

**Supplementary Table S1.** Comparison of avian- and human-like amino acids in viral proteins of influenza A viruses

Protein	Amino acid*			References†
	Position	Avian-like	Human-like	
PB2	9*	D	N	
	44	A	S	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	64	M	T	Finkelstein <i>et al.</i> (2007)
	81	T	M	Shaw <i>et al.</i> (2002)
	199*	A	S	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	271	T	A	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	368*	R	K	
	475	L	M	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	567	D	N	Finkelstein <i>et al.</i> (2007)
	588	A	I	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	613	V	T	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	627*	E	K	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	661	A	T	Shaw <i>et al.</i> (2002)
	674	A	T	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	702	K	R	Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
PB1	327	R	K	Chen <i>et al.</i> (2006)
	336	V	I	Chen <i>et al.</i> (2006)
PB1-F2	73	K	R	Chen <i>et al.</i> (2006)
	76	V	A	Chen <i>et al.</i> (2006)
	79	R	Q	Chen <i>et al.</i> (2006)
	82	L	S	Chen <i>et al.</i> (2006)
	87	E	G	Chen <i>et al.</i> (2006)
PA	28	P	L	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	55	D	N	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	57	R	Q	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	65	S	L	Shaw <i>et al.</i> (2002)
	100	V	A	Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	142*	K	N, E	
	225	S	C	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	241	C	Y	Shaw <i>et al.</i> (2002)
	268	L	I	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	312	K	R	Shaw <i>et al.</i> (2002)
	337	A	S	Finkelstein <i>et al.</i> (2007)
	356	K	R	Chen <i>et al.</i> (2006)
	382	E	D	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	400	Q, T, S	L	Shaw <i>et al.</i> (2002)
	404	A	S	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	409	S	N	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	421*	S	I	
552	T	S	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)	
NP	16	G	D	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	31	R	K	Shaw <i>et al.</i> (2002)
	33*	V	I	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	61	I	L	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)

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Protein	Amino acid*		References†	
	Position	Avian-like		Human-like
	100*	R	V, I	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	109	I	V	Chen <i>et al.</i> (2006)
	127	E	D	Shaw <i>et al.</i> (2002)
	136	L	M	Shaw <i>et al.</i> (2002)
	214	R	K	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	283*	L	P	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	293	R	K	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	305	R	K	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	313	F	Y	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
	357*	Q	K	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	372	E	D	Chen <i>et al.</i> (2006)
	375	D	G, E	Shaw <i>et al.</i> (2002)
	422	R	K	Chen <i>et al.</i> (2006)
	442	T	A	Chen <i>et al.</i> (2006)
	455	D	E	Chen <i>et al.</i> (2006)
M1	115	V	I	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	121	T	A	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
	137	T	A	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007); Shaw <i>et al.</i> (2002)
M2	11	T	I	Chen <i>et al.</i> (2006)
	16	E	G	Shaw <i>et al.</i> (2002)
	20	S	N	Chen <i>et al.</i> (2006); Shaw <i>et al.</i> (2002)
	28	I	I, V	Shaw <i>et al.</i> (2002)
	55	L	F	Shaw <i>et al.</i> (2002)
	57	Y	H	Chen <i>et al.</i> (2006)
	78	Q	K	Shaw <i>et al.</i> (2002)
	86	V	A	Chen <i>et al.</i> (2006)
NS1	81	I	M	Finkelstein <i>et al.</i> (2007)
	215	P	T	Finkelstein <i>et al.</i> (2007)
	227	E	R	Chen <i>et al.</i> (2006); Finkelstein <i>et al.</i> (2007)
NS2	70	S	G	Chen <i>et al.</i> (2006)
	107	L	F	Chen <i>et al.</i> (2006)

\*We analysed protein sequences in the Influenza Sequence Database and identified 75 host-specific amino acids conserved in human and avian influenza viruses. Human-like amino acids at positions flagged with an asterisk were tested for their contributions to avian virus replication in a mouse model.

†Host-specific amino acids identified in this study that have also been described in papers published by others.

## References

- Chen, G. W., Chang, S. C., Mok, C. K., Lo, Y. L., Kung, Y. N., Huang, J. H., Shih, Y. H., Wang, J. Y., Chiang, C. & other authors (2006). Genomic signatures of human versus avian influenza A viruses. *Emerg Infect Dis* **12**, 1353–1360. [Medline](#)
- Finkelstein, D. B., Mukatira, S., Mehta, P. K., Obenauer, J. C., Su, X., Webster, R. G. & Naeve, C. W. (2007). Persistent host markers in pandemic and H5N1 influenza viruses. *J Virol* **81**, 10292–10299. [Medline](#)
- Shaw, M., Cooper, L., Xu, X., Thompson, W., Krauss, S., Guan, Y., Zhou, N., Klimov, A., Cox, N. & other authors (2002). Molecular changes associated with the transmission of avian influenza A H5N1 and H9N2 viruses to humans. *J Med Virol* **66**, 107–114. [Medline](#)

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