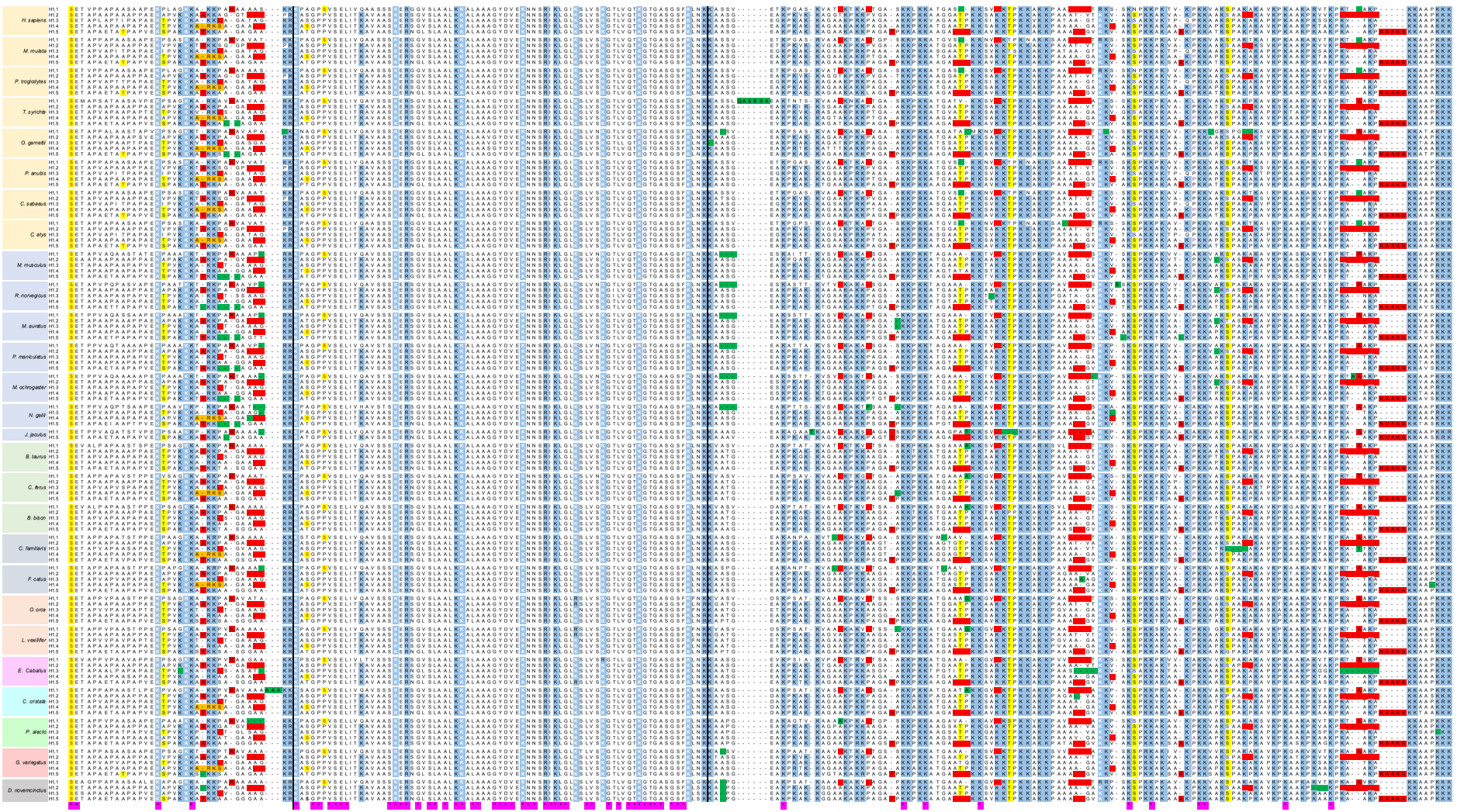

Figure S1. Multiple sequence alignment of histone H1.1-H1.5 subtypes. The 130 sequences are clustered by species. The limits of the domains are indicated by vertical lines. Insertion/deletions present in paralogous comparisons are highlighted in red; insertions/deletions present in orthologous comparisons are highlighted in green. The conserved positions of basic residues among paralogous sequences are highlighted in light-blue. In white, lysines post-translationally modified; in yellow, phosphorylated residues; in orange, the ARKS peptide, containing the methyl-phos switch that controls H1.4 interactions with the heterochromatin protein (HP1); asterisks mark conserved positions in the alignment.

Figure S2: Alignment of orthologous sequences of histone H1.1-H1.5 subtypes. The 130 sequences are clustered by subtype. The limits of the conserved and isolated by vertical lines. Insertions/deletions present in orthologous comparisons are highlighted in green. The conserved positions of basic residues among paralogous sequences are highlighted in light blue. In vertebrates, various post-translationally modified residues, in orange the ARKS peptide, containing the methyl-phos switch that controls H1.4 interaction with the heterochromatin protein (HP1), asterisks mark conserved positions in the alignment.

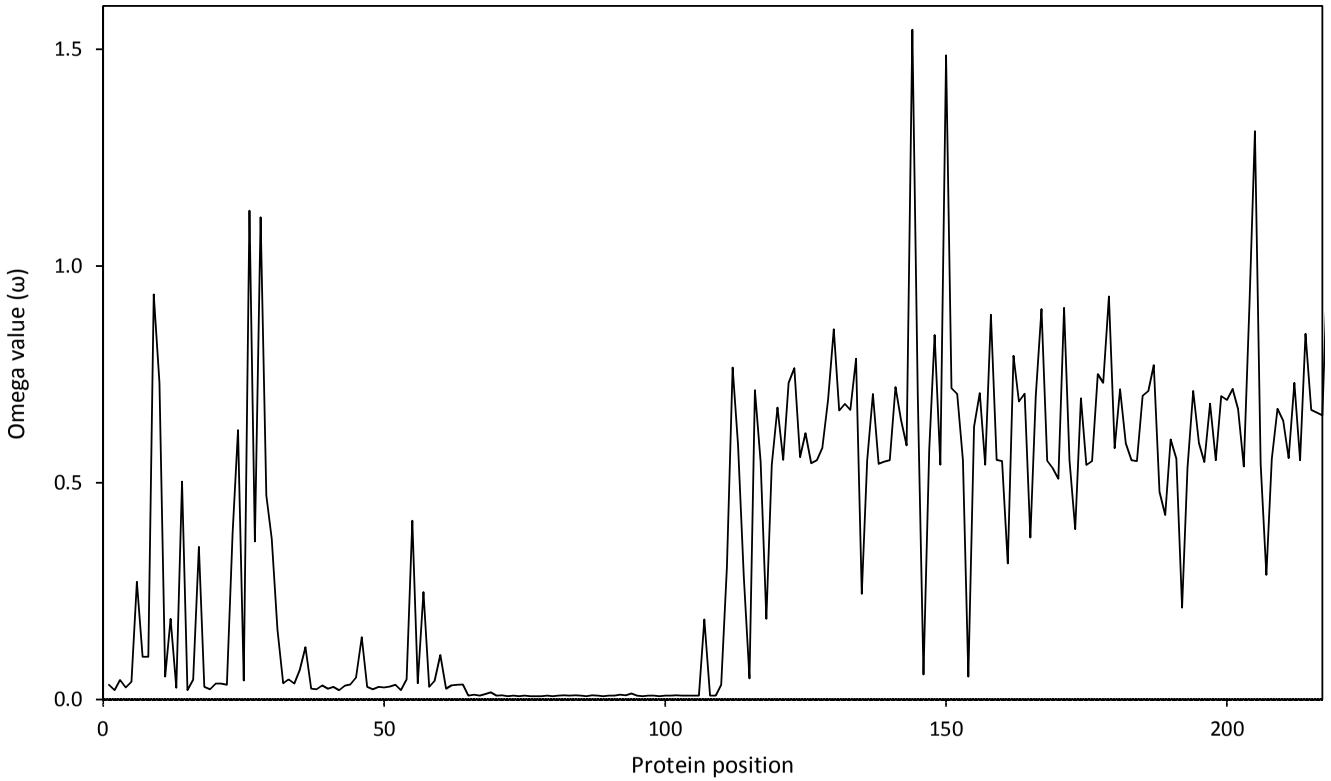

Figure S3. Representation of the ω values for each site along H1.3. The ω values of the individual residues were estimated with the accepted model of the M0-M3 pair for each of the three partitions.

