

SUPPLEMENTARY MATERIAL

Table S1: Presence and absence of the 14 coagulation genes in each of the 47 genomes used in this study.

Clades	Scientific name	Common name	FGA	FGB	FGG	F2	F3	F5	F7	F8	F9	F10	F11	F12	F13A	F13B
Primates	<i>Callithrix jacchus</i>	Marmoset	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Homo sapiens</i>	Human	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Macaca mulatta</i>	Macaque	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Nomascus leucogenys</i>	Gibbon	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Otolemur garnettii</i>	Bushbaby	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Pongo abelii</i>	Orangutan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Primates	<i>Pan troglodytes</i>	Chimpanzee	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Cavia porcellus</i>	Guinea Pig	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Dipodomys ordii</i>	Kangaroo rat	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Mus musculus</i>	Mouse	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Oryctolagus cuniculus</i>	Rabbit	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Ochotona princeps</i>	Pika	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Rattus norvegicus</i>	Rat	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glires	<i>Ictidomys tridecemlineatus</i>	Squirrel	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Ailuropoda melanoleuca</i>	Panda	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Bos taurus</i>	Cow	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Canis lupus familiaris</i>	Dog	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Equus caballus</i>	Horse	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Felis catus</i>	Cat	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Mustela putorius furo</i>	Ferret	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laurasiatheria	<i>Sus scrofa</i>	Pig	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Atlantogenata	<i>Choloepus hoffmanni</i>	Sloth	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes
Atlantogenata	<i>Dasyopus novemcinctus</i>	Armadillo	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

<i>Atlantogenata</i>	<i>Echinops telfairi</i>	Lesser hedgehog tenrec	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Atlantogenata</i>	<i>Loxodonta africana</i>	Elephant	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Atlantogenata</i>	<i>Procavia capensis</i>	Hyrax	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Mammals</i>	<i>Macropus eugenii</i>	Wallaby	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Mammals</i>	<i>Monodelphis domestica</i>	Opossum	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Mammals</i>	<i>Ornithorhynchus anatinus</i>	Platypus	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
<i>Mammals</i>	<i>Sarcophilus harrisii</i>	Tasmanian devil	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<i>Sauropsida</i>	<i>Anolis carolinensis</i>	Anole lizard	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Anas platyrhynchos</i>	Duck	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Ficedula albicollis</i>	Flycatcher	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Gallus gallus</i>	Chicken	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Meleagris gallopavo</i>	Turkey	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Pelodiscus sinensis</i>	Chinese softshell turtle	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Sauropsida</i>	<i>Taeniopygia guttata</i>	Zebra Finch	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
<i>Other</i>	<i>Latimeria chalumnae</i>	Coelacanth	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
<i>Tetrapoda</i>	<i>Xenopus tropicalis</i>	Xenopus	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
<i>Fishes</i>	<i>Danio rerio</i>	Zebrafish	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Gasterosteus aculeatus</i>	Stickleback	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Gadus morhua</i>	Cod	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Oreochromis niloticus</i>	Tilapia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Oryzias latipes</i>	Medaka	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Tetraodon nigroviridis</i>	Tetraodon	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Takifugu rubripes</i>	Fugu	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
<i>Fishes</i>	<i>Xiphophorus maculatus</i>	Platyfish	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No

Table S2a: Positively selected genes of the coagulation cascade within different groups of species as calculated with the site model in this study.

	Vertebrates	Fishes	Sauropsida	Mammals	Laurasiatheria	Glires	Primates
<i>FGA</i>	No	No	No	Yes	Yes	No	No
<i>FGB</i>	No	No	No	No	No	No	Yes
<i>FGG</i>	No	No	No	No	No	No	No
<i>F2</i>	Yes	No	No	No	No	No	No
<i>F3</i>	No	No	Yes	Yes	No	No	No
<i>F5</i>	Yes	No	No	Yes	No	No	Yes
<i>F7</i>	Yes	No	No	No	No	No	No
<i>F8</i>	No	No	No	Yes	No	No	Yes
<i>F9</i>	No	No	No	Yes	No	No	No
<i>F10</i>	Yes	No	No	No	No	No	No
<i>F11</i>	No	No	No	No	No	No	No
<i>F12</i>	No	No	No	No	No	No	No
<i>F13A</i>	Yes	No	No	No	No	No	No
<i>F13B</i>	No	No	No	No	Yes	No	No

