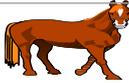
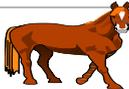




# Les virus grippaux émergents (H5N1 ou H7N9) en 2016

**Bruno LINA**

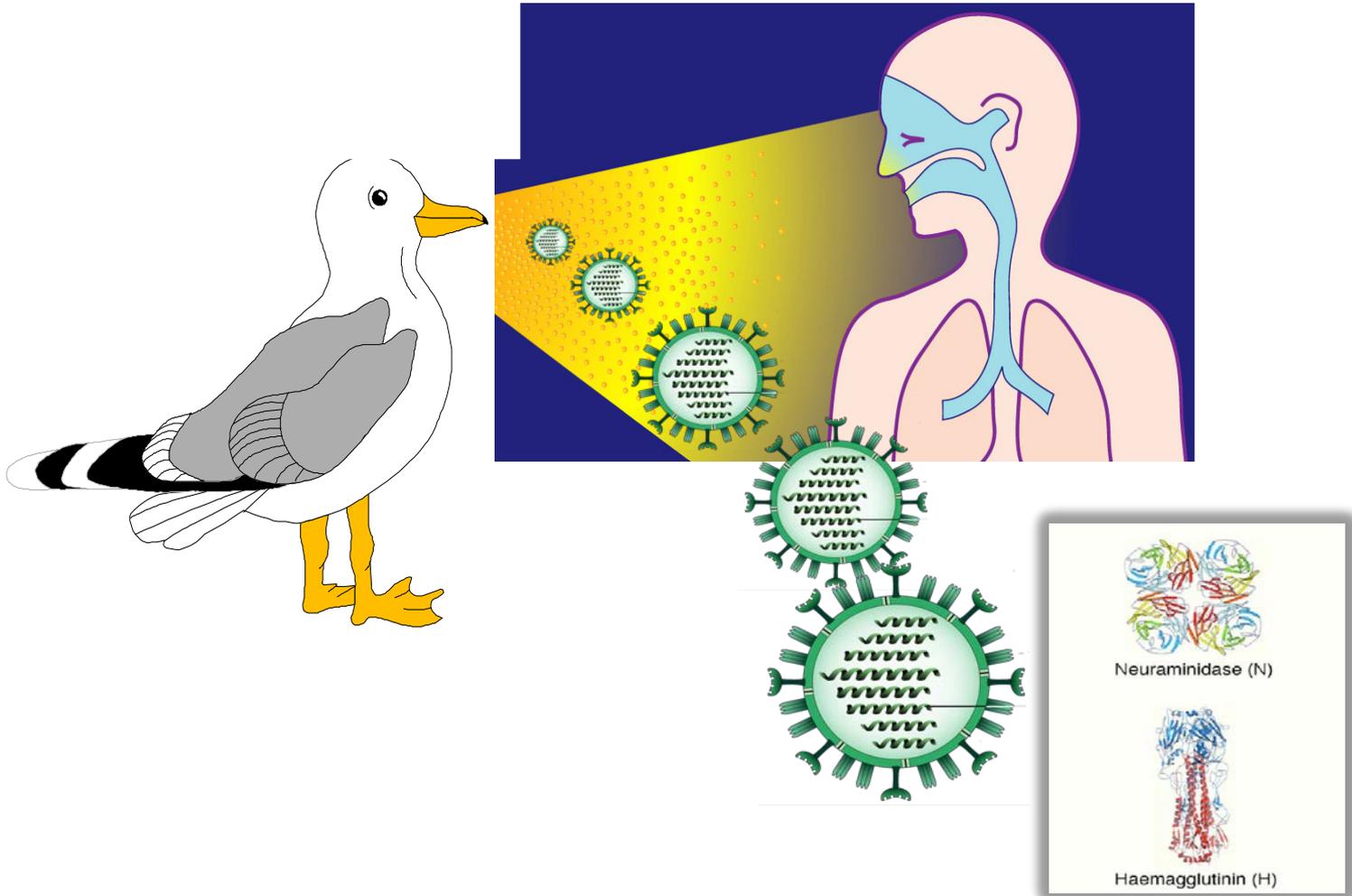
CNR des virus influenza, Institut des Agents Infectieux, Hôpital de la Croix-Rousse, Lyon  
Virpath, CIRI, INSERM U1111, CNRS UMR5308, ENS Lyon, UCBL, Lyon, France

