

Table S11. Nucleotide Substitutions in *CST1* gene in introns and regulatory regions

Genomic Coordinates (hg19)	Gene Region	Modern human	Altai Neanderthal (Variant Frequency)	Chagyrskaya Neanderthal (Variant Frequency)	Vindija Neanderthal (Variant Frequency)	Denisovan (Variant Frequency)	Codon → amino acid
23,731,947	Upstream regions	G	A (2%)*	G (100%)	A (14%)	G (100%)	
23,731,940	Upstream regions	C	C (100%)	T (12%)	T (7%)*	C (100%)	
23,731,864	Upstream regions	G	G (100%)	G (100%)	A (15%)	G (100%)	
23,731,815	Upstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)	
23,731,810	Upstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)	
23,731,800	Upstream regions	C	C (100%)	T (13%)	C (100%)	C (100%)	
23,731,770	Upstream regions	C	C (100%)	C (100%)	T (17%)	C (100%)	
23,731,769	Upstream regions	C	T (2%)*	T (8%)*	T (17%)	C (100%)	
23,731,741	Upstream regions	C	C (100%)	T (30%)	C (100%)	C (100%)	
23,731,738	Upstream regions	C	T (3%)*	T (20%)	C (100%)	C (100%)	
23,731,721	Upstream regions	C	T (87%)	T (100%)	T (71%)	T (95%)	
23,731,719	Upstream regions	C	T (90%)	T (100%)	T (79%)	T (96%)	
23,731,705	Upstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)	
23,731,665	Upstream regions	T	G (100%)	G (89%)	G (88%)**	G (94%)	
23,731,653	Upstream regions	C	T (95%)	T (100%)	T (100%)**	T (100%)	
23,731,624	Upstream regions	C	C (100%)	T (9%)*	T (17%)	C (100%)	
23,731,620	Upstream regions	C	C (100%)	T (7%)*	T (17%)	C (100%)	
23,731,619	Upstream regions	C	C (100%)	T (7%)*	T (17%)	C (100%)	
23,731,589	Upstream regions	G	C (58%)	C (60%)	C (54%)	C (36%)	
23,731,571	5'UTR	G	G (100%)	G (100%)	A (13%)	G (100%)	
23,731,563	5'UTR	G	G (100%)	A (11%)	A (5%)*	G (100%)	
23,731,560	5'UTR	C	T (69%)	T (47%)	T (42%)	T (56%)	
23,731,557	5'UTR	G	G (100%)	G (100%)	A (11%)	G (100%)	
23,731,551	5'UTR	G	G (100%)	A (19%)	A (5%)*	G (100%)	
23,731,550	5'UTR	G	G (100%)	A (13%)	A (5%)*	G (100%)	
23,731,527	5'UTR	A	G (34%)	G (21%)	G (43%)	G (21%)	
23,731,479	Exon 1 (Signal)	<u>G</u> AC	<u>G</u> AC (100%)	<u>A</u> AC (11%)	<u>A</u> AC (4%)*	<u>G</u> AC (100%)	CUG→L <sub>8(sp)</sub> UUG→L <sub>8(sp)</sub>
23,731,453	Exon 1 (Signal)	<u>C</u> AC	<u>C</u> AC (98%)	<u>C</u> AC (100%)	<u>C</u> AT (11%)	<u>C</u> AC (100%)	GUG→V <sub>16(sp)</sub> GUA→V <sub>16(sp)</sub>

