

Supplementary tables

Supplementary table S1. Positions at which a substitution has occurred on the human lineage where at least one ancestral allele is present in the archaic humans.

hg18 coordinate	hg18 base	outgroup base	archaic human state	published Neandertal consensus	captured Neandertal bases	Denisovan bases	HGDP individuals	HGDP derived base fraction	dbSNP132 chromosomes	dbSNP132 derived base fraction	dbSNP132 ID	potential C->T
113,814,079	C	T	anc	X	TTTT	TTTTT	50	0.06	17	0.06	rs2396729	No
113,818,561	C	T	anc	T	TTTTT	TTT	50	0.03	434	0.03	rs7807690	No
113,820,420	T	C	anc	C	CCCCC	CCC	50	0.03	435	0.04	rs2396723	No
113,821,349	C	T	anc/der	X	CCCCCCCCCCCCCTC	CCCC	50	1.00	-	-	-	Yes
113,830,397	G	A	anc	X	X	A	49	0.04	428	0.03	rs6969741	Yes
113,832,887	G	A	anc	A	AA	AAA	50	1.00	168	0.93	rs75755264	No
113,834,376	A	T	anc	X	TTTTTT	TTT	50	0.42	429	0.47	rs7795397	No
113,834,774	A	G	anc	X	G	GG	50	0.03	414	0.05	rs6966777	No
113,834,778	G	C	anc	X	C	C	50	0.53	-	-	-	No
113,859,679	A	G	anc	G	GGGGG	G	50	0.18	2520	0.12	rs10255943	No
113,860,981	C	T	anc	X	T	TTTT	44	0.98	548	0.97	rs17137020	No
113,861,403	T	C	anc/der	X	CC	T	49	1.00	118	0.97	rs115887906	No
113,865,140	C	T	anc/der	C	CCCCCCCCCCCCCT	CC	50	0.99	-	-	-	Yes
113,866,166	A	T	anc	T	TT	TTTT	50	0.97	2	0.50	rs73434173	No
113,870,786	C	G	anc	G	GG	GGGG	45	0.59	1988	0.39	rs10228494	No
113,870,825	G	A	anc/der	A	G	X	50	1.00	-	-	-	Yes
113,874,900	G	A	anc/der	G	GGGGGGGGGGG	AG	50	1.00	118	0.98	rs116785628	Yes
113,875,021	G	C	anc	C	CC	C	50	1.00	414	0.97	rs7788102	No
113,877,694	T	C	anc	C	CCCCC	CC	49	1.00	558	0.98	rs17137029	No
113,879,080	C	A	anc	X	AAA	A	50	0.54	1984	0.39	rs10262103	No
113,880,427	G	A	anc	A	AA	X	50	0.99	2	0.50	rs73434180	No
113,880,438	G	A	anc	A	AAA	A	50	1.00	118	0.90	rs115295546	No
113,883,593	G	A	anc	A	AAAA	AA	50	1.00	1760	0.96	rs17137034	No
113,890,947	A	G	anc	X	GG	GG	48	0.99	144	0.98	rs17137041	No
113,892,689	T	A	anc	X	AAAA	A	47	0.99	663	0.96	rs6466487	No
113,894,830	C	G	anc	X	G	G	50	0.17	14	0.21	rs10225528	No
113,894,893	C	T	anc/der	X	CCCCCCCCCT	C	50	1.00	-	-	-	Yes
113,895,542	T	G	anc	G	GGG	GGGG	50	0.98	1793	0.95	rs17137045	No
113,897,804	C	T	anc	X	TT	TTT	50	0.20	1989	0.14	rs4727799	No
113,897,862	G	A	anc	A	AA	AA	50	0.97	1616	0.94	rs17137047	No
113,900,762	C	T	anc	T	X	TT	50	0.97	2	0.50	rs57915188	No
113,904,117	G	A	anc	A	X	A	42	0.52	13	0.15	rs7783012	No
113,905,348	C	T	anc	T	X	X	50	0.04	852	0.03	rs2396752	Yes
113,905,456	G	A	anc	A	A	A	46	1.00	1640	0.95	rs718378	No
113,906,142	A	C	anc	C	CC	CCC	50	0.99	-	-	-	No
113,906,379	G	A	anc/der	X	GAGAGGG	GG	50	1.00	-	-	-	No
113,906,666	G	A	anc	A	AAAAA	X	50	0.51	568	0.42	rs2189010	No
113,908,774	G	A	anc/der	X	GG	A	50	0.99	-	-	-	Yes
113,911,896	C	G	anc	G	G	X	41	0.56	569	0.43	rs6974757	No
113,912,746	A	G	anc	X	X	G	31	0.05	1090	0.05	rs17312861	No