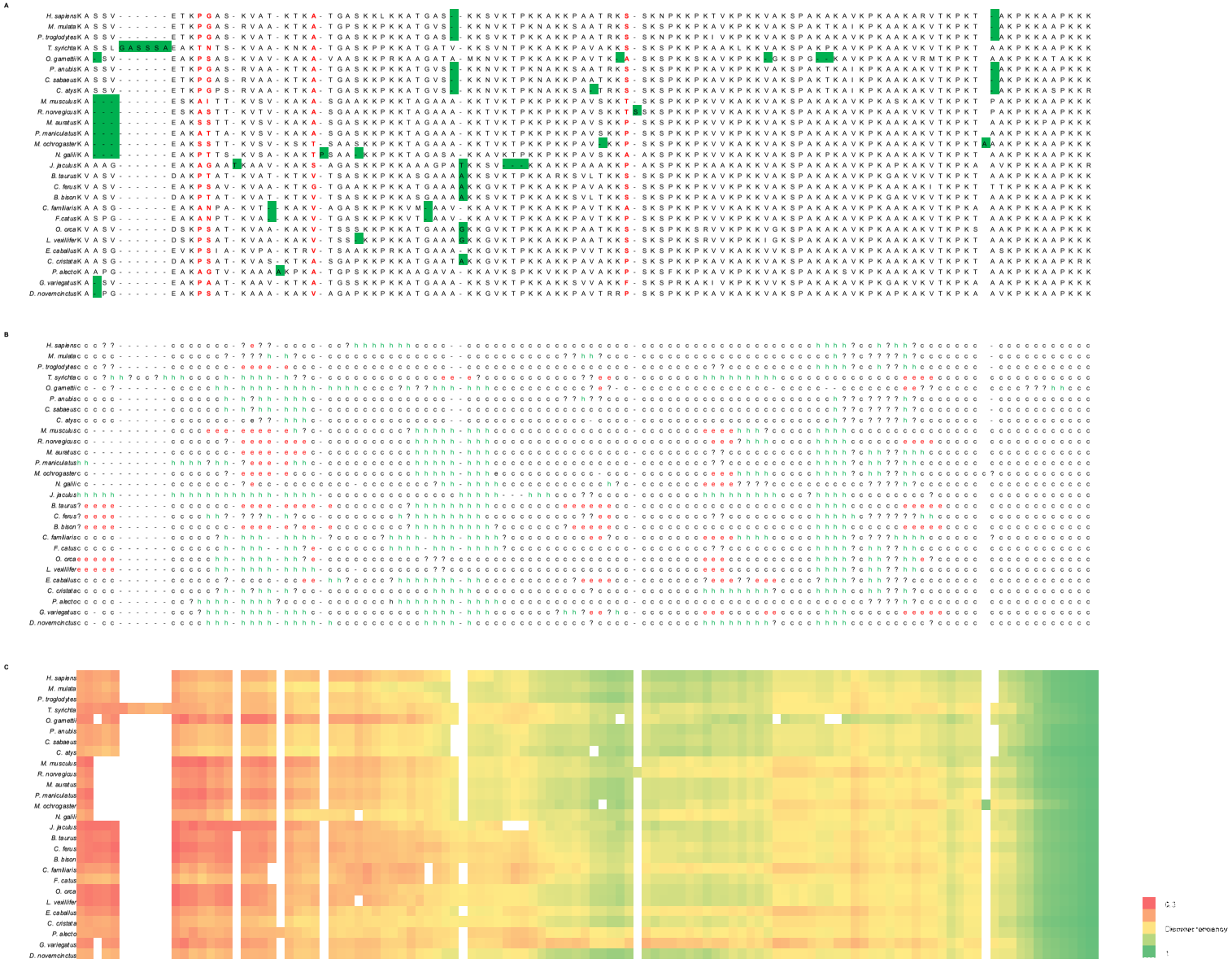

Figure S4. Positive selection in the CTD of H1.1. A, multiple sequence alignment of the 27 H1.1 sequences. In red, positively selected sites; in green, indels present in H1.1 sequences. B, consensus secondary structure prediction for each sequence. The analysis was performed at the Network Protein sequence analysis server available at http://npsa-pbil.ibcp.fr/. The different secondary structure motifs are labeled as follows: h, α-helix; e, extended strand; c, random coil; ?, ambiguous states; -, indel in the sequence alignment. C, heat map of disorder tendency by residue as predicted by IUPred.

Table S1. NCBI accession numbers of the sequences of the H1 subtypes

Order	Specie	Subtype	Accession number
Primates	*Homo sapiens*	1	X57130.1
		2	X57129.1
		3	M60747.1
		4	M60748.1
		5	M60747.1
	Macaca mulatta	1	NM_001193709.1
		2	XM_001084417.2
		3	NM_001193819.1
		4	XM_001086509.2
		5	NM_001194063.1
	Pan troglodytes	1	XM_527252.3
		2	XM_001172525.4
		3	XM_001172808.2
		4	XM_527259.5
		5	XM_009450699.1
	Tarsius syrichta	1	XM_008073507.1
		2	XM_008073501.1
		3	XM_008057602.1
		4	XM_008057598.1
		5	XM_008072231.1
	Otolemur garnettii	1	XM_003788783.1
		2	XM_003788780.1
		3	XM_003788782.2
		4	XM_003788781.2
		5	XM_003801852.1
	Papio anubis	1	XM_003897152.2
		2	XM_003897161.2
		3	XM_003897183.2
		4	XM_003897174.2
		5	XM_003897220.2
	Chlorocebus sabaeus	1	XM_007973498.1
		2	XM_007973490.1
		3	XM_007973474.1
		4	XM_007973482.1
		5	XM_007973405.1
	Cerocebus atys	1	XM_012031534.1
		2	XM_012031541.1
		3	XM_012031557.1
		4	XM_012031550.1
		5	XM_012076101.1
Rodentia	*Mus muculus*	1	L26164.1
		2	z46227
		3	Z381281.1
		4	L26163.1
		5	Z46227.1
	Rattus norvegicus	1	NM_001106113.1
		2	XM_001071565.2
		3	M31229.1
		4	X67320.1
		5	NM_001109417.1
	Mesocricetus auratus	1	XM_005066469.2
		2	XM_005066464.2
		3	XM_013110574.1
		4	XM_005066470.2
		5	XM_005086676.1
	Peromyscus maniculatus	1	XM_006993141.1
		2	XM_006993149.1
		3	XM_006993163.1
		4	XM_006993156.1
		5	XM_006988862.1
	Microtus ochrogaster	1	XM_005354954.2
		2	XM_005354949.2
		3	XM_005354944.2
		4	XM_005354943.2
		5	XM_005369908.2
	Nannospalax galili	1	XM_008831889.1
		3	XM_008831856.1
		4	XM_008831872.1
		5	XM_008826638.1
	Jaculus jaculus	1	XM_004670840.1
		5	XM_004670829.1
Artiodactyla	*Bos taurus*	1	XM_001252377.3
		2	NM_001083425
		3	NM_001101066.1
		4	XM_870179.5
		5	XM_010818459.1
	Camelus ferus	1	XM_006182196.1
		2	XM_006182177.1
		3	XM_006182164.1
		4	XM_006182173.1
		5	XM_006194163.1
	Bison bison	1	XM_010843447.1
		2	XM_010843443.1
		3	XM_010843422.1
		4	XM_010843433.1
		5	XM_010834036.1
Carnivora	*Canis lupus familiaris*	1	XM_545380.2
		2	XM_005640102.1
		3	XM_005640112.1
		4	XM_545391.2
		5	XM_545427.4
	Felis catus	1	XM_006931397.2
		2	XM_003985723.3
		3	XM_003985709.3
		4	XM_003985718.3
		5	XM_003985684.1
Cetacea	*Orcinus Orca*	1	XM_004273503.1
		2	XM_004273490.2
		3	XM_004273472.2
		4	XM_004273489.2
		5	XM_012539194.1
	Lipotes vexillifer	1	XM_007471242.1
		2	XM_007471233.1
		3	XM_007471246.1
		4	XM_007471225.1
		5	XM_007449250.1
Perissodactyla	*Equus caballus*	1	XM_001496648.1
		2	XM_005603619.1
		3	XM_005603627.1
		4	XM_001916031.3
		5	XM_001505032.2
Soricomorpha	*Condylura cristata*	1	XM_004694872.1
		2	XM_004694866.1
		3	XM_004694854.1
		4	XM_004694861.2
		5	XM_004695423.1
Chiroptera	*Pteropus alecto*	1	XM_006923490.2
		2	XM_006923482.1
		3	XM_006923470.1
		4	XM_006923477.1
		5	XM_006923450.1
Dermoptera	*Galeopterus variegatus*	1	XM_008587631.1
		2	XM_008587623.1
		3	XM_008567844.1
		4	XM_008587616.1
		5	XM_008581933.1
Cingulata	*Dasypus novemcinctus*	1	XM_004463490.1
		2	XM_004463497.1
		3	XM_004463518.2
		5	XM_004481848.2