Table S2b: Positively selected genes of the coagulation cascade in different branches of the taxonomic tree of vertebrates as calculated in the branch-site model in this study. Within brackets () are given the results from the Selectome Database for comparison. (-) means that the results for the gene family are not available in Selectome.

Gene	Codons analysed	Actinopterygii	Sarcopterygii	Tetrapoda	Amniota	Sauropsida	Mammals	Theria	Eutheria
<i>FGA</i>	135	Yes (No)	Yes (No)	No (No)	No (Yes)	No (No)	No (No)	No (No)	No (No)
<i>FGB</i>	315	Yes (Yes)	Yes (Yes)	Yes (No)	Yes (Yes)	Yes (No)	Yes (Yes)	No (Yes)	No (No)
<i>FGG</i>	299	No (No)	No (No)	No (No)	No (No)	No (No)	No (Yes)	No (No)	No (No)
<i>F2</i>	391	Yes (No)	Yes (No)	Yes (Yes)	Yes (Yes)	No (No)	Yes (No)	No (-)	Yes (Yes)
<i>F3</i>	122	No (No)	No (No)	No (No)	No (No)	No (No)	No (No)	No (No)	No (No)
<i>F5</i>	488	Yes (-)	Yes (-)	Yes (-)	Yes (-)	No (-)	No (-)	No (-)	No (-)
<i>F7</i>	126	(-) (Yes)	(-) (Yes)	No (No)	No (No)	No (No)	No (No)	No (No)	No (No)
<i>F8</i>	701	Yes (-)	Yes (-)	Yes (-)	Yes (-)	Yes (-)	Yes (-)	No (-)	No (-)
<i>F9</i>	218	Yes (Yes)	Yes (Yes)	No (Yes)	Yes (Yes)	Yes (Yes)	No (No)	No (No)	Yes (Yes)
<i>F10</i>	197	No (Yes)	No (Yes)	No (Yes)	Yes (Yes)	No (Yes)	No (Yes)	No (No)	No (No)
<i>F11</i>	152	No (-)	No (-)	No (-)	No (-)	No (-)	No (-)	No (-)	No (-)
<i>F12</i>	306	No (-)	No (-)	No (-)	Yes (-)	No (-)	Yes (-)	No (-)	No (-)
<i>F13A</i>	388	Yes (Yes)	Yes (Yes)	Yes (Yes)	Yes (No)	No (No)	No (No)	No (Yes)	No (No)
<i>F13B</i>	245	(-) (-)	(-) (-)	No (-)	Yes (-)	No (-)	No (-)	No (-)	No (-)

Figure Legends

Supplementary Figure S1. Schematic representation of the workflow of this study. The programs (Methods) and the order in which they were employed to provide the multiple sequence alignments of sufficient quality and the phylogenetic trees is shown. This procedure enabled the calculation of selective pressures using CodeML.

Supplementary Figure S2. The probabilities of negative, neutral and positive selection were plotted against the amino acid position for the other 11 coagulation genes of the 14 across the Primates. This extends Figure 4 in the main text in which only the three genes for FIX, FVIII and FXI are shown. The probability values were obtained from CodeML analyses of the seven primate sequences (grey, negative selection; yellow, neutral selection; green, positive selection).

Supplementary Figure S3. Summary of the seven *Primates* sequences to show the degree of positive selection during evolution and the pathogenic mutations at each site for (a) FVIII, (b) FIX, and (c) FXI. The point mutations in the coding regions were obtained from the disease-causing databases for (a) FVIII, (b) FIX, and (c) FXI. Red and orange denote ≥ 4 mutations and 1-3 mutations respectively. The probabilities of positive selection were taken from the CodeML runs for the seven primate sequences. Because FVIII is a large protein with 2351 residues, the figure was divided into three parts to accommodate the sequence length.