23,731,363	Exon 1	<u>CGG</u>	<u>CGG</u> (100%)	<u>CGA</u> (12%)	<u>CGG</u> (100%)	<u>CGG</u> (100%)	GCC→A <sub>27</sub> GCU→A <sub>27</sub>
23,731,354	Exon 1	<u>AAG</u>	<u>AAA</u> (5%)*	<u>AAA</u> (13%)	<u>AAG</u> (10%)	<u>AAG</u> (10%)	UUC→F <sub>30</sub> UUU→F <sub>30</sub>
23,731,294	Exon 1	<u>CAT</u>	<u>CAA</u> (57%)	<u>CAT</u> (100%)	<u>CAA</u> (52%)	<u>CAT</u> (100%)	GUA→V <sub>50</sub> GUU→V <sub>50</sub>
23,731,282	Exon 1	<u>TCC</u>	<u>TCC</u> (100%)	<u>TCC</u> (100%)	<u>TCI</u> (13%)	<u>TCC</u> (100%)	AGG→R <sub>54</sub> AGA→R <sub>54</sub>
23,731,254	Intron 1	C	C (100%)	C (100%)	T (11%)	C (100%)	
23,731,251	Intron 1	C	C (100%)	T (6%)*	T (13%)	C (100%)	
23,731,248	Intron 1	G	G (100%)	G (100%)	A (11%)	G (100%)	
23,731,123	Intron 1	C	G (2%)*	T (14%)	C (100%)	C (100%)	
23,731,102	Intron 1	C	C (100%)	T (13%)	T (15%)	C (100%)	
23,731,048	Intron 1	G	G (100%)	A (3%)*	A (11%)	G (100%)	
23,731,032	Intron 1	C	C (100%)	C (100%)	T (13%)	C (100%)	
23,731,017	Intron 1	C	C (100%)	C (100%)	T (14%)	T (3%)*	
23,731,007	Intron 1	C	C (100%)	T (4%)*	T (11%)	C (100%)	
23,731,005	Intron 1	C	C (100%)	C (96%)	T (14%)	C (100%)	
23,730,890	Intron 1	C	C (100%)	C (100%)	T (14%)	C (100%)	
23,730,888	Intron 1	C	C (100%)	T (4%)*	T (11%)	C (100%)	
23,730,886	Intron 1	G	G (100%)	A (22%)	A (11%)	G (100%)	
23,730,885	Intron 1	G	G (100%)	A (5%)*	A (11%)	G (100%)	
23,730,873	Intron 1	C	C (100%)	C (100%)	T (15%)	C (100%)	
23,730,867	Intron 1	G	G (100%)	A (7%)*	A (25%)	G (100%)	
23,730,841	Intron 1	C	C (100%)	C (100%)	T (18%)	C (100%)	
23,730,803	Intron 1	C	C (100%)	C (100%)	T (14%)	C (100%)	
23,730,798	Intron 1	C	C (100%)	T (11%)	C (100%)	C (100%)	
23,730,797	Intron 1	C	C (100%)	T (6%)*	T (13%)	C (100%)	
23,730,777	Intron 1	C	C (100%)	T (12%)	T (5%)*	C (100%)	
23,730,775	Intron 1	C	C (100%)	T (12%)	T (11%)	C (100%)	
23,730,772	Intron 1	C	C (100%)	T (13%)	C (100%)	C (100%)	
23,730,761	Intron 1	G	G (100%)	A (19%)	A (8%)*	G (100%)	
23,730,760	Intron 1	G	G (100%)	A (13%)	A (18%)	G (100%)	
23,730,754	Intron 1	G	G (100%)	A (11%)	G (100%)	G (100%)	
23,730,747	Intron 1	G	G (100%)	G (100%)	A (14%)	G (100%)	
23,730,692	Intron 1	C	C (100%)	T (13%)	T (11%)*	C (100%)	
23,730,682	Intron 1	C	C (100%)	T (13%)	T (14%)**	T (4%)*	
23,730,677	Intron 1	C	C (97%)	T (13%)	C (100%)	C (100%)	