Table S2. Assessment of the multiple alignment quality

Multiple alignment	SP-score		
	NAFTT	PROBCONS	MUSCLE
ClustalW alignment (130 H1 sequences)	0.945	0.950	0.948
Curated alignment (130 H1 sequences)	0.951	0.956	0.954
Peptidase M13 (reference alignment)	0.879	0.885	0.882
SH2 (reference alignment)	0.895	0.902	0.741

The scores were calculated at http://www.mtt.fi/AlignmentQuality/ as described by Ahola et al., 2008. The scores of two reference sequence alignments are shown for additional comparison.

Table S3. Nucleotide substitution models used for phylogenetic tree reconstruction

Analysis	Dataset	Number of sequences	Number of parameters	Base frequency				I	α	Model Selected
				A	C	G	T			
Branch-analysis	H1.1-H1.5	130	261	0.200	0.300	0.300	0.200	0.26	0.87	T92+G+I
Site-specific by partitions	H1.1.1	27	60	0.16828	0.33586	0.3277	0.16816	0	0.679	GTR+G
	H1.1.2	27	60	0.26922	0.22752	0.34046	0.1628	0	0.346	GTR+G
	H1.1.3	27	60	0.33274	0.26045	0.28563	0.12118	0	0.682	GTR+G
	H1.2.1	25	56	0.17403	0.32254	0.34353	0.1599	0	0.264	GTR+G
	H1.2.2	25	56	0.26901	0.24393	0.31572	0.17133	0	0.328	GTR+G
	H1.2.3	25	56	0.34803	0.28556	0.3018	0.3018	0	0.52	GTR+G
	H1.3.1	26	58	0.20155	0.28513	0.34417	0.16915	0	0.363	GTR+G
	H1.3.2	26	58	0.29179	0.22876	0.30547	0.17397	0	0.276	GTR+G
	H1.3.3	26	58	0.35821	0.26518	0.29305	0.08357	0	0.788	GTR+G
	H1.4.1	25	56	0.24629	0.29227	0.32805	0.1334	0	0.269	GTR+G
	H1.4.2	25	56	0.34132	0.29014	0.31105	0.05749	0	0.277	GTR+G
	H1.5.1	27	60	0.19935	0.3046	0.3353	0.16075	0	0.277	GTR+G
	H1.5.2	27	60	0.28251	0.24912	0.31444	0.15394	0	0.339	GTR+G
	H1.5.3	27	60	0.33394	0.25563	0.32202	0.08841	0	0.333	GTR+G
Site-specific by domains	H1.1 NTD	27	60	0.24021	0.34748	0.28003	0.13228	0.0	1176	GTR+G
	H1.1 GD	27	61	0.20819	0.28886	0.32826	0.17470	0.337	0.794	GTR+G+I
	H1.1 CTD	27	61	0.36162	0.26531	0.27593	0.09715	0.223	1444	GTR+G+I
	H1.2 NTD	25	57	0.18667	0.37750	0.33000	0.10583	0.400	0.916	GTR+G+I
	H1.2 GD	25	56	0.22123	0.29614	0.31982	0.16281	0.0	0.199	GTR+G
	H1.2 CTD	25	57	0.32870	0.28465	0.31813	0.06852	0.223	0.951	GTR+G+I
	H1.3 NTD	26	59	0.26433	0.29396	0.30214	0.13957	0.283	2651	GTR+G+I
	H1.3 GD	26	58	0.22318	0.30128	0.31579	0.15975	0.0	0.239	GTR+G
	H1.3 CTD	26	58	0.34112	0.28963	0.30730	0.06195	0.0	0.798	GTR+G
	H1.4 NTD	25	57	0.19983	0.39132	0.32666	0.08219	0.538	2311	GTR+G+I
	H1.4 GD	25	57	0.21772	0.30684	0.31982	0.15561	0.595	3502	GTR+G+I
	H1.4 CTD	25	56	0.36693	0.29051	0.30810	0.03445	0.0	0.344	GTR+G
	H1.5 NTD	27	61	0.25072	0.32681	0.32174	0.10072	0.471	1800	GTR+G+I
	H1.5 GD	27	61	0.22466	0.29711	0.31189	0.16634	0.588	3821	GTR+G+I
	H1.5 CTD	27	61	0.34656	0.28108	0.30829	0.06407	0.280	0.597	GTR+G+I

The best nucleotide substitution model for each alignment was calculated with jModelTest using maximum likelihood methods (Posada, 2008). I, proportion of invariable sites; α, gamma shape. The H1.1-H1.5 dataset includes the 130 sequences analyzed in this study. Phylogenetic trees were also reconstructed when the sequences were analyzed by partitions, taking into account the recombination breakpoints and when the sequences were analyzed by structural domains: N-terminal domain (NTD), globular domain (GD) and C-terminal domain (CTD).

Table S4. Frequency of indels in the 130 protein sequences of the H1.1-H1.5 subtypes

Subtype	H1.1					H1.2					H1.3					H1.4					H1.5				
Species	**Residues**	**PI**	**FreqPI**	**OI**	**FreqOI**	**Residues**	**PI**	**FreqPI**	**OI**	**FreqOI**	**Residues**	**PI**	**FreqPI**	**OI**	**FreqOI**	**Residues**	**PI**	**FreqPI**	**OI**	**FreqOI**	**Residues**	**PI**	**FreqPI**	**OI**	**FreqOI**
M. musculus	212	7	0.03302	2	0.00943	211	4	0.01896	1	0.00474	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	222	6	0.02703	1	0.00450
R. norvegicus	213	7	0.03286	3	0.01408	211	4	0.01896	1	0.00474	220	1	0.00455	1	0.00455	218	2	0.00917	0	0.00000	221	5	0.02262	2	0.00905
B. taurus	217	6	0.02765	1	0.00461	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
M. mulata	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
H. sapiens	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
T. syrichta	222	7	0.03153	1	0.00450	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	223	6	0.02691	1	0.00448
C. cristata	220	6	0.02727	2	0.00909	211	4	0.01896	1	0.00474	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
C. familiaris	214	7	0.03271	2	0.00935	212	4	0.01887	0	0.00000	217	1	0.00461	2	0.00922	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
P. alecto	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	219	1	0.00457	1	0.00457	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
O. garnettii	210	6	0.02857	5	0.02381	212	4	0.01887	0	0.00000	219	1	0.00457	1	0.00457	218	2	0.00917	0	0.00000	223	6	0.02691	1	0.00448
C. equus	216	7	0.03241	0	0.00000	212	4	0.01887	0	0.00000	210	1	0.00476	4	0.01905	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
C. felis	213	7	0.03286	3	0.01408	212	4	0.01887	0	0.00000	221	1	0.00452	1	0.00452	217	2	0.00922	1	0.00461	225	6	0.02667	0	0.00000
G. variegatus	215	7	0.03256	1	0.00465	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	224	5	0.02232	1	0.00446
P. troglodytes	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
C. ferus	217	6	0.02765	1	0.00461	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	217	2	0.00922	1	0.00461	225	6	0.02667	0	0.00000
B. bison	217	6	0.02765	1	0.00461	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
P. anubis	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
C. sabaeus	214	6	0.02804	2	0.00935	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
C. atys	213	6	0.02817	3	0.01408	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
M. auratus	212	7	0.03302	2	0.00943	210	4	0.01905	2	0.00952	219	1	0.00457	1	0.00457	218	2	0.00917	0	0.00000	220	5	0.02273	3	0.01364
P. maniculatus	212	7	0.03302	2	0.00943	211	4	0.01896	1	0.00474	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	1	0.00444
O. orca	217	6	0.02765	1	0.00461	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
L. vexillifer	216	6	0.02778	2	0.00926	212	4	0.01887	0	0.00000	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	225	6	0.02667	0	0.00000
M. ochrogaster	213	7	0.03286	3	0.01408	211	4	0.01896	1	0.00474	220	1	0.00455	0	0.00000	218	2	0.00917	0	0.00000	222	6	0.02703	1	0.00450
D. novemcinctus	215	7	0.03256	1	0.00465	207	3	0.01449	3	0.01449	219	1	0.00457	1	0.00457						224	6	0.02679	1	0.00446
N. galili	211	6	0.02844	4	0.01896						218	1	0.00459	2	0.00917	217	2	0.00922	1	0.00461	222	6	0.02703	1	0.00450
J. jaculus	214	5	0.02336	4	0.01869																224	6	0.02679	1	0.00446
		average	**0.02970**		**0.00971**		average	**0.01872**		**0.00191**		average	**0.00456**		**0.00249**		average	**0.00918**		**0.00055**		average	**0.02628**		**0.00233**
		P-value < 0.0001	***				P-value< 0.0001	***				P-value< 0.001	**				P-value< 0.0001	***			P-value< 0.0001	***		

