17503834	C	T	C	TT	0

Same as Chimp

Same as Neandertal allele

Your genotype

Neandertal



White Paper 23-05

Neanderthal Ancestry Estimator

Authors:

Eric Y. Durand edurand@23andme.com

Created: 5 December 2011

Last Edited: 8 January 2012

Summary:

Neanderthal ancestry estimator is a 23andMe feature that enables customers to find out how much of their genome is of Neanderthal ancestry. This document is a technical description of the feature.

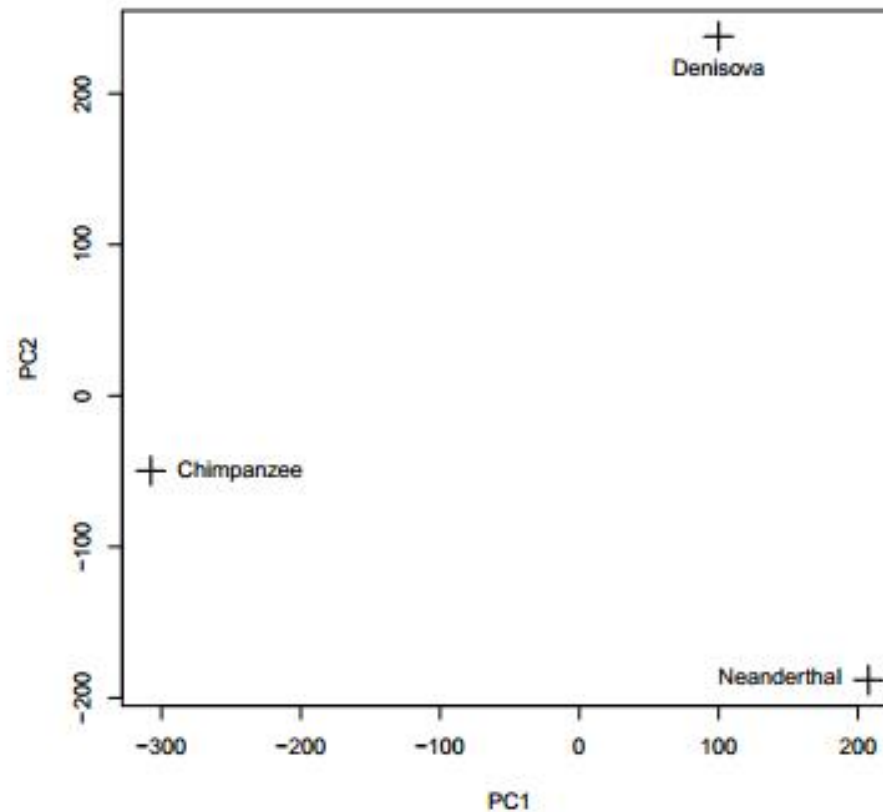


Figure 1: PCA on the Neanderthal, Denisovan and Chimpanzee genomes. We used the subset of the genomes that was defined on the 23andMe genotyping platform. PC1 differentiates archaic humans from the Chimpanzee while PC2 separates Neanderthal from Denisova.

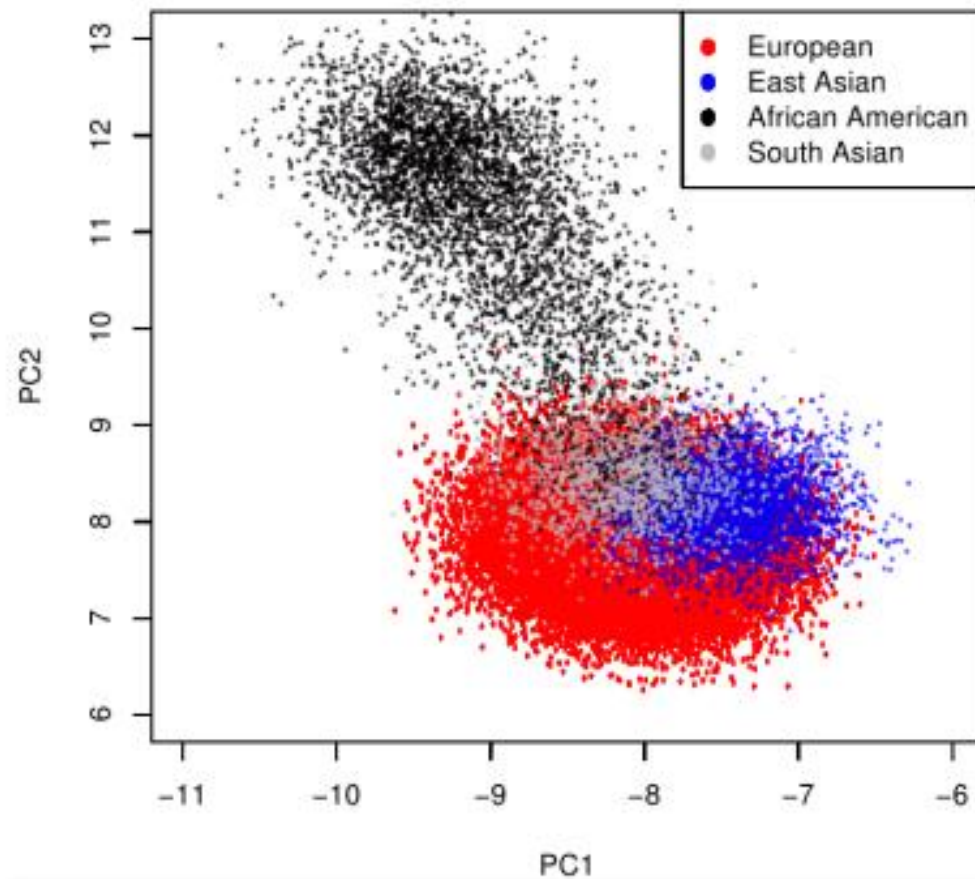


Figure 2: Projection of customer genotypes onto PC1 and PC2. Customers of European, East-Asian and South-Asian ancestry are shifted towards Neanderthal compared to African-Americans.

Got Neanderthal DNA?

An estimated **2.5%** of your DNA is from Neanderthals.

stuart kim (You)



2.5%

35th percentile

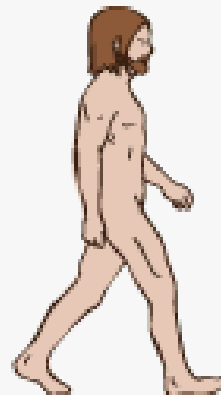
Average Eastern
Asian user



2.6%

MODERN HUMANS

- Higher brow
- Narrower shoulders
- Slightly taller



NEANDERTHALS

- Heavy eyebrow ridge
- Long, low, bigger skull
- Prominent nose with developed nasal chambers for cold-air protection