23,730,674	Intron 1	C	C (100%)	T (13%)	C (100%)	C (100%)	
23,730,629	Intron 1	C	C (100%)	T (6%)*	T (13%)	C (100%)	
23,730,625	Intron 1	G	G (100%)	G (100%)	C (4%)*	C (32%)	
23,730,607	Intron 1	G	G (100%)	A (5%)*	A (13%)	G (100%)	
23,730,549	Intron 1	C	C (98%)	T (16%)	T (6%)*	C (97%)	
23,730,536	Intron 1	G	G (100%)	A (11%)	A (3%)*	G (100%)	
23,730,522	Intron 1	C	C (100%)	T (17%)	T (3%)*	C (100%)	
23,730,494	Intron 1	G	G (98%)	A (13%)	A (4%)*	G (100%)	
23,730,475	Intron 1	C	C (100%)	T (7%)*	T (11%)	C (100%)	
23,730,436	Intron 1	C	C (100%)	C (94%)	T (20%)	C (100%)	
23,730,434	Intron 1	C	C (100%)	C (100%)	T (18%)	C (100%)	
23,730,234	Intron 1	G	A (2%)*	G (100%)	A (18%)	G (100%)	
23,730,227	Intron 1	C	C (100%)	C (100%)	T (14%)	C (100%)	
23,730,034	Intron 1	G	G (100%)	G (100%)	A (11%)	G (100%)	
23,729,973	Intron 1	A	A (100%)	G (41%)	G (55%)	A (100%)	
23,729,898	Intron 1	C	C (100%)	T (13%)	C (100%)	T (5%)*	
23,729,871	Intron 1	C	T (2%)*	T (4%)*	T (11%)	C (100%)	
23,729,870	Intron 1	C	T (2%)*	T (11%)	C (100%)	C (100%)	
23,729,858	Intron 1	C	C (100%)	T (12%)	T (5%)*	C (100%)	
23,729,857	Intron 1	G	G (97%)	G (100%)	A (11%)	G (100%)	
23,729,837	Intron 1	G	G (100%)	G (100%)	G (100%)	A (47%)	
23,729,814	Intron 1	C	C (100%)	T (3%)*	T (11%)	C (100%)	
23,729,812	Intron 1	C	C (100%)	C (100%)	T (14%)	C (100%)	
23,729,793	Intron 1	G	A (4%)*	A (4%)*	A (14%)	A (4%)*	
23,729,764	Exon 2	<b>TG<u>G</u></b>	TG <u>G</u> (98%)	TG <u>A</u> (14%)	TG <u>A</u> (4%)*	TG <u>G</u> (100%)	ACC→T <sub>57</sub> ACG→T <sub>57</sub>
23,729,737	Exon 2	<b>CT<u>G</u></b>	CT <u>G</u> (100%)	CT <u>A</u> (13%)	CT <u>A</u> (9%)*	CT <u>A</u> (3%)*	GAC→D <sub>66</sub> GAU→D <sub>66</sub>
23,729,722	Exon 2	<b>G<u>C</u><u>G</u></b>	G <u>C</u> <u>I</u> (48%)	G <u>C</u> <u>I</u> (45%)	G <u>C</u> <u>I</u> (54%)	G <u>C</u> <u>I</u> (44%)	CGC→R <sub>71</sub> CGA→R <sub>71</sub>
23,729,689	Exon 2	<b>CT<u>G</u></b>	CT <u>G</u> (100%)	CT <u>A</u> (3%)*	CT <u>A</u> (13%)	CT <u>G</u> (100%)	GAC→D <sub>82</sub> GAU→D <sub>82</sub>
23,729,635	Intron 2	C	C (100%)	T (4%)*	T (13%)	C (100%)	
23,729,616	Intron 2	G	G (100%)	A (11%)	A (3%)*	G (100%)	
23,729,609	Intron 2	C	C (100%)	C (100%)	T (13%)	C (100%)	
23,729,602	Intron 2	C	T (3%)*	C (100%)	T (13%)	C (100%)	
23,729,584	Intron 2	G	G (100%)	G (100%)	G (100%)	A (87%)	
23,729,579	Intron 2	T	G (10%)*	T (100%)	G (16%)	T (100%)	

23,729,567	Intron 2	C	C (100%)	C (100%)	T (20%)	C (100%)
23,729,556	Intron 2		InsAC (50%)	InsAC (40%)**	InsAC (23%)	InsAC (56%)**
23,729,550	Intron 2	C	C (100%)	C (100%)	A (20%)	C (100%)
23,729,549	Intron 2	C	C (100%)	C (100%)	A (20%)	C (100%)
23,729,544	Intron 2	C	T (26%)	C (100%)**	T (33%)*	C (100%)**
23,729,514	Intron 2	C	T (31%)	T (14%)**	T (17%)**	T (25%)**
23,729,500	Intron 2	T	C (42%)	C (45%)	C (56%)**	C (30%)
23,729,496	Intron 2	C	T (48%)	T (55%)	T (50%)**	T (45%)
23,729,486	Intron 2	T	G (63%)	G (54%)	G (63%)**	G (62%)
23,729,484	Intron 2	C	C (100%)	T (13%)	T (9%)*	C (100%)
23,729,481	Intron 2	C	C (100%)	T (7%)*	T (17%)	C (100%)
23,729,464	Intron 2	C	C (100%)	T (12%)	C (100%)	T (5%)*
23,729,449	Intron 2	G	G (100%)	A (13%)	G (100%)	G (100%)
23,729,373	Intron 2	G	G (100%)	G (92%)	T (60%)	G (100%)
23,729,337	Intron 2	A	A (100%)	G (70%)	G (26%)	A (100%)
23,729,302	Intron 2	C	C (100%)	T (13%)	T (5%)*	C (97%)
23,729,301	Intron 2	C	C (100%)	T (13%)	C (100%)	C (96%)
23,729,299	Intron 2	C	C (100%)	T (13%)	C (100%)	T (4%)*
23,729,298	Intron 2	C	C (100%)	T (13%)	T (5%)*	C (100%)
23,729,296	Intron 2	C	C (100%)	T (13%)	T (11%)	C (97%)
23,729,287	Intron 2	C	C (100%)	T (6%)*	T (11%)	C (100%)
23,729,286	Intron 2	C	C (100%)	T (6%)*	T (11%)	C (100%)
23,729,264	Intron 2	C	C (100%)	C (100%)	T (17%)	C (100%)
23,729,253	Intron 2	C	C (100%)	T (3%)*	T (17%)	C (100%)
23,729,232	Intron 2	C	C (100%)	T (5%)*	T (13%)	C (100%)
23,729,187	Intron 2	C	A (100%)	A (100%)**	A (100%)**	A (100%)**
23,729,184	Intron 2	C	G (100%)	G (100%)**	G (100%)**	G (100%)**
23,729,134	Intron 2	G	C (100%)	C (93%)	C (90%)	C (100%)
23,729,117	Intron 2	G	G (100%)	A (11%)	A (4%)*	G (100%)
23,729,090	Intron 2	A	A (100%)	A (100%)	A (100%)	G (76%)
23,729,056	Intron 2	C	C (100%)	C (100%)	T (12%)	C (100%)
23,729,045	Intron 2	G	G (100%)	A (11%)	G (100%)	G (100%)
23,729,041	Intron 2	G	G (100%)	A (6%)*	A (13%)	G (100%)
23,729,029	Intron 2	G	G (98%)	G (96%)	A (14%)	G (100%)
23,728,986	Intron 2	C	T (87%)	T (74%)	T (64%)	C (100%)