The indels were counted from the global H1.1-H1.5 alignment. Indels present only in paralog comparisons are referred to as paralog indels (PI).Indels present only in ortholog comparisons are referred to as ortholog indels (OI). All the indels were counted only once as explained in the Materials and Method section. The frequency was calculated as the total number of each type of indel present in each protein sequence divided by the number of residues. p-values were calculated with a Mann-Whitney U-test and correspond to the probability that the ortholog and paralog indel frequencies are the same for each subtype. **, very significant, *** extremely significant.

Table S5. Positive selection detection in mammalian H1.1-H1.5 gene-family using branch-site methods

Software	Foreground branches	Parameter estimates	lnL	LRT	p-value	Positively selected sites (PSS)[a]
PAML	H1.1	MA1:p_0= 0.77453, p_1=0.09771, p_{2a}=0.11345 p_{2b}=0.01431 FG: ω_0= 0.05829, ω_1=1.0, ω_2=1.0 MA:p_0= 0.79614, p_1=0.1000, p_{2a}=0.09227 p_{2b}=0.01159 FG: ω_0= 0.05889, ω_1=1.0, ω_2=16.57223	-22758 -22746	23.39	0.00000132	**20**(0.99677), **39**(0.99917), **51**(0.99090) **125** (0.99339) **136**(0.98696), **178**(0.99759)
	H1.2	MA1: p_0= 0.28625, p_1=0.05408, p_{2a}=0.55484 p_{2b}=0.10482 FG: ω_0= 0.09829, ω_1=1.0, ω_2=1.0 MA: p_0= 0.81330, p_1=0.15874, p_{2a}=0.02872 p_{2b}=0.00539 FG: ω_0= 0.09829, ω_1=1.0, ω_2=999.0	-22537 -22528	17.62	0.00002697	none
	H1.3	MA1: p_0= 0.63170, p_1=0.12550, p_{2a}=0.20255 p_{2b}=0.04024 FG: ω_0= 0.09799, ω_1=1.0, ω_2=1.0 MA: p_0= 0.82179, p_1=0.16175, p_{2a}=0.01375 p_{2b}=0.00271 FG: ω_0= 0.09795, ω_1=1.0, ω_2=516.7444	-22542 -22537	9.94	0.00161726	none
	H1.4	MA1: p_0= 0.80905, p_1=0.15974, p_{2a}=0.02606 p_{2b}=0.00515 FG: ω_0= 0.09862, ω_1=1.0, ω_2=1.0 MA: p_0= 0.83357, p_1=0.15849, p_{2a}=0.00667 p_{2b}=0.00127 FG: ω_0= 0.09929, ω_1=1.0, ω_2=77.98072	-22544 -22542	3.93	0.04743194	none
	H1.5	MA1: p_0= 0.78606, p_1=0.15558, p_{2a}=0.04871 p_{2b}=0.00964 FG: ω_0= 0.09839, ω_1=1.0, ω_2=1.0 MA: p_0= 0.80051, p_1=0.15848, p_{2a}=0.03424 p_{2b}=0.00678 FG: ω_0= 0.09838, ω_1=1.0, ω_2=1.74071	-22544 -22544	0.032	0.85802766	N.A
BUSTED	H1.1	Null: BG: ω1=0.0435 (97%), ω2=0.684 (2.5%), ω3=14.6 (0.31%) FG: ω_1=0.00 (74%), ω_2=0.919 (0.0%), ω_3=1.00 (26%) Sel: BG: ω_1=0.0429 (97%), ω_2=0.742 (2.6%), ω_3=15.2 (0.28%) FG: ω_1=0.0121 (81%), ω_2=0.919 (0.0%), ω_3=158 (12%)	-16255 -16246	17.56	0.000152997	**20(0.0006), 39(0.002),** 41(0.04)**, 51(0.003), 125(0.02),** 131(0.01)**, 136(0.003), 178(0.001),** 214(0.02)
	H1.2	Null: BG: ω_1=0.0570 (97%), ω_2=0.691 (2.8%), ω_3=11.0 (0.48%) FG: ω_1=1.00 (48%), 0.888 (0.0%), 1.00 (52%) Sel: BG: ω_1=0.0569 (97%), ω_2=0.750 (2.8%), ω_3=424 (2.5%) FG: ω_1=0.104 (90%), ω_2=0.998 (7.4%), ω_3=27.1 (1.7%)	-22292 -22285	12.62	0.001816797	-
	H1.3	Null: BG: ω_1=0.0558 (96%), ω_2=0.657 (3.3%), ω_3=12.4 (0.45%) FG: ω_1=0.0421 (0.0%), ω_2=0.80 (81%), ω_3=1.00 (19%) Sel: BG: ω_1=0.0485 (93%), ω_2=0.479 (6.2%), ω_3=12.9 (0.44%) FG: ω_1=0.159 (87%), ω_2=0.215 (12%), ω_3=10000 (1.3%)	-22290 -22287	7.14	0.028128288	-
	H1.4	Null: BG: ω_1=0.0576 (97%), ω_2=0.737 (2.6%), ω_3=12.4 (0.45%) FG: ω_1=0.00 (91%), 0.002 (1.0%), 1.00 (8.2%) Sel: BG: ω_1=0.0534 (95%), ω_2=0.586 (4.2%), ω_3=12.5 (0.45%) FG: ω_1=0.00 (93%), ω_2=0.002 (5.1%), ω_3=27.1 (1.7%)	-22291 -22288	6.12	0.046669824	-
	H1.5	Null: BG: ω_1=0.0576 (97%), ω_2=0.772 (2.5%), ω_3=12.9 (0.43%) FG: ω_1=0.00 (34%), ω_2=0.905 (0.0%), ω_3=1.00 (66%) Sel: BG: ω_1=0.0556 (96%), ω_2=0.659 (3.3%), ω_3=13.3 (0.43%) FG: ω_1=0.230 (84%), ω_2=0.774 (12%), ω_3=925 (4.0%)	-22287 -22283	8.08	0.0174845489	-

PAML analyses were performed using a maximum likelihood phylogenetic tree (Figure 2). Branches labeled in Figure 3 were used as foreground branches. The branch-site model A (MA), allowing sites with ω>1 was compared with a null model that does not allowed for positive selection, using a likelihood ratio test (LRT). The proportion of sites in each category and the ω-values for the foreground branch are shown. BUSTED was used as implemented at datamonkey.org/busted using the paralog alignment. The model allowing positive selection (Sel) was compared with the Null model, using a LRT test. [a] in parenthesis the Bayes Empirical Bayes (BEB) posterior probabilities estimated by PAML or the p-values estimated by BUSTED are shown. PSS are reported in the selected branch (p-values < 0.001 in both analyses). Only those sites with a BEB posterior probability > 0.95 for PAML and a p-value < 0.05 for BUSTED are shown. In bold, sites that are confirmed by the two methods. The positions of the positively selected sites are referred to the multiple sequence alignment in Figure 1. N.A not allowed, as the null model was accepted. -, not calculated.

