Supplementary Table 1. MAE and BAE calls for genes used in the study. *In a separate file.*

Supplementary Table 2. Genetic diversity and functional GO categories.
Nucleotide diversity of MAE and BAE genes annotated with specific functional categories (Gene Ontology, GO) that have been shown to be over- or under-represented among MAE genes [5]. For a given GO term, the number and proportion of associated MAE and BAE genes, $\boldsymbol{\pi}$ at 4-fold degenerate sites (4fd), $\boldsymbol{\pi}$ at non-CpG-prone 4-fold degenerate sites (Non-CpG), fold difference in $\boldsymbol{\pi}$ of each category between MAE and BAE, and bootstrap-based p-values (N=10,000) for difference in $\boldsymbol{\pi}$ between MAE and BAE genes are shown. Non-CpG $\boldsymbol{\pi}$ was adjusted for 1.06-fold non-CpG mutation rate difference. Note that some genes are annotated with multiple GO terms. BP: Biological Process, CC: Cellular Component.

GO term (GO accession number)	Number and proportion of overall genes		Nucleotide diversity (π in 4fd)		Nucleotide diversity (π in non-CpG 4fd)		Fold difference in π (MAE/BAE)		P-value	
	MAE (N=4,227)	BAE (N=6,006)	MAE	BAE	MAE	BAE	4fd	Non-CpG	4fd	Non-CpG
multicellular organismal process (GO:0032501, BP)	1,560 (36.9%)	1,452 (24.2%)	0.0011	0.0007	0.0006	0.0005	1.44	1.24	$< 1x10^{-4}$	0.0105
plasma membrane (GO:0005886, CC)	1,123 (26.6%)	833 (13.9%)	0.0011	0.0007	0.0006	0.0005	1.63	1.37	$< 1x10^{-4}$	0.0094
extracellular region (GO:0005576, CC)	1,119 (26.5%)	1,116 (18.6%)	0.0012	0.0007	0.0006	0.0005	1.60	1.26	$< 1x10^{-4}$	0.0314
anatomical structure development (GO:0048856, BP)	1,237 (29.3%)	1,160 (19.3%)	0.0010	0.0007	0.0006	0.0005	1.37	1.16	$< 1x10^{-4}$	0.0695
organelle (GO:0043226, CC)	2,789 (66.0%)	4,807 (80.0%)	0.0011	0.0007	0.0006	0.0005	1.46	1.22	$< 1x10^{-4}$	0.0015
intracellular (GO:0005622, CC)	2,949 (69.8%)	5,081 (84.6%)	0.0011	0.0007	0.0006	0.0005	1.48	1.26	$< 1x10^{-4}$	$< 1x10^{-4}$
None of the above	606 (14.3%)	684 (11.4%)	0.0010	0.0007	0.0007	0.0005	1.31	1.33	$1x10^{-4}$	0.0234

Supplementary Table 3. Analysis of d_N/d_S in MAE and BAE genes.
The number of nonsynonymous substitutions per non-synonymous site (d_N), and the number of synonymous substitutions per synonymous site (d_S) [8] were aggregated across all genes in each set. 95% Confidence intervals were computed by bootstrapping (1000 replicates).

	Number of genes	dN	dS	Num Syn sites	Num NonSyn sites	dN/dS	CI lo	CI hi
MAE	2512	4049	7824	688713.1	1716705	0.21	0.20	0.22
BAE	4114	6166	11548	1268083	3231334	0.21	0.20	0.22

Supplementary Table 4. Analysis of selective constraint in MAE and BAE genes.

Z-scores are binned by constraint [7]. P-values are given by two-sided Fisher's exact test. See also Supplementary Fig. 10.

	Z score bin	Number of genes	% MAE	% BAE	P-value
less than average constraint	Z < -1	999	4.27	3.91	0.44
	-1 < Z < -0.5	1073	5.68	4.60	0.03
	-0.5 < Z < -0.01	1642	9.89	8.26	0.02
average constraint	-0.01 < Z < 0.01	88	0.33	0.42	0.60
greater than average constraint	0.01< Z < 1	4541	29.23	29.90	0.63
	1< Z < 2	3924	26.18	27.28	0.40
	2< Z < 3.09	2553	17.40	18.63	0.22
highly constrained	Z > 3.09	1003	7.01	6.99	1.00

Supplementary Table 5. D*e novo* mutation rate in MAE and BAE genes.
In a separate file.

Supplementary Table 6. Nucleotide diversity in recombination rate bins.
In a separate file.

Supplementary Table 7. Nucleotide diversity in recombination rate bins with strict read depth mask and divergence-based correction for CpG mutation bias.
In a separate file.

Supplementary Table 8. Difference in NC values between MAE and BAE genes across recombination rates. Recombination rates bins were created using the deCODE sex-averaged genetic map (10kb resolution). Recombination rate (***r***) for different bins is reported for MAE and BAE as mean (SD). A P-value for each derived allele frequency bin (DAF) was computed using Mann-Whitney rank-sum test. P-values are one-sided, with alternative hypotheses following younger age for BAE genes. Combined p-values were computed by meta-analysis using Stouffer's Z-score method, weighted by sample size.

	Number of tested SNPs		**Recombination rate, mean(sd)**		**P-value**
	MAE	**BAE**	**MAE**	**BAE**	
r = 0	2556	5142	0	0	1.05×10^{-7}
0<r< 0.5	1621	2399	0.17(0.16)	0.15(0.15)	7.04×10^{-7}
0.5<r<1	851	741	0.74(0.15)	0.71(0.15)	0.04
1<r<1.5	530	391	1.24(0.15)	1.22(0.15)	0.05
1.5<r<2	322	217	1.75(0.14)	1.72(0.14)	0.89

Supplementary Table 9. Multivariate regression model for Time to Most Recent Common Ancestor (T_{MRCA}). The T_{MRCA} estimates were log-transformed for the regression analysis. Binary variable used to describe expression status (MAE=1, BAE=0; See Methods). See Methods for description of other variables.

Variable	Coefficient	Std. Error	P-value
Intercept	10.75	0.011	**$< 2 \times 10^{-16}$**
MAE/BAE	0.054	0.010	**7.47×10^{-08}**
Recombination rate	0.077	0.0059	**$< 2 \times 10^{-16}$**
Gene expression	0.000054	0.000029	6.03×10^{-02}
Expression breadth	0.041	0.016	**1.14×10^{-02}**
Gene length	-0.000002	0.000003	5.80×10^{-01}
Selective constraint	-0.039	0.0037	**$< 2 \times 10^{-16}$**

Supplementary Table 10. Genes in the study for which balancing selection has been reported. *In a separate file.*

Supplementary Table 11. Analysis of human-chimpanzee trans-species polymorphisms. *In a separate file.*

Supplementary Table 12. Analysis of derived alleles predating the human-Neanderthal split. *In a separate file.*

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