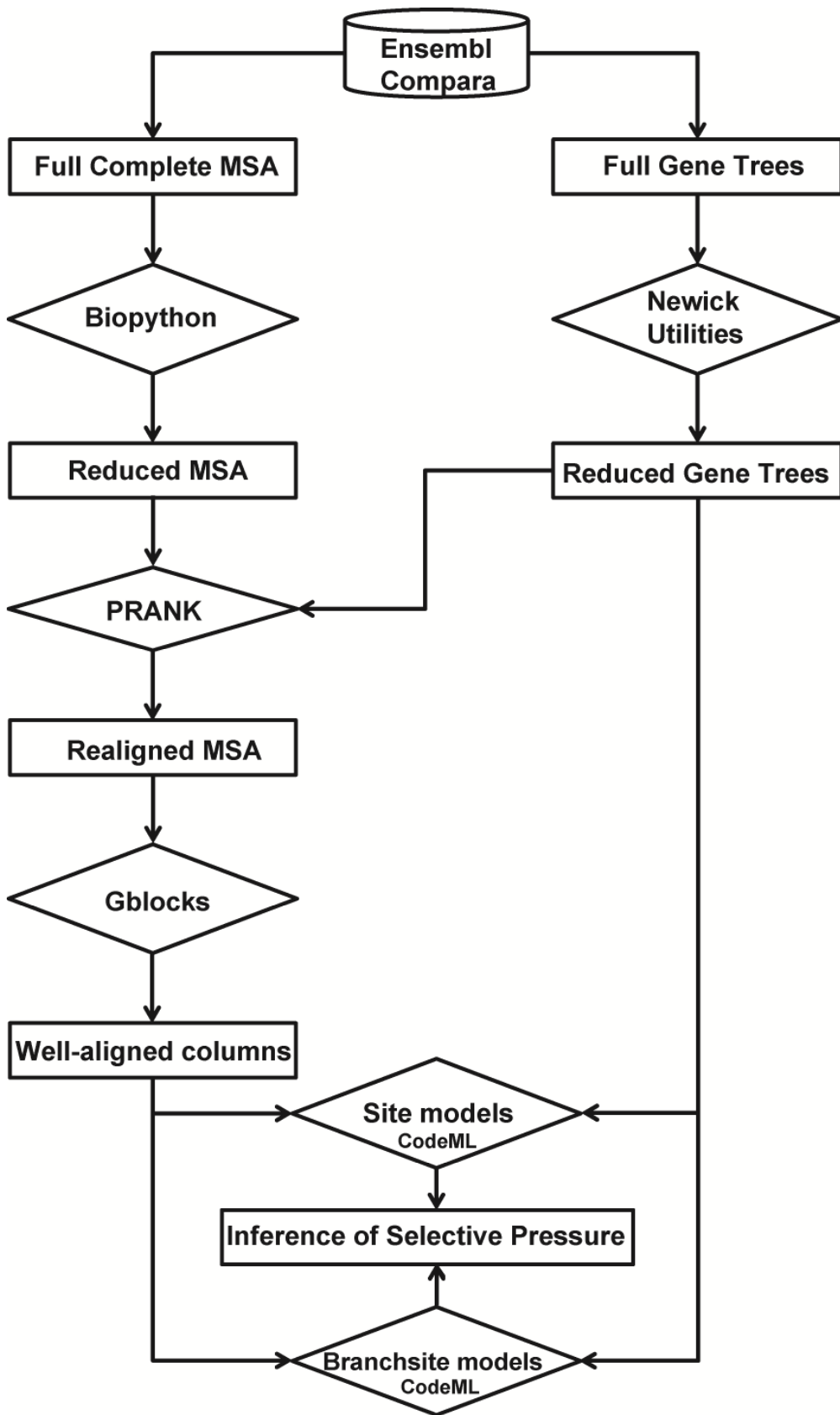


FIGURE S1