H1				
H2				
H3				
H4				
H5				
H6				
H7				
H8				
H9				
H10				
H11				
H12				
H13				
H14				
H15				
H16				

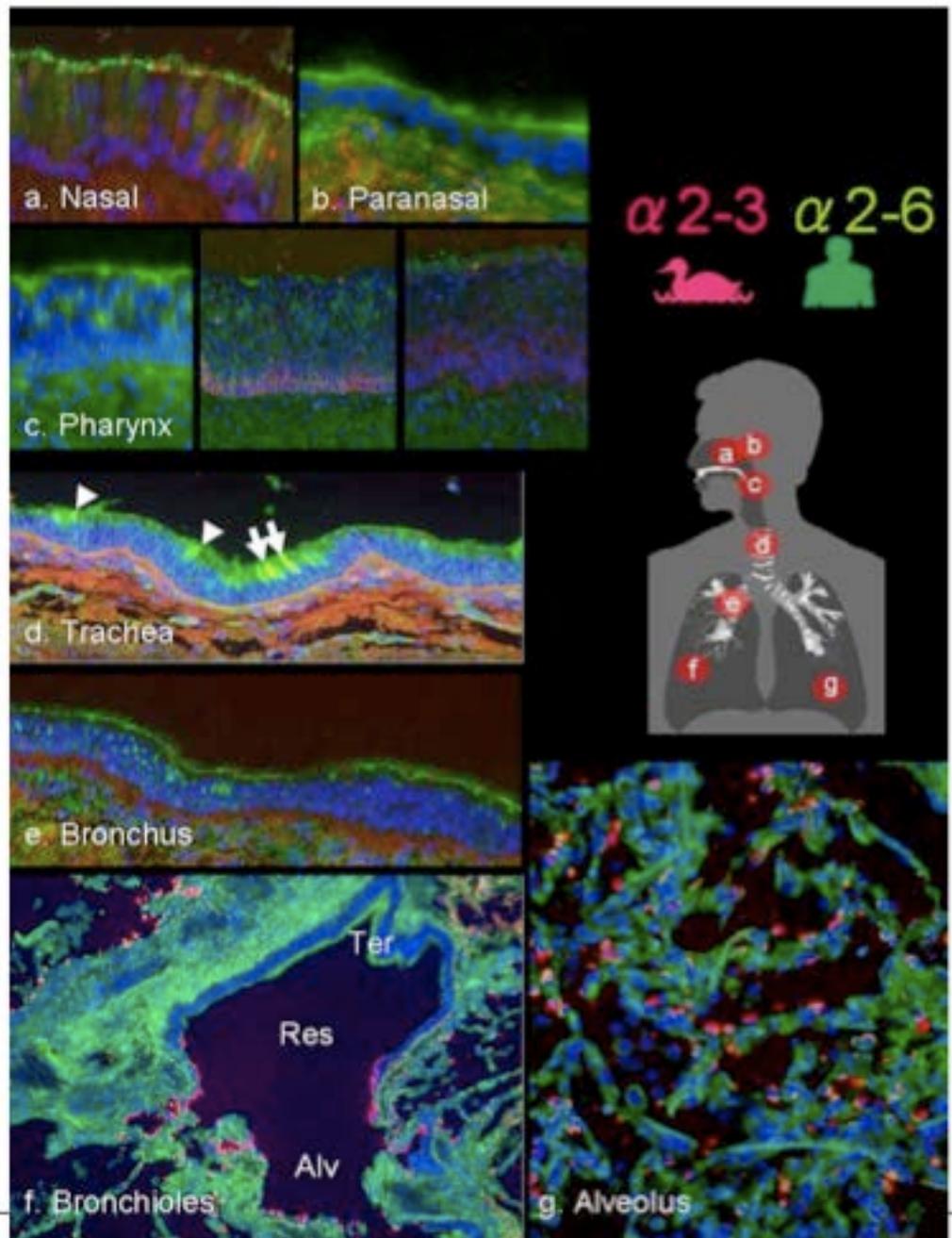
N1				
N2				
N3				
N4				
N5				
N6				
N7				
N8				
N9				

**Les hôtes des  
différents sous-types  
de virus influenza A  
aviaires**

# Grippe aviaire : pas de transmission à l'homme

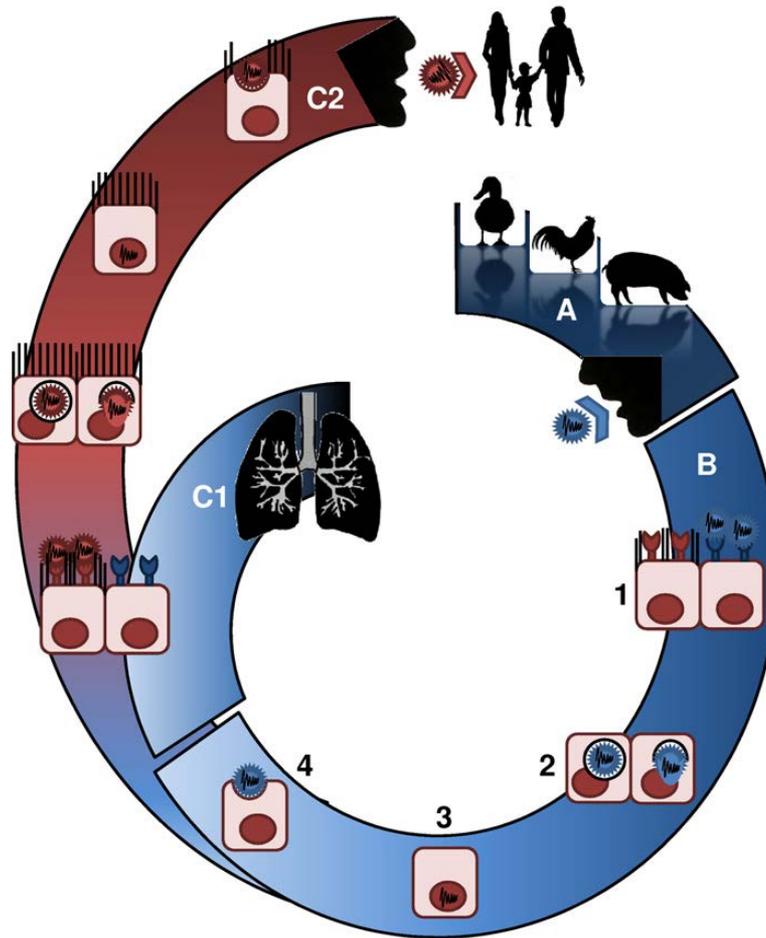


# Distribution des récepteurs $\alpha$ 2-6 et $\alpha$ 2-3 dans le tractus respiratoire



# Analyse de risque :

« the bottleneck of upper respiratory tract adaptation »



**Table 2**

Known mutations and associated mechanisms of adaptation of zoonotic influenza viruses to human hosts via the crossing of virus–cell interaction barriers.