113,913,053	G	A	anc/der	X	GGG	A	47	1.00	-	-	-	-	Yes
113,914,443	G	A	anc	A	X	A	8	1.00	2	0.50	rs111549411	No	
113,915,130	G	A	anc/der	X	A	GGG	32	0.98	4	0.25	rs62467874	Yes	
113,916,373	G	A	anc	X	AAA	A	49	0.52	2543	0.40	rs10249234	No	
113,916,739	C	T	anc	X	TTTTTTT	T	49	0.97	2	0.50	rs73436138	No	
113,920,823	T	A	anc/der	X	TTTTTT	AAAA	50	1.00	-	-	-	No	
113,925,176	A	G	anc	X	GGG	X	47	0.49	572	0.43	rs1989903	No	
113,925,295	C	T	anc/der	C	C	TT	48	0.99	-	-	-	No	
113,925,987	G	C	anc	X	X	CC	40	0.47	569	0.43	rs2040658	No	
113,929,064	G	A	anc/der	G	GAGGG	X	27	1.00	-	-	-	Yes	
113,930,643	C	T	anc	X	TTTT	X	49	0.51	2897	0.43	rs10266297	No	
113,935,479	A	G	anc	G	GGG	G	49	0.46	422	0.35	rs2189015	No	
113,935,567	C	A	anc	A	AAAAAA	X	50	0.43	412	0.38	rs2396753	No	
113,936,205	A	G	anc/der	G	AGGGG	X	50	0.94	508	0.97	rs17137063	No	
113,936,812	T	C	anc/der	X	CCCCCCT	CC	50	0.95	2	0.50	rs73429307	No	
113,940,210	C	T	anc	X	X	T	8	0.88	2	0.50	rs113503202	Yes	
113,940,339	T	C	anc	C	X	CC	19	0.92	2	0.50	rs977429	No	
113,946,190	G	A	anc/der	A	GGAAAA	A	49	0.22	1350	0.12	rs9969232	No	
113,946,224	G	T	anc/der	T	GGTTTTTT	T	49	0.96	2	0.50	rs73429327	No	
113,949,976	G	A	anc	A	X	X	46	0.53	2611	0.33	rs6980093	Yes	
113,951,735	C	T	anc	X	T	X	49	0.97	2	0.50	rs73429330	Yes	
113,954,693	G	C	anc	C	CCCCCC	C	50	0.95	2	0.50	rs73429339	No	
113,957,488	A	G	anc	G	GGGGGG	GG	50	0.88	1786	0.90	rs11764740	No	
113,967,298	A	G	anc	X	G	G	49	0.34	419	0.37	rs10262462	No	
113,971,334	G	A	anc	A	X	AA	28	0.43	13	0.15	rs7458242	No	
113,981,851	T	G	anc	X	G	X	26	0.50	10	0.20	rs1859100	No	
113,989,930	G	A	anc/der	G	AGGGGGGG	GG	50	0.99	-	-	-	Yes	
113,991,185	A	G	anc	G	GGGGGGG	GG	50	0.79	1985	0.70	rs12532920	No	
113,994,870	C	G	anc	X	GG	GG	50	0.93	563	0.93	rs11760306	No	
113,999,148	G	A	anc	A	AAA	A	50	0.16	426	0.14	rs2189012	No	
114,000,820	A	G	anc/der	G	X	AA	47	1.00	-	-	-	No	
114,003,040	G	A	anc	A	AAAAAAA	A	50	0.80	1967	0.72	rs7812028	No	
114,008,122	C	T	anc/der	C	CCCT	CCC	50	1.00	-	-	-	Yes	
114,010,959	C	A	anc	A	AAAAAAA	A	50	0.18	2127	0.17	rs1229761	No	
114,011,398	C	T	anc/der	C	CTC	X	48	1.00	-	-	-	Yes	
114,011,399	A	G	anc	G	GGG	X	48	0.08	440	0.16	rs1229760	No	
114,020,913	T	C	anc	C	C	CC	48	0.91	288	0.81	rs78332146	No	
114,022,318	A	C	anc	C	CCCC	X	50	0.93	416	0.93	rs10279820	No	
114,023,745	C	T	anc	T	TTTTTTTTT	X	50	0.93	1969	0.85	rs10085693	No	
114,023,793	A	T	anc	T	TTT	T	50	0.94	1981	0.86	rs10085404	No	
114,024,116	G	C	anc	X	CCC	CCC	50	0.00	564	0.01	rs1229757	No	
114,026,093	C	T	anc/der	T	CC	CC	46	0.99	-	-	-	Yes	
114,027,966	T	C	anc	X	CCCCCC	X	49	0.92	4	0.75	rs10231706	No	
114,029,131	C	T	anc/der	C	CCCCCT	CCC	47	1.00	-	-	-	Yes	
114,031,269	A	G	anc	G	X	GGG	50	0.92	360	0.82	rs28587831	No	
114,032,883	C	T	anc	T	TTTTTTTTT	TTT	50	0.93	1764	0.85	rs6953053	No	
114,039,257	A	G	anc	X	X	G	44	0.96	360	0.83	rs75273999	No	
114,042,420	A	G	anc	G	X	GG	8	1.00	120	0.94	rs10260142	No	
114,045,598	C	A	anc	A	A	X	45	0.91	310	0.87	rs10246561	No	
114,046,825	T	A	anc	X	A	X	37	0.95	360	0.84	rs11980684	No	
114,054,076	G	A	anc	A	AA	AAA	41	0.94	416	0.93	rs11768229	No	
114,054,869	T	C	anc/der	C	CCCCTCCCC	X	50	0.93	2072	0.85	rs1456025	No	
114,055,016	G	A	anc/der	X	GAG	X	50	1.00	-	-	-	Yes	
114,063,482	G	A	anc	A	AAA	AAAA	49	0.04	548	0.04	rs1869840	No	
114,066,271	T	C	anc	X	CCC	C	45	0.26	1977	0.22	rs6951781	No	

