Epidémiologie récente de la grippe : le vaccin tétravalent est-il la solution?

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Journée du Groupe Vaccination-Prévention de la SPILF
18 mai 2018

Quelques éléments de compréhension de la réponse immunitaire contre la grippe

Basiques de la réponse immunitaire

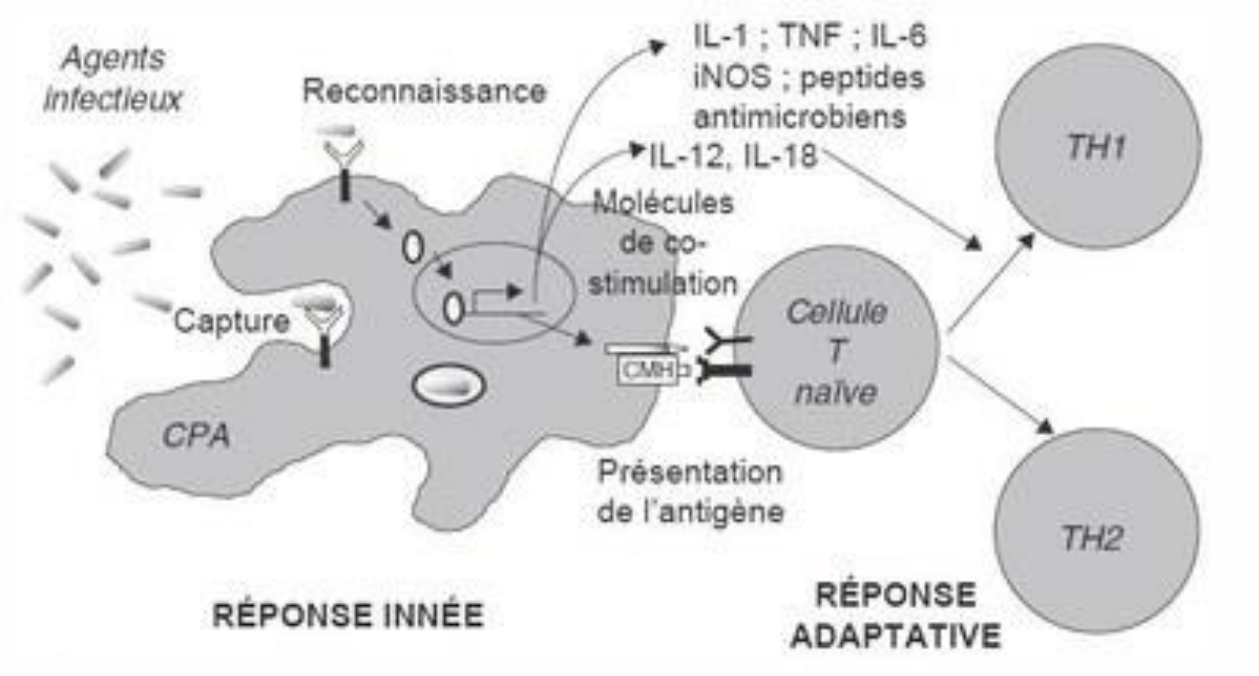
- La réponse immunitaire comporte plusieurs composants:
  - Réponse innée
  - Réponse adaptative primaire
  - Réponse adaptative mémoire

- Sa qualité et son action dépends en fonction de l'âge
  - Défaillante aux extrêmes de la vie
  - Efficace entre ces deux extrêmes

- Elle est globalement très performante, permettant de maitriser le risque infectieux et le risque tumoral

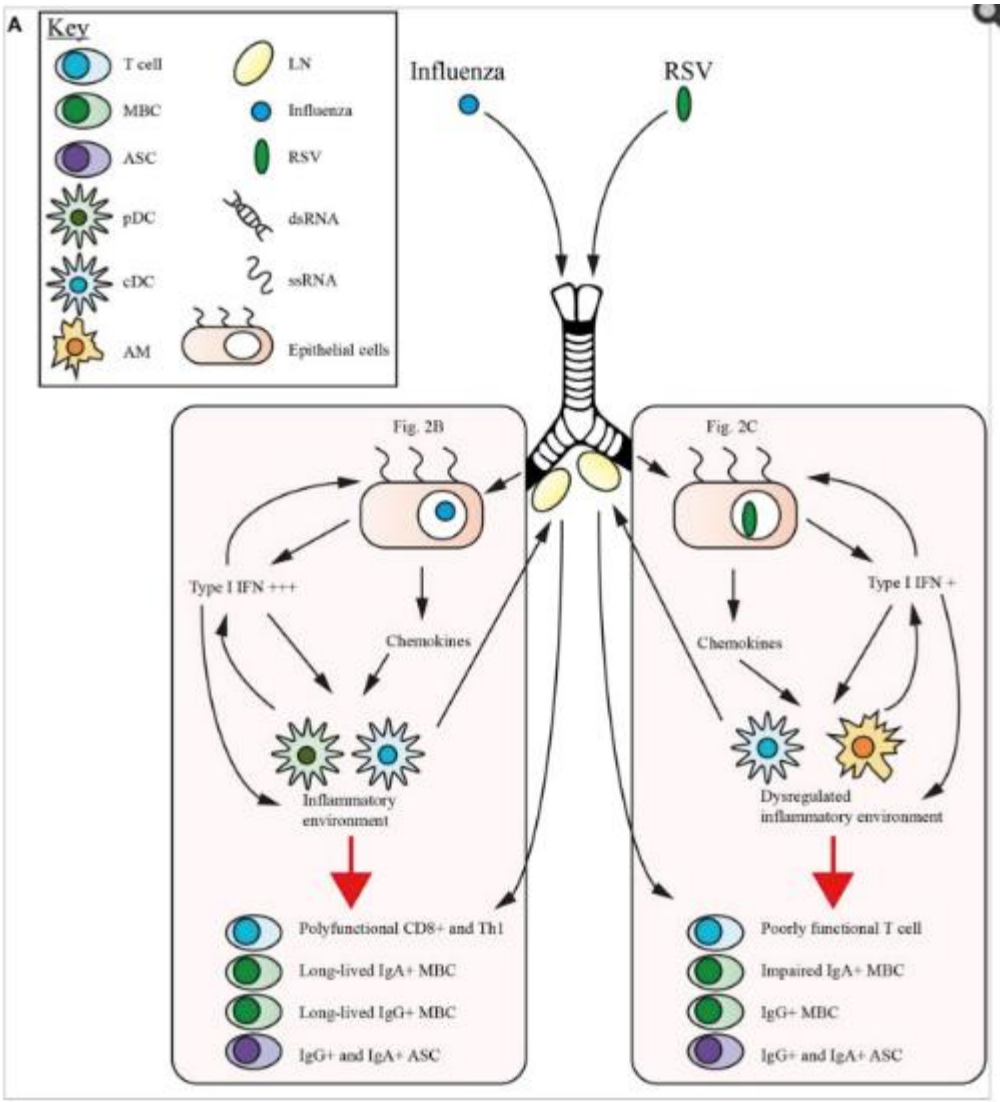
- Elle a un mode de fonctionnement complexe qui s'adapte en fonction des pathogènes rencontrés.

Phase 1 : la réponse innée



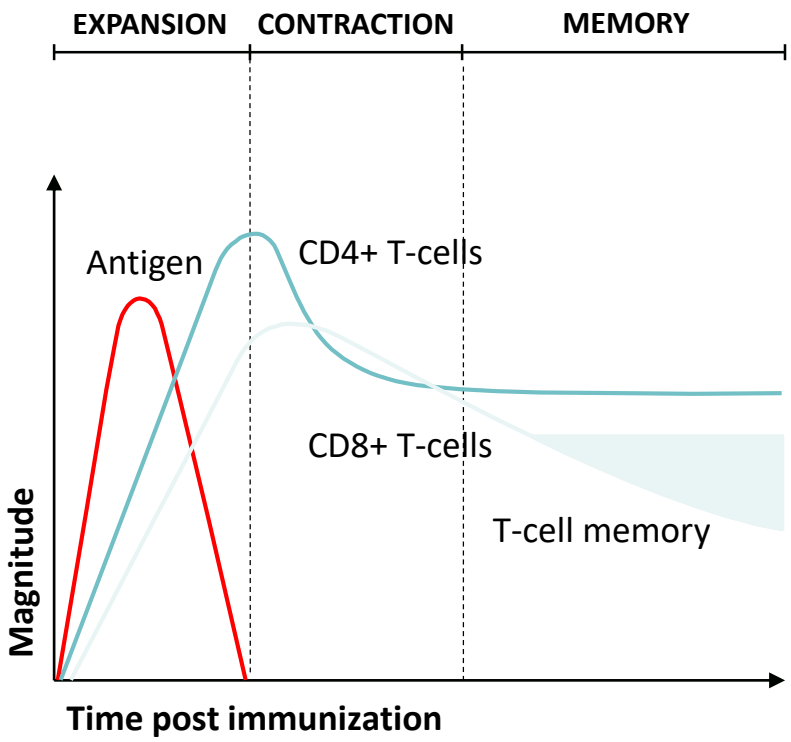
– Les deux bras du système immunitaire des vertébrés.

Il existe des différences sur les voies d'activation de la réponse immunitaire innée en fonction des pathogènes

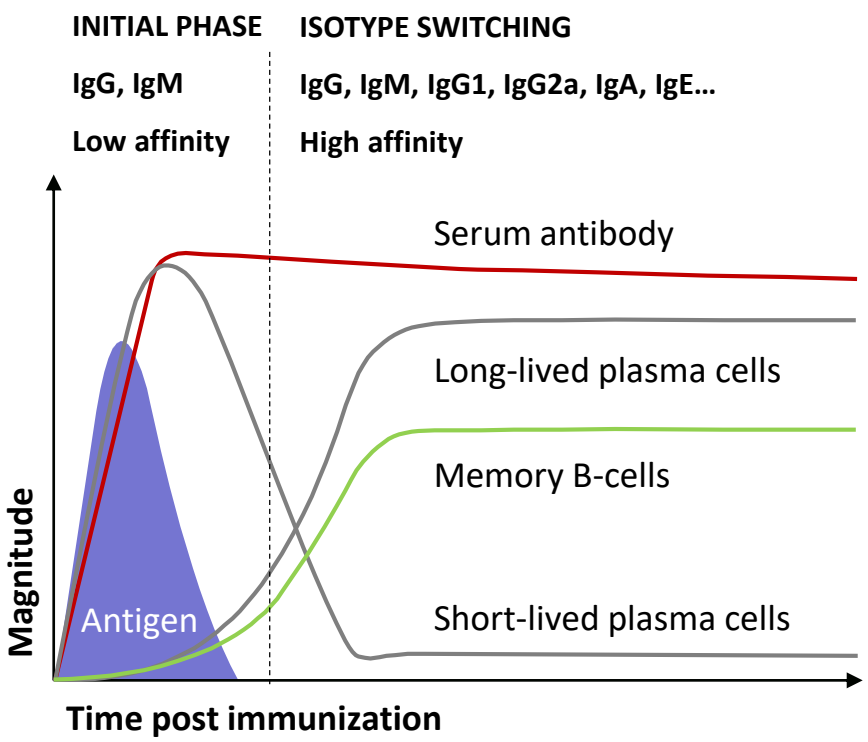


Phase 2 : la réponse adaptative

Cellular adaptive immune responses



Humoral adaptive immune response



Seder RA and Ahmed R. *Nat Immun* 2003;9:835-842.

Si on tente de détailler (simplement)

CD4 T cells

IFNg, TNFa, IL-2, Chemokines, CD40L

Cytokine release
T help
Switch isotypique

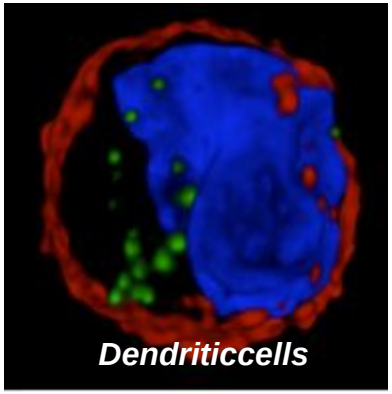
Virus elimination
Control of the viral infection

Neutralization
Inhibition
Phagocytosis
ADCC

B cells

Systemic response
(IgG, IgA)

Mucosal response
(IgGIgA)



from A SmedSörensen
MHC class II (red) virus (green)

CD8 cytotoxic T cells

Killing of infectedcells

Effector CD8 T cells

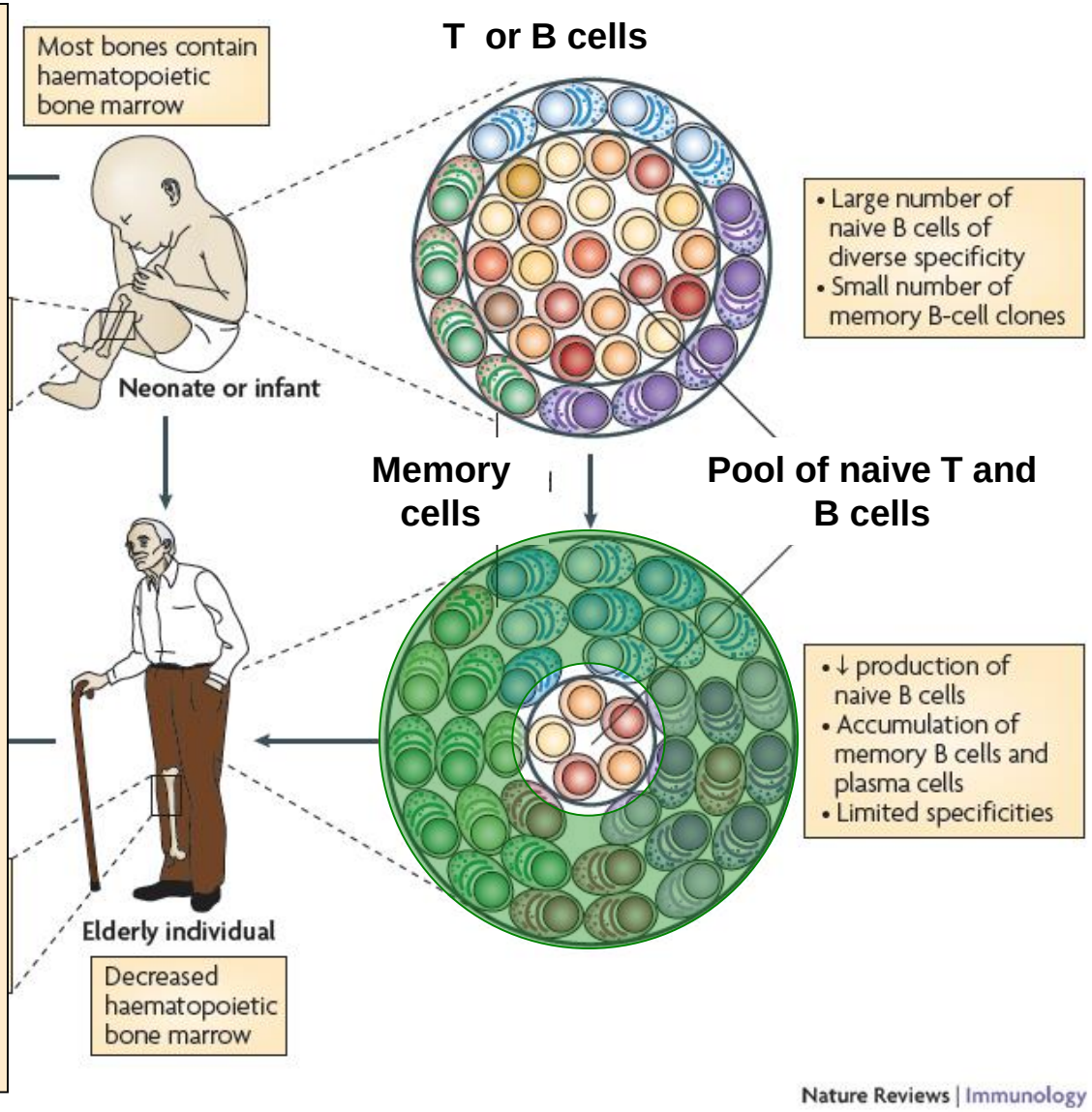
IFNg, TNFa, IL-2, Chemokines, CD40L

NK cells

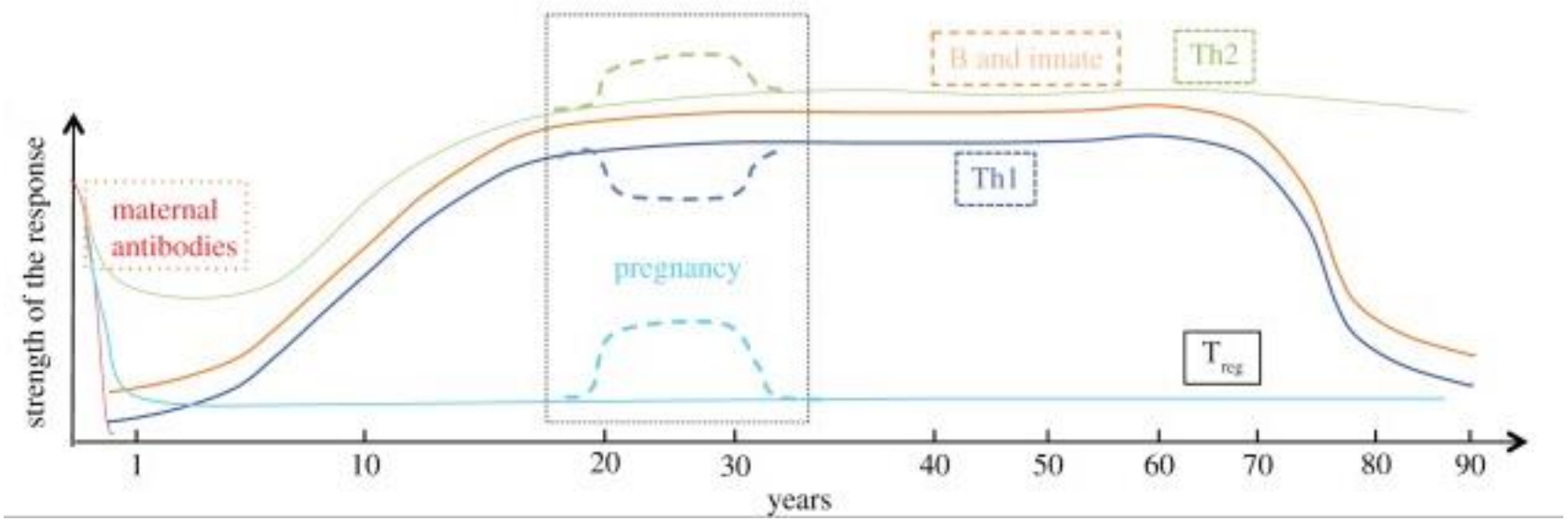
- **IgA: first line of defense in respiratory tract (prevent viral infection)**
  Renegar et al 2004
- **Mucosal T cell response**
  Arulanandam et al 2001