Virus–cell interaction barrier	Protein	Mutation	Adaptive mechanism	Ref.		
Virus attachment	HA	N154S	Increases $\alpha$ 2,6 binding in H5 subtype	[194]		
		N182K	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194,195]		
		E190D	Increases $\alpha$ 2,6 binding in H1 subtype	[86,196]		
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		Q222L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]		
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		Q226L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H2, H3, H4, H5 and H9 subtypes	[81,86,198,199]		
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Viral replication	PB1 + PB2	Unknown	Increases polymerase activity of HPAIV H5N1 in human cells (unknown mechanism)	[126]		
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	Virus release Viral escape from host immune responses		NA	I275V	Increases $\alpha$ 2,6 substrate specificity in N2 subtype	[133]
HA		Antigenic shift	Escapes pre-existing humoral immunity	[134]		
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NS1		P42S	Prevents double-stranded RNA-mediated activation of NF- $\kappa$ B and IRF-3 pathways during HPAIV H5N1 infection	[140]		
		L103F + I106M	Allows binding of HPAIV H5N1 NS1 protein and CPSF30 resulting in decreased INF- $\beta$ mRNA production	[141]		
		PDZ domain ligand in C-terminus	Disruption of protein-protein interactions, including impairment of IFN-stimulated signaling, disruption of tight junctions, and reduction of apoptosis	[142–145]		
	PB1-F2	N66S	Unknown mechanism associated with apoptosis pathway regulation	[150]		

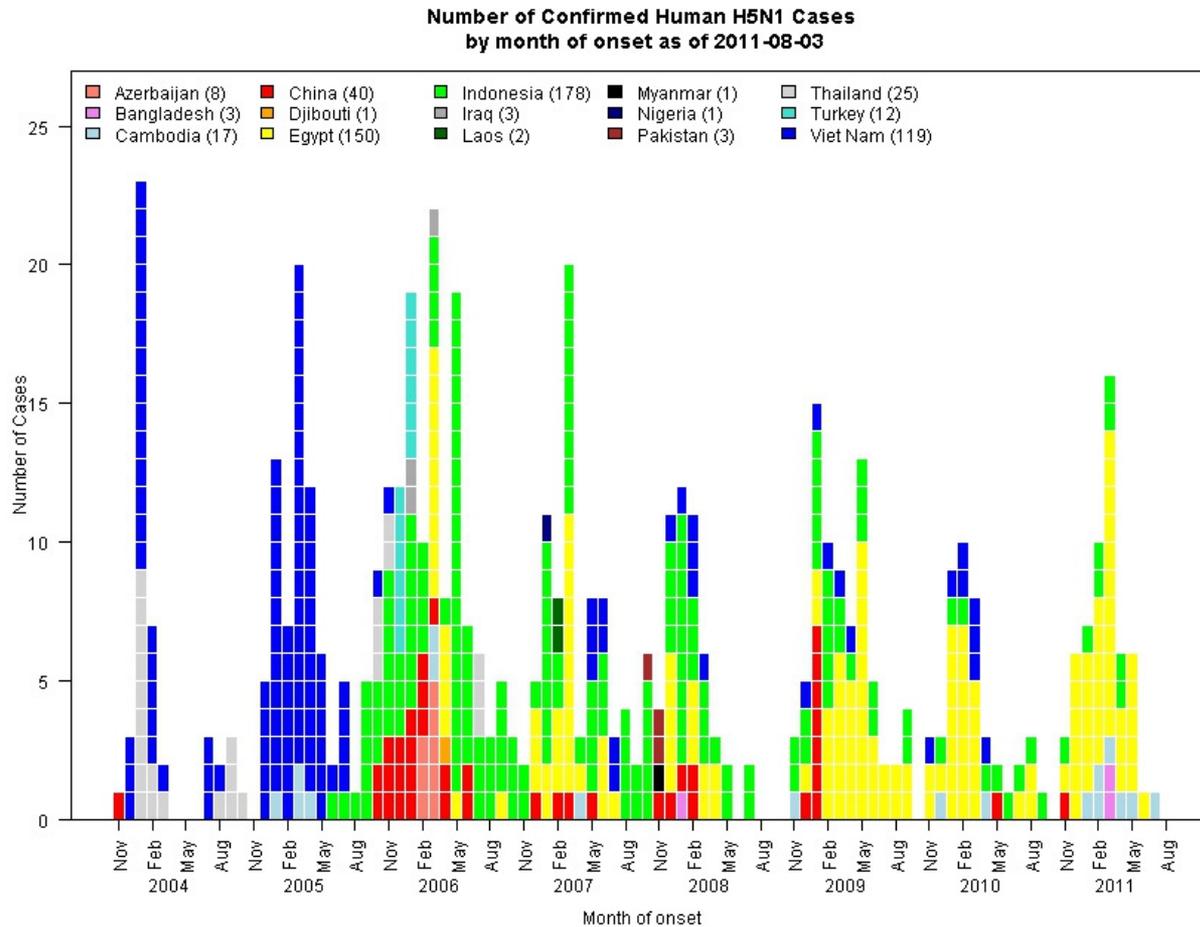
Longue liste de facteurs limitants avant transmission inter-humaine