Table S6. Positive selection analysis with the PAML site-models of mammalian H1.1-H1.5

Subtype	Partition	Model with positive selection			Null model			LRT	P-value	Positively selected sites
		Model	lnL	Parameters	Model	lnL	Parameters			
H1.1	1-52	M3	-1769.39	p_0= 0.36490; p_1= 0.30553; p_2= 0.32957 ω_0=0.02814; ω_1= 0.34716; ω_2= 0.34716	M0	-1787.88	ω= 0.20499	36.98	**1.82E-07**	none
		M2	-1786.32	p_0= 0.90476; p_1=0.06605; p_2=0.02919 ω_0=0.18251; ω_1= 1.00000; ω_2= 1.00000	M1	-1786.32	p_0= 0.90476; p_1= 0.09524 ω_0= 0.18251; ω_1=1.00000	0	1	N.A
		M8	-1772.02	p0 = 0.99999 p = 0.88147 q = 2.86509 (p1 = 0.00001) ω= 2.92008	M7	-1772.02	p = 0.88148 q = 2.86511	-0.00125	1	N.A
	53-115	M3	-960.94	p_0= 0.39047; p_1= 0.48566; p_2=0.12387 ω_0=0.01365; ω_1= 0.01365; ω_2= 0.14633	M0	-965.22	ω= 0.02709	8.54	**0.073547**	N.A
		M2	-965.22	p_0= 1.00000; p_1=0.00000; p_2=0.00000 ω_0= 0.02709; ω_1= 1.00000; ω_2= 1.00000	M1	-965.22	p_0= 0.99999; p_1= 0.00001 ω_0= 0.02709; ω_1=1.00000	0.00096	0.99952	N.A
		M8	-961.95	p0 = 0.99999 p = 0.88147 q = 2.86509 (p1 = 0.00001) ω= 2.92008	M7	-961.95	p = 0.88148 q = 2.86511	-0.00105	1	N.A
	116-231	M3	-3106.35	p_0= 0.24277; p_1= 0.62201; p_2= 0.13521 ω_0=0.10262; ω_1=0.53889; ω_2= 1.66986	M0	-3134.12	ω= 0.53147	55.54	**2.51E-11**	121, 124, 125**, 127, 131, 136*, 153, 157, 187*
		M2	-3109.03	p_0= 0.60737; p_1= 0.34786; p_2= 0.04477 ω_0=0.25915; ω_1= 1.00000; ω_2= 2.21518	M1	-3110.55	p_0= 0.59453; p_1= 0.40547 ω_0= 0.24403; ω_1=1.00000	3.04	0.05515	N.A
		M8	-3106.73	p0 = 0.90339 p = 1.26847 q = 1.52416 (p1 = 0.09661) ω= 1.83443	M7	-3110.72	p = 0.81967 q = 0.70183	8.00	0.01834	124, 125*, 127, 136, 157, 187
H1.2	1-48	M3	-939.85	p_0= 0.30837; p_1= 0.58857; p_2= 0.10306 ω_0= 0.02109; ω_1= 0.02109; ω_2= 0.49211	M0	-954.76	ω= 0.05996	29.82	**5.32E-06**	N.A
		M2	-942.26	p_0= 0.92522; p_1= 0.07478; p_2= 0.00000 ω_0= 0.02777; ω_1= 1.00000; ω_2= 1.00000	M1	-942.26	p_0= 0.92522; p_1= 0.07478 ω_0= 0.02777; ω_1=1.00000	0	1	N.A
		M8	-941.15	p_0 = 0.99999 p = 0.18222 q = 2.08534 (p_1= 0.00001) ω= 1.67482	M7	-941.15	p = 0.18222 q =2.08538	-0.00075	1	N.A
	49-121	M3	-1181.56	p_0= 0.36682; p_1= 0.50335; p_2= 0.12982 ω_0= 0.00767; ω_1= 0.00767; ω_2= 0.29038	M0	-1196.48	ω= 0.03047	29.85	**5.25E-06**	none
		M2	-1187.34	p_0= 0.95000; p_1= 0.04864; p_2= 0.00136 ω_0= 0.01801; ω_1= 1.00000; ω_2= 1.00000	M1	-1187.34	p_0= 0.95000; p_1= 0.05000 ω_0= 0.01801; ω_1= 1.00000	0	1	N.A
		M8	-1181.99	p0 = 0.99999 p = 0.11736 q = 2.24592 (p1 = 0.00001) ω= 1.00000	M7	-1181.99	p = 0.11736 q = 2.24568	-0.00061	1	N.A
	122-213	M3	-1812.17	p_0= 0.29607; p_1= 0.64760; p_2= 0.05633 ω_0= 0.12816; ω_1= 0.43868; ω_2= 1.46988	M0	-1815.06	ω= 0.36899	5.79	0.215763	N.A
		M2	-1812.62	p_0= 0.85508; p_1= 0.10284; p_2= 0.04207 ω_0= 0.28915; ω_1= 1.00000; ω_2= 1.24249	M1	-1812.63	p_0= 0.83565; p_1= 0.16435 ω_0= 0.28239; ω_1=1.00000	0.01	0.99369	N.A
		M8	-1812.28	p0 = 0.94660 p = 2.54204 q = 4.79463 (p1 = 0.05340) ω= 1.44601	M7	-1812.58	p = 1.51608 q = 2.31640	0.59	0.7427	N.A
H1.3	1-64	M3	-1427.63	p_0= 0.74199; p_1= 0.19879; p_2= 0.05922 ω_0= 0.02175; ω_1= 0.34467; ω_2= 1.13951	M0	-1469.13	ω= 0.12383	83.00	**4.02E-17**	9, 28*, 31*
		M2	-1431.93	p_0= 0.83153; p_1= 0.11816; p_2= 0.05032 ω_0= 0.03877; ω_1= 1.00000; ω_2= 1.00000	M1	-1431.93	p_0= 0.83152; p_1= 0.16848 ω_0= 0.03877; ω_1=1.00000	0	1	N.A
		M8	-1428.36	p_0 = 0.97219 p = 0.19379 q = 1.24876 (p_1= 0.02781) ω= 1.25867	M7	-1428.77	p = 0.18712 q = 1.02115	0.82	0.663915	N.A
	65-110	M3	-630.74	p_0= 0.93972; p_1= 0.03595; p_2= 0.02433 ω_0= 0.00839; ω_1= 0.00840; ω_2= 0.22890	M0	-631.35	ω= 0.01037	1.24	0.871551	N.A
		M2	-631.35	p_0= 1.00000; p_1= 0.00000; p_2= 0.00000 ω_0= 0.01037; ω_1= 1.00000; ω_2= 1.00000	M1	-631.36	p_0= 0.99999; p_1= 0.00001 ω_0= 0.01037; ω_1= 1.00000	0.000358	0.999821	N.A
		M8	-631.26	p0 = 0.99999 p = 0.57997 q = 43.13267 (p1 = 0.00001) ω= 86.80246	M7	-631.19	p = 1.13586 q = 99.00000	-0.15	1	N.A
	111-222	M3	-2766.21	p_0= 0.16848; p_1= 0.76043; p_2= 0.07109 ω_0= 0.04772; ω_1= 0.64346; ω_2=1.75678	M0	-2779.74	ω= 0.53524	27.07	**1.93E-05**	151, 157, 214
		M2	-2768.86	p_0= 0.35701; p_1= 0.51658; p_2= 0.12642 ω_0= 0.15071; ω_1= 1.00000; ω_2= 1.24249	M1	-2768.86	p_0= 0.35701; p_1= 0.64299 ω_0=0.15071; ω_1=1.00000	0	1	N.A
		M8	-2767.12	p0 = 0.97957 p = 0.76486 q = 0.50674 (p1 = 0.02043) ω= 1.90160	M7	-2767.18	p = 0.71583 q = 0.43860	0.13	0.936687	N.A
H1.4	1-140	M3	-2305.78	p_0= 00.22457; p_1= 0.56611; p_2= 0.20932 ω_0= 0.00000; ω_1= 0.01017; ω_2= 0.20575	M0	-2318.62	ω= 0.03998	25.67	**3.68E-05**	none
		M2	-2312.19	p_0= 0.96144; p_1= 0.03276; p_2= 0.00579 ω_0= 0.02756; ω_1= 1.00000; ω_2= 1.00000	M1	-2312.19	p_0= 0.96144; p_1= 0.03856 ω_0= 0.02756; ω_1=1.00000	0	1	N.A
		M8	-2305.67	p_0 = 0.99999 p = 0.18647 q = 3.27993 (p_1= 0.00001) ω= 1.35165	M7	-2305.67	p = 0.18647 q = 3.27981	-0.00122	1	N.A
	140-218	M3	-1190.20	p_0= 0.56370; p_1= 0.03958; p_2= 0.39672 ω_0= 0.10563; ω_1= 0.10563; ω_2= 1.24083	M0	-1196.81	ω= 0.53596	13.21	**0.010287**	149**,151, 152**,154, 157**, 160, 169, 172, 188, 191**, 194, 201, 202, 203, 209, 213**, 214, 230, 232
		M2	-1190.20	p_0= 0.60328; p_1= 0.00000; p_2= 0.39672 ω_0= 0.10563; ω_1= 1.00000; ω_2= 1.24082	M1	-1190.42	p_0= 0.49929; p_1= 0.50071 ω_0= 0.05472; ω_1= 1.00000	0.43	0.806122	N.A
		M8	-1190.21	p0 =0.60429 p = 11.92795 q = 99.00000 (p1 = 0.39571) ω= 1.24171	M7	-1190.50	p = 0.02748 q = 0.02359	0.59	0.7436	N.A
H1.5	1-53	M3	-1202.65	p_0= 0.06362; p_1= 0.76578; p_2= 0.17060 ω_0= 0.01486; ω_1= 0.01486; ω_2= 0.32264	M0	-1218.63	ω= 0.06133	31.96	**1.95E-06**	none
		M2	-1212.51	p_0= 0.88977; p_1= 0.10322; p_2=0.00701 ω_0= 0.02772; ω_1= 1.00000; ω_2= 1.00000	M1	-1212.51	p_0= 0.88977; p_1= 0.11023 ω_0= 0.02772; ω_1=1.00000	0	1	N.A
		M8	-1203.62	p_0 = 0.99999 p = 0.20277 q = 2.69826 (p_1= 0.00001) ω= 1.00000	M7	-1203.61	p = 0.20277 q = 2.69821	-0.00068	1	N.A
	54-133	M3	-1391.30	p_0= 0.47566; p_1= 0.42878; p_2= 0.09556 ω_0= 0.00000; ω_1= 0.07160; ω_2= 0.27972	M0	-1399.42	ω= 0.04856	16.24	**0.002711**	none
		M2	-1396.94	p_0= 0.96937; p_1= 0.02915; p_2= 0.00147 ω_0= 0.03950; ω_1= 1.00000; ω_2= 1.00000	M1	-1396.94	p_0= 0.96937; p_1= 0.03063 ω_0= 0.03950; ω_1= 1.00000	0	1	N.A
		M8	-1391.40	p0 = 0.99999 p = 0.35114 q = 5.45228 (p1 = 0.00001) ω= 1.45537	M7	-1391.40	p = 0.35114 q = 5.45229	0	1	N.A
	133-225	M3	-2067.75	p_0= 0.27086; p_1= 0.58430; p_2= 0.14485 ω_0= 0.01022; ω_1= 0.25335; ω_2= 1.14689	M0	-2079.16	ω= 0.27133	22.83	**0.000137**	149*, 151, 186, 187*, 214, 218
		M2	-2068.83	p_0= 0.80304; p_1= 0.12666; p_2= 0.07031 ω_0= 0.14728; ω_1= 1.00000; ω_2= 1.00000	M1	-2068.83	p_0= 0.80303; p_1= 0.19697 ω_0= 0.14728; ω_1=1.00000	0	1	N.A
		M8	-2068.08	p0 = 0.87268 p = 0.96016 q = 3.87603 (p1 = 0.12732) ω= 1.13818	M7	-2068.44	p = 0.48386 q = 1.10061	0.72	0.6964	N.A