Limites de ce systeme aux capacités illimitées

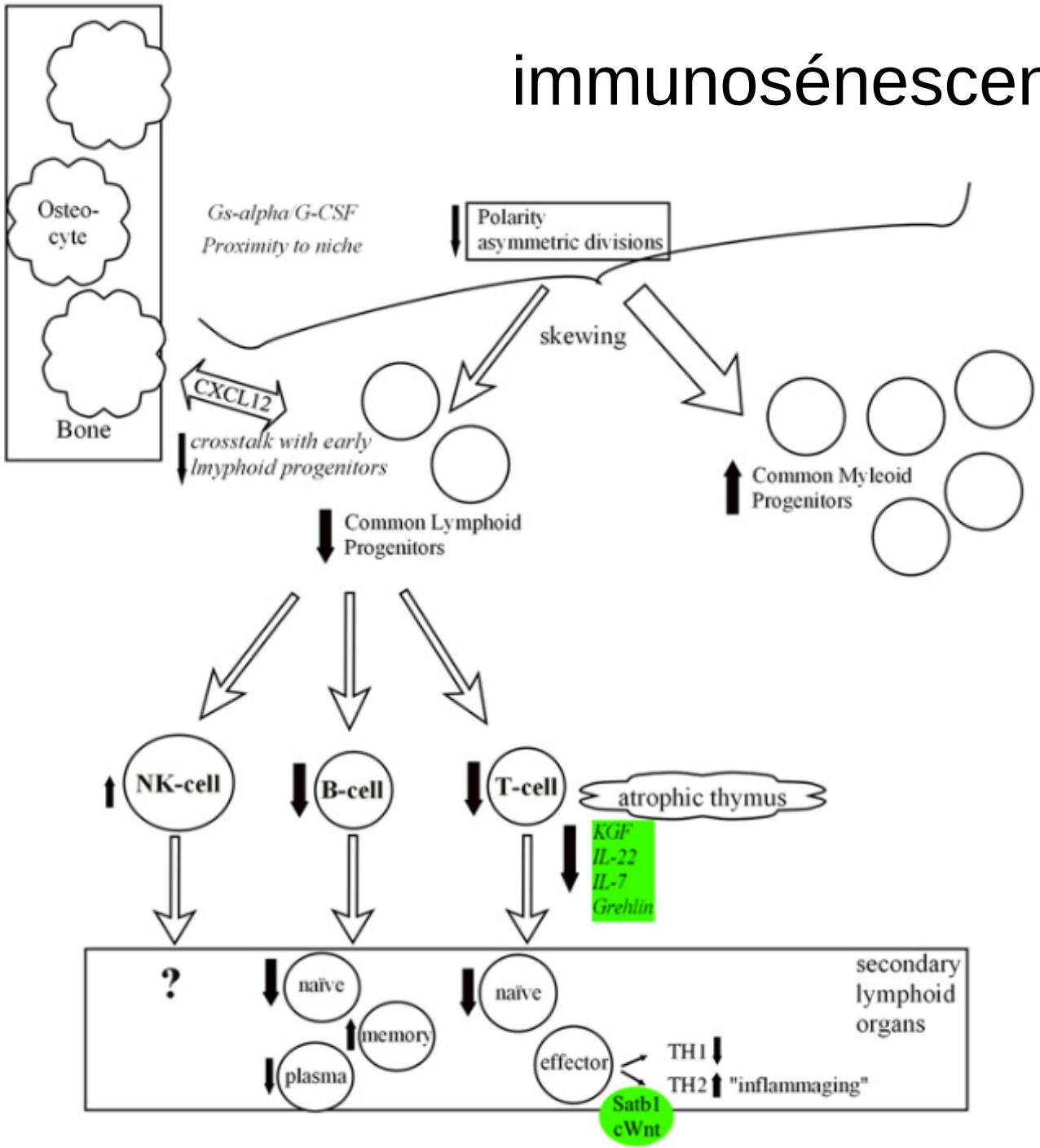
- Target groups:
  - Without immunological experience (or little)
  - **With immunological experience (multiple infection/ multiple vaccination)**
  - With long-term immunological experience **<u>but aged immune system</u>**



Evolution de la réponse immunitaire en fonction de l'age



immunosénescence



TH2 inflammation

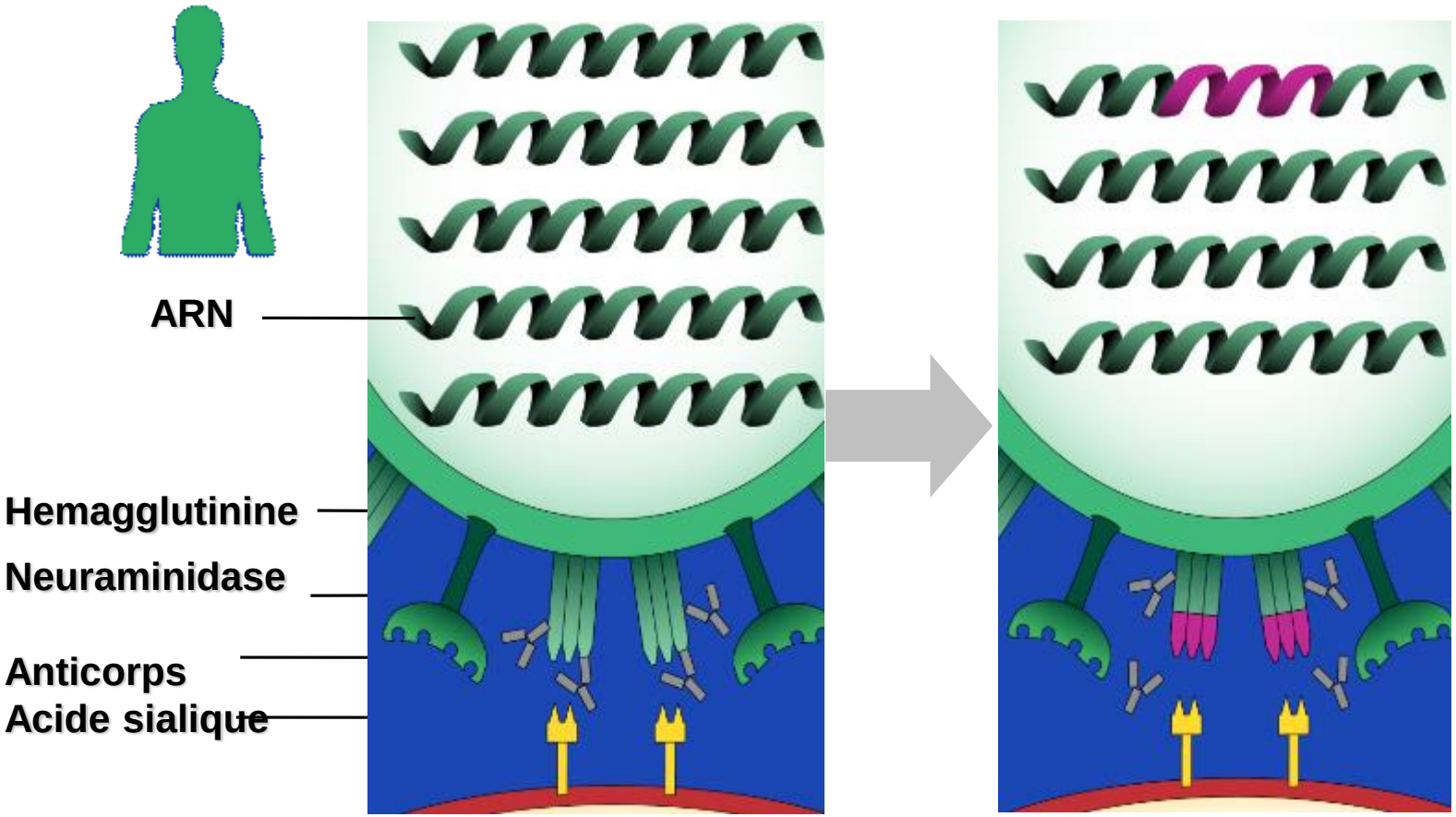
immunosénescence

Features	Increase	Decrease	No change
Innate immunity			
Phagocytosis	–	√	√
Free radical production	√	√	–
Chemotaxis	–	√	–
Cytokine production	√	–	–
Myeloid cell number	√	–	–
Adaptive immunity			
Naïve cell number	–	√	–
Memory cell number	√	–	–
T regulatory cell number	√	–	–
T regulatory cell function	–	√	–
Proliferation	–	√	–
IL-2 production	–	√	–
B regulatory cell number/function	–	√	–
B cell immunoglobulin production	–	√	–
B cell autoantibody production	√	–	–

Changes are indicated with a checkmark (√) and, absence of changes with a horizontal bar (—).

Les défis de la vaccination contre la grippe

L’evolution permanente et imprévisible des virus



Les vaccins actuels n'induisent qu'une réponse humorale

CD4 T cells

IFNγ, TNFα, IL-2, Chemokines, CD40L

Cytokine release
T help
Switch isotypique

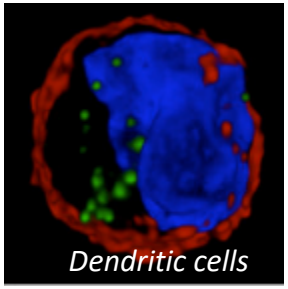
Y Y Y Y Y

Neutralization
Inhibition
Phagocytosis
ADCC

B cells

Systemic response
(IgG, IgA)

Mucosal response
(IgG, IgA)



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MHC class II (red) virus (green)

CD8 cytotoxic T cells

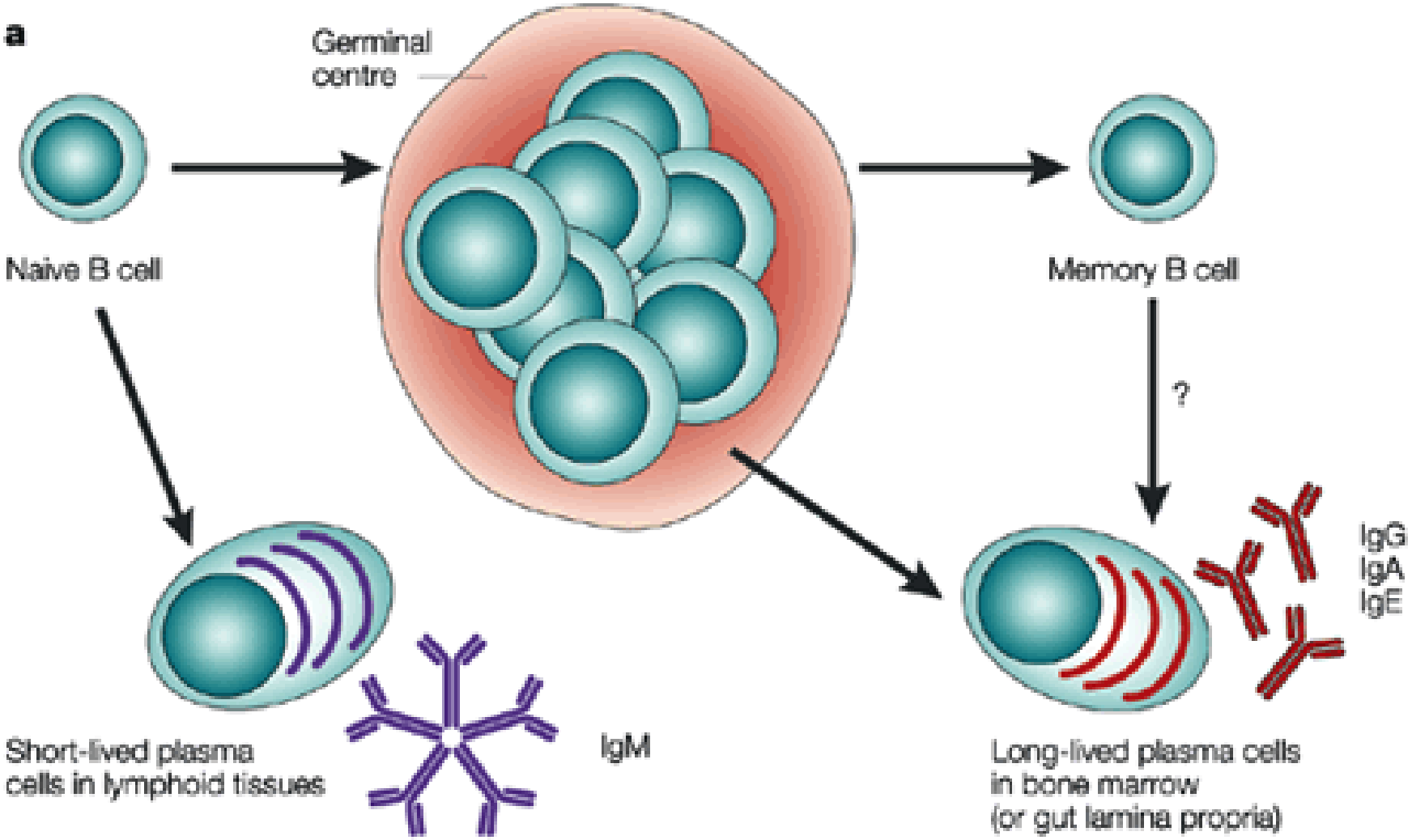
Effector CD8 T cells

NK cells

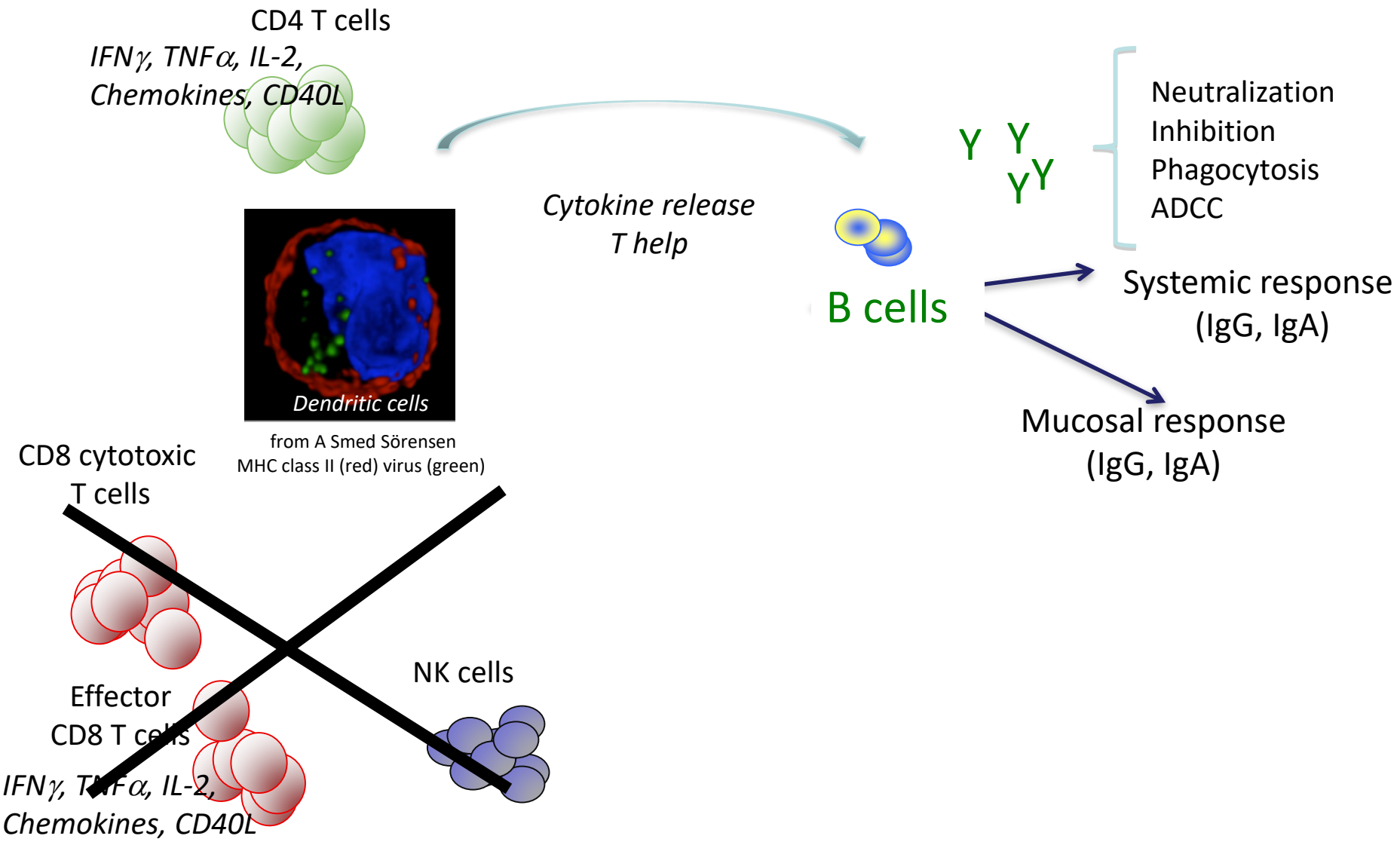
IFNγ, TNFα, IL-2, Chemokines, CD40L

- IgA: first line of defense in respiratory tract (prevent viral infection) *Renegar et al 2004*
- Mucosal T cell response *Arulanandam et al 2001*

B cell differentiation



Immune responses to inactivated influenza vaccines in elderly



Conclusion

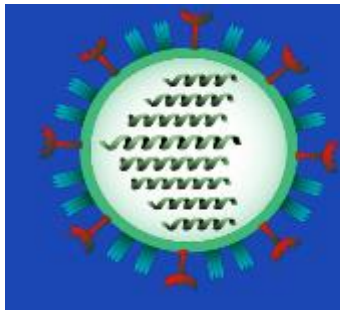
- La réponse immunitaire est performante mais variable en fonction de l'age
- Les vaccins utilisent efficacement le système immunitaire
- Les cibles de la vaccination sont ceux qui répondent le moins bien à la stimulation immunitaire (tant pour la réponse post infectieuse que la réponse post vaccinale)
- Les vaccins inactivés induisent une réponse très spécifique de souche
- Tous ces éléments « fragilisent » le vaccin, mais ne remettent pas en cause les politiques de vaccination
- Ils entrainent la nécessité de préparer de meilleurs vaccins

Les défis des vaccins contre la grippe

- Le bon choix des souches vaccinales est crucial
- La prévision de l’évolution des virus doit aussi aider au choix
- Les vaccins doivent être bien évalués

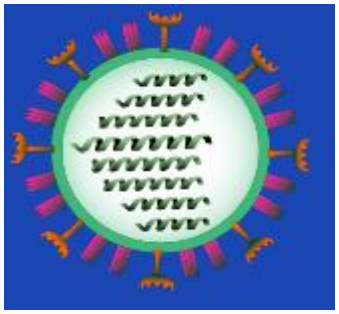
Types, sous-types & lignages des virus influenza circulant