# Alerte N° 1 : virus H5

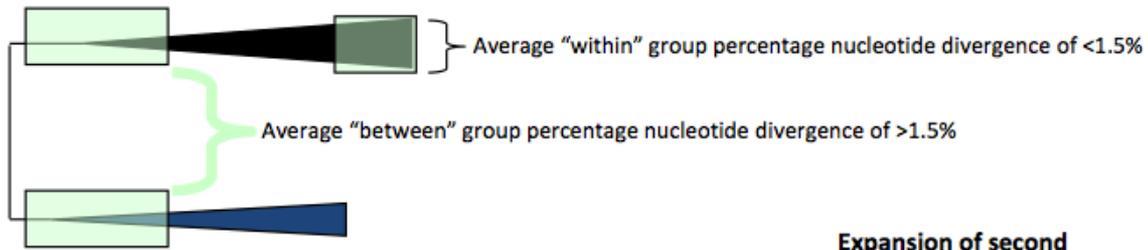
(H5N1, H5N6, H5N8, H5N9)

850 cas / 449 décès

# Saisonnalité et distribution des cas rapportés



# Evolution of the Asian H5 Hemagglutinin

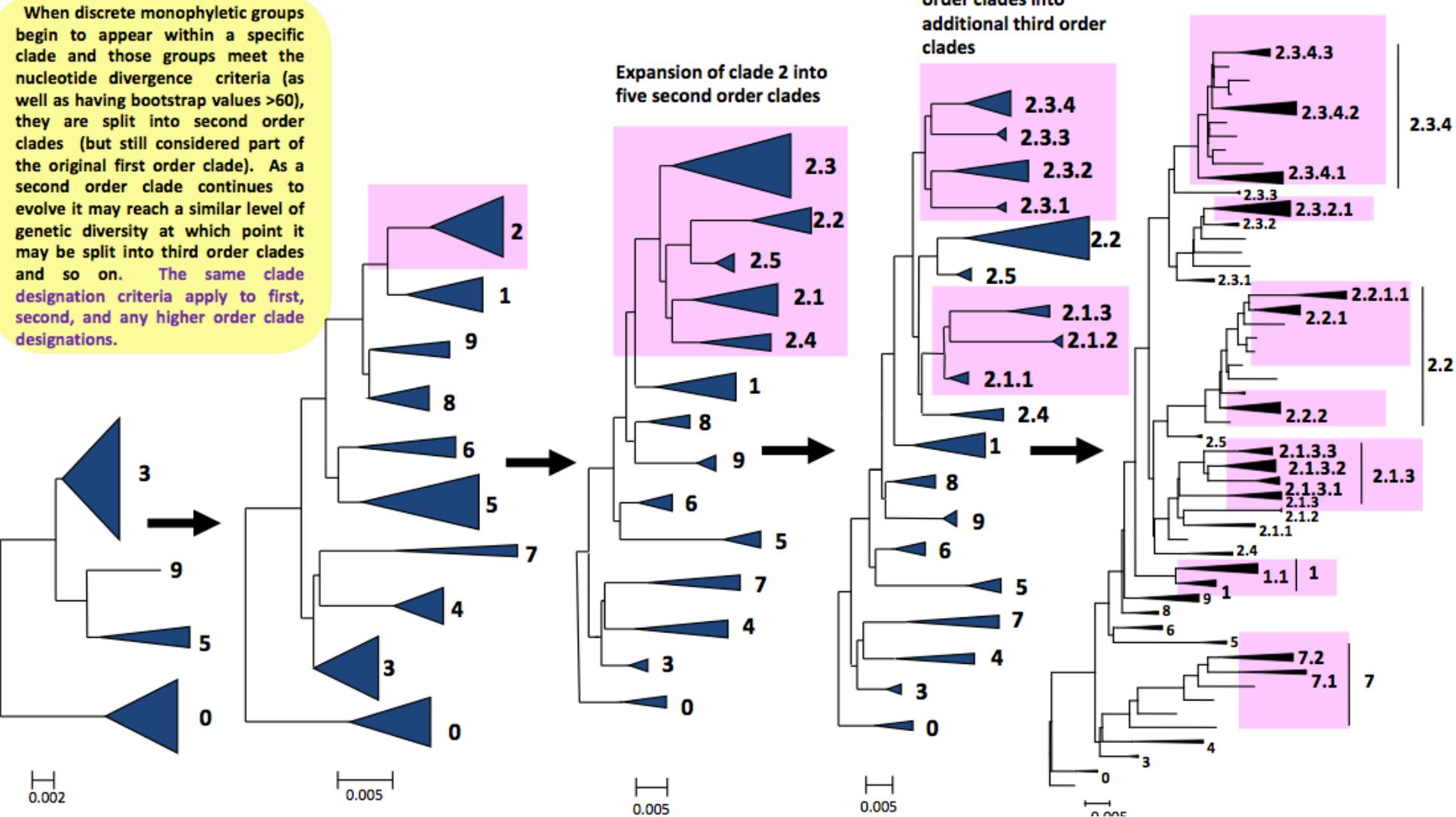


Expansion of first, second and third order clades into additional second, third and fourth order clades

Expansion of second order clades into additional third order clades

Expansion of clade 2 into five second order clades

When discrete monophyletic groups begin to appear within a specific clade and those groups meet the nucleotide divergence criteria (as well as having bootstrap values  $>60$ ), they are split into second order clades (but still considered part of the original first order clade). As a second order clade continues to evolve it may reach a similar level of genetic diversity at which point it may be split into third order clades and so on. The same clade designation criteria apply to first, second, and any higher order clade designations.