Considering the recombination breakpoints reported in the GARD analysis, the sequences were partitioned before running Codeml and a maximum likelihood phylogenetic tree was reconstructed for each partition with PhyML, using the best fitted nucleotide substitution model (Table S2). The model pairs compared in each partition were M0-M3; M1-M2 and M7-M8. lnL, log likelihood; LRT, likelihood ratio test. In bold, p-values > 0.05, that allowed to accept the model with positive selection. Sites with posterior probabiliy >0.5 are listed; *, posterior probability > 0.9; **, posterior probabily > 0.95. The positions of the positively selected sites are referred to the multiple sequence alignment in Figure 1. N.A, not allowed, as the null model was accepted.

Table S7. Analysis of variance (ANOVA) of the averaged omega ratios by domains.

Subtype	Parameters	NTD	GD	CTD	Source of variation	Degrees of freedom	Sum of squares	Mean square	F-value	p-value	Tukey HSD test	
											Compared means	Significance
	Mean	0.2907	0.0537	0.587	Between domains	2	12.7511	6.3755			NTD vs GD	p< 0.01
H1.1	Variance	0.0194	0.0044	0.1169	Within domains	214	13.2683	0.0620	102.83	<0.0001	NTD vs CTD	p< 0.01
											GD vs CTD	p< 0.01
	Mean	0.0943	0.0239	0.362	Between domains	2	5.4445	2.7222			NTD vs GD	p< 0.01
H1.2	Variance	0.0135	0.0012	0.018	Within domains	209	2.3335	0.0112	243.81	<0.0001	NTD vs CTD	p< 0.01
											GD vs CTD	p< 0.01
	Mean	0.2319	0.0334	0.6180	Between domains	2	16.0360	8.018			NTD vs GD	p< 0.01
H1.3	Variance	0.0607	0.0043	0.0383	Within domains	217	6.4784	0.0298	268.57	<0.0001	NTD vs CTD	p< 0.01
											GD vs CTD	p< 0.01
	Mean	0.0552	0.0274	0.4062	Between domains	2	7.5035	3.7518			NTD vs GD	nonsignificant
H1.4	Variance	0.0050	0.0007	0.0924	Within domains	215	10.2864	0.0478	78.42	<0.0001	NTD vs CTD	p< 0.01
											GD vs CTD	p< 0.01
	Mean	0.0801	0.0431	0.2641	Between domains	2	2.4959	1.2479			NTD vs GD	nonsignificant
H1.5	Variance	0.0102	0.0027	0.0306	Within domains	222	3.9999	0.018	69.26	<0.0001	NTD vs CTD	p< 0.01
											GD vs CTD	p< 0.01

The omega ratios per residue resultant of the accepted model from the pair M7-M8 were averaged by domains. The analysis of variance was performed at http://vassarstats.net/. The Tukey HSD test was performed to do a pairwise comparison of the means by domain

Table S8. Positive selection analysis with PAML site-models of the individual domains of mammalian H1.1-H1.5