H1N1

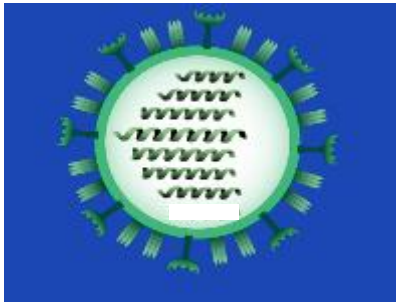


Type A

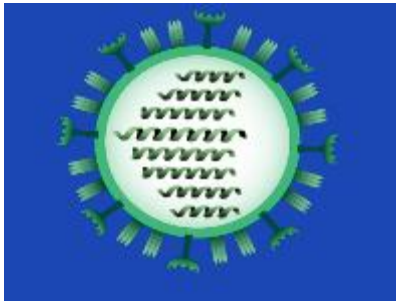
H3N2



Type C

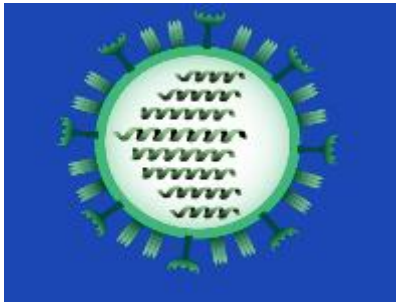


Yamagata

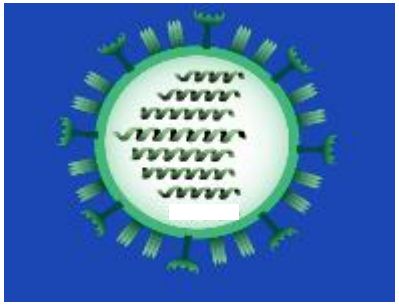


Type B

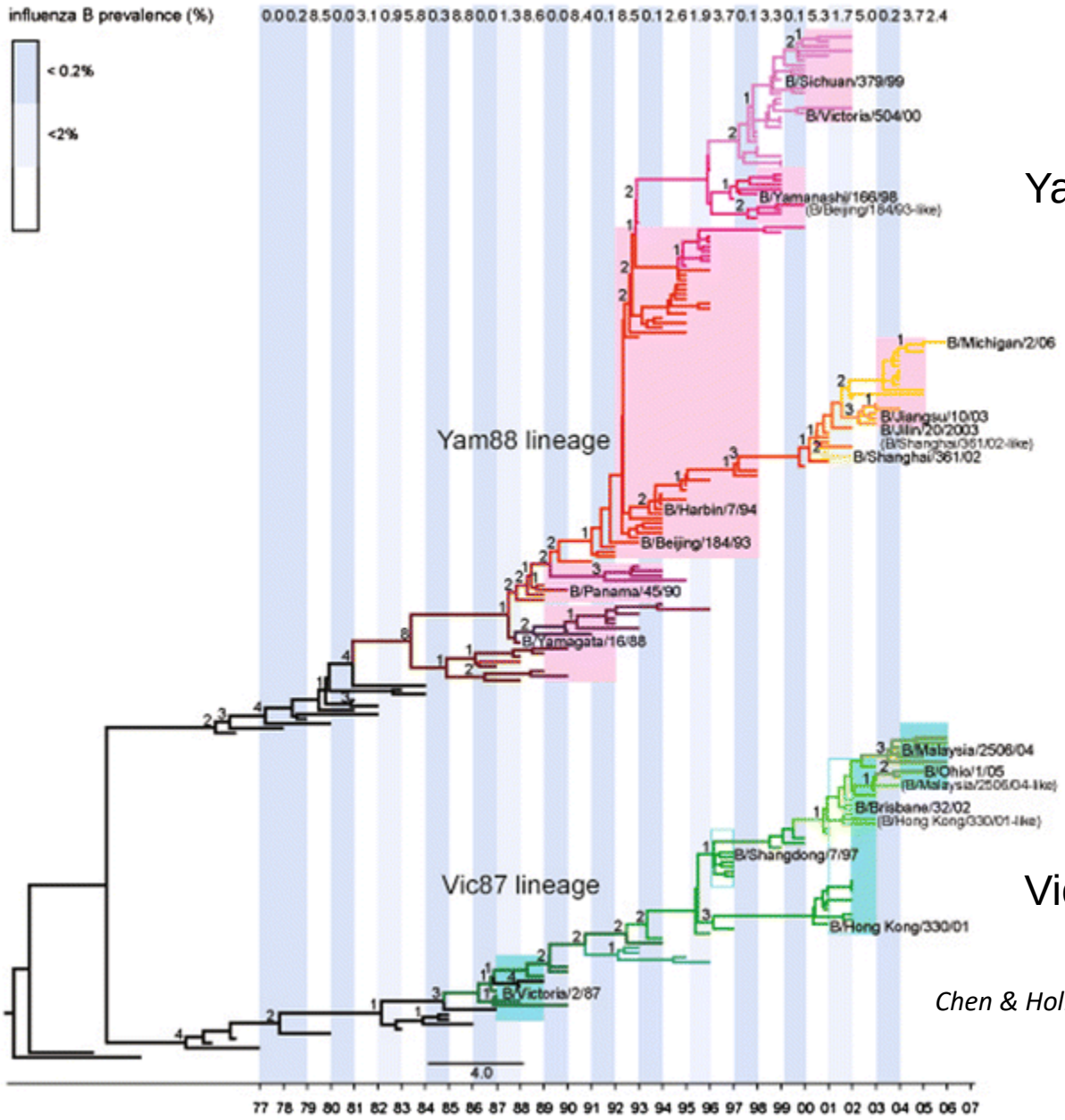
Victoria



Type D



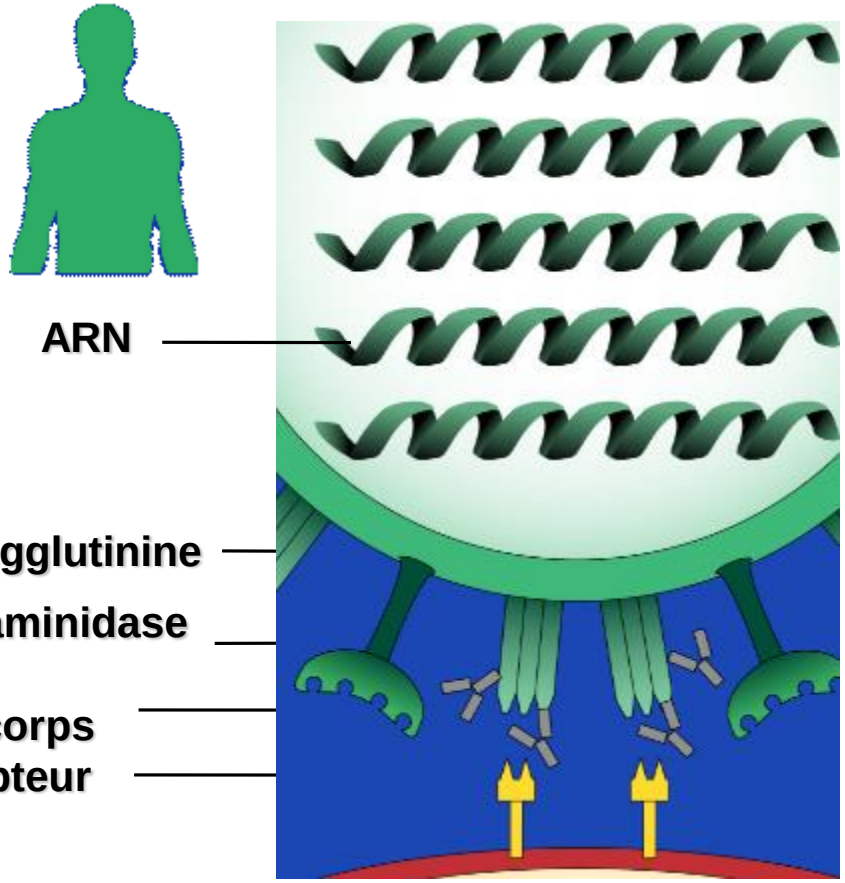
Evolution des Influenza B ayant conduit au quadrivalent

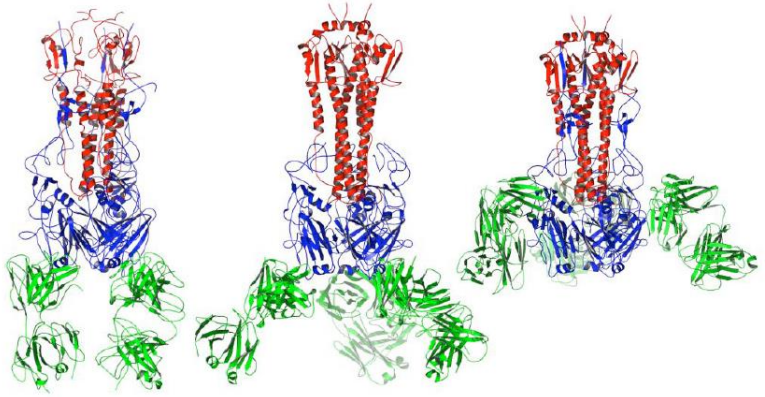


Chen & Holmes 2008

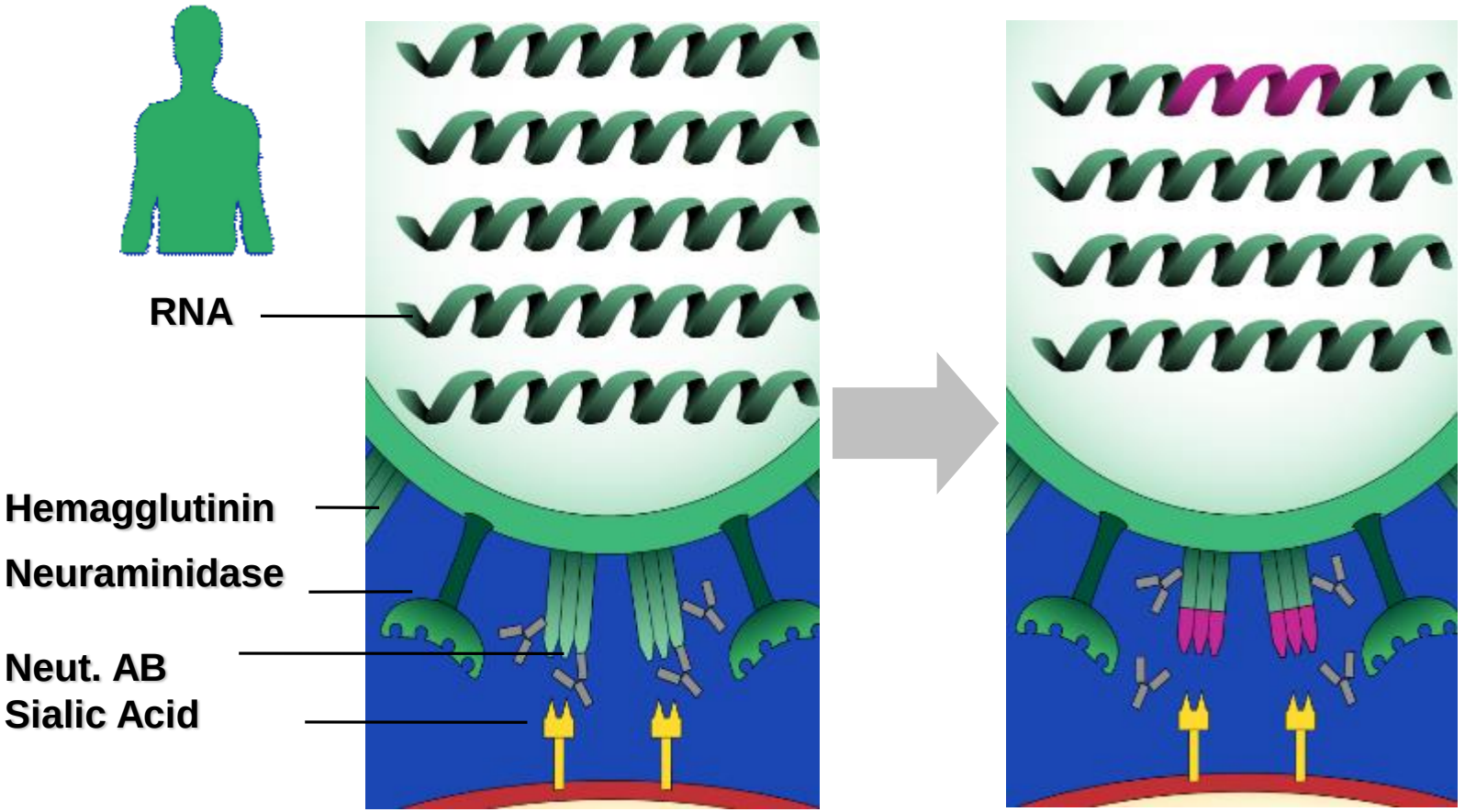
2 lineages de virus influenza B différents cocirculent depuis 1988

Protection par les anti-corps spécifiques

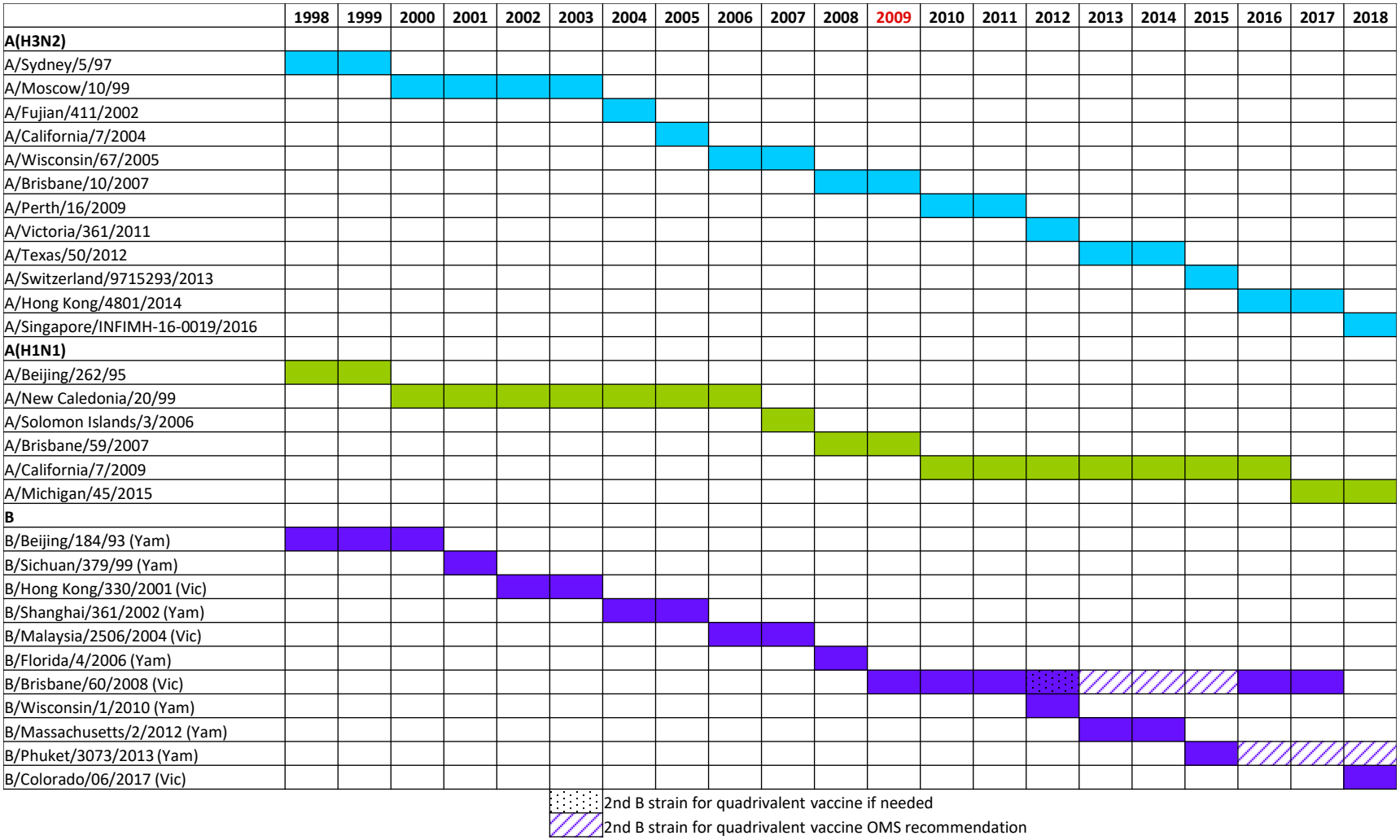




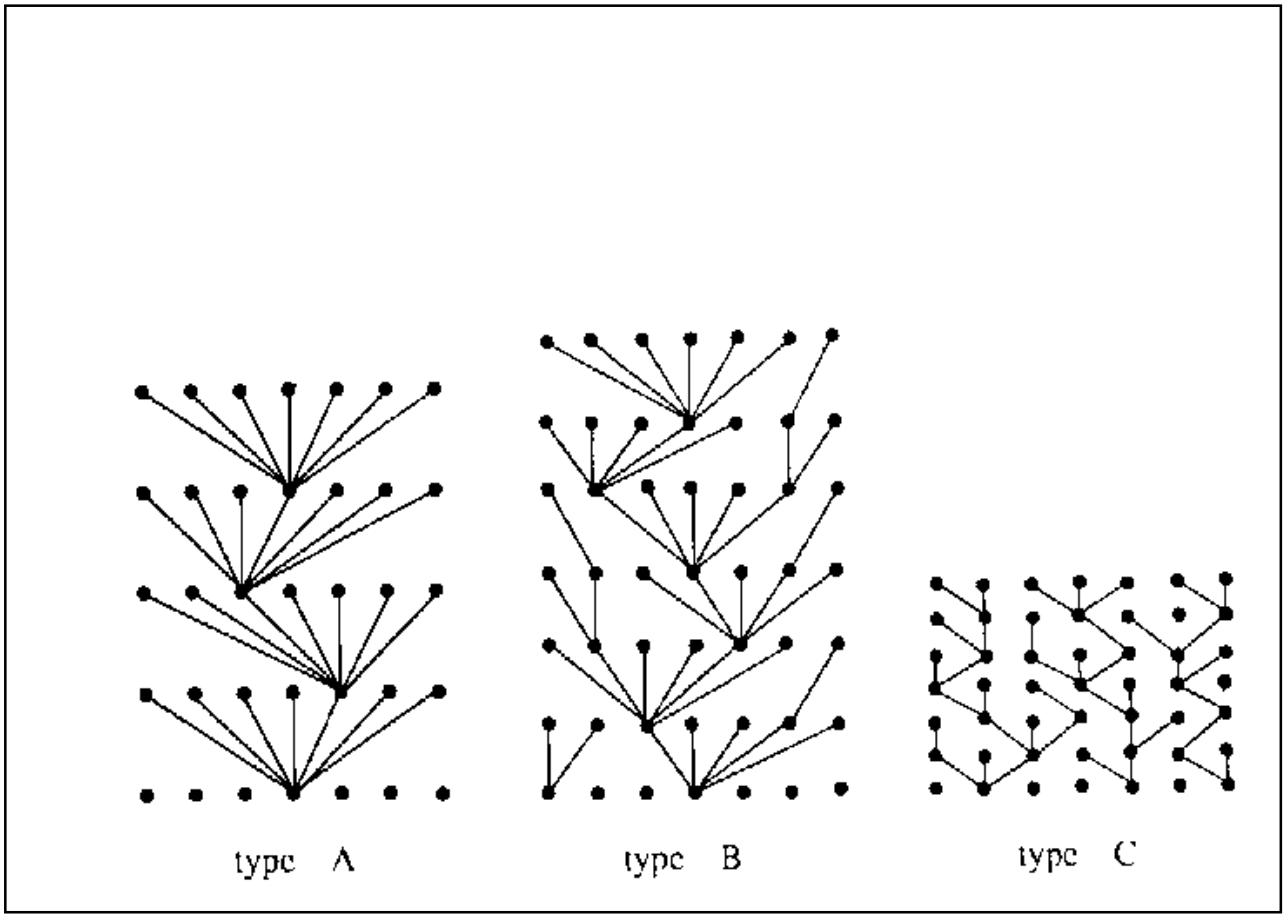
Glissement antigénique : échappement immunitaire