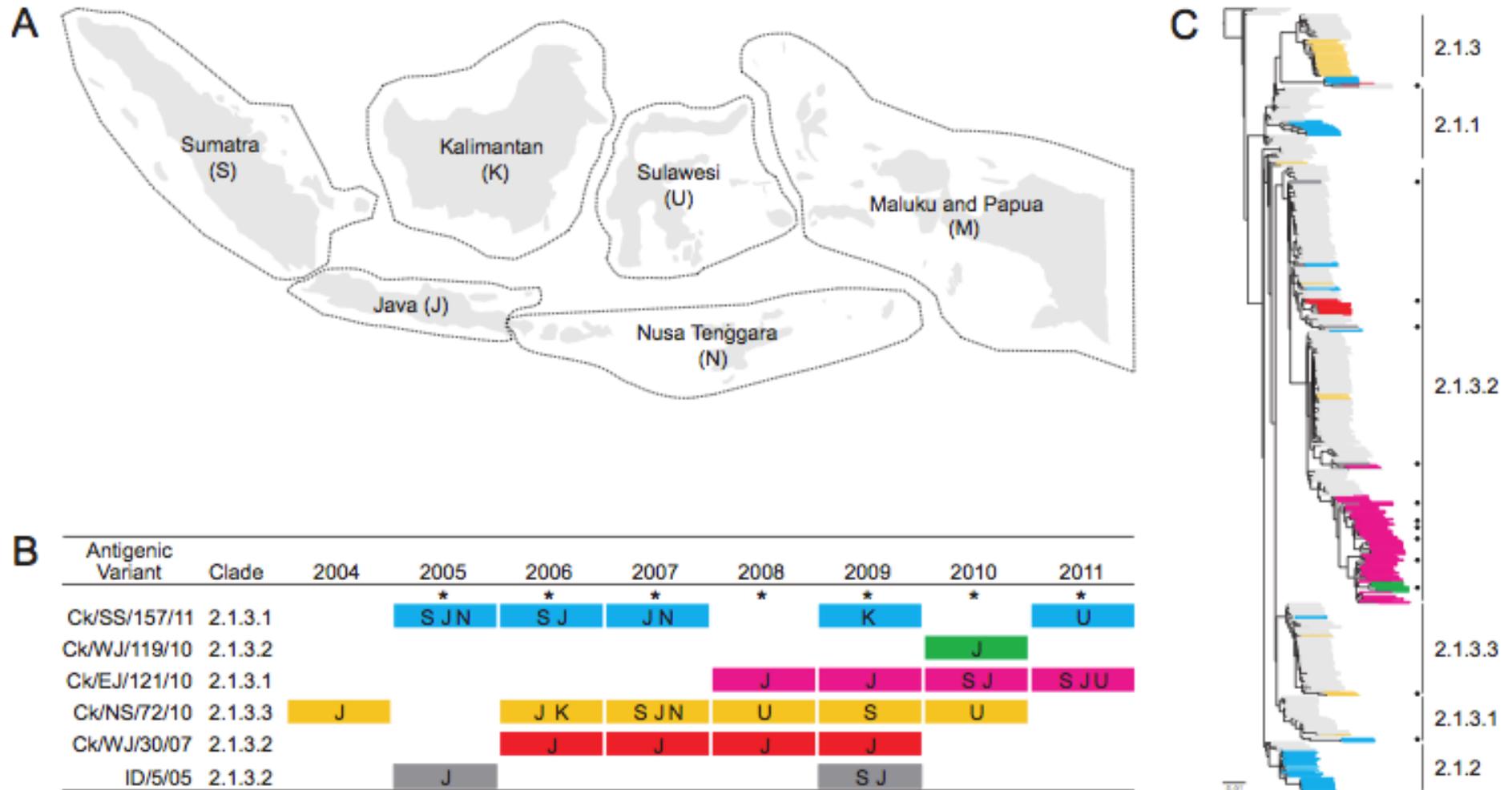
2.3.4

2.2

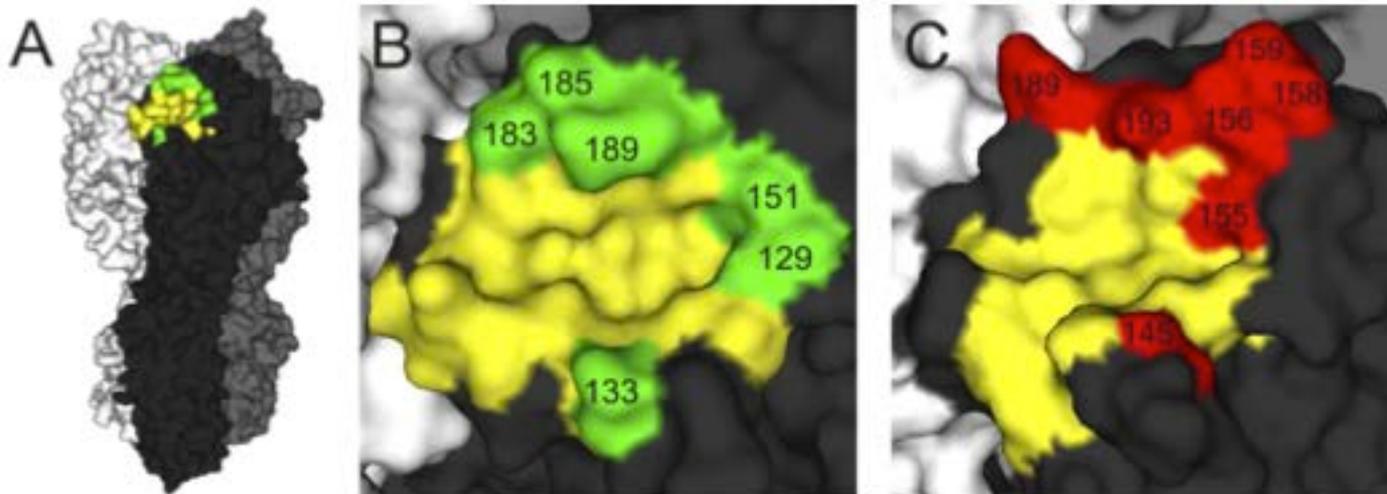
2.1.3

7

# Emergence et distribution des différents clades de H5N1 en Indonésie



Ce virus présente des similitudes avec les variants observés dans la grippe saisonnière humaine