Subtype	Partition	Model with positive selection			Null model			LRT	P-value	Positively selected sites
		Model	lnL	Parameters	Model	lnL	Parameters			
H1.1	NTD	M3	-1394.70	p_0= 0.17839; p_1= 0.76263; p_2= 0.05898 ω_0=0.02746; ω_1= 0.51075; ω_2= 1.34945	M0	-1411.00	ω= 0.39503	32.27	**1.68E-06**	13
		M2	-1403.30	p_0= 0.53611; p_1=0.41159; p_2=0.05230 ω_0=0.21139; ω_1= 1.00000; ω_2= 1.00000	M1	-1403.30	p_0= 0.53611; p_1= 0.46389 ω_0= 0.21139; ω_1=1.00000	0	1	N.A
		M8	-1396.60	p0 = 0.99999 p = 0.83561 q = 0.90082 (p1 = 0.00001) ω= 1.00000	M7	-1397.00	p = 0.83561 q = 0.90080	-0.40	1	N.A
	GD	M3	-1320.22	p_0= 0.42141; p_1= 0.42457; p_2=0.15401 ω_0=0.01337; ω_1= 0.01337; ω_2= 0.12319	M0	-1325.00	ω= 0.02772	10.13	0.0383	N.A
		M2	-1325.28	p_0= 1.00000; p_1=0.00000; p_2=0.00000 ω_0= 0.02772; ω_1= 1.00000; ω_2= 1.00000	M1	-1325.04	p_0= 0.99999; p_1= 0.00001 ω_0= 0.02772; ω_1=1.00000	0	0.9994	N.A
		M8	-961.95	p0 = 0.99999 p = 0.55239 q = 17.00464 (p1 = 0.00001) ω= 1.00000	M7	-1321.00	p = 0.55239 q = 17.00463	0	1	N.A
	CTD	M3	-3126.54	p_0= 0.25601; p_1= 0.61834; p_2= 0.12565 ω_0=0.10317; ω_1=0.58190; ω_2= 1.75727	M0	-3155.00	ω= 0.55344	57.25	**1.10E-11**	124, 130, 131**, 133, 137, 143*, 159, 163, 188*
		M2	-3109.03	p_0= 0.60737; p_1= 0.34786; p_2= 0.04477 ω_0=0.25915; ω_1= 1.00000; ω_2= 2.21518	M1	-3131.55	p_0= 0.55409; p_1= 0.44591 ω_0= 0.23332; ω_1=1.00000	3.43	0.1798	N.A
		M8	-3106.73	p0 = 0.90881 p = 1.13701 q = 1.24024 (p1 = 0.09119) ω= 1.91401	M7	-3131.72	p = 0.76174 q = 0.60865	8.08	**0.01782**	130, 131*, 133, 143, 163, 188
H1.2	NTD	M3	-690.58	p_0= 0.32827; p_1= 0.53262; p_2= 0.13911 ω_0= 0.04347; ω_1= 0.04347; ω_2= 0.94823	M0	-705.87	ω= 0.13502	30.58	**3.73E-06**	none
		M2	-690.60	p_0= 0.86290; p_1= 0.07947; p_2= 0.05763 ω_0= 0.04402; ω_1= 1.00000; ω_2= 1.00000	M1	-690.60	p_0= 0.86290; p_1= 0.13710 ω_0= 0.04402; ω_1=1.00000	0	1	N.A
		M8	-692.53	p_0 = 0.99999 p = 0.20658 q = 0.99525 (p_1= 0.00001) ω= 2.02409	M7	-692.53	p = 0.20659 q =0.99525	0	1	N.A
	GD	M3	-1100.10	p_0= 0.27878; p_1= 0.42483; p_2= 0.29639 ω_0= 0.00000; ω_1= 0.00000; ω_2= 0.02825	M0	-1100.76	ω= 0.00776	1.32	0.857602	none
		M2	-1100.76	p_0= 1.00000; p_1= 0.00000; p_2= 0.00000 ω_0= 0.00776; ω_1= 1.00000; ω_2= 1.00000	M1	-1100.76	p_0= 0.99999; p_1= 0.00001 ω_0= 0.00776; ω_1= 1.00000	0	0.999261	N.A
		M8	-1100.13	p0 = 0.99999 p = 0.25028 q = 26.50296 (p1 = 0.00001) ω= 10.87047	M7	-1100.12	p = 0.25030 q =26.51017	0	1	N.A
	CTD	M3	-2131.31	p_0= 0.37216; p_1= 0.32322; p_2= 0.30432 ω_0= 0.10713; ω_1= 0.53443; ω_2= 0.53443	M0	-2135.56	ω= 0.34494	8.51	0.074665	none
		M2	-2133.10	p_0= 0.85212; p_1= 0.12322; p_2= 0.02467 ω_0= 0.27389; ω_1= 1.00000; ω_2= 1.00000	M1	-2133.10	p_0= 0.85212; p_1= 0.14788 ω_0= 0.27389; ω_1=1.00000	0	1	N.A
		M8	-2131.65	p0 = 0.98571 p = 1.54259 q =2.69390 (p1 = 0.01420) ω= 1.45608	M7	-2131.68	p = 1.39825 q = 2.30813	0.06	0.96985	N.A
H1.3	NTD	M3	-886.48	p_0= 0.54586; p_1= 0.37982; p_2= 0.07431 ω_0= 0.02494; ω_1= 0.39819; ω_2= 1.63394	M0	-913.51	ω= 0.24263	54.06	**5.11E-11**	28*, 31**
		M2	-889.39	p_0= 0.73581; p_1= 0.18393; p_2= 0.08027 ω_0= 0.06756; ω_1= 1.00000; ω_2= 1.00000	M1	-889.39	p_0= 0.73581; p_1= 0.26419 ω_0= 0.06756; ω_1=1.00000	0	1	N.A
		M8	-886.48	p0 = 0.93254 p = 0.36880 q = 1.53450 (p1= 0.06746) ω= 1.64522	M7	-887.70	p = 0.25146 q = 0.68312	2.44	0.294741	N.A
	GD	M3	-1146.03	p_0= 0.43225; p_1= 0.25374; p_2= 0.31400 ω_0= 0.00000; ω_1= 0.02952; ω_2= 0.02953	M0	-1146.62	ω= 0.01620	1.18	0.880967	N.A
		M2	-1146.62	p_0= 1.00000; p_1= 0.00000; p_2= 0.00000 ω_0= 0.01620; ω_1= 1.00000; ω_2= 1.00000	M1	-1146.62	p_0= 0.99999; p_1= 0.00001 ω_0= 0.01620; ω_1= 1.00000	0	1	N.A
		M8	-1146.13	p0 = 0.99999 p = 0.91004 q = 51.47618 (p1 = 0.00001) ω= 1.00000	M7	-1146.13	p = 0.91001 q = 51.47487	0	1	N.A
	CTD	M3	-2781.38	p_0= 0.16502; p_1= 0.75793; p_2= 0.07705 ω_0= 0.04829; ω_1= 0.64271; ω_2=1.72365	M0	-2794.91	ω= 0.53524	27.06	**1.93E-05**	151, 157, 214
		M2	-2783.99	p_0= 0.35527; p_1= 0.52774; p_2= 0.11699 ω_0= 0.15442; ω_1= 1.00000; ω_2= 1.00000	M1	-2783.99	p_0= 0.35527; p_1= 0.64473 ω_0=0.15442; ω_1=1.00000	0	1	N.A
		M8	-2782.27	p0 = 0.97807 p = 0.76895 q = 0.50007 (p1 = 0.02193) ω= 1.87312	M7	-2782.34	p = 0.71873 q = 0.43073	0	0.936483	N.A
H1.4	NTD	M3	-575.51	p_0= 0.31303; p_1= 0.34054; p_2= 0.34643 ω_0= 0.00122; ω_1= 0.00122; ω_2= 0.17872	M0	-578.03	ω= 0.05146	5.03	0.284109	N.A
		M2	-578.03	p_0= 1.00000; p_1= 0.00000; p_2= 0.00000 ω_0= 0.05146; ω_1= 1.00000; ω_2= 1.00000	M1	-578.03	p_0= 0.99999; p_1= 0.00001 ω_0= 0.05146; ω_1= 1.00000	0	0.999894	N.A
		M8	-575.69	p0 = 0.99999 p = 0.27252 q = 3.97468 (p1 = 0.00001) ω= 2.56483	M7	-575.69	p = 0.27253 q = 3.97487	0	1	N.A
	GD	M3	-978.19	p_0= 0.32324; p_1= 0.31938; p_2= 0.35737 ω_0= 0.00520; ω_1= 0.00520; ω_2= 0.00520	M0	-978.19	ω= 0.00520	0	1	none
		M2	-978.19	p_0= 1.00000; p_1= 0.00000; p_2= 0.00000 ω_0= 0.00520; ω_1= 1.00000; ω_2= 41.27124	M1	-978.19	p_0= 0.96144; p_1= 0.03856 ω_0= 0.00520; ω_1=1.00000	0	0.999258	N.A
		M8	-978.27	p_0 = 0.99999 p = 0.57187 q = 99.00000 (p_1= 0.00001) ω= 1.00000	M7	-978.27	p = 0.57187 q = 99.00000	0	1	N.A
	CTD	M3	-1849.41	p_0= 0.48578; p_1= 0.33273; p_2= 0.18149 ω_0= 0.10554; ω_1= 0.96916; ω_2= 0.96917	M0	-1855.69	ω= 0.48708	12.55	**0.013679**	157, 191
		M2	-1849.42	p_0= 0.49888; p_1= 0.39243; p_2= 0.10869 ω_0= 0.11025; ω_1= 1.00000; ω_2= 1.24082	M1	-1849.42	p_0= 0.49888; p_1= 0.50112 ω_0= 0.11025; ω_1= 1.00000	0	1	N.A
		M8	-1850.16	p0 =0.98154 p = 0.41906 q = 0.40335 (p1 = 0.01846) ω= 2.37149	M7	-1850.21	p = 0.36980 q = 0.32600	0.09	0.954987	N.A
H1.5	NTD	M3	-782.62	p_0= 0.33843; p_1= 0.39289; p_2= 0.26868 ω_0= 0.01508; ω_1= 0.01508; ω_2= 0.30089	M0	-791.21	ω= 0.07664	17.18	**0.001784**	none
		M2	-788.34	p_0= 0.87538; p_1= 0.10081; p_2=0.02381 ω_0= 0.03947; ω_1= 1.00000; ω_2= 1.00000	M1	-788.34	p_0= 0.87538; p_1= 0.124623 ω_0= 0.03947; ω_1=1.00000	0	1	N.A
		M8	-783.05	p_0 = 0.99999 p = 0.27828 q = 2.70330 (p_1= 0.00001) ω= 1.00000	M7	-783.05	p = 0.27828 q = 2.70325	0	1	N.A
	GD	M3	-1259.24	p_0= 0.05766; p_1= 0.84022; p_2= 0.10213 ω_0= 0.00494; ω_1= 0.00495; ω_2= 0.18456	M0	-1270.96	ω= 0.02055	23.44	**0.000103**	none
		M2	-1268.87	p_0= 0.98207; p_1= 0.00079; p_2= 0.01714 ω_0= 0.01564; ω_1= 1.00000; ω_2= 1.00000	M1	-1268.87	p_0= 0.98207; p_1= 0.01793 ω_0= 0.01564; ω_1= 1.00000	0	1	N.A
		M8	-1259.46	p0 = 0.99999 p = 0.10058 q = 3.45503 (p1 = 0.00001) ω= 1.00000	M7	-1259.46	p = 0.10058 q = 3.45504	0	1	N.A
	CTD	M3	-2641.96	p_0= 0.47929; p_1= 0.44192; p_2= 0.07879 ω_0= 0.08707; ω_1= 0.36677; ω_2= 1.45759	M0	-2654.30	ω= 0.26325	24.68	**5.84E-05**	140, 149*, 185, 187*, 214, 218
		M2	-2643.12	p_0= 0.82648; p_1= 0.10794; p_2= 0.06558 ω_0= 0.16216; ω_1= 1.00000; ω_2= 1.00000	M1	-2643.12	p_0= 0.82648; p_1= 0.17352 ω_0= 0.16216; ω_1=1.00000	0	1	N.A
		M8	-2642.31	p0 = 0.91210 p = 1.77210 q = 6.46942 (p1 = 0.08790) ω= 1.39165	M7	-2643.79	p = 0.73402 q = 1.69066	2.96	0.227754	N.A