Evolution permanente des prototypes des virus circulants

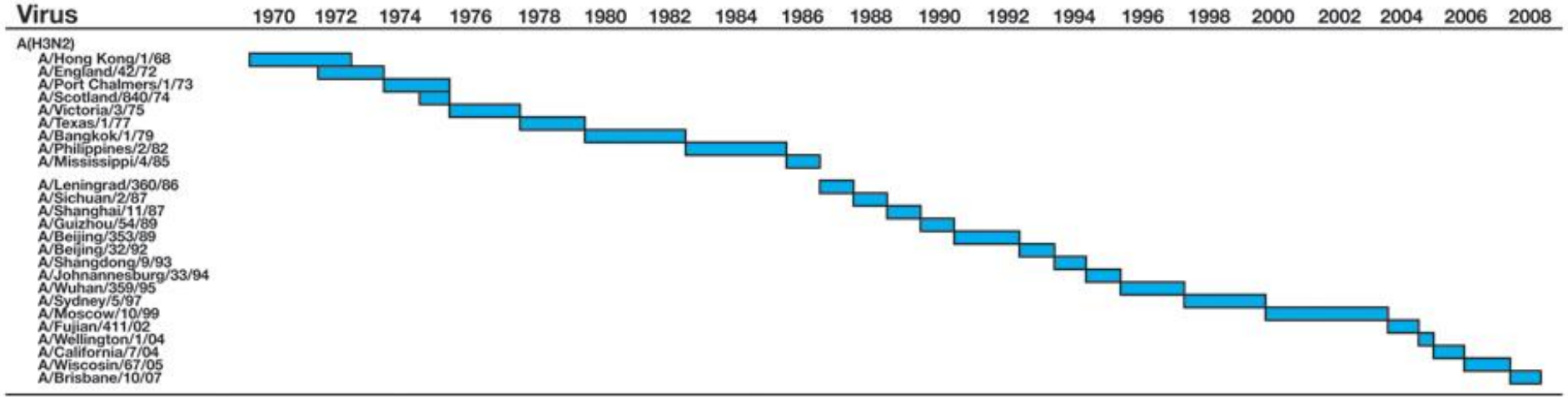


Modèle d'évolution des virus saisonniers A et B et impact pour leur surveillance



Yamashita et al.Virology, 1988

Exemple : l'évolution de H3N2 (1968 - 2009)



Méthode « classique » de comparaison des virus : Les tableaux d'IHA

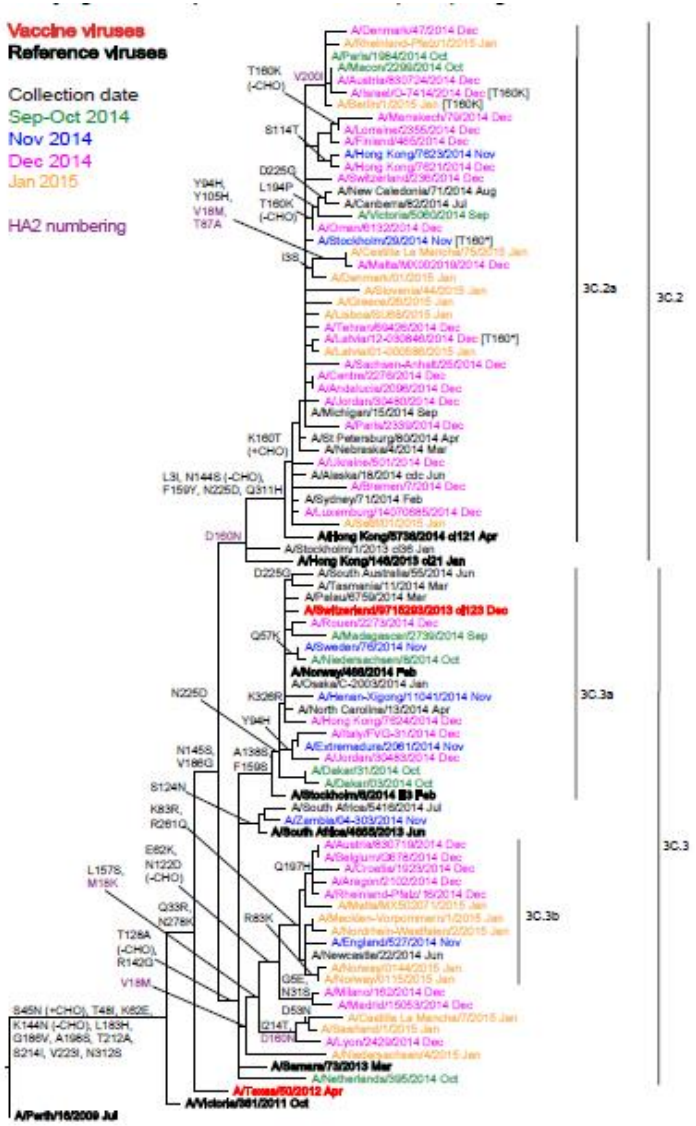
Table 9-7. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2015-01-20

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] — Post infection ferret antisera										
				A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12	A/Texas 50/12 Egg F42/13	A/Samara 73/13 F24/13	A/HK 146/13 F40/13	A/Stock 6/14 T/C F14/14	A/Stock 6/14 Egg F20/14	A/Switz 9715293/13 NIB F13/14	A/Switz 9715293/13 F26/14	A/HK 6738/14 T/C F30/14	A/HK 6738/14 NIB F53/14
					3C.1	3C.1	3C.3	3C.2	3C.3a	3C.3a Isolate 2	3C.3a	3C.3a cl123	3C.2a	3C.2a cl 121
REFERENCE VIRUSES														
A/Perth/16/2009		2009-07-04	E3/E3	640	160	160	160	320	40	160	<	80	<	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT5	80	160	160	320	160	320	160	80	160	160	40
A/Texas/50/2012	3C.1	2012-04-16	E5/E2	640	1280	1280	640	640	160	640	80	640	160	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	160	320	320	640	640	320	320	160	320	320	40
A/Hong Kong/146/2013	3C.2	2013-01-11	E3/E3	320	640	640	640	1280	80	640	40	640	320	40
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	<	40	40	160	80	320	160	160	160	160	40
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1 Isolate 2	80	160	160	80	160	160	320	80	640	160	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	<	40	40	160	80	320	160	160	160	80	<
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1 clone 123	40	160	160	160	320	320	320	80	1280	320	40
A/Hong Kong/6738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	<	40	40	160	160	160	80	80	80	160	<
A/Hong Kong/6738/2014	3C.2a	2014-04-30	E5/E1 clone121	40	40	40	160	80	160	80	40	40	320	640
TEST VIRUSES														
A/Marseille/2180/2014	3C.2a	2014-09-11	MDCK3/SIAT1	<	<	<	80	40	80	40	<	40	80	<
A/Netherland d/388/2014	3C.3a	2014-10-27	SIAT3/SIAT1	<	40	40	160	80	320	160	160	160	80	<
A/Lyon/2387/2014		2014-12-08	MDCK2/SIAT1	<	<	40	80	80	320	80	40	80	80	<
A/Lyon/2388/2014		2014-12-08	MDCK2/SIAT1	80	160	80	320	160	320	80	40	80	80	<
A/Lyon-CHU/21.88/2014	3C.3	2014-12-10	MDCK2/SIAT1	80	160	160	320	320	320	160	80	160	160	<
A/Lyon/2428/2014	3C.3	2014-12-15	MDCK2/SIAT1	80	160	160	320	320	320	160	80	160	160	<
A/Nimes/2454/2014	3C.3a	2014-12-18	MDCK2/SIAT1	<	<	40	160	80	320	80	80	80	80	<
						Vaccine SH2014 NH 2014/15						Vaccine SH2015		

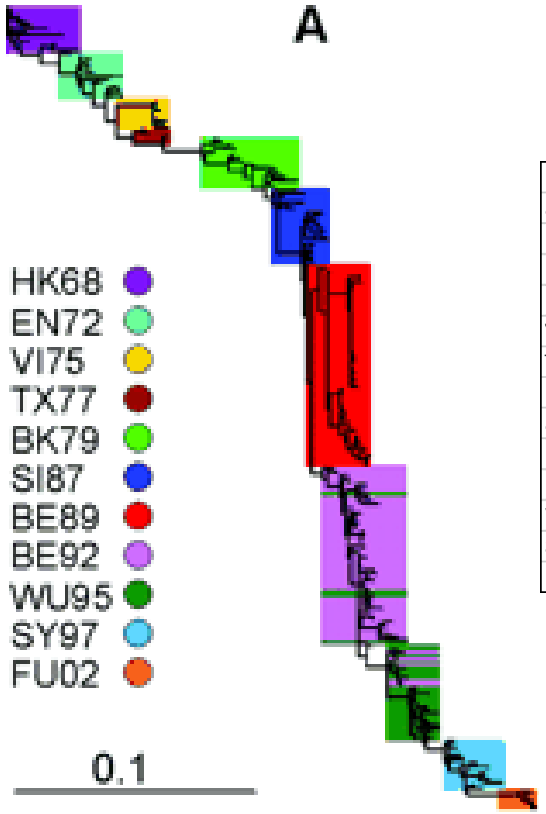
1. < = <40

Sequences in phylogenetic trees

Méthode « moléculaire » de comparaison des virus



Comparaison par analyse des distances antigeniques (D Smith 2003)



	serums	HK68	EN72	VI75	TX77	BK79	SI87	BE89	BE92	WU95	SY97	FU02
Souche												
HK68		2560	320	90	5	0	0					
EN72		320	2560	320	90	5	0	0				
VI75		90	320	2560	320	90	5	0	0			
TX77		5	90	320	2560	320	90	5	0	0		
BK79		0	5	90	320	2560	320	90	5	0	0	
SI87		0	0	5	90	320	2560	320	90	5	0	0
BE89			0	0	5	90	320	2560	320	90	5	0
BE92				0	0	5	90	320	2560	320	90	5
WU95					0	0	5	90	320	2560	320	90
SY97						0	0	5	90	320	2560	320
FU02							0	0	5	90	320	2560


Nord
Pas-de-Calais-
Picardie
Normandie
Ile-
de-
France
Alsace-
Champagne-Ardenne-
Lorraine
Bretagne
Pays-de-
la-Loire
Centre-
Val-de-Loire
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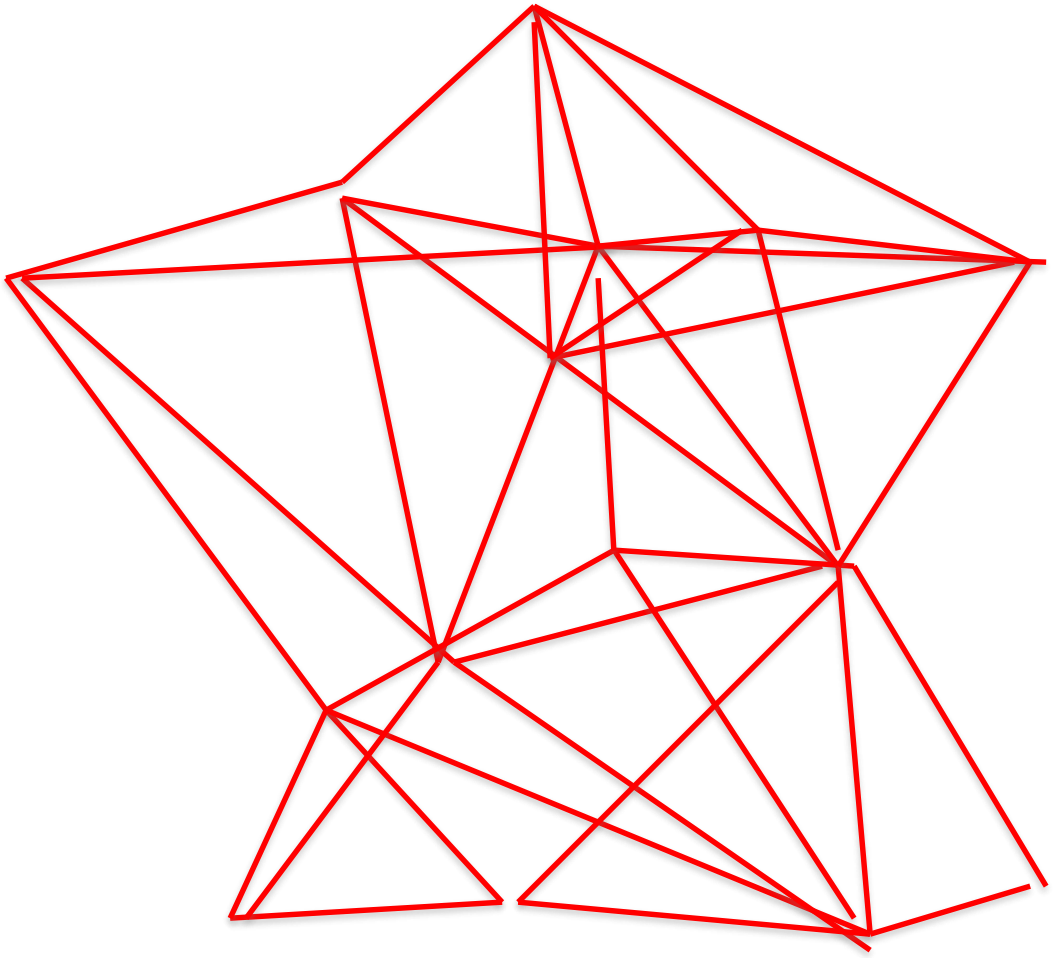
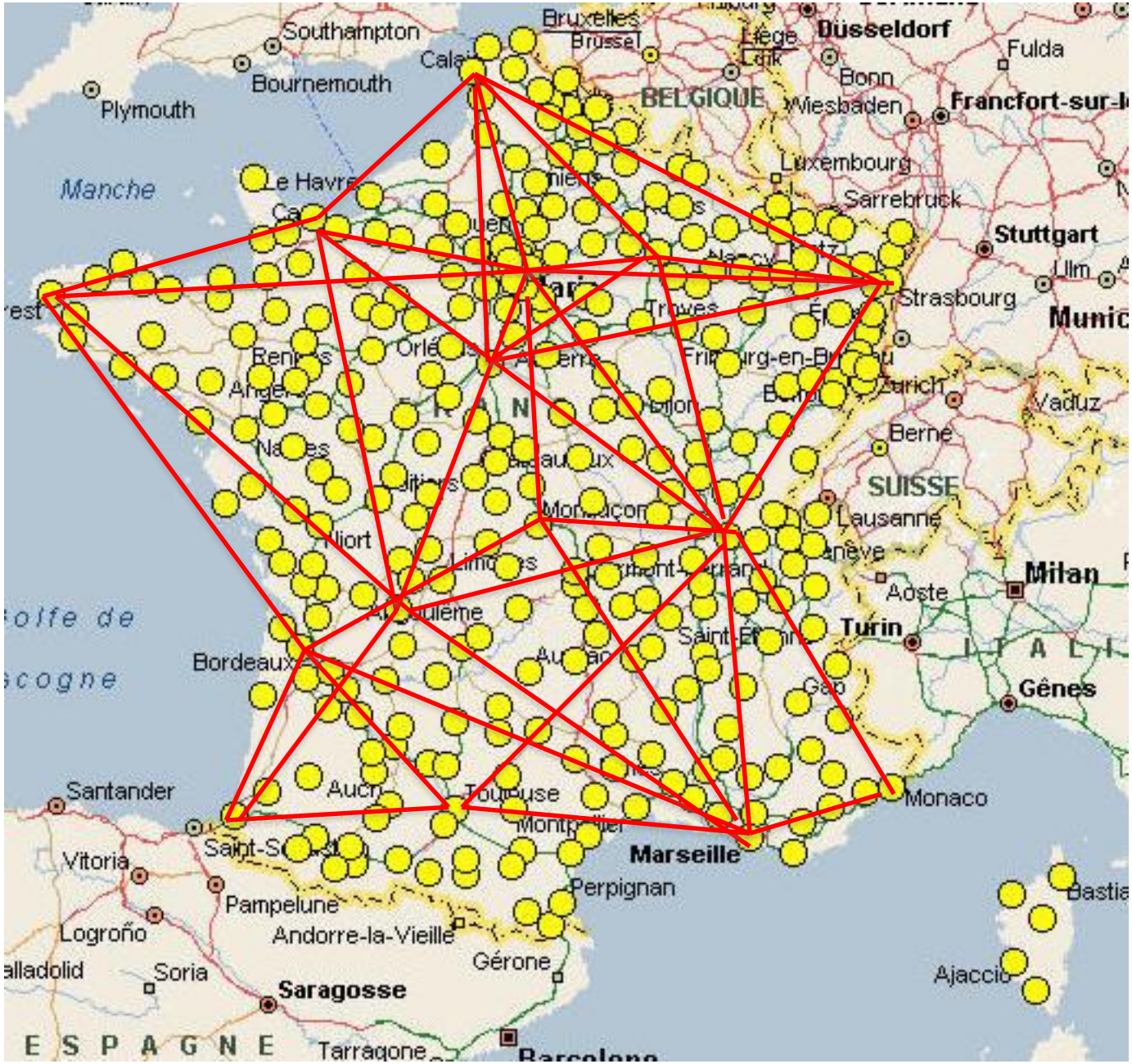
Languedoc-Roussillon-
Midi-Pyrénées
Provence-Alpes-
Côte-d'Azur