114,076,877	T	A	anc	X	AAA	X	30	0.98	118	0.97	rs114972925	No
114,077,449	A	T	anc	T	T	X	46	0.90	414	0.93	rs7795372	No
114,078,671	G	A	anc	A	X	A	38	0.60	-	-	-	No
114,090,425	G	A	anc	A	AA	X	48	0.72	706	0.57	rs1563408	No
114,097,289	G	T	anc	X	TTTT	T	50	0.75	2208	0.80	rs12705971	No
114,097,629	T	G	anc	G	X	G	46	1.00	-	-	-	No
114,100,435	A	G	anc	G	GGGGGGGG	G	50	0.74	1982	0.79	rs12705973	No
114,106,380	C	T	anc	T	X	X	21	1.00	-	-	-	Yes
114,109,179	A	G	anc	X	G	GG	49	0.59	1048	0.56	rs17291908	No
114,119,482	G	T	anc	T	TTTTTT	TTTTT	50	0.75	1000	0.82	rs12705977	No
114,121,279	T	C	anc	C	CCCC	C	50	0.76	1986	0.81	rs12671330	No
114,124,717	A	G	anc	G	GGGGGGGGG	GGGGG	50	0.48	14	0.07	rs10231331	No
114,125,548	C	T	anc	X	TTTTTTT	TTT	50	0.46	1990	0.42	rs11769707	No
114,130,812	T	A	anc	X	AAAAAAA	X	50	0.42	1199	0.41	rs4730639	No
114,130,838	T	C	anc	X	CCC	C	50	0.24	2209	0.26	rs4730640	No
114,132,736	T	C	anc	X	CC	CCC	48	0.04	2093	0.10	rs662217	No
114,132,911	G	T	anc	X	TTTTT	TTT	50	1.00	-	-	-	No
114,133,773	T	G	anc	A	GGGGGG	GGG	50	0.34	3048	0.42	rs647318	No
114,135,889	T	G	anc	X	GG	G	46	0.31	1974	0.42	rs617433	No
114,136,272	A	G	anc	X	GGGG	GGG	50	0.06	1664	0.11	rs605421	No
114,138,763	A	G	anc	G	GGGGGGGG	G	50	0.74	570	0.79	rs13312596	No
114,142,086	A	G	anc	G	GG	GGGGG	50	0.47	17	0.24	rs12536642	No
114,142,238	A	G	anc	G	GGGGGGG	X	50	0.46	2525	0.47	rs12705988	No
114,142,429	A	G	anc	G	GGG	GG	50	0.78	-	-	-	No
114,143,224	C	G	anc	G	GGGGG	GGGGGGGG	50	0.04	428	0.06	rs593549	No
114,149,689	G	A	anc	A	AAAAAAA	AAAA	50	0.78	6	0.17	rs7808219	No
114,151,634	A	C	anc	X	C	X	32	0.82	1876	0.79	rs4727801	No
114,152,579	G	T	anc	X	T	T	49	0.46	396	0.42	rs10252522	No
114,152,972	T	G	anc	G	G	GGG	42	0.37	153	0.28	rs656172	No
114,153,154	A	C	anc	C	C	X	24	0.00	155	0.02	rs599661	No
114,154,215	T	C	anc	X	X	C	1	0.00	177	0.40	rs776467	No
114,154,473	A	C	anc	X	X	CCCC	1	1.00	10	0.30	rs776466	No
114,155,106	C	T	anc	T	X	TT	21	0.92	4	0.50	rs626204	No
114,155,656	C	A	anc	X	AAAAAA	AA	49	0.57	9	0.11	rs613196	No
114,156,241	T	C	anc	C	X	CC	11	0.64	9	0.33	rs600286	No
114,158,140	A	G	anc	X	G	GGGGG	37	0.51	13	0.23	rs582035	No
114,158,307	C	T	anc	X	X	TT	6	1.00	-	-	-	No
114,158,488	A	G	anc	X	GGG	GG	20	0.33	-	-	-	No
114,160,335	A	G	anc/der	G	GAGGGGGGG	G	50	0.02	1877	0.04	rs631945	No
114,162,516	A	G	anc	G	GGG	GGGGG	50	0.73	2548	0.79	rs601926	No
114,165,268	G	A	anc	A	AAAAA	AA	50	0.55	568	0.44	rs666187	No
114,166,677	A	G	anc	X	G	X	49	0.54	422	0.44	rs776460	No
114,169,625	A	G	anc	G	GGG	G	47	0.05	962	0.14	rs589252	No
114,172,544	A	T	anc	X	TTT	TT	50	0.53	12	0.25	rs609138	No
114,174,277	C	T	anc	X	TTTTTT	TT	50	0.53	2954	0.47	rs624667	No
114,174,892	T	A	anc/der	T	TTTTTTTTTTTTTT	AAA	50	0.78	2282	0.79	rs675236	No
114,174,997	T	A	anc	A	AAAAAA	AAA	50	0.07	16	0.06	rs621566	No
114,185,561	C	T	anc	T	TTTTTT	TT	50	0.09	1663	0.16	rs4727803	No
114,187,168	G	A	anc/der	X	A	G	50	0.99	118	0.97	rs115841770	Yes
114,188,108	T	C	anc	C	CCCC	CCC	50	0.54	2536	0.59	rs1839115	No
114,188,235	A	G	anc	X	G	X	49	0.50	384	0.56	rs4727804	No
114,189,494	A	G	anc	G	GG	G	50	0.56	770	0.64	rs12534908	No
114,189,787	A	G	anc	G	GG	GG	50	0.09	572	0.11	rs6963018	No
114,192,967	G	A	anc	A	AAA	AAAA	50	0.10	1639	0.15	rs1448344	No
114,193,945	A	T	anc	X	TT	X	49	1.00	-	-	-	No