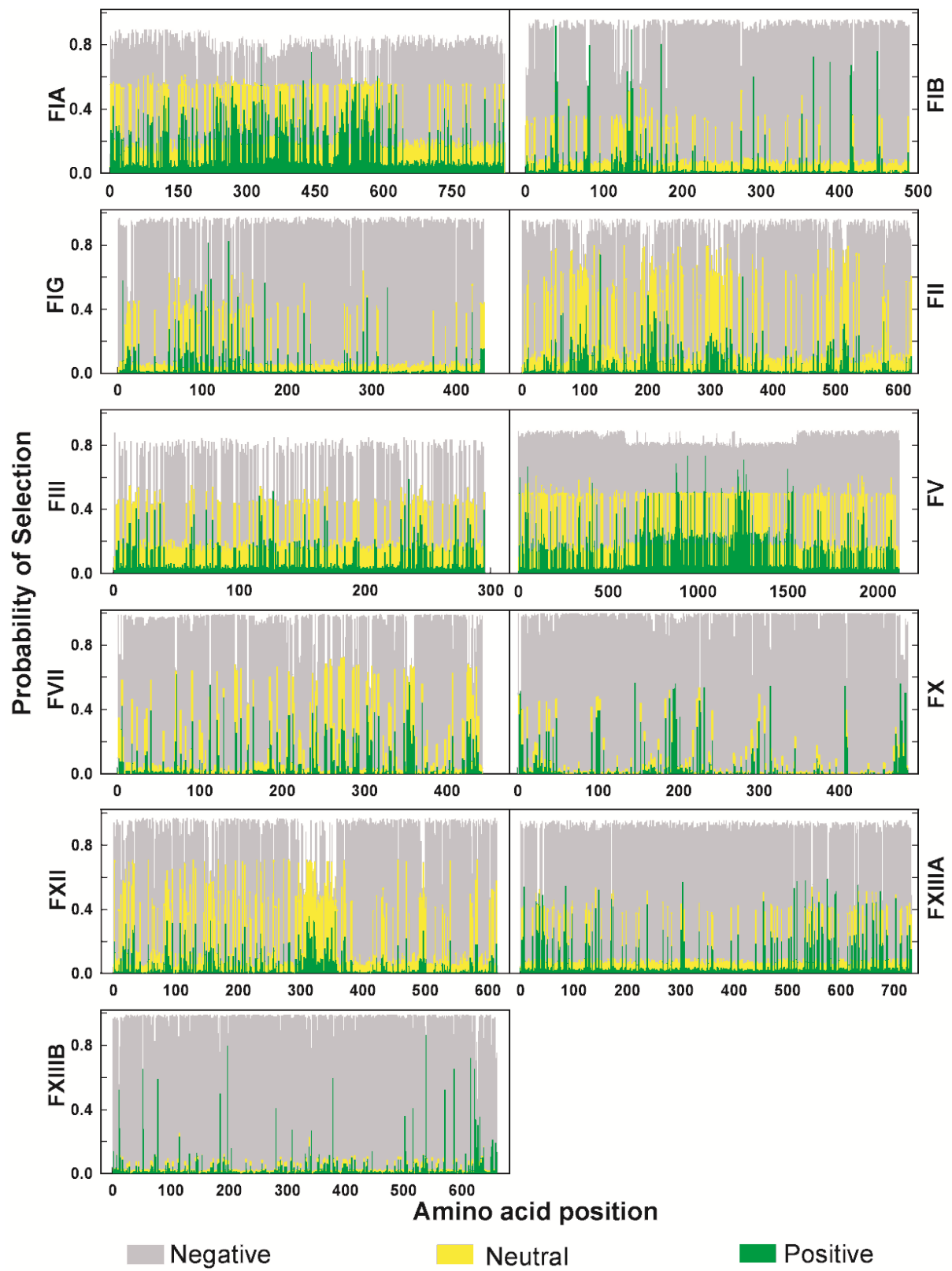


FIGURE S2