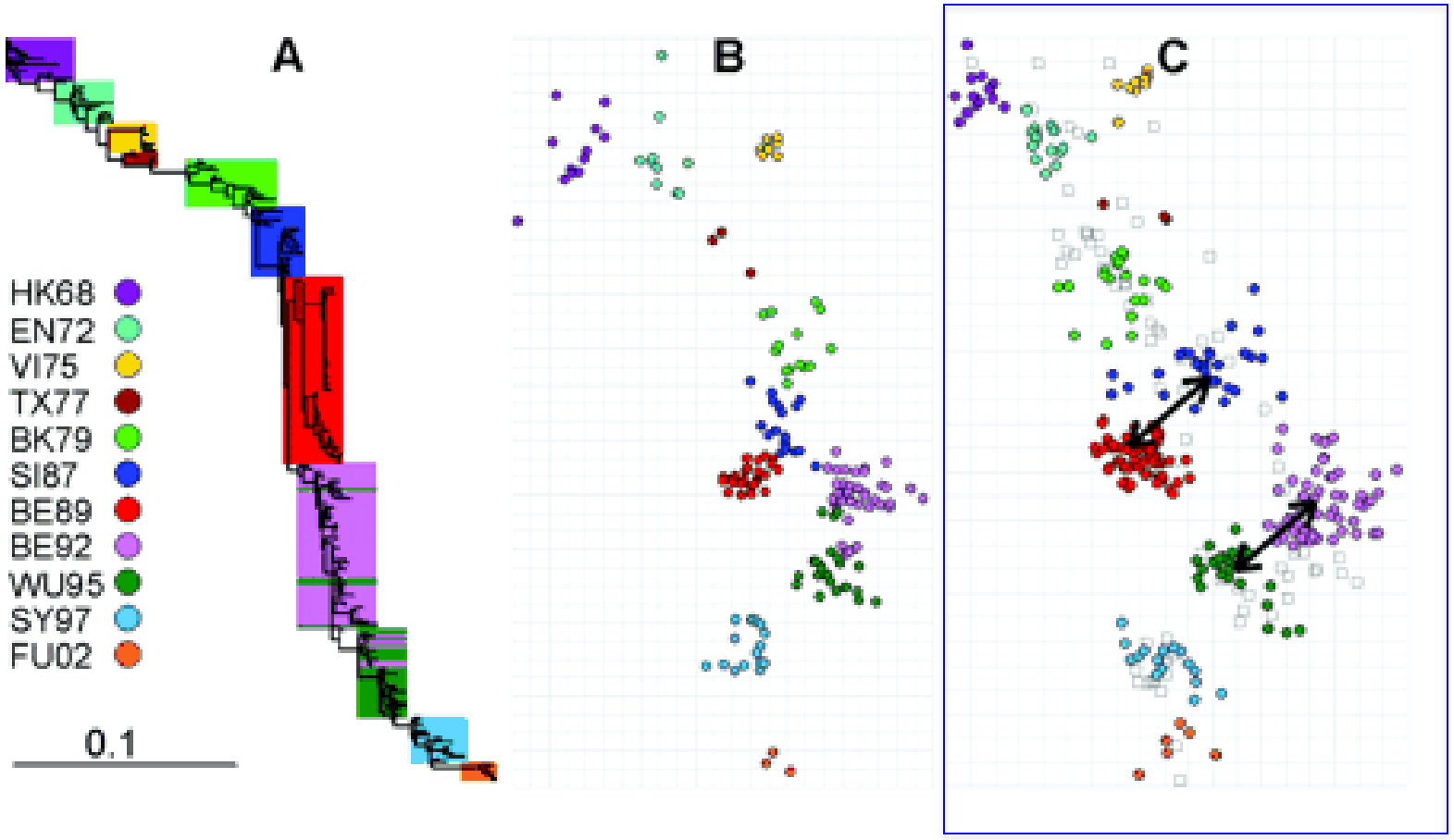
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF
1	Column1	Column2	Column3	Column4	Column5	Column6	Column7	Column8	Column9	Column10	Column11	Column12	Column13	Column14	Column15	Column16	Column17	Column18	Column19	Column20	Column21	Column22	Column23	Column24	Column25	Column26	Column27	Column28	Column29	Column30	Column31	Column32
2		Agen	Ajaccio	Albi	Alençon	Amiens	Angers	Angoulême	Annecy	Arras	Auch	Aurillac	Auxerre	Avignon	Bar-le-Duc	Bastia	Beauvais	Belfort	Besançon	Blois	Bobigny	Bordeaux	Bourg-en-Bresse	Bourges	Caen	Cahors	Carcassonne	Chambéry	Charleville-Mézières	Chartres	Chaumont	Châlons-en-Champagne
3	Agen																															
4	Ajaccio	846																														
5	Albi	182	790																													
6	Alençon	620	1299	790																												
7	Amiens	854	1223	843	319																											
8	Angers	553	1346	723	142	431																										
9	Angoulême	254	1072	424	350	585	297																									
10	Annecy	776	683	735	726	676	799	648																								
11	Arras	901	1270	867	404	64	477	631	723																							
12	Auch	72	793	153	682	917	616	317	737	964																						
13	Aurillac	252	745	159	678	702	479	271	476	753	252																					
14	Auxerre	593	924	581	355	305	429	427	377	353	656	420																				
15	Avignon	444	410	402	875	826	949	685	353	873	406	356	526																			
16	Bar-le-Duc	963	1065	1047	466	281	539	693	501	287	1025	689	212	666																		
17	Bastia	769	148	728	1211	1162	1285	1010	398	1209	731	681	862	348	1003																	
18	Beauvais	803	1172	769	206	60	379	533	624	152	865	655	252	773	326	1109																
19	Belfort	993	881	952	685	636	759	764	286	644	955	647	337	571	242	642	584															
20	Besançon	906	882	864	598	548	671	676	217	556	867	538	249	483	279	735	496	96														
21	Blois	547	1122	716	149	319	190	277	662	366	609	498	219	723	426	1060	263	546	463													
22	Bobigny	738	1107	726	241	139	314	468	560	174	800	590	187	708	252	1044	87	515	432	202												
23	Bordeaux	141	960	311	484	719	418	120	903	767	204	379	620	572	827	897	668	946	864	411	601											
24	Bourg-en-Bres	734	710	692	616	566	689	605	109	621	695	436	267	311	398	648	514	264	181	578	448	861										
25	Bourges	493	965	508	356	384	355	328	505	431	557	341	143	566	491	903	332	429	346	177	265	481	463									
26	Caen	728	1319	938	101	291	243	458	772	323	790	802	401	920	491	1256	208	727	644	414	242	590	661	478								
27	Cahors	85	832	111	681	709	491	210	586	756	146	132	506	445	816	770	658	801	719	413	591	273	544	406	805							
28	Carcassonne	208	629	166	814	917	749	450	573	964	169	310	746	242	887	566	865	787	704	741	798	336	531	613	1012	205						
29	Chambéry	702	634	660	752	702	825	611	50	749	664	442	403	279	544	367	651	418	336	627	584	829	161	467	798	699	497					
30	Charleville-M	942	1191	931	445	248	518	672	627	235	1005	792	286	792	140	1129	306	515	461	407	230	804	523	471	470	794	1010	669				
31	Chartres	665	1141	631	134	222	207	395	594	273	728	517	222	743	333	1079	170	549	467	130	108	527	483	194	238	519	725	619	312			
32	Chaumont	948	924	906	457	384	531	684	361	390	910	580	164	525	90	862	347	277	194	419	271	817	257	337	503	808	743	402	290	325		
33	Châlons-en-C	902	1073	890	405	219	478	632	509	226	964	754	167	674	70	1010	266	426	343	366	190	764	405	430	430	756	892	550	126	273	174	
34	Châteauroux	397	979	445	376	404	218	231	519	451	460	295	201	580	511	916	352	533	450	108	285	384	477	101	500	311	520	480	489	215	394	451



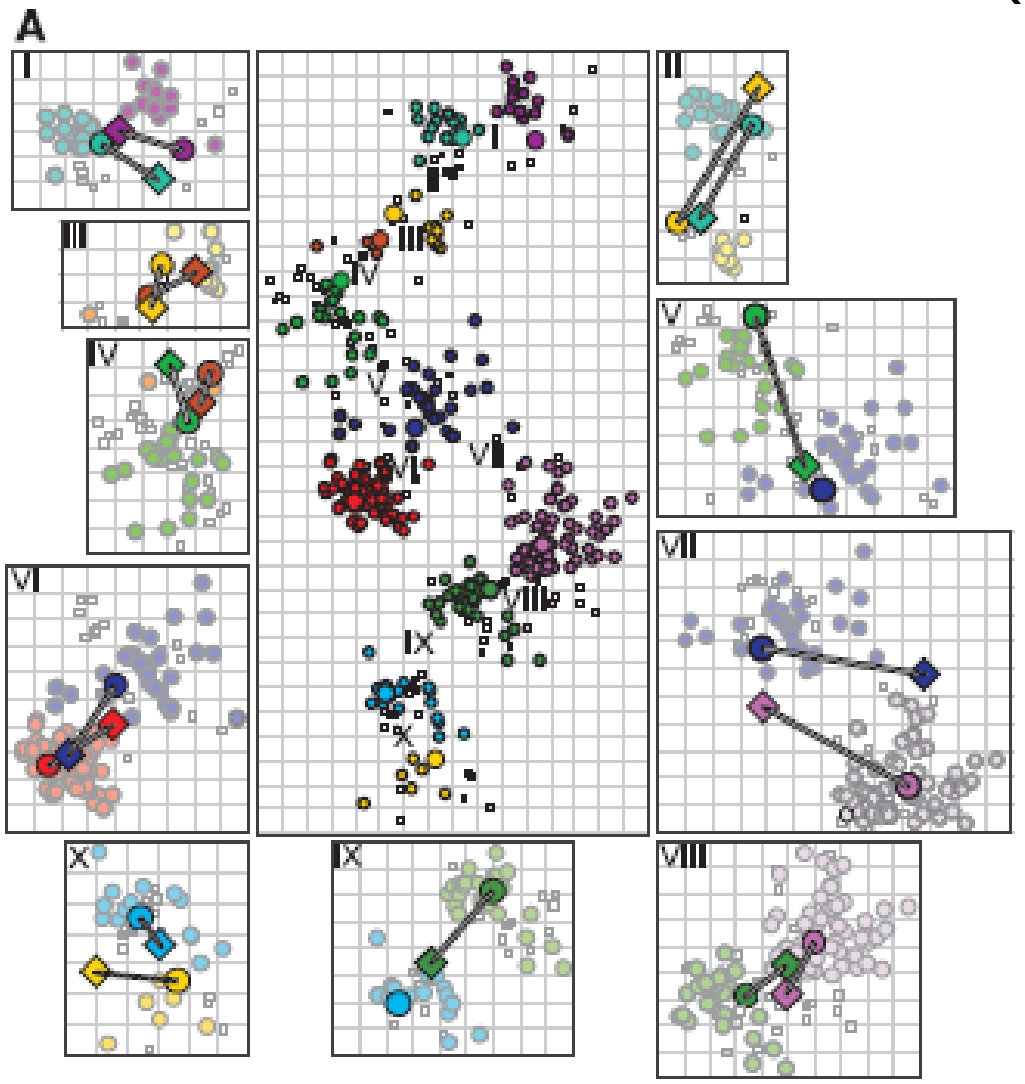

Southampton
Bournemouth
Plymouth
Manche
Le Havre
Bruxelles
Brussel
Liège
Luik
Düsseldorf
Fulda
Bonn
BELGIQUE
Wiesbaden
Francfort-sur-l
Luxembourg
Sarrebruck
Stuttgart
Ulm
Strasbourg
Munic
Zurich
Vaduz
Berne
SUISSE
Lausanne
Genève
Milan
Aoste
Turin
ITALIE
Gênes
Monaco
Marseille
Perpignan
Bastia
Ajaccio
Golfe de
Gascogne
Bordeaux
Niort
Angers
Nantes
Orléans
Troyes
Dijon
Besançon
Montbéliard
Mulhouse
Fribourg-en-Brisgau
Saint-Étienne
Gap
Montpellier
Toulouse
Auch
Santander
Vitoria
Pampelune
Logroño
Andorre-la-Vieille
Gérone
Soria
Saragosse
Tarragone
Barcelone
ESPAGNE

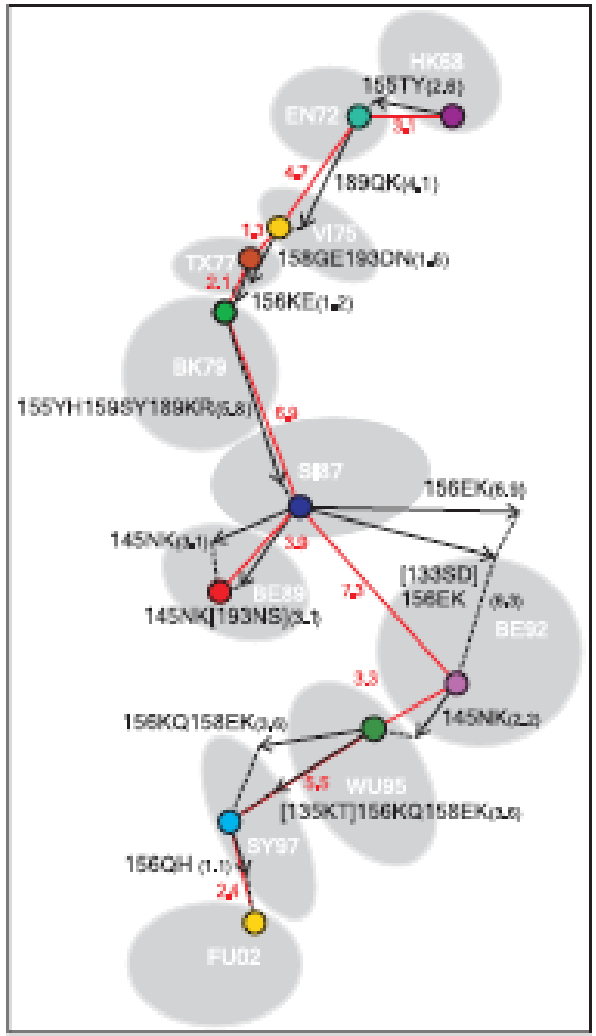
Antigenic distances Model (D Smith 2003)

After refining

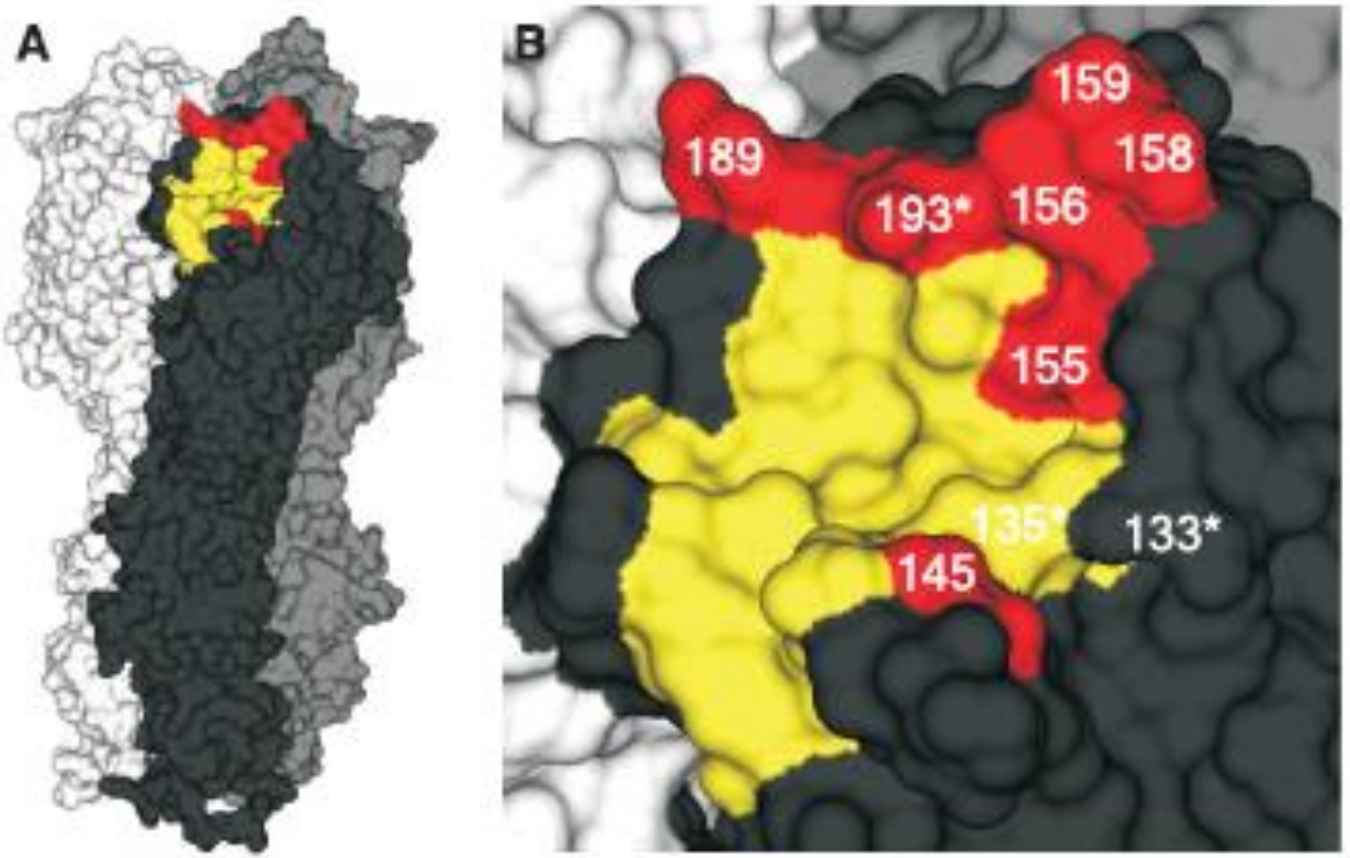


Understanding the antigenic evolution of H3N2 between 1968 and 2002 (Fouchier)