The sequences were partitioned by structural domains before running Codeml and a maximum likelihood phylogenetic tree was reconstructed for each partition with PhyML, using the best fitted nucleotide substitution model (Table S2). The model pairs compared in each partition were M0-M3; M1-M2 and M7-M8. lnL, log likelihood; LRT, likelihood ratio test. In bold, p-values > 0.05, that allowed to accept the model with positive selection. Sites with posterior probabiliy >0.5 are listed; *, posterior probability > 0.9; **, posterior probabily > 0.95. The positions of the positively selected sites are referred to the sequence alignment in Figure 1. N.A, not allowed, as the null model was accepted.

Table S9. Positive selection analysis of H1.1 partition 3 with REL and ADAPTSITE

REL				ADAPTSITE		
Position	Bayes factor	Posterior probability	Selection	Position	p-value	Selection
116	228.54	0.999672	N	116	0.007	N
117	2927.73	0.999974	N	117	0.001	N
123	378.95	0.999802	N	123	0.03	N
124	87.96	0.868544	P	125	0.037	P
125	70.76	0.842647	P	130	0.034	N
129	517.10	1	N	135	0.02	N
133	104.91	0.999285	N	140	0	N
143	778.73	0.999904	N	143	0.001	N
147	295.29	0.999746	N	144	0.004	N
155	328.33	0.999771	N	145	0.039	N
156	1172.55	0.999936	N	146	0.016	N
158	1.47E+15	1	N	149	0.002	N
160	225.47	0.999667	N	151	0.003	N
167	283.51	0.999735	N	155	0	N
169	111.81	0.999329	N	156	0	N
179	822.44	0.999909	N	157	0.008	N
180	300.77	0.99975	N	160	0.002	N
181	38860.9	0.999998	N	166	0.024	N
183	668.03	0.998877	N	168	0.014	N
184	305.14	0.999754	N	169	0.002	N
188	4.29E+12	1	N	181	0.009	N
190	3.16E+05	0.999762	N	182	0.006	N
192	339.64	0.999779	N	183	0.005	N
193	183.45	0.999591	N	184	0.031	N
196	292.08	0.999743	N	185	0.048	N
197	128.19	0.999999	N	186	0.006	N
198	128.95	0.999418	N	190	0.032	N
199	203.89	0.999632	N	192	0.031	N
202	292.33	0.999743	N	193	0.002	N
203	206.05	0.999636	N	196	0.007	N
204	1.12E+14	1	N	198	0	N
205	2.77E+05	0.999729	N	203	0.001	N
206	150.90	0.999503	N	205	0.001	N
207	184.38	0.999593	N	206	0.01	N
210	342.59	0.999781	N	207	0.002	N
211	794.09	0.999055	N	210	0.031	N
213	3.59E+12	1	N	211	0.005	N
214	1.61E+05	0.999534	N	214	0.01	N
215	283.51	0.999735	N	216	0	N
216	1504.86	0.99995	N	217	0.031	N
217	358.42	0.999791	N	218	0.001	N
221	301.71	0.999751	N	221	0.001	N
222	130594.00	0.999425	N	222	0.034	N
228	303.91	0.999753	N	229	0.031	N
229	318869.00	0.999765	N	230	0.006	N
230	299.93	0.99975	N	231	0.018	N
234	283.51	0.999735	N	234	0	N

The positions are referred to the multiple sequence alignment in Figure 1. In red, basic residues. P, positive selection; N, negative selection.

Table S10. Percentages of the different amino acid types in H1.1

Species	Basic	Acid	Polar	Hydrophobic	Aromatic
H. sapiens	38.8	1.0	19.4	40.8	0.0
M. mulata	37.9	1.0	20.4	40.8	0.0
P. troglodytes	38.8	1.0	18.4	41.7	0.0
T. syrichta	35.2	0.9	18.5	45.4	0.0
O. garnettii	37.0	1.0	15.0	45.0	0.0
P. anubis	37.9	1.0	20.4	40.8	0.0
C. sabaeus	37.9	1.0	19.4	41.7	0.0
C. atys	38.2	1.0	21.6	39.2	0.0
M. musculus	39.2	1.0	15.7	44.1	0.0
R. norvegicus	38.8	1.0	16.5	43.7	0.0
M. auratus	39.2	1.0	15.7	44.1	0.0
P. maniculatus	39.2	1.0	13.7	46.1	0.0
M. ochrogaster	39.2	1.0	16.7	43.1	0.0
N. galili	39.2	1.0	13.7	46.1	0.0
J. jaculus	37.5	1.0	7.7	53.8	0.0
B. taurus	37.7	0.9	17.9	43.4	0.0
C. ferus	37.7	0.9	13.2	48.1	0.0
B. bison	37.7	0.9	17.9	43.4	0.0
C. familiaris	38.8	1.0	9.7	49.5	0.0
F.catus	38.8	1.0	12.6	47.6	0.0
O. orca	37.7	0.9	17.0	44.3	0.0
L. vexillifer	38.1	1.0	16.2	44.8	0.0
E. caballus	42.1	1.1	15.8	41.1	0.0
C. cristata	38.1	0.0	13.3	48.6	0.0
P. alecto	37.7	0.9	9.4	50.9	0.9
G. variegatus	38.5	1.0	13.5	46.2	1.0
D. novemcinctus	38.5	1.0	8.7	51.9	0.0

Amino acid composition for each sequence was obtained with Protparam (Expasy) and averaged by amino acid type. Basic, K and R; Acid, D and E; Polar, S, T and N; Hydrophobic, A, G, I, L, M, P, V; Aromatic, F