114,195,911	G	A	anc	X	AAAAAAAAA	X	50	1.00	-	-	-	No
114,197,212	T	A	anc/der	X	A	TT	50	1.00	526	0.99	rs17137249	No
114,200,474	T	C	anc	C	C	X	41	0.13	307	0.02	rs10258661	No
114,201,330	G	A	anc	X	AA	A	49	0.12	572	0.11	rs1375092	No
114,205,509	G	A	anc	A	X	AAA	15	0.11	17	0.06	rs289202	No
114,209,534	G	A	anc/der	A	AAAAAAAAAAAA	GG	50	1.00	-	-	-	No
114,212,742	G	A	anc	A	AAAAAA	AAA	50	0.07	435	0.08	rs289204	No
114,213,766	A	T	anc	T	TTTTTTTT	TTT	50	0.04	578	0.04	rs289205	No
114,216,057	G	A	anc/der	G	GGAGGG	GGG	50	1.00	-	-	-	Yes
114,217,805	G	A	anc	A	AAAAA	A	50	0.11	1662	0.13	rs1448347	No
114,218,555	A	G	anc/der	A	AAA	GG	49	1.00	-	-	-	No
114,218,918	G	C	anc	X	CCCCC	CCC	50	0.08	381	0.08	rs1448348	No
114,219,989	T	C	anc/der	T	TTT	CCC	50	1.00	-	-	-	No
114,220,703	A	G	anc	G	X	GG	50	0.98	4	0.25	rs61202485	No
114,222,933	C	T	anc	T	TT	TT	50	0.97	4	0.25	rs73716989	No
114,223,616	G	A	anc	A	AA	X	50	0.09	1663	0.12	rs1375093	No
114,227,035	C	T	anc/der	X	CCCC	TTT	50	1.00	-	-	-	No
114,229,333	C	T	anc	T	TTT	TT	50	0.08	431	0.10	rs1375095	No
114,232,470	C	T	anc	T	TTTTTT	TTT	50	0.09	16	0.13	rs1989799	No
114,234,135	C	T	anc	X	TTT	T	50	0.00	-	-	-	No
114,235,715	C	T	anc/der	C	CTCT	CCC	50	0.94	120	0.98	rs117936540	No
114,237,836	C	T	anc/der	C	CCCCCCCC	TCCCC	50	1.00	-	-	-	Yes
114,238,219	G	A	anc/der	X	GGG	AGGG	50	1.00	-	-	-	Yes
114,239,333	T	A	anc	A	AAAAAAA	A	50	0.11	6119	0.06	rs2034380	No
114,239,582	G	A	anc	A	AAAAAAA	AAA	50	0.09	1658	0.19	rs10241162	No
114,241,271	C	A	anc/der	C	CCCAC	CCCC	50	0.99	-	-	-	No
114,241,882	G	A	anc/der	G	GAGGGGGG	GG	50	1.00	-	-	-	Yes
114,242,444	T	G	anc	G	GG	G	50	0.08	534	0.11	rs6466495	No
114,243,461	C	A	anc/der	A	CC	X	47	1.00	-	-	-	No
114,244,039	C	A	anc	X	X	AA	10	0.10	12	0.08	rs289196	No
114,244,511	G	A	anc	X	X	AA	0	NA	-	-	-	No
114,244,989	C	T	anc	X	X	T	6	0.43	8	0.13	rs7455681	Yes
114,245,557	T	C	anc/der	C	TTT	X	49	1.00	-	-	-	No
114,246,898	C	A	anc/der	C	CACCCCC	CCCCC	50	0.99	-	-	-	No
114,247,394	T	G	anc	G	GGG	GG	50	0.99	414	1.00	rs10264546	No