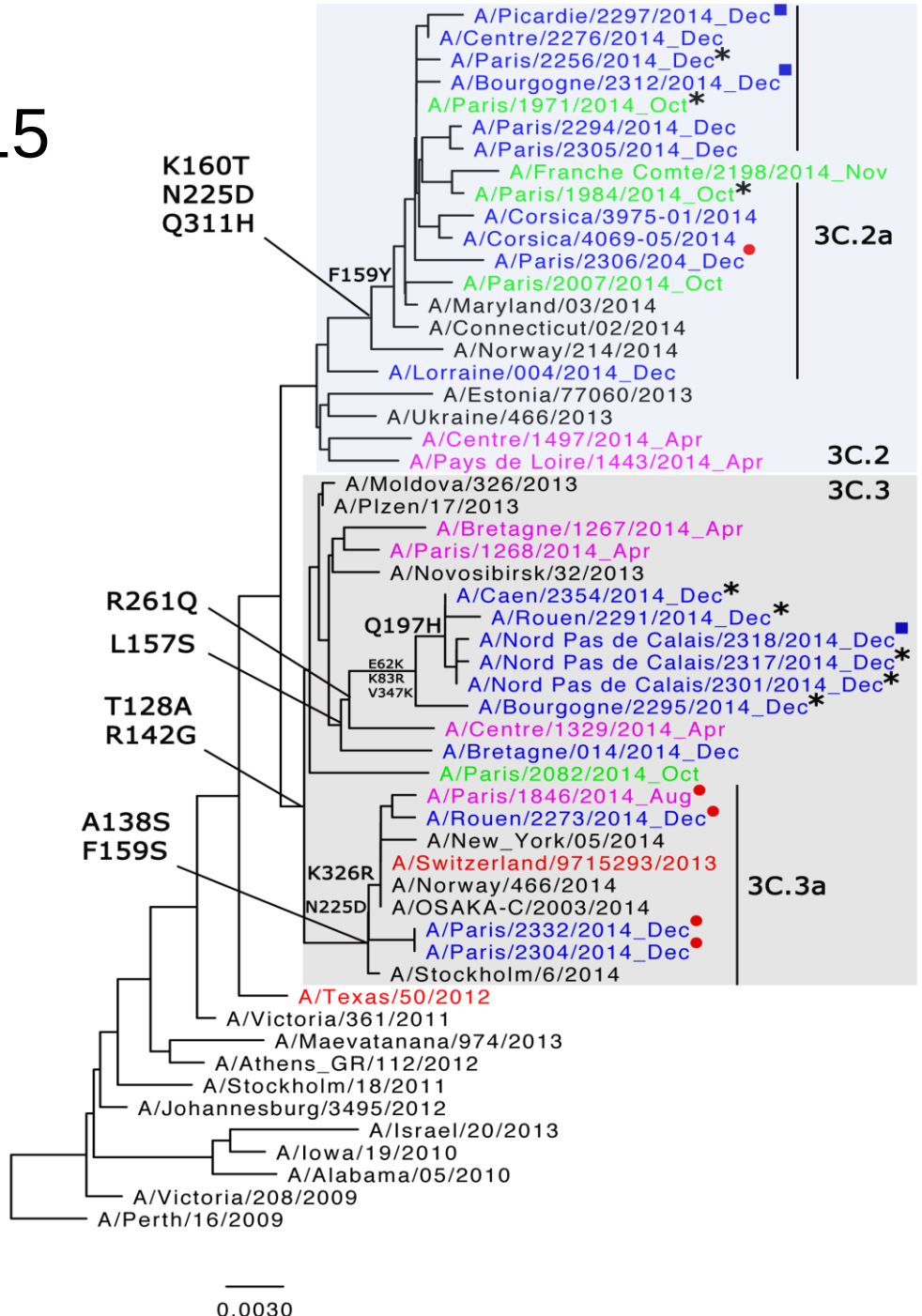


Beyond the antigenic sites : the H3N2 major amino acid sites



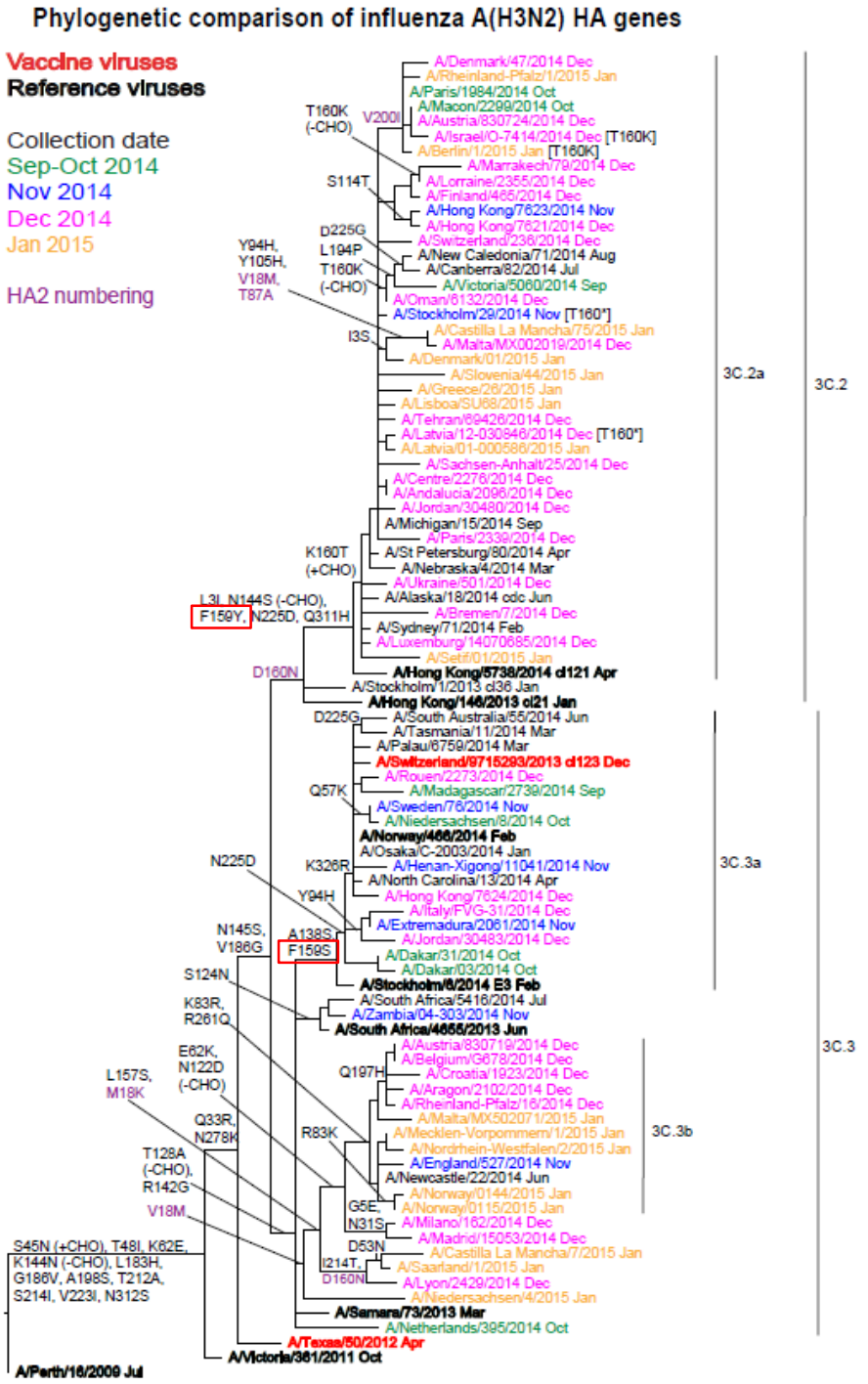
Real-time use: 2014-15

- ● switzerland –like
- ★Texas-like
- ■ indeterminates

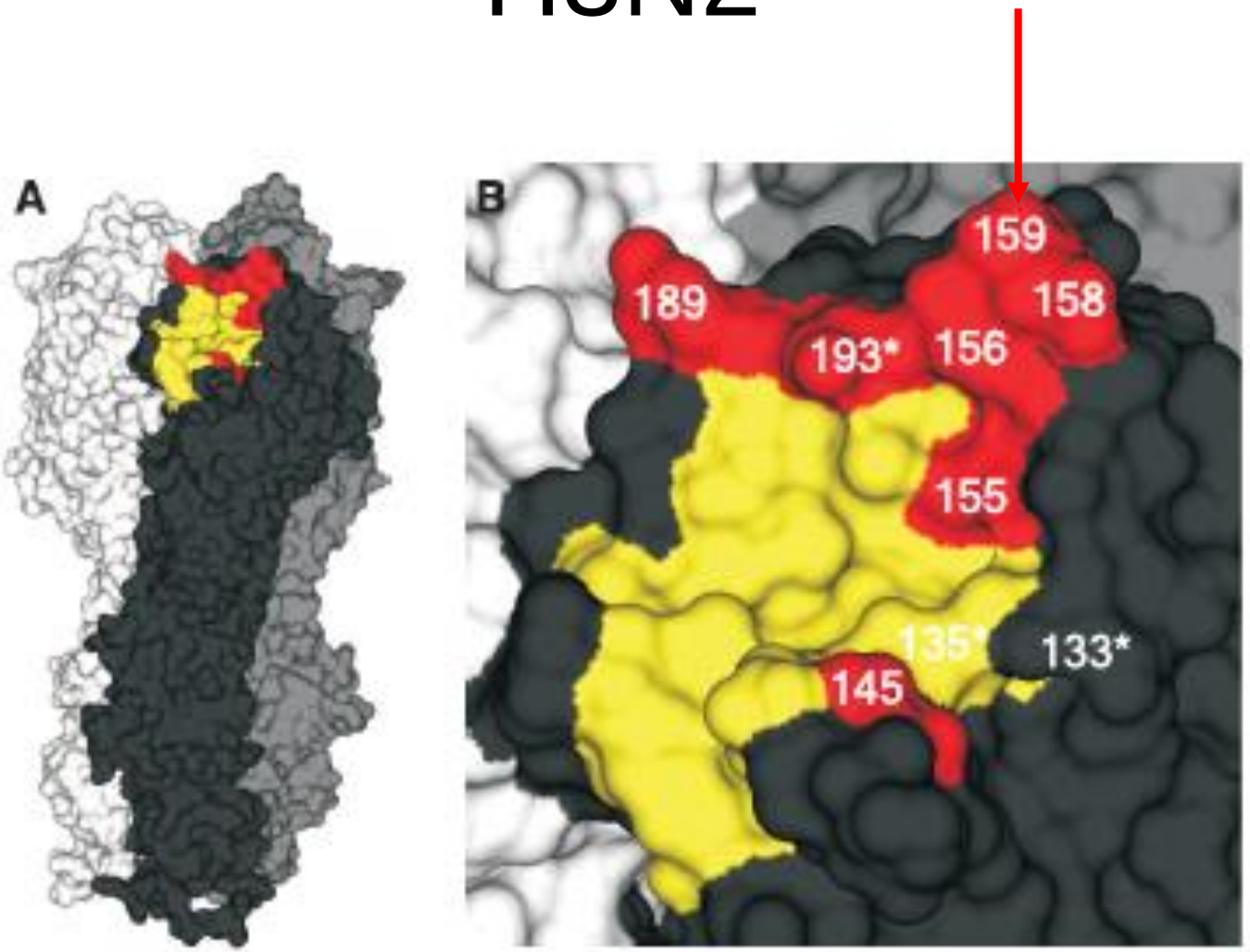


2014-2015

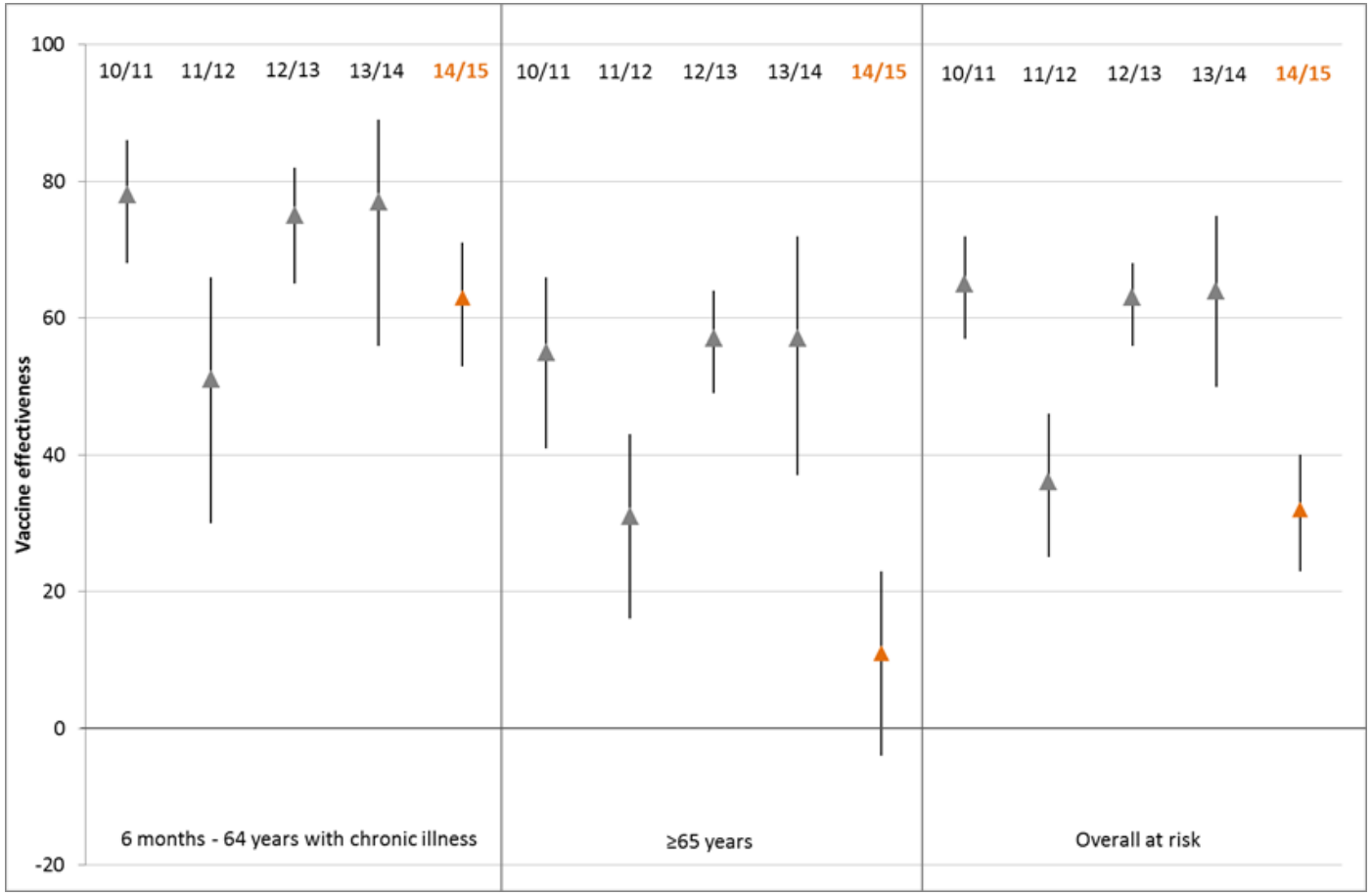
Data available at the vaccine composition meeting



H3N2

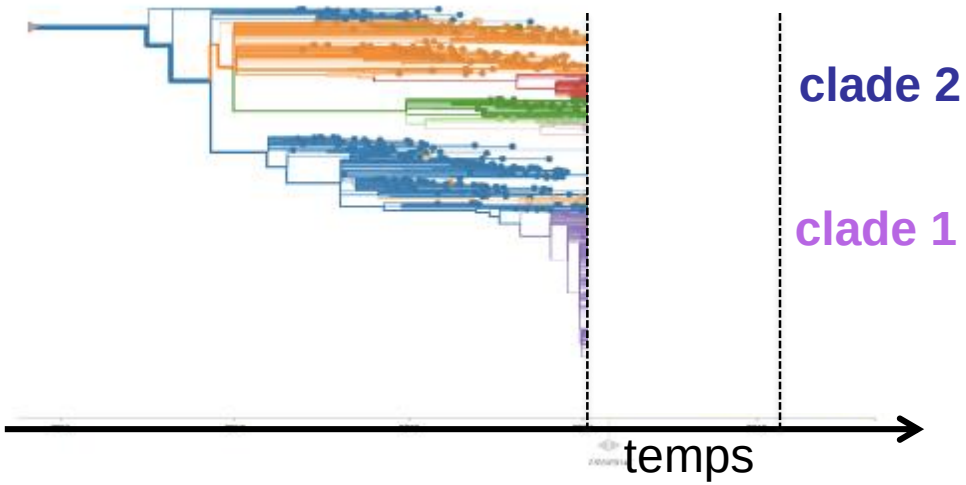


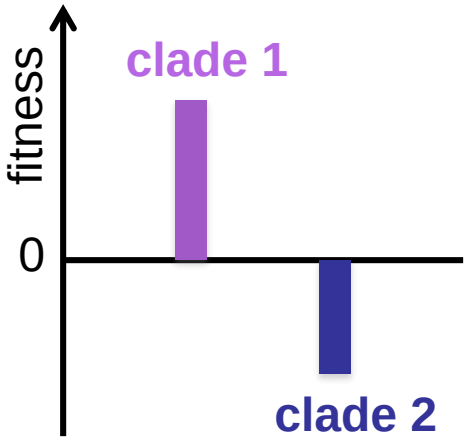
Impact: decrease in vaccine efficacy

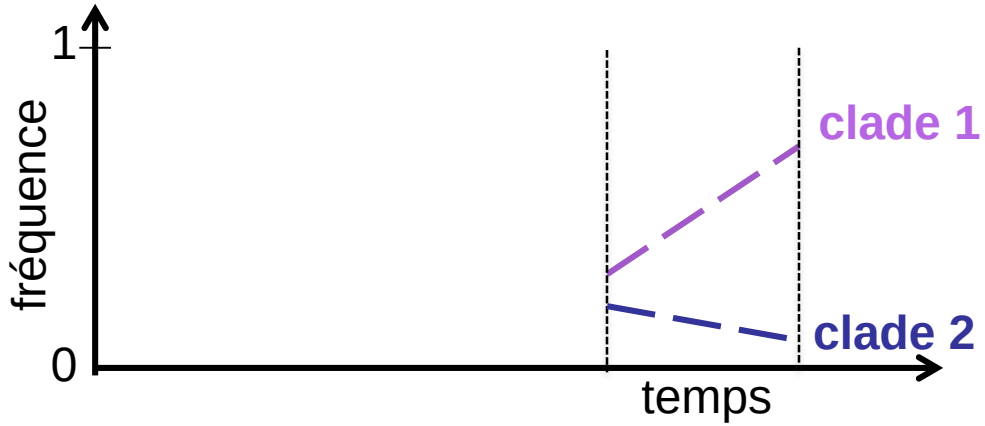


Comment réaliser une étude de fitness ?