# De moins en moins de cas H5 en Asie

**Table 1: Cumulative number laboratory-confirmed human cases (C) and deaths (D) of influenza A (H5N1) virus infection reported to WHO (January 2003 to 4 April 2016), Western Pacific Region.**

Country	2003-2010		2011		2012		2013		2014		2015		2016		Total	
	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D
Cambodia	10	8	8	8	3	3	26	14	9	4	0	0	0	0	56	37
China	40	26	1	1	2	1	2	2	2	0	6	1	0	0	53	31
Lao PDR	2	2	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Viet Nam	119	59	0	0	4	2	2	1	2	2	0	0	0	0	127	64
<b>Total</b>	<b>171</b>	<b>95</b>	<b>9</b>	<b>9</b>	<b>9</b>	<b>6</b>	<b>30</b>	<b>17</b>	<b>13</b>	<b>6</b>	<b>6</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>238</b>	<b>134</b>

# H5Nx

Virus attachment **NO**

Virus fusion **NO**

Virus répliation **OK**

Virus release **OK**

Immune response **OK**

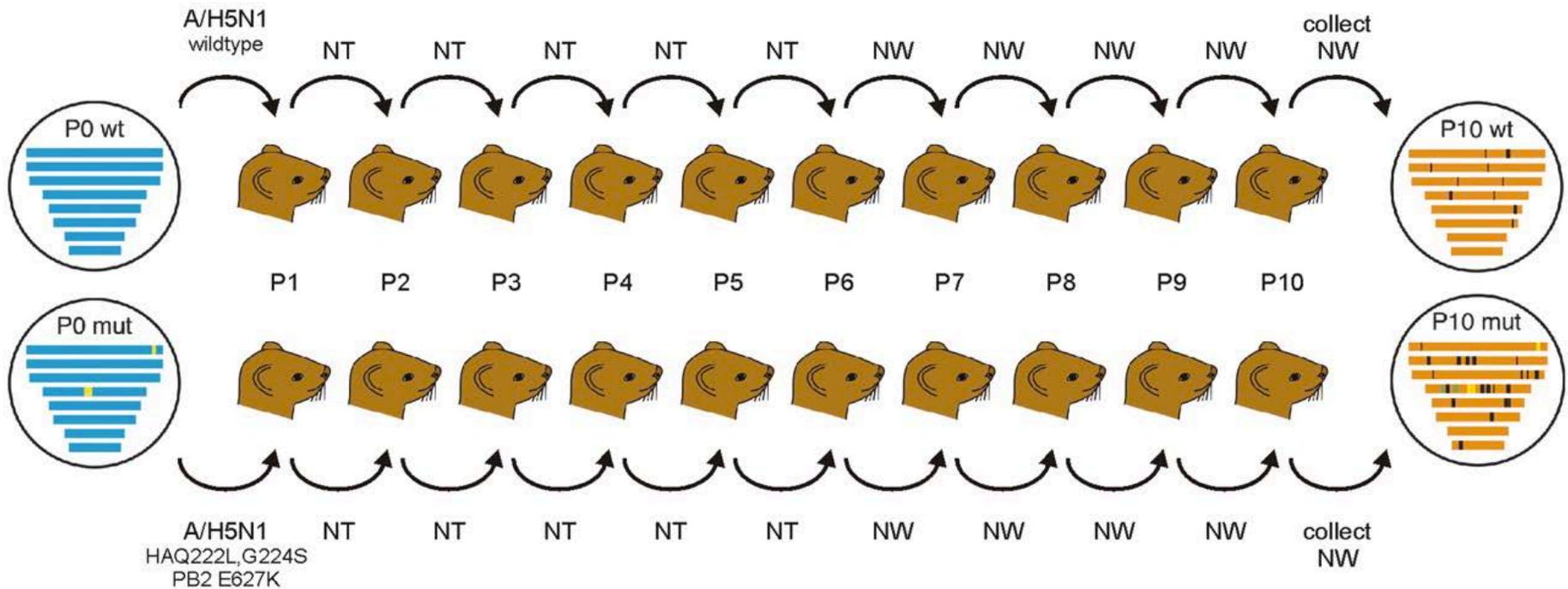
Virulence **OK**

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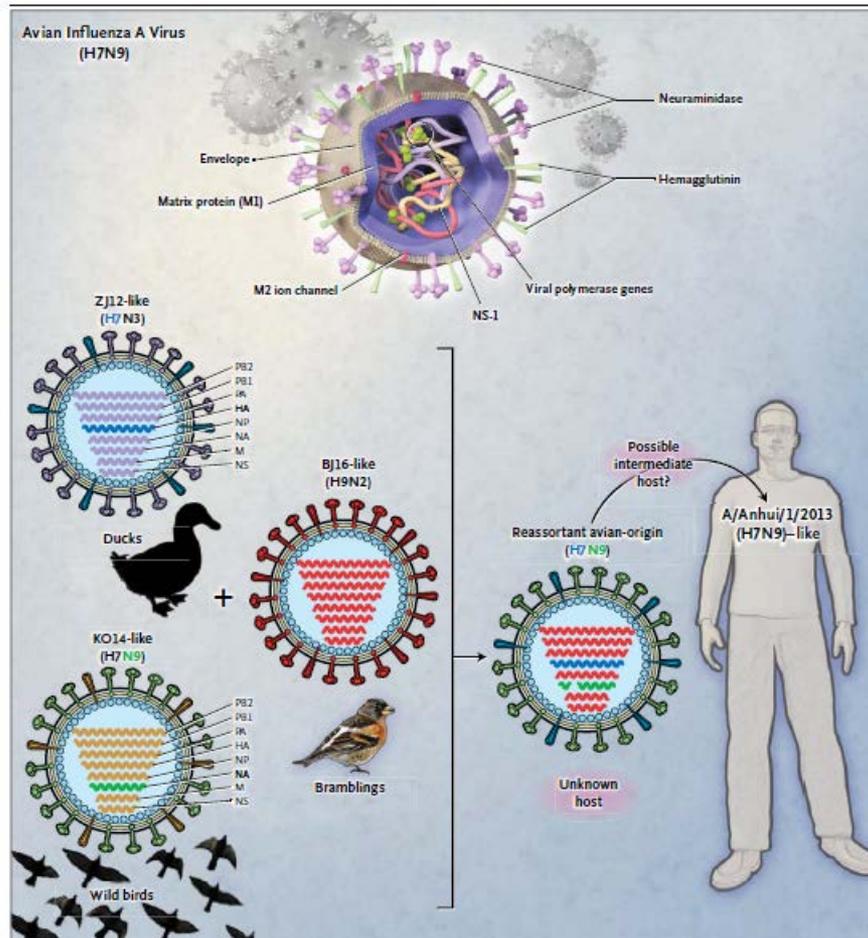
# Pas de transmission interhumaine, mais...



