Virus	**α2,3 SL**	**α2,6 SL** K_d [μg/ml]
A/Perth/16/2009	91.4±12316	0.008 ±0.018
A/California/04/2009	1.0±1.8	0.06977 ±.05
A/harbor seal/NH/179629/2011	5.2±15.1	0.063 ±0.09
A/long-tailed duck/ME/295/2011	1.1±0.6	0.37 ±0.61
A/ruddy duck/IL/3471/2009	87.66±6472	106 ±18147
A/mallard/Alberta/551/2009	0.23±0.05	55.41 ±6478
A/mallard/Alberta/50/1979	0.33±0.07	24 ±1647
A/mallard/Alberta/274/1979	1.1±0.5	93.7 ±11939
A/duck/Ukraine/1/1963	0.51±0.07	16.7±78.7

Supplementary Table 1: Dissociation constants (K_d) [μg/ml] ± standard deviation for H3N8 and human seasonal influenza viruses on absorbance from binding assays

		Antisera		
Virus	**Subtype**	α Harbor Seal (Ferret # 1131)	α Harbor Seal (Ferret # 1132)	α pH1N1 (Ferret # ARC349)
A/California/04/2009	pH1N1	-	-	640
A/Perth/16/2009	H3N2	-	-	-
A/harbor seal/NH/179629/2011	H3N8	240	320	-
A/ruddy duck/IL/3471/2009	H3N8	80	120	-
A/long-tailed duck/ME/295/2011	H3N8	80	80	-
A/mallard/Alberta/551/2009	H3N8	40	40	-
A/mallard/Alberta/50/1979	H3N8	40	40	-
A/mallard/Alberta/274/1979	H3N8	40	40	-

Supplementary Table 2: Cross reaction of seal antisera against H3N8 and human seasonal influenza viruses

Subtype	Strains	Compared to other subtypes?	Sialic Acid Linkage	Replication *in vitro*	Replication in mice	Replication in ferrets	Transmission in ferrets	Reference
H7	H7N7 H7N3 H7N2	No	ND	ND	Yes	ND	ND	1
H1 and H6	H1N9 H6N1	Yes to each other	α2-3	ND	ND	Yes	Direct contact with H1N9 only	2
H7	H7N3 (5 viruses)	No	ND assume α2-3	ND	Yes	Yes	ND	3
H7	H7N7 H7N3 H7N2	No	α2-3 and α2-6	ND	ND	Yes	Direct contact with a few viruses	4
H9	reassortant virus H9N2 HA/NA on human H3N2 backbone	No	GOF towards α2-6	ND	ND	Yes	respiratory droplet with mutations	5
H6	H6N1 H6N2 H6N5 H6N8	No	α2-3 and α2-6	ND	Yes	Yes	Direct contact in 1 of 2 H6N5	6
H1	pdmH1N1 (4 viruses)	No	α2-6	ND	Yes	Yes	Yes respiratory	7
H1	H1N1 (31 viruses)	No	ND assume α2-3	ND	Yes	Yes	Direct with 1 virus	8
Mixed	H2, H3, H4, H6, H7, H11	Yes	ND	Yes	Yes	ND	ND	9
H2	H2N2 (23 viruses)	No	α2-3	Yes	Yes	Yes	Direct with 3 viruses	10
H3	H3N2 H3N3 H3N8	No	α2-3 and α2-6	ND	Yes	Yes	ND	11

H9	H9N2 (10 viruses) H3N2 used as transmission control	No	α2-3 and α2-6	ND	ND	Yes	Direct with 2 of 5 viruses	12
H4	H4N6 (5 viruses)	No	ND assume α2-3	ND	Yes	ND	ND	13
H5	H5N1 H3N2 control reassortant	No	ND	ND	ND	Yes	No H5N1	14
H9	H9N2 (12 viruses)	No	ND assume α2-3 and α2-6	Yes	Yes	Yes	Direct with 4 of 12 viruses	15
H5	H5N1 (4 viruses)	No	ND assum e α2-3	ND	Yes	Yes	No transmission	16
H5	Pathogenicity studies limited to H5N1 (2 viruses)	No	ND	ND	Yes	Yes	No transmission	17
H5	H5N1 (11 viruses)	No	ND	ND	Yes	Yes	No transmission	18
H6	H6N1 H6N2 H6N5 H6N8 H6N9	No	ND	ND	Yes	Yes	ND	19
H5	H5N2 (2 viruses)	No	ND assume α2-3	Yes	Yes	ND	ND	20
H7	H7N9 (3 viruses) H1N1 used as positive control	No	Yes	Yes	Yes	Yes	Respiratory transmission in 1 of 3 animals with 1 virus	21

Supplementary Table 3: Avian influenza viruses assessed for mammalian pathogenicity and transmission

Supplementary Table References:

1 Belser, J. A. *et al.* Pathogenesis of Avian Influenza (H7) Virus Infection in Mice and Ferrets: Enhanced Virulence of Eurasian H7N7 Viruses Isolated from Humans. *Journal of Virology* **81**, 11139-11147, doi:10.1128/jvi.01235-07 (2007).

2 Driskell, E. A. *et al.* Low Pathogenic Avian Influenza Isolates from Wild Birds Replicate and Transmit via Contact in Ferrets without Prior Adaptation. *PLoS ONE* **7**, e38067, doi:10.1371/journal.pone.0038067 (2012).