Marta Luksza & Michael Lässig

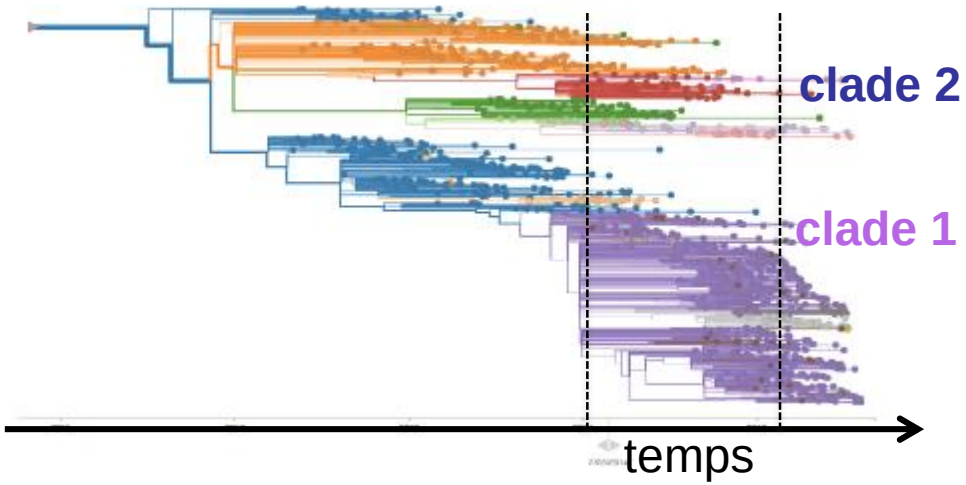


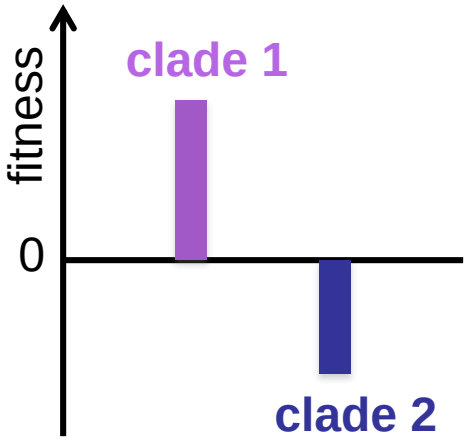


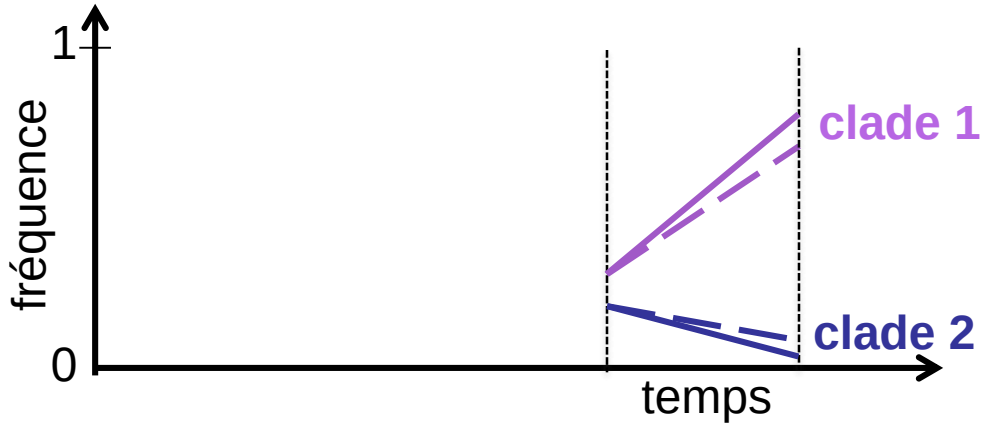


Les données fournies en temps réel permettent de mieux estimer

Marta Luksza & Michael Lässig



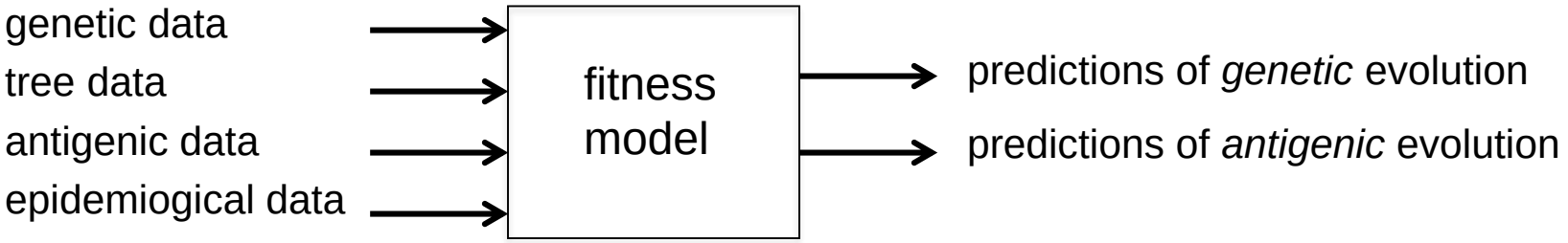




Marta Luksza & Michael Lässig

Donc un modele d‘étude de firness doit intégrer de nombreuses données

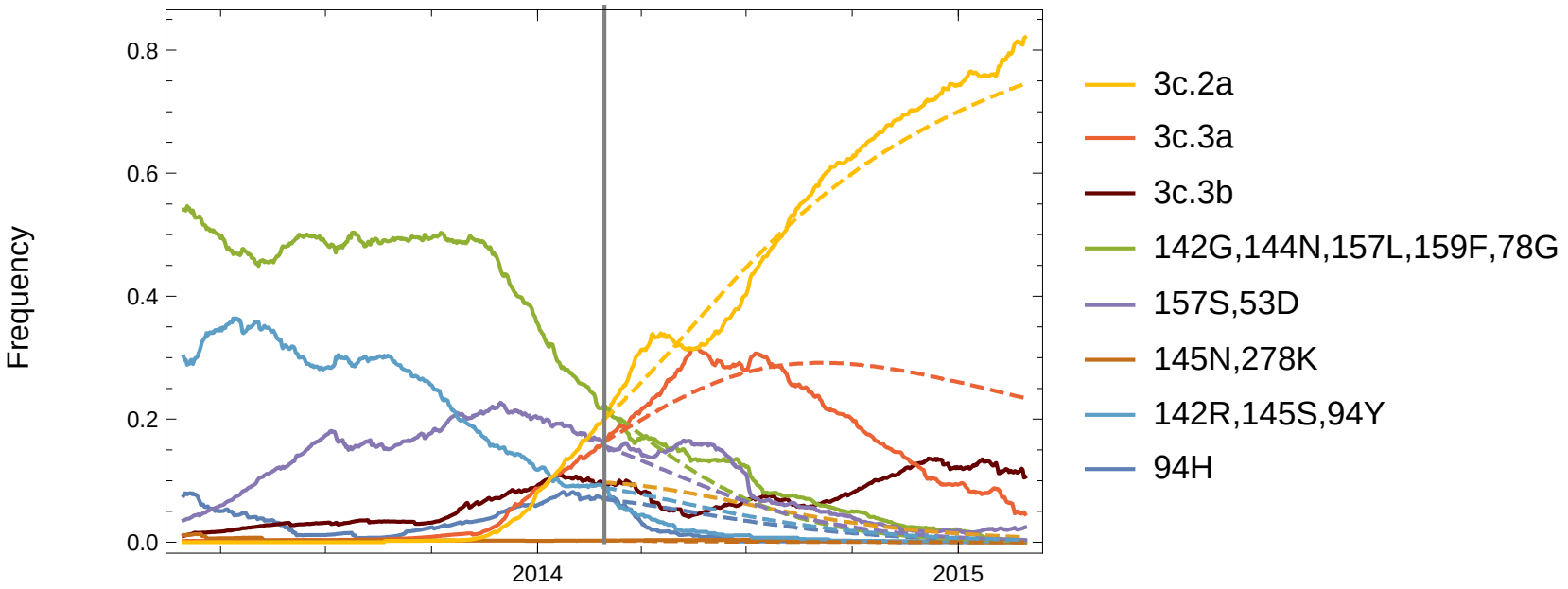
Fitness models integrate data into predictions



Marta Luksza & Michael Lässig

Predictions and vaccine strain selection

Phase 2: Clade frequency prediction

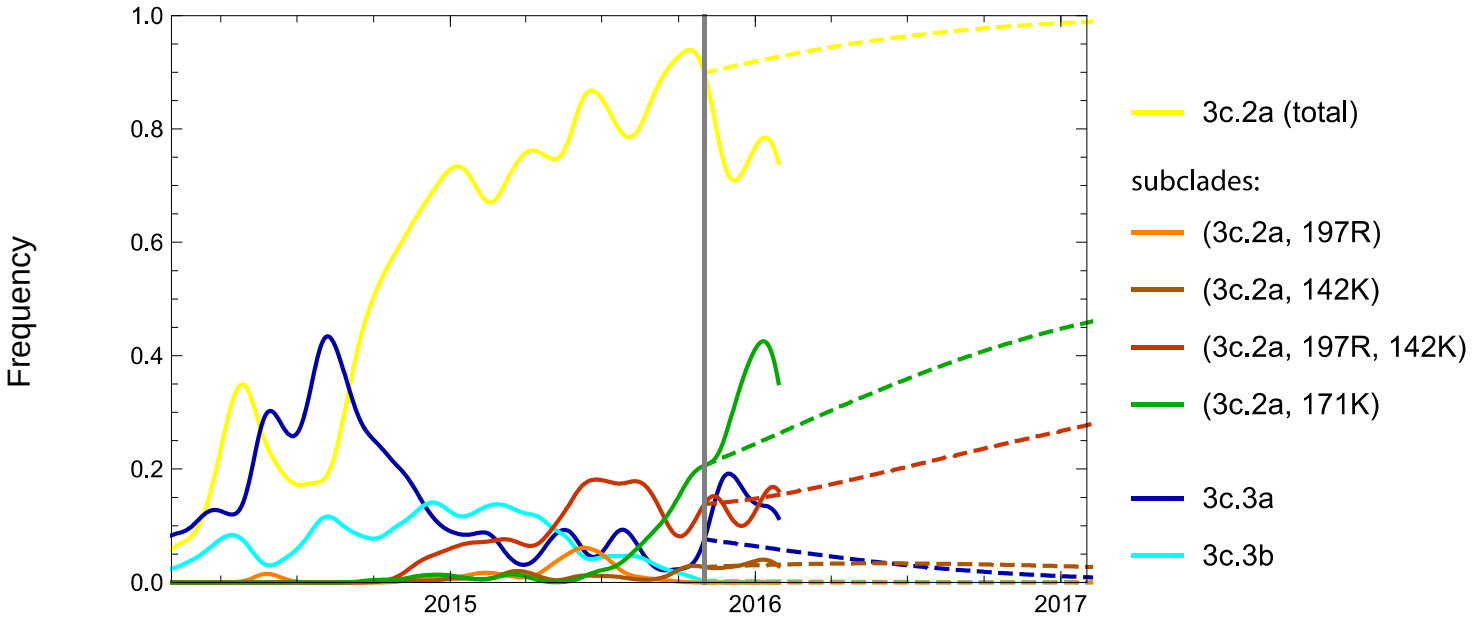


Prediction start date: February 28, 2014
Prediction period: one year

Marta Luksza & Michael Lässig

Mise en oeuvre de l‘outil prédiction pour le vaccine strain selection meeting

Phase 2: Clade frequency prediction



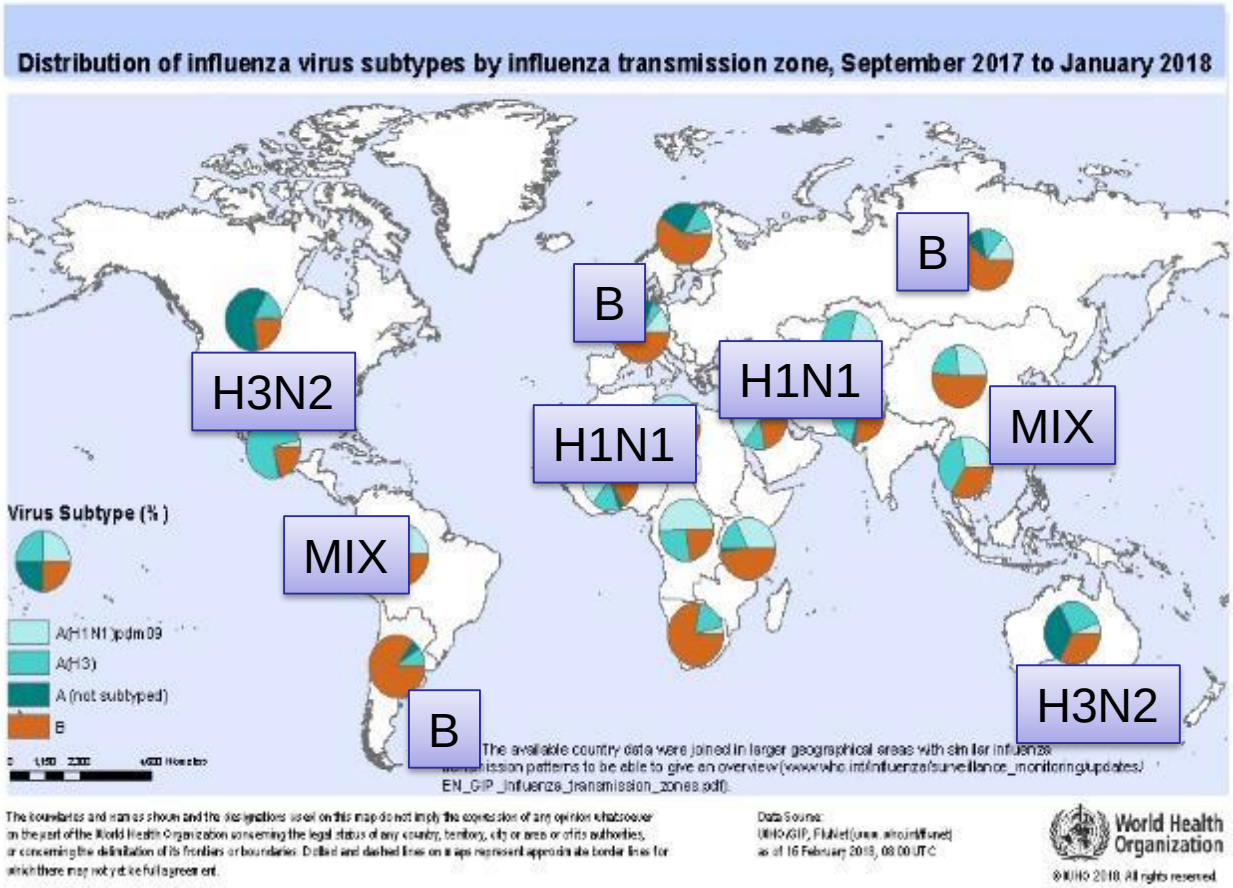
Prediction start date: February 28, 2016
Prediction period: one year

Marta Luksza & Michael Lässig

Pour choisir le bon candidat vaccin, il faut :

- Avoir de nombreux virus a analyser
- Avoir des comparaison antigéniques entre les virus
- Cartographier les distances antigéniques entre les représentants des virus circulants
- Definir les clades génétiques des virus circulants et comparer les fitness respectifs des différents clades génétiques
- Choisir un représentant du groupe viral le plus récent pour avoir la meilleure immunité post vaccinale (et donc protection) possible
- Vérifier que la protection induite croise sur les différents clades génétiques circulants

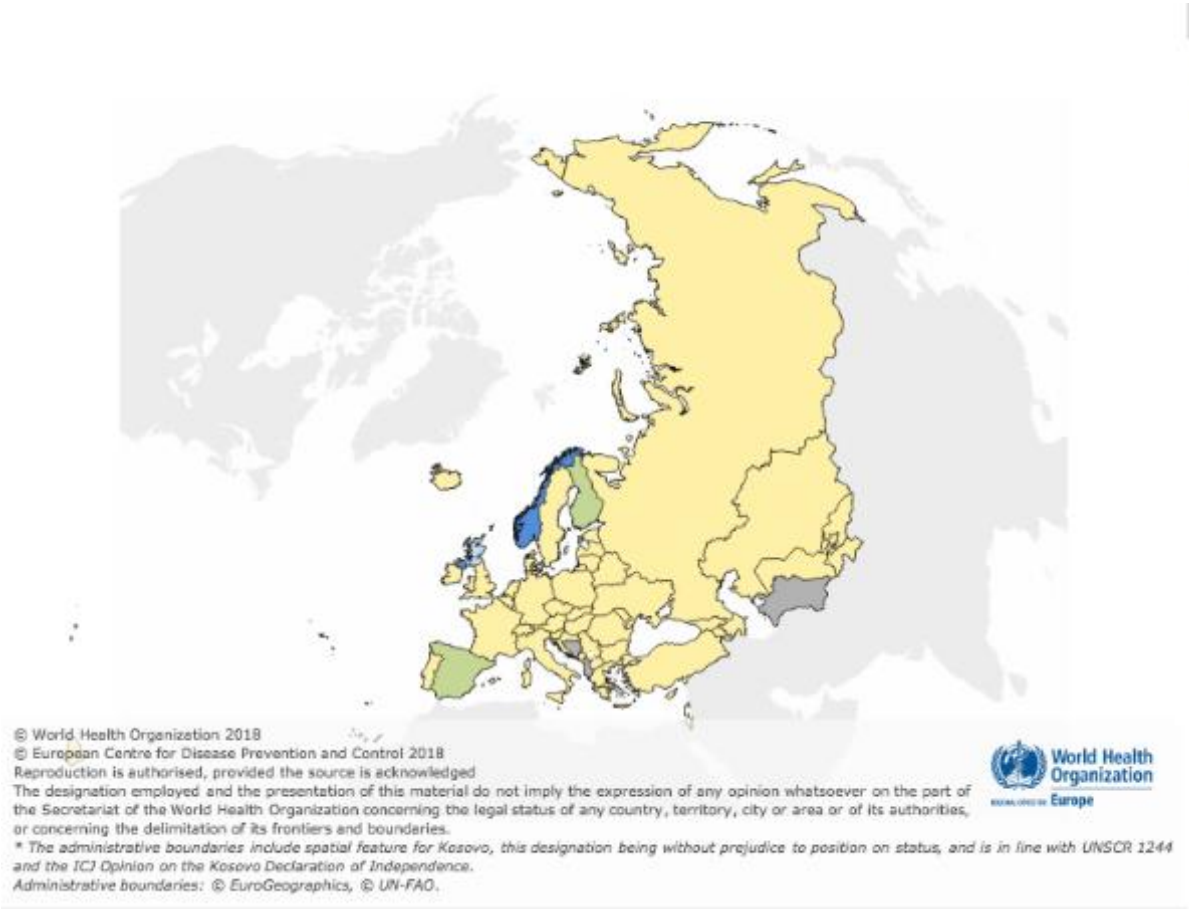
Influenza as observed between Sep 2017 and Jan 2018



A European focus

- Europe is supposed to be a single transmission zone (homogeneous epidemiology)
- The ECDC and WHO are monitoring the epidemic (weekly reports)
  - Intensity
  - Dominant subtype
- Euromomo is monitoring the mortality associated to influenza