Supplementary table S2. Individuals from the Human Genome Diversity Panel used for making the sequencing library.

HGDP-CEPH ID	Sex	Population	Geographic origin	Continent
HGDP00980	Female	Biaka Pygmies	Central African Republic	Africa
HGDP00471	Female	Mbuti Pygmies	Democratic Republic of Congo	Africa
HGDP00909	Female	Mandenka	Senegal	Africa
HGDP00920	Female	Yoruba	Nigeria	Africa
HGDP01414	Female	Bantu N.E.	Kenya	Africa
HGDP01254	Female	Mozabite	Algeria (Mzab)	Africa
HGDP00607	Female	Bedouin	Israel (Negev)	Asia
HGDP00557	Female	Druze	Israel (Carmel)	Asia
HGDP00679	Female	Palestinian	Israel (Central)	Asia
HGDP00151	Female	Makrani	Pakistan	Asia
HGDP00192	Female	Sindhi	Pakistan	Asia
HGDP00232	Female	Pathan	Pakistan	Asia
HGDP00286	Female	Kalash	Pakistan	Asia
HGDP00336	Female	Burusho	Pakistan	Asia
HGDP00783	Female	Han	China	Asia
HGDP01098	Female	Tujia	China	Asia
HGDP01188	Female	Yizu	China	Asia
HGDP01196	Female	Miaozu	China	Asia
HGDP01209	Female	Oroqen	China	Asia
HGDP01215	Female	Daur	China	Asia
HGDP01223	Female	Mongola	China	Asia
HGDP01234	Female	Hezhen	China	Asia
HGDP01251	Female	Xibo	China	Asia
HGDP01305	Female	Uygur	China	Asia
HGDP01314	Female	Dai	China	Asia
HGDP01323	Female	Lahu	China	Asia
HGDP01334	Female	She	China	Asia
HGDP01345	Female	Naxi	China	Asia
HGDP01354	Female	Tu	China	Asia
HGDP00955	Female	Yakut	Siberia	Asia
HGDP00754	Female	Japanese	Japan	Asia
HGDP00712	Female	Cambodian	Cambodia	Asia
HGDP00544	Female	Papuan	New Guinea	Oceania
HGDP00656	Female	NAN Melanesian	Bougainville	Oceania
HGDP00513	Female	French	France	Europe
HGDP01363	Female	French Basque	France	Europe
HGDP00667	Female	Sardinian	Italy	Europe
HGDP01156	Female	North Italian	Italy (Bergamo)	Europe
HGDP01168	Female	Tuscan	Italy	Europe
HGDP00794	Female	Orcadian	Orkney Islands	Europe
HGDP01381	Female	Adygei	Russia Caucasus	Europe
HGDP00881	Female	Russian	Russia	Europe
HGDP01038	Female	Pima	Mexico	America
HGDP00854	Female	Maya	Mexico	America
HGDP00702	Female	Colombian	Colombia	America
HGDP00995	Female	Karitiana	Brazil	America
HGDP00830	Female	Surui	Brazil	America
HGDP00987	Male	San	Namibia	Africa
HGDP00015	Male	Brahui	Pakistan	Asia
HGDP00096	Male	Balochi	Pakistan	Asia
HGDP00111	Male	Hazara	Pakistan	Asia

Supplementary table S3. Recent substitutions that are fixed or at high frequency in present-day humans.