3 Aamir, U. B. *et al.* Zoonotic potential of highly pathogenic avian H7N3 influenza viruses from Pakistan. *Virology* **390**, 212-220, doi:http://dx.doi.org/10.1016/j.virol.2009.05.008 (2009).

4 Belser, J. A. *et al.* Contemporary North American influenza H7 viruses possess human receptor specificity: Implications for virus transmissibility. *Proceedings of the National Academy of Sciences* **105**, 7558-7563, doi:10.1073/pnas.0801259105 (2008).

5 Sorrell, E. M., Wan, H., Araya, Y., Song, H. & Perez, D. R. Minimal molecular constraints for respiratory droplet transmission of an avian–human H9N2 influenza A virus. *Proceedings of the National Academy of Sciences* **106**, 7565-7570, doi:10.1073/pnas.0900877106 (2009).

6 Nam, J.-H. *et al.* Emergence of Mammalian Species-infectious and -pathogenic Avian Influenza H6N5 Virus with No Evidence of Adaptation. *Journal of Virology*, doi:10.1128/jvi.05038-11 (2011).

7 Maines, T. R. *et al.* Transmission and Pathogenesis of Swine-Origin 2009 A(H1N1) Influenza Viruses in Ferrets and Mice. *Science* **325**, 484-487, doi:10.1126/science.1177238 (2009).

8 Koçer, Z. A., Krauss, S., Stallknecht, D. E., Rehg, J. E. & Webster, R. G. The Potential of Avian H1N1 Influenza A Viruses to Replicate and Cause Disease in Mammalian Models. *PLoS ONE* **7**, e41609, doi:10.1371/journal.pone.0041609 (2012).

9 Driskell, E. A., Jones, C. A., Stallknecht, D. E., Howerth, E. W. & Tompkins, S. M. Avian influenza virus isolates from wild birds replicate and cause disease in a mouse model of infection. *Virology* **399**, 280-289, doi:http://dx.doi.org/10.1016/j.virol.2010.01.005 (2010).

10 Jones, J. C. *et al.* Risk Assessment of H2N2 Influenza Viruses from the Avian Reservoir. *Journal of Virology*, doi:10.1128/jvi.02526-13 (2013).

11 Baz, M. *et al.* Replication and Immunogenicity of Swine, Equine, and Avian H3 Subtype Influenza Viruses in Mice and Ferrets. *Journal of Virology* **87**, 6901-6910, doi:10.1128/jvi.03520-12 (2013).

12 Wan, H. *et al.* Replication and Transmission of H9N2 Influenza Viruses in Ferrets: Evaluation of Pandemic Potential. *PLoS ONE* **3**, e2923, doi:10.1371/journal.pone.0002923 (2008).

13 Kang, H.-M. *et al.* Genetic and antigenic characteristics of H4 subtype avian influenza viruses in Korea and their pathogenicity in quails, domestic ducks and mice. *Journal of General Virology* **94**, 30-39, doi:10.1099/vir.0.046581-0 (2013).

14 Maines, T. R. *et al.* Lack of transmission of H5N1 avian–human reassortant influenza viruses in a ferret model. *Proceedings of the National Academy of Sciences* **103**, 12121-12126, doi:10.1073/pnas.0605134103 (2006).

15 SJCEIRS Working Group. Assessing the fitness of distinct clades of influenza A (H9N2) viruses. *Emerg Microbes Infect* **2**, e75, doi:10.1038/emi.2013.75 (2013).

16 Kwon, H.-i. *et al.* Genetic characterization and pathogenicity assessment of highly pathogenic H5N1 avian influenza viruses isolated from migratory wild birds in 2011, South Korea. *Virus Research* **160**, 305-315, doi:http://dx.doi.org/10.1016/j.virusres.2011.07.003 (2011).

17 Nguyen, D. C. *et al.* Isolation and Characterization of Avian Influenza Viruses, Including Highly Pathogenic H5N1, from Poultry in Live Bird Markets in Hanoi, Vietnam, in 2001. *Journal of Virology* **79**, 4201-4212, doi:10.1128/jvi.79.7.4201-4212.2005 (2005).
18 Maines, T. R. *et al.* Avian Influenza (H5N1) Viruses Isolated from Humans in Asia in 2004 Exhibit Increased Virulence in Mammals. *Journal of Virology* **79**, 11788-11800, doi:10.1128/jvi.79.18.11788-11800.2005 (2005).
19 Gillim-Ross, L. *et al.* Avian Influenza H6 Viruses Productively Infect and Cause Illness in Mice and Ferrets. *Journal of Virology* **82**, 10854-10863, doi:10.1128/jvi.01206-08 (2008).
20 Karlsson, E. A. *et al.* Prevalence and characterization of influenza viruses in diverse species in Los Llanos, Colombia. *Emerg Microbes Infect* **2**, e20, doi:10.1038/emi.2013.20 (2013).
21 Watanabe, T. *et al.* Characterization of H7N9 influenza A viruses isolated from humans. *Nature* **501**, 551-555, doi:10.1038/nature12392

http://www.nature.com/nature/journal/v501/n7468/abs/nature12392.html - supplementary-information (2013).