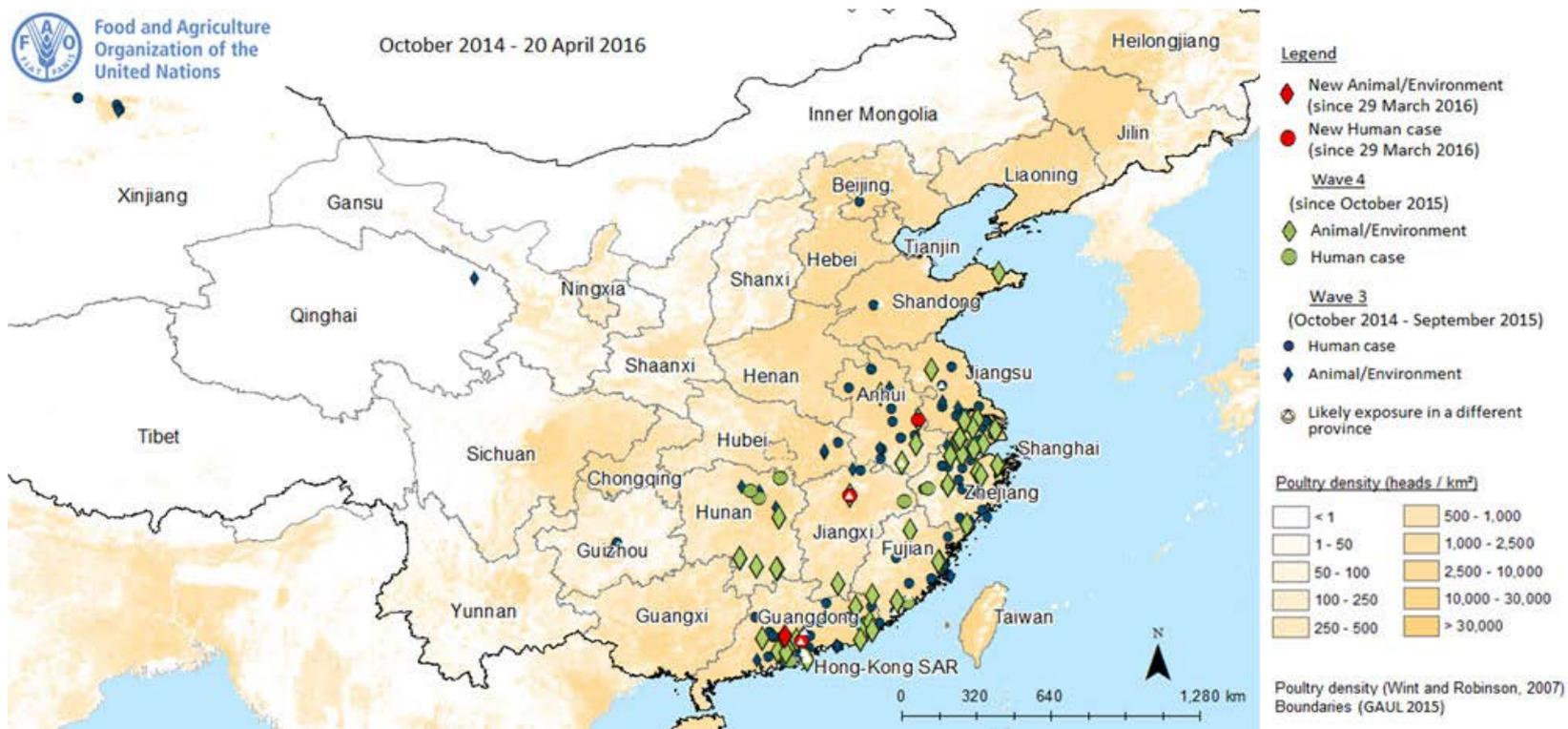
# Alerte N° 2 : virus H7N9

790 cas / 378 décès

# Assemblage du virus



# Localisation exclusive en Chine, rares cas exportés



# Saisonnalité et distribution des cas

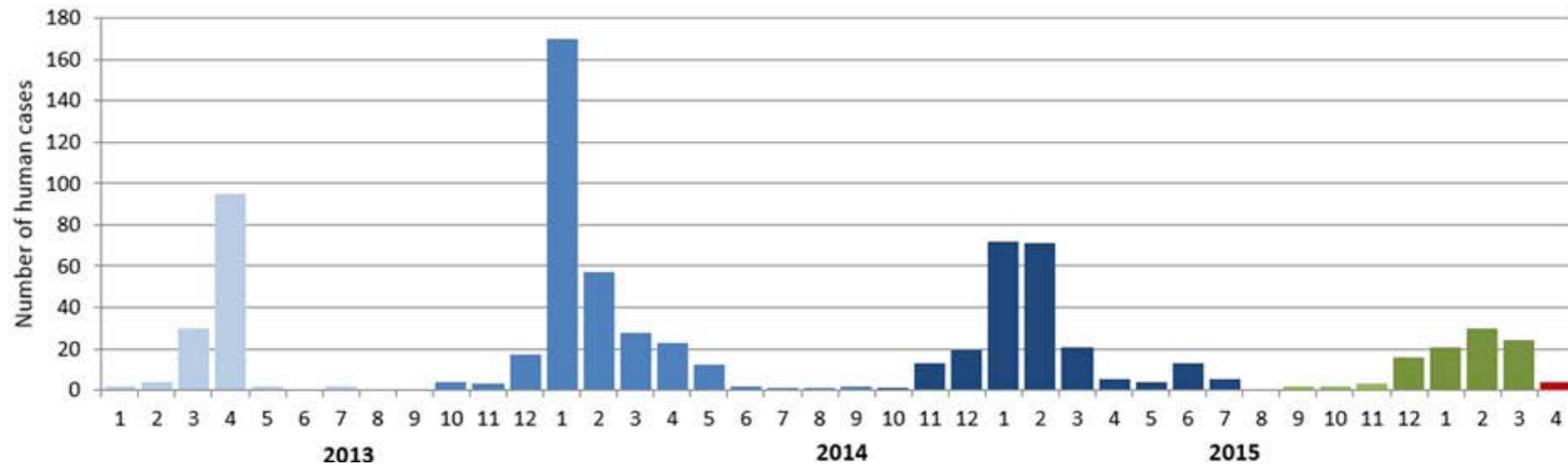