hg18 coordinate	hg18 base	outgroup base	archaic human state	published Neandertal consensus	captured Neandertal bases	Denisovan bases	HGDP individuals	HGDP derived base fraction	dbSNP132 chromosomes	dbSNP132 derived base fraction	dbSNP132 ID	PhastCons vertebrate conservation score
113,832,887	G	A	anc	A	AA	AAA	50	1.00	168	0.93	rs75755264	0.98
113,860,981	C	T	anc	X	T	TTTT	44	0.98	548	0.97	rs17137020	0.0
113,861,403	T	C	anc/der	X	CC	T	49	1.00	118	0.97	rs115887906	0.0
113,866,166	A	T	anc	T	TT	TTTT	50	0.97	2	0.50	rs73434173	0.0
113,875,021	G	C	anc	C	CC	C	50	1.00	414	0.97	rs7788102	0.0
113,877,694	T	C	anc	C	CCCCC	CC	49	1.00	558	0.98	rs17137029	0.03
113,880,427	G	A	anc	A	AA	X	50	0.99	2	0.50	rs73434180	0.0
113,880,438	G	A	anc	A	AAA	A	50	1.00	118	0.90	rs115295546	0.0
113,883,593	G	A	anc	A	AAAA	AA	50	1.00	1760	0.96	rs17137034	0.0
113,890,947	A	G	anc	X	GG	GG	48	0.99	144	0.98	rs17137041	0.0
113,892,689	T	A	anc	X	AAAA	A	47	0.99	663	0.96	rs6466487	0.08
113,895,542	T	G	anc	G	GGG	GGGG	50	0.98	1793	0.95	rs17137045	0.0
113,897,862	G	A	anc	A	AA	AA	50	0.97	1616	0.94	rs17137047	0.0
113,900,762	C	T	anc	T	X	TT	50	0.97	2	0.50	rs57915188	0.0
113,905,456	G	A	anc	A	A	A	46	1.00	1640	0.95	rs718378	0.0
113,906,142	A	C	anc	C	CC	CCC	50	0.99	-	-	-	0.0
113,906,379	G	A	anc/der	X	GAGAGGG	GG	50	1.00	-	-	-	0.0
113,916,739	C	T	anc	X	TTTTTTT	T	49	0.97	2	0.50	rs73436138	0.0
113,920,823	T	A	anc/der	X	TTTTTT	AAAA	50	1.00	-	-	-	0.0
113,925,295	C	T	anc/der	C	C	TT	48	0.99	-	-	-	0.0
113,936,812	T	C	anc/der	X	CCCCCCTT	CC	50	0.95	2	0.50	rs73429307	0.0
113,946,224	G	T	anc/der	T	GGTTTTTT	T	49	0.96	2	0.50	rs73429327	0.0
113,951,735	C	T	anc	X	T	X	49	0.97	2	0.50	rs73429330	0.0
113,954,693	G	C	anc	C	CCCCC	C	50	0.95	2	0.50	rs73429339	0.0
114,000,820	A	G	anc/der	G	X	AA	47	1.00	-	-	-	0.0
114,039,257	A	G	anc	X	X	G	44	0.96	360	0.83	rs75273999	0.06
114,076,877	T	A	anc	X	AAA	X	30	0.98	118	0.97	rs114972925	1.0
114,097,629	T	G	anc	G	X	G	46	1.00	-	-	-	0.0
114,106,380	C	T	anc	T	X	X	21	1.00	-	-	-	0.0
114,132,911	G	T	anc	X	TTTTT	TTT	50	1.00	-	-	-	0.05
114,158,307	C	T	anc	X	X	TT	6	1.00	-	-	-	0.04
114,193,945	A	T	anc	X	TT	X	49	1.00	-	-	-	0.0
114,195,911	G	A	anc	X	AAAAAAAAA	X	50	1.00	-	-	-	0.0
114,197,212	T	A	anc/der	X	A	TT	50	1.00	526	0.99	rs17137249	0.0
114,209,534	G	A	anc/der	A	AAAAAAAAAAAA	GG	50	1.00	-	-	-	0.0
114,218,555	A	G	anc/der	A	AAA	GG	49	1.00	-	-	-	0.0
114,219,989	T	C	anc/der	T	TTT	CCC	50	1.00	-	-	-	0.0
114,220,703	A	G	anc	G	X	GG	50	0.98	4	0.25	rs61202485	0.0
114,222,933	C	T	anc	T	TT	TT	50	0.97	4	0.25	rs73716989	0.0
114,227,035	C	T	anc/der	X	CCCC	TTT	50	1.00	-	-	-	0.0
114,241,271	C	A	anc/der	C	CCCAC	CCCC	50	0.99	-	-	-	0.0
114,243,461	C	A	anc/der	A	CC	X	47	1.00	-	-	-	0.0
114,244,511	G	A	anc	X	X	AA	0	N.A.	-	-	-	0.05
114,245,557	T	C	anc/der	C	TTT	X	49	1.00	-	-	-	0.0
114,246,898	C	A	anc/der	C	CACCCCC	CCCCC	50	0.99	-	-	-	0.0
114,247,394	T	G	anc	G	GGG	GG	50	0.99	414	1.00	rs10264546	0.0

Supplementary table S4. UCSCgenome browser (NCBI Build 36.1) annotation tracks used in this study.

