

Table S1: Summary of HA mutations screened in the nine H10 AIV strains under study (Italy 1994-2007) and known to be associated with zoonotic potential, as previously reviewed [36].

Subtype tested	Amino acid change/Motif (H3 numbering)	Phenotypic consequences	References
H5N1	D101N	Increased virus binding to $\alpha 2-6$	[38]
	S126N	Increased virus binding to $\alpha 2-6$	[39]
	S137A	Increased pseudovirus binding to $\alpha 2-6$	[40]
	A138V	Increased infectivity in SIATCells	[41,42]
	G143R	Increased virus binding to $\alpha 2-6$	[43]
	S158N	Increased virus binding to $\alpha 2-6$	[39]
	S159N	Increased virus binding to $\alpha 2-6$	[39]
	T160A	Increased virus binding to $\alpha 2-6$, increased transmission in guinea pigs	[39,44]
	N186K/D	Increased virus binding to $\alpha 2-6$	[39]
	D187G	Increased virus binding to $\alpha 2-6$	[45]
	E190G	Increased virus binding to $\alpha 2-6$, maintained $\alpha 2-3$ binding, decreased virulence in mice	[45,46]
	T192I	Increased pseudovirus binding to $\alpha 2-6$	[43]
	K193R/T	Increased virus binding to $\alpha 2-6$	[39]
	Q196R/H	Increased virus binding to $\alpha 2-6$	[45]
	N197K	Increased virus binding to $\alpha 2-6$	[43]
	V214I	Increased virus binding to $\alpha 2-6$	[47]
	S221P	Increased virus binding to $\alpha 2-6$	[48]

	S221P+K216E	Increased virus binding to $\alpha 2-6$	[48]
	Q226L	Increased virus binding to $\alpha 2-6$, decreased binding to $\alpha 2-3$	[49]
	S227N	Increased virus binding to $\alpha 2-6$	[49]
	G228S	Increased virus binding to $\alpha 2-6$	[50]
	E83K+S128P	Increased virus binding to $\alpha 2-6$	[43]
	E83K+S128P+R496K	Increased virus binding to $\alpha 2-6$	[43]
	E83K+S128P+N197K+R496K	Increased virus binding to $\alpha 2-6$	[43]
	E83K+N197K	Increased virus binding to $\alpha 2-6$	[43]
	E83K+N197K+R496K	Increased virus binding to $\alpha 2-6$	[43]
	E83K+R496K	Increased virus binding to $\alpha 2-6$	[43]
	H110Y+T160A+Q226L+G228S	Airborne transmissible in ferrets,	[51,52]
	S114R+T115I	Increased virulence in chickens and mice, increased pH of fusion	[53]
	S128P+N197K	Increased virus binding to $\alpha 2-6$	[43]
	S128P+N197K+R496K	Increased virus binding to $\alpha 2-6$	[43]
	S128P+R496K	Increased virus binding to $\alpha 2-6$	[43]
	P239S	Increased virus binding to $\alpha 2-6$	[43]
	E255K	Increased virus binding to $\alpha 2-6$	[45]
	S137A+T192I	Increased pseudovirus binding to $\alpha 2-6$	[43]
	G143R+N186K	Decreased binding to $\alpha 2-3$, increased virus binding to $\alpha 2-6$	[49]
	K387I	Decreased pH of fusion, increased HA stability, increased replication, decreased virulence in mice, efficiency and virulence in mice	[54,55,56]
	N158S+Q226L	Increased virus binding to $\alpha 2-6$	[57]
	N158S+Q226L+N248D	Increased virus binding to $\alpha 2-6$	[57]

