

**Table S3.** List of H4 AIVs and genotypes with key molecular markers in China

Subtype	Genotype	isolate	HA	PB2			PB1			PA	NP		M2					
			Altered receptor specificity	Enhanced virus polymerase activity and virulence in mice	Host signature amino acids through statistical methods (avian to human)										Increased resistance to amantadine and rimantadine			
					V214I	K482R	D9N	M64T	T105M	K702R	R327K	R57Q	S409N	V33I	D455E	L26F	V27I/A	S31N
H4N2	G3	A/duck/Guangdong/S1469/2010	V	K	D	M	T	K	R	R	S	V	D	L	I	S		
	G4	A/wild bird/China/Y13/2019	V	K	D	M	T	R	R	R	S	V	D	L	I	S		
	G4	A/duck/Hunan/S11313/2012	V	R	D	M	T	K	R	R	S	V	D	L	V	S		
	G9	A/duck/Jiangsu/1-15/2011	V	K	D	M	A	K	R	R	S	V	D	L	V	N		
	G10	A/duck/Hubei/S2213/2012	V	K	D	M	T	K	R	R	S	V	D	L	I	S		
	G14	A/duck/Hubei/S2227/2012	V	K	D	M	T	K	R	R	N	V	D	L	I	S		
	G15	A/duck/Hunan/01.16 YYGK227-P/2014	V	K	D	M	T	K	K	R	S	V	D	L	V	S		
	G16	A/Environment/Hunan/28094/2014	V	K	D	M	T	K	R	R	S	V	D	L	I	S		
	G17	A/duck/Zhejiang/925170/2014	V	K	D	M	T	K	R	R	N	V	D	L	V	S		
	G17	A/duck/Zhejiang/925161/2014	V	K	D	M	T	K	R	R	N	V	D	L	V	S		
	G18	A/duck/Zhejiang/727145/2014	V	K	D	M	T	K	R	R	N	V	D	L	V	S		
	G18	A/duck/Zhejiang/77140/2014	V	K	D	M	T	K	R	R	N	V	D	L	V	S		
	G18	A/duck/Zhejiang/77127/2014	V	K	D	M	T	K	R	R	N	V	D	L	V	S		
	G20	A/Environment/Guangdong/34254/2019	V	K	D	M	T	K	R	R	S	V	D	L	A	S		
	G22	A/Environment/Guangxi/09909/2021	V	K	D	M	T	K	R	R	S	V	D	L	V	N		
	G23	A/Environment/Guangdong/34255/2019	V	K	D	M	T	K	R	R	S	V	D	L	A	S		
H4N6	G2	A/mallard/Yan chen/2005	V	K	D	M	T	R	R	R	S	V	D	L	V	S		
	G3	A/mallard/ZhaLong/88/2004	V	K	D	I	A	K	R	R	S	V	D	L	V	S		
	G4	A/duck/Shanghai/Y20/2006	V	K	D	M	M	K	R	R	S	V	D	L	V	S		
	G5	A/duck/Hunan/S1012/2009	V	K	D	M	T	K	R	R	S	V	E	L	V	S		
	G6	A/duck/Shanghai/421-2/2009	I	K	D	M	T	K	R	R	S	V	D	L	V	S		
	G7	A/Environment/Hubei/02/2009	V	K	D	M	T	K	K	R	S	V	D	L	V	S		
	G7	A/duck/Yunnan/YN-1/2011	V	K	D	M	T	K	R	Q	S	V	D	L	V	S		
	G7	A/Environment/Hunan/00600/2020	V	K	D	M	T	R	R	R	S	V	D	L	V	S		
	G8	A/weiyangshui/Jiangxi/14/2009	V	K	D	M	T	K	R	R	S	V	D	L	I	S		
	G8	A/duck/Guangxi/S2090/2012	V	K	D	M	M	K	R	R	S	V	D	L	V	S		
	G8	A/duck/Anhui/S4155/2009	V	K	D	M	T	K	R	R	S	I	D	L	V	S		

	G8	A/duck/Anhui/S2193/2012	V	K	D	M	T	K	R	R	S	V	D	L	V	N
	G8	A/duck/Guangxi/149D24/2013	V	K	D	M	T	K	K	R	S	V	D	L	V	S
	G9	A/duck/Shanghai/67-2/2009	V	K	D	M	T	K	R	R	S	V	D	L	I	S
	G9	A/duck/Shanghai/46-2/2009	V	K	D	M	T	K	R	R	S	V	D	L	I	S
	G9	A/duck/Shanghai/44-2/2009	V	K	D	M	T	K	R	R	S	V	D	L	I	S
	G15	A/duck/Zhejiang/D2-1/2013	V	K	D	M	A	K	R	R	S	V	D	L	V	S
	G23	A/Environment/Chongqing/33933/2018	V	K	D	M	T	K	R	Q	S	V	D	L	V	S
	G24	A/Environment/Sichuan/39514/2019	V	K	D	T	T	K	R	R	S	V	D	L	V	S
<b>H4N8</b>	G1	A/chicken/Guangdong/S1010/2010	V	K	D	M	T	K	R	R	S	V	D	F	I	S
	G3	A/Mallard/Hubei/chenhu VII09/2015	V	K	D	M	T	K	R	R	S	I	D	L	V	S
	G3	A/goose/Hunan/S2466/2011	V	K	N	M	T	K	R	R	S	V	D	L	V	S
	G5	A/greylag goose/Changsha/CS-1983/2013	V	K	D	M	T	K	R	R	S	V	D	L	I	S
	G6	A/greylag goose/Changsha/CS-510/2013	V	K	D	M	T	K	R	R	S	V	D	L	I	S
	G9	A/chicken/Jiangsu/YC/2015	V	K	D	M	T	K	R	R	S	V	D	L	A	S