Gene and gene prediction tracks	UCSC genes Alt events (alternative splicing, alternative promoter and similar events) CCDS RefSeq genes Ensembl genes RNA genes (non-coding RNA genes)
mRNA and EST track	Spliced ESTs
Regulation tracks	HAIB methyl-seq (average methylation status in CpG islands) HAIB Methyl27 (methylation status of specific CpG dinucleotides) HAIB TFBS (transcription factor binding sites) TFBS conserved (conserved transcription factor binding sites) TS miRNA sites (conserved mammalian microRNA) LI/UCSD TAF1 sites (TAF1 binding) Vista enhancers UCSF brain methylation
ENCODE regulation tracks	Transcription Transcription factor ChIP-seq DNaseI hypersensitivity clusters

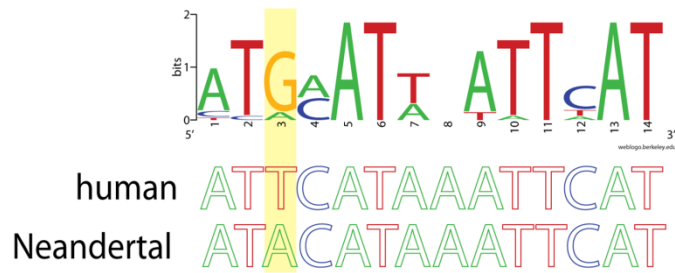
Supplementary table S5. Transgenic mouse enhancer assay.

stage	tissue	number of mice tested	
		derived	ancestral
E11.5	whole embryo	11	6
P4	brain	6	4
P28	brain	4	3
P60	brain	4	3
	heart	4	3
	esophagus	4	3
	lungs	4	3

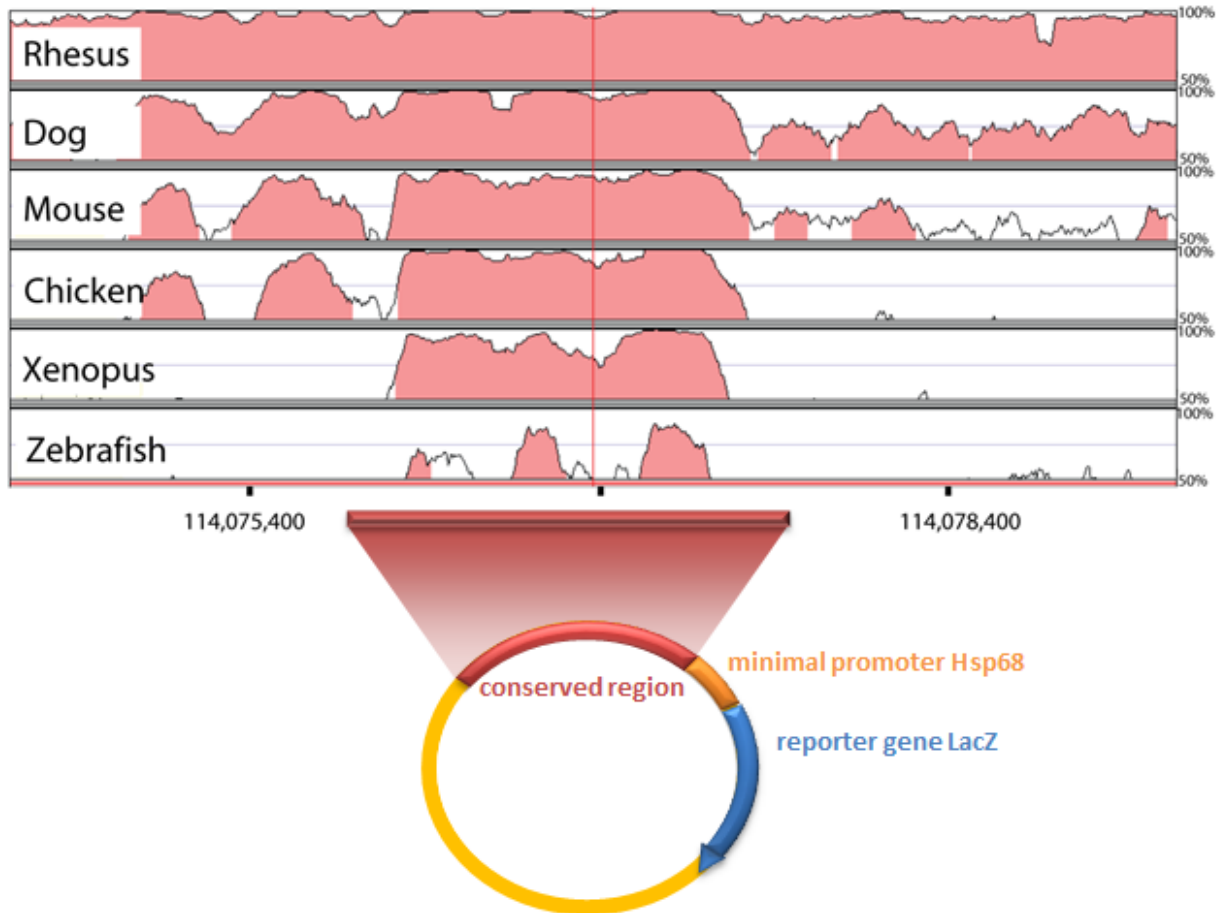
Supplementary table S6. Frequencies of the ancestral allele in various populations at the position 114,076,877 obtained from 1,000 genomes project, phase I.