23,728,979	Intron 2	T	C (6%)*	C (43%)	C (9%)*	T (100%)	
23,728,951	Intron 2	G	G (100%)	A (13%)	G (100%)	G (100%)	
23,728,934	Intron 2	C	C (100%)	T (4%)*	T (15%)	C (100%)	
23,728,927	Intron 2	G	G (98%)	G (100%)	A (12%)	G (100%)	
23,728,925	Intron 2	G	G (100%)	A (13%)	G (100%)	G (100%)	
23,728,910	Intron 2	G	G (100%)	A (14%)	A (4%)*	G (100%)	
23,728,909	Intron 2	G	G (100%)	A (11%)	A (9%)*	G (100%)	
23,728,893	Intron 2	C	C (100%)	T (13%)	T (11%)	C (100%)	
23,728,890	Intron 2	G	G (100%)	A (12%)	G (100%)	G (100%)	
23,728,882	Intron 2	C	T (87%)	T (65%)	T (68%)	C (100%)	
23,728,881	Intron 2	C	C (100%)	T (6%)*	T (11%)	C (100%)	
23,728,878	Intron 2	G	G (100%)	G (100%)	A (11%)	G (100%)	
23,728,873	Intron 2	C	T (2%)*	C (100%)	T (11%)	C (100%)	
23,728,872	Intron 2	C	C (100%)	T (5%)*	T (13%)	C (100%)	
23,728,805	Intron 2	G	G (100%)	A (13%)	A (11%)	G (100%)	
23,728,797	Intron 2	T	C (11%)	T (100%)	C (25%)	T (100%)	
23,728,751	Intron 2	C	C (100%)	T (4%)*	T (11%)	C (100%)	
23,728,749	Intron 2	C	C (98%)	T (11%)	C (100%)	C (100%)	
23,728,719	Intron 2	A	A (95%)	A (96%)	A (100%)	delA (21%)	
23,728,687	Intron 2	G	G (98%)	A (5%)*	A (14%)	G (100%)	
23,728,661	Intron 2	C	C (100%)	T (11%)	C (100%)	C (100%)	
23,728,658	Intron 2	C	C (100%)	T (6%)*	T (20%)	C (100%)	
23,728,656	Intron 2	C	C (100%)	T (6%)*	T (13%)	C (100%)	
23,728,649	Intron 2	C	C (100%)	C (100%)	T (11%)	C (100%)	
23,728,648	Intron 2	C	C (100%)	T (9%)*	T (18%)	C (100%)	
23,728,641	Intron 2	C	T (8%)*	T (5%)*	T (14%)	C (100%)	
23,728,639	Intron 2	G	G (100%)	G (100%)	A (13%)	G (100%)	
23,728,635	Intron 2	G	G (100%)	A (12%)	A (15%)	G (100%)	
23,728,557	Intron 2	G	G (100%)	A (11%)	A (9%)*	G (100%)	
23,728,556	Intron 2	G	G (100%)	A (11%)	A (9%)*	G (100%)	
23,728,550	Intron 2	G	G (100%)	G (100%)	A (15%)	G (100%)	
23,728,547	Intron 2	G	G (100%)	A (11%)	A (4%)*	G (100%)	
23,728,546	Intron 2	G	G (100%)	A (11%)	G (100%)	G (100%)	
23,728,486	Exon 3	TCC	TCC (100%)	TCT (4%)*	TCT (17%)	TCC (100%)	AGG→R111 AGA→R111