H5N1	S159N+T160A	Increased virus binding to $\alpha 2-6$	[39]
	S159N+T160A+S227N	Increased virus binding to $\alpha 2-6$, reduced lethality and systemic spread in mice	[58]
	T160A+K193T+N224K+Q226L	Increased virus binding to $\alpha 2-6$	[59]
	T160A+Q226L	Increased virus binding to $\alpha 2-6$	[39]
	T160A+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[39]
	T160A+S227N	Increased virus binding to $\alpha 2-6$	[39]
	N186K+Q226L+S227N+G228S	Increased virus binding to $\alpha 2-6$	[49]
	N186K+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[49]
	E187G+E190D+K193S+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[60]
	E187G+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[45]
	D187G+S227N	Increased virus binding to $\alpha 2-6$	[45]
	N186K+Q196R+Q226L+S227N+G228S	Increased virus binding to $\alpha 2-6$	[49]
	E190G+Q226E+G228S	Increased virus binding to $\alpha 2-6$	[45]
	K193R+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[59]
	Q196R+Q226L+S227N+G228S	Increased virus binding to $\alpha 2-6$	[49]
	Q196R+Q226L+G228S	Increased virus binding to $\alpha 2-6$	[49]
	Q196R+S227N	Increased virus binding to $\alpha 2-6$	[49]
	N197K+R496K	Increased virus binding to $\alpha 2-6$	[43]
	K222Q+S227R	Increased virus binding to $\alpha 2-3$ and $\alpha 2-6$	[61]
	Q226L+S227N+G228S	Increased virus binding to $\alpha 2-6$	[49]
	Q226L+G228S	Increased virus binding to $\alpha 2-6$; decreased antiviral response in host; reduced tissue tropism in guinea pigs	[45,49,50]
	326 to 329 (R-X-R K-R)	Polybasic cleavage motif sequence required for high pathogenicity avian influenza viruses	[62]

	N158D+N224K+Q226L+T318I	Transmissible among ferrets	[63]
H7N9	G186V	Increased virus binding to $\alpha 2-3$	[64]
	Q226L	Increased virus binding to $\alpha 2-3$, decreased binding to $\alpha 2-6$	[65,66]
	L226I	Decreased binding to $\alpha 2-3$	[65]
	G228S	Decreased binding to $\alpha 2-3$ and $\alpha 2-6$ receptors	[67]
	K393E	Increased pH of fusion, decreased HA stability	[36,37]
	V186N, N228K	Increased virus binding to $\alpha 2-6$	[67]
	V186K/G+K193T+G228S	Increased virus binding to $\alpha 2-6$,	[67]
	V186N+N224K+G228S	Increased virus binding to $\alpha 2-6$,	[67]
	K193T+G228S	Dual $\alpha 2-3$ and $\alpha 2-6$ binding	[67]
	N224K+G228S	Increased virus binding to $\alpha 2-6$	[67]
H7N7	Q226L+G228S	Increased virus binding to $\alpha 2-6$	[68]
H9N2	N158D	Decreased virulence in mice	[69]
	T190V	Enhances binding affinity to mammalian cells and replication in mammalian cells	[70]
	Q226L	Increased virus binding to $\alpha 2-6$, enhanced replication in mammalian cells and in ferrets, enhanced contact transmission in ferrets	[71,72]
	T189A+G192R	Enhanced replication in ferrets, transmitted via aerosols among ferrets,	[73]

H6N1	P186L	Decreased binding to $\alpha 2-3$	[74]
	G225D	Increased virus binding to $\alpha 2-6$	[75]
H6N2	E190V	Decreased binding to $\alpha 2-3$ and $\alpha 2-6$	[76]
	Q226L	Increased virus binding to $\alpha 2-6$	[76]
	G228S	Decreased virus binding to $\alpha 2-3$	[76]
H4N6	Q226L	Increased virus binding to $\alpha 2-6$	[77]
	G228A/S	Increased binding to $\alpha 2-6$, dual receptor specificity	[77]
	Q226L+G228S	Increased virus binding to $\alpha 2-6$	[77]
H1N1	G228S	Increased viral replication in mammalian cells and virulence in mice	[78]
H10N8	Q226L	Loss of binding to $\alpha 2-3$	[79,80]
	G228S	Decreased binding to $\alpha 2-3$, no binding to $\alpha 2-6$	[80]
	Q226L+G228S	Loss of binding to $\alpha 2-3$, no gain of binding to $\alpha 2-6$,	[79,80]
H13N6	V186N	Increased binding to $\alpha 2-6$, decreased binding to $\alpha 2-3$	[81]