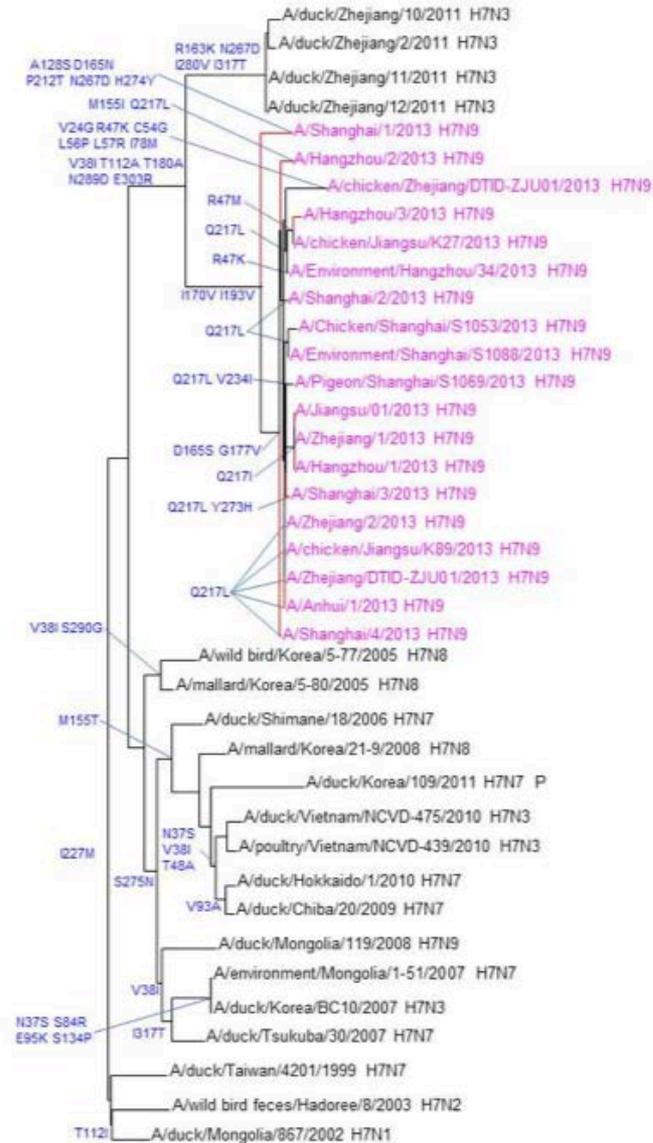


Fig. 1A  
HA



# H7N9

Virus attachment **OK**

Virus fusion **OK**

Virus replication **OK**

Virus release **OK**

Immune response **OK**

Virulence **OK**

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