23,728,419	3'UTR	G	G (100%)	G (100%)	A (20%)	G (100%)
23,728,418	3'UTR	G	G (100%)	A (10%)*	A (20%)	G (100%)
23,728,417	3'UTR	G	G (100%)	A (27%)	G (100%)	G (100%)
23,728,359	3'UTR	C	A (15%)	A (22%)**	A (13%)	C (100%)
23,728,341	3'UTR	C	C (100%)	C (100%)	T (11%)	C (95%)
23,728,332	3'UTR	G	G (100%)	G (100%)	A (11%)	G (100%)
23,728,314	3'UTR	C	C (100%)	C (100%)	T (13%)	C (100%)
23,728,301	3'UTR	C	C (100%)	T (15%)	C (100%)	C (100%)
23,728,291	3'UTR	C	C (100%)	T (12%)	C (100%)	C (100%)
23,728,238	3'UTR	G	G (100%)	G (100%)	A (14%)	G (100%)
23,728,233	3'UTR	G	T (100%)	T (89%)**	T (90%)	T (100%)**
23,728,222	3'UTR	G	G (100%)	G (100%)	A (14%)	G (100%)
23,728,157	Downstream regions	C	T (100%)	T (100%)**	T (100%)	T (100%)
23,728,128	Downstream regions	G	G (96%)	A (14%)	G (100%)	G (100%)
23,728,103	Downstream regions	G	C (25%)	C (35%)	C (42%)	G (100%)
23,728,101	Downstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)
23,728,094	Downstream regions	G	G (100%)	A (3%)*	A (14%)	G (100%)
23,728,083	Downstream regions	G	A (23%)	A (25%)	A (43%)	A (5%)*
23,728,058	Downstream regions	C	T (3%)*	T (38%)	T (60%)	C (100%)
23,728,056	Downstream regions	C	C (100%)	C (100%)	T (15%)	C (100%)
23,728,055	Downstream regions	G	G (100%)	G (100%)	A (15%)	G (94%)
23,727,966	Downstream regions	C	T (3%)*	T (11%)	C (100%)	C (100%)
23,727,961	Downstream regions	C	T (8%)*	C (100%)	T (13%)	C (100%)
23,727,953	Downstream regions	C	C (100%)	T (10%)*	T (14%)	C (100%)
23,727,940	Downstream regions	G	G (100%)	A (12%)	A (5%)*	G (100%)
23,727,928	Downstream regions	G	G (100%)	A (26%)	G (100%)	G (100%)
23,727,927	Downstream regions	G	G (100%)	A (11%)	A (4%)*	G (100%)
23,727,917	Downstream regions	T	C (100%)	C (100%)	C (100%)	C (100%)**
23,727,909	Downstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)
23,727,891	Downstream regions	C	C (100%)	C (100%)	T (20%)	C (100%)
23,727,890	Downstream regions	C	C (100%)	C (100%)	T (13%)	C (100%)
23,727,884	Downstream regions	G	G (100%)	A (13%)	G (100%)	G (100%)
23,727,875	Downstream regions	C	C (100%)	T (5%)*	T (13%)	C (100%)

23,727,874	Downstream regions	C	C (100%)	C (100%)	T (25%)	C (100%)
23,727,849	Downstream regions	C	C (97%)	T (12%)	C (100%)	C (100%)
23,727,828	Downstream regions	C	G (96%)	G (91%)	G (90%)	G (95%)
23,727,761	Downstream regions	T	T (100%)	C (13%)	T (100%)	T (100%)
23,727,757	Downstream regions	G	G (100%)	A (4%)*	A (12%)	G (100%)
23,727,756	Downstream regions	G	G (100%)	A (4%)*	A (16%)	G (100%)
23,727,735	Downstream regions	G	A (100%)	A (100%)	A (100%)	G (100%)
23,727,707	Downstream regions	C	C (100%)	T (12%)	C (100%)	C (100%)
23,727,697	Downstream regions	T	G (100%)	G (86%) A (14%)	G (92%)	G (100%)
23,727,695	Downstream regions	G	G (100%)	A (14%)	A (4%)*	G (100%)
23,727,628	Downstream regions	C	C (100%)	T (4%)*	T (11%)	C (100%)

n.a.: not available; the variant frequency is referred to the percentage of the highlighted base in the sequenced ancient hominine genome, with\* frequency≤10% and \*\* counts<10. In light orange are underlined the variants fixed at 100% in modern human compared to ancient hominines.