continent	population	number of chromosomes	fraction ancestral
Africa	ASW	122	0.11
Africa	LWK	194	0.08
Africa	YRI	176	0.09
Europe	CEU	174	0.00
Europe	FIN	186	0.00
Europe	GBR	176	0.00
Europe	IBS	28	0.00
Europe	TSI	196	0.00
East Asia	CHB	194	0.00
East Asia	CHS	200	0.00
East Asia	JPT	178	0.00
America	CLM	120	0.01
America	MXL	132	0.02
America	PUR	110	0.00

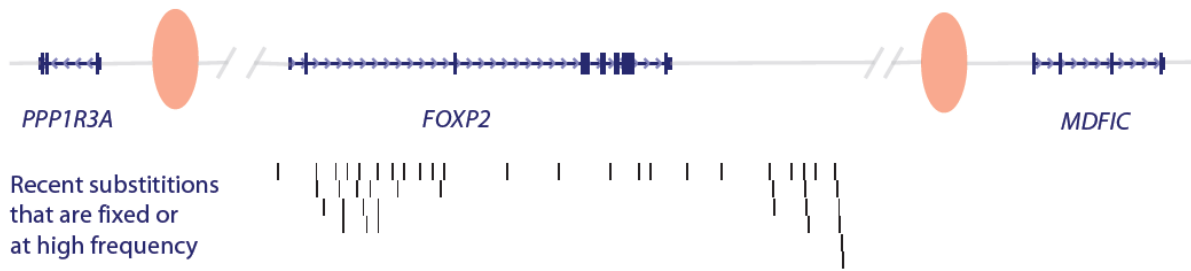
Supplementary figures



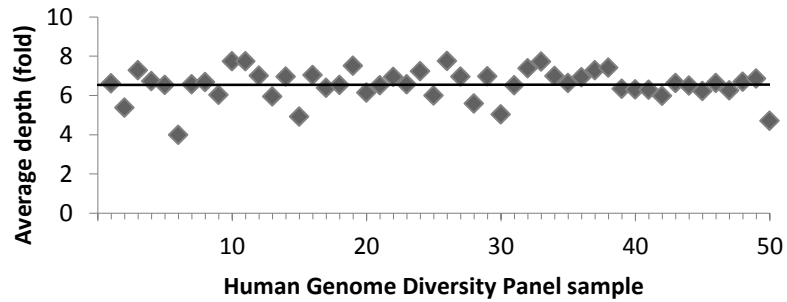
Supplementary fig. S1. POU3F2 binding motif (Rhee et al. 1998) drawn with WebLogo (Crooks et al. 2004) and aligned to the sequences of a Neanderthal and a human. Position 114,076,877 is indicated by a yellow box.



Supplementary fig. S2. Plasmid used for transgenic mouse enhancer assay. Region that is 1,829 long, surrounding the POU3F2 binding site (red line), was inserted in a plasmid in front of a minimal promoter and a reporter gene.



Supplementary fig. S3. Insulators around the *FOXP2* gene. Insulators are depicted as red ellipses and transcripts are depicted in blue.



Supplementary fig. S4. Average sequencing depth of the 50 HGDP samples. Black line represents average depth of all 50 samples.

References

Crooks GE, Hon G, Chandonia JM, Brenner SE 2004. WebLogo: a sequence logo generator. *Genome Res* 14: 1188-1190.

Rhee JM, Gruber CA, Brodie TB, Trieu M, Turner EE 1998. Highly cooperative homodimerization is a conserved property of neural POU proteins. *J Biol Chem* 273: 34196-34205.