Week 46


Dominant type
A
A(H1)
A(H3)
B
None
No data
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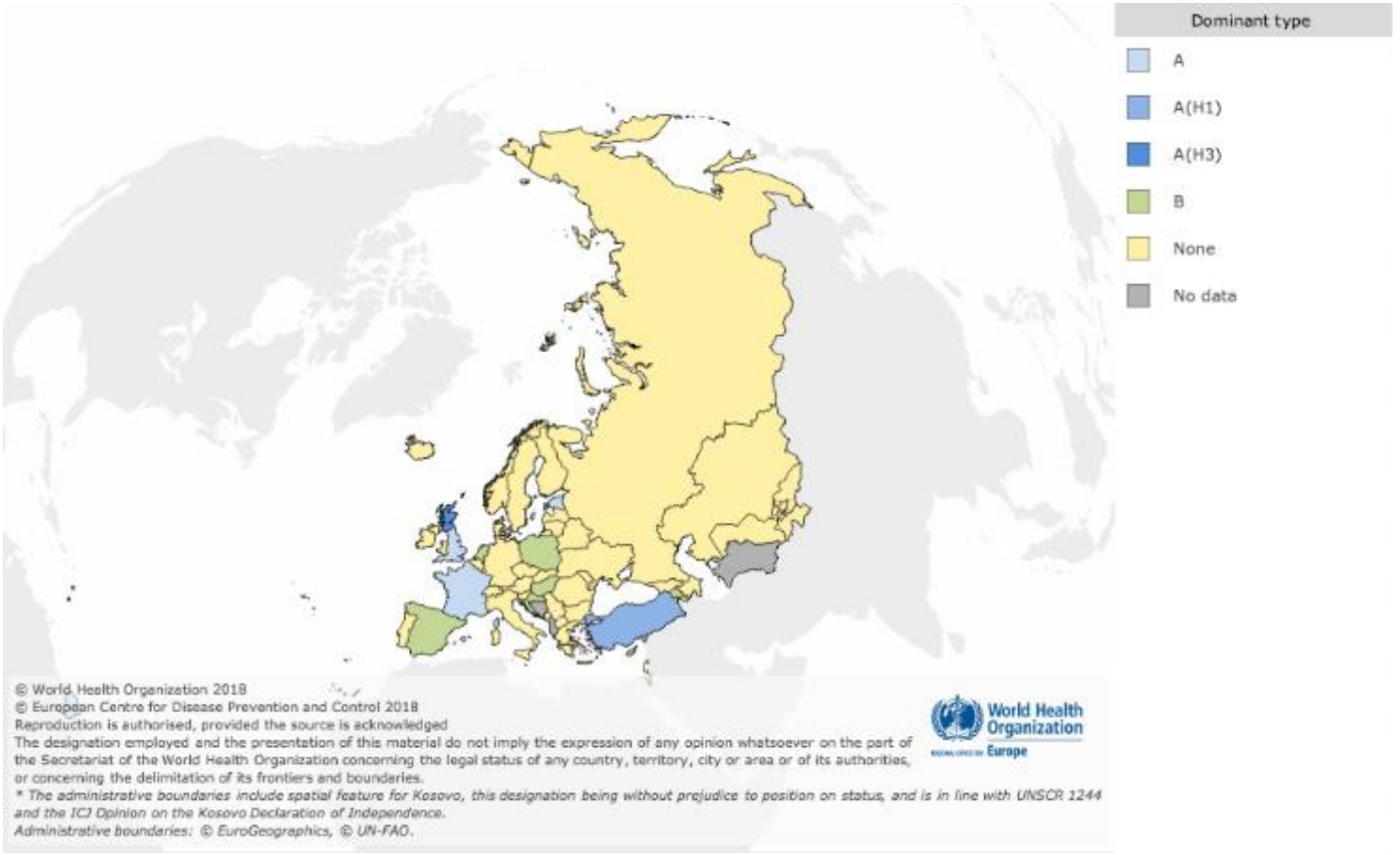
Europe

Week 48


Dominant type
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A(H1)
A(H3)
B
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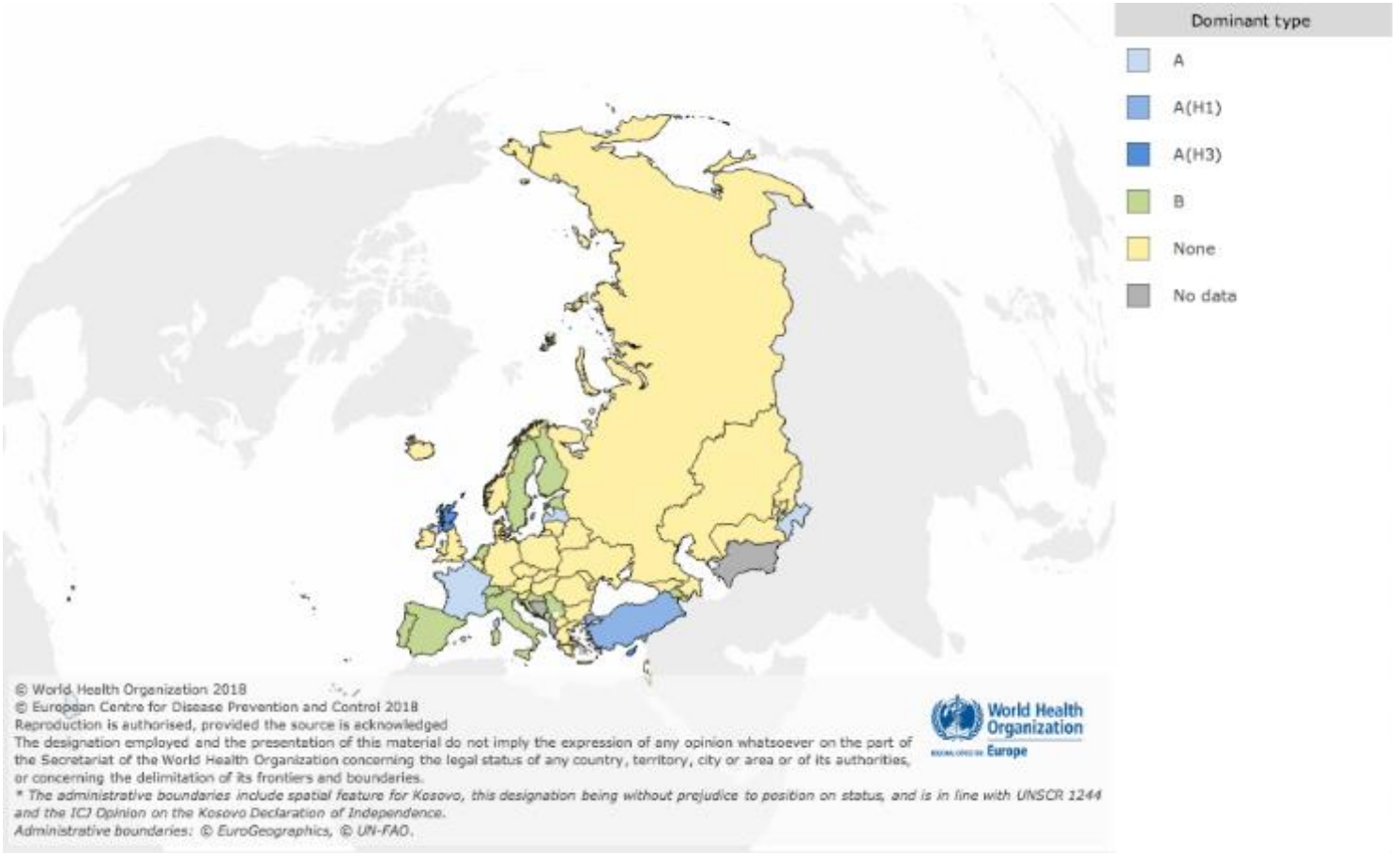
Europe

Week 50


Dominant type
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A(H3)
B
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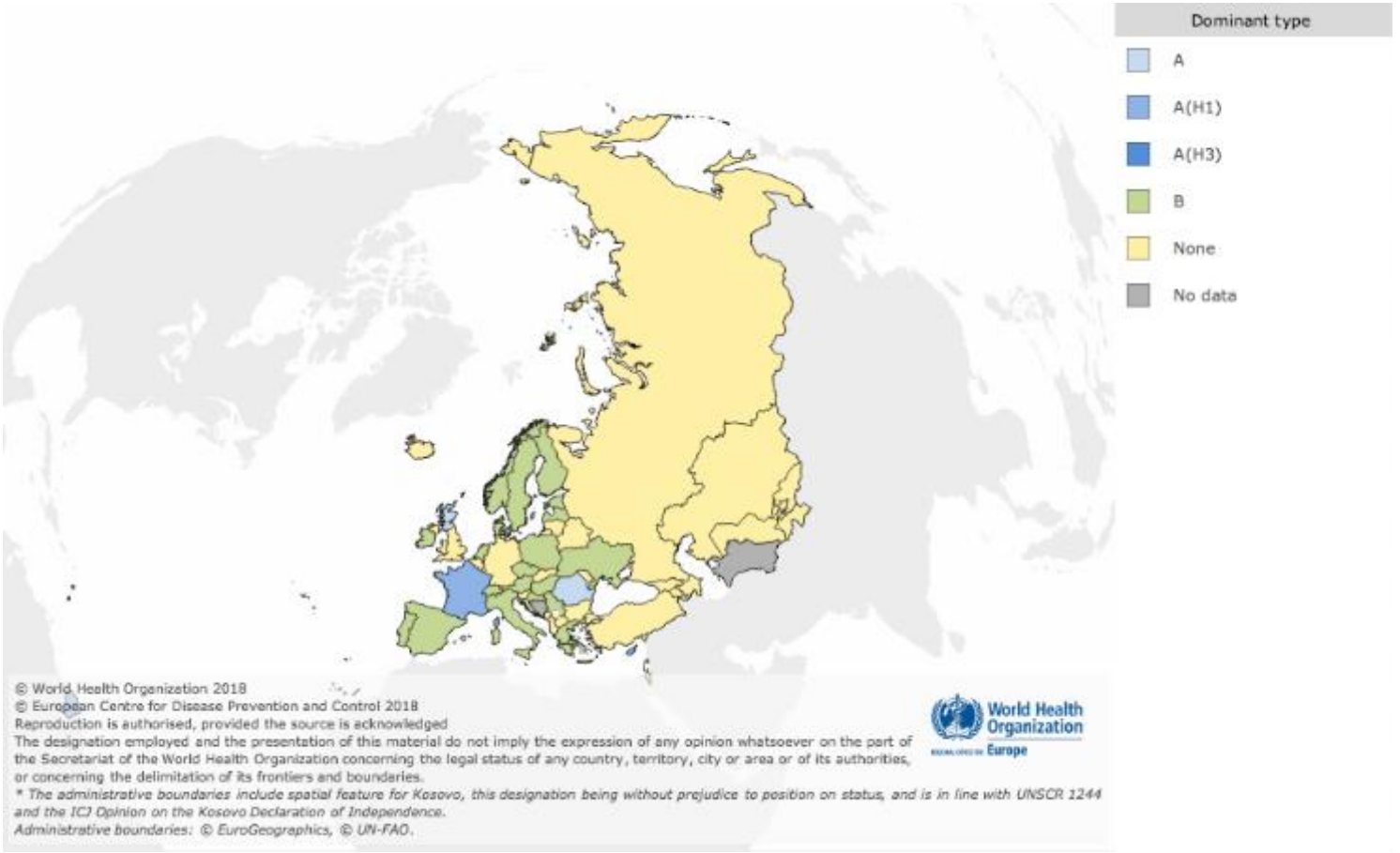
Europe

Week 1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A(H3)
B
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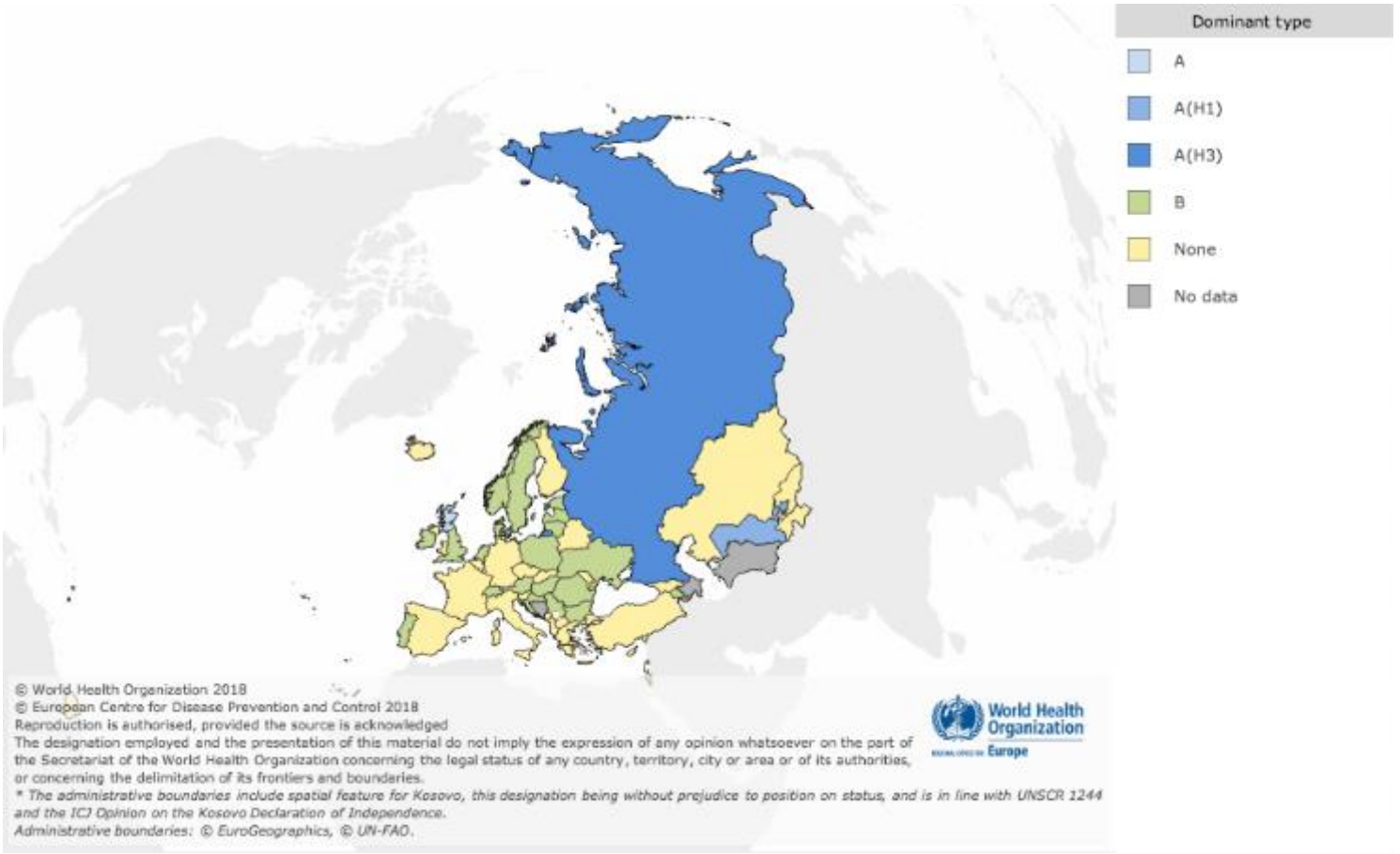
Week 3


Dominant type
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A(H3)
B
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No data
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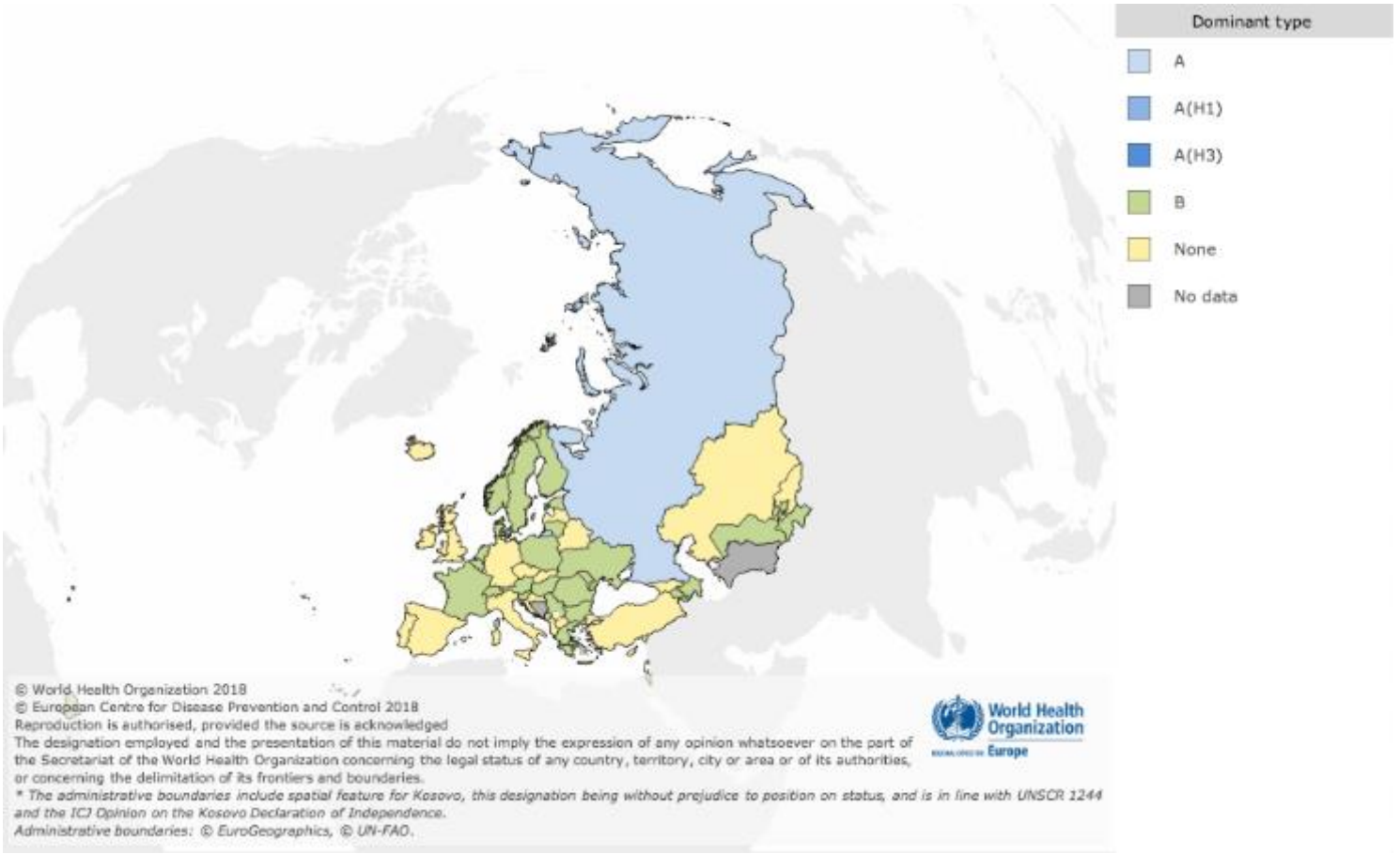
Week 5


Dominant type
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A(H3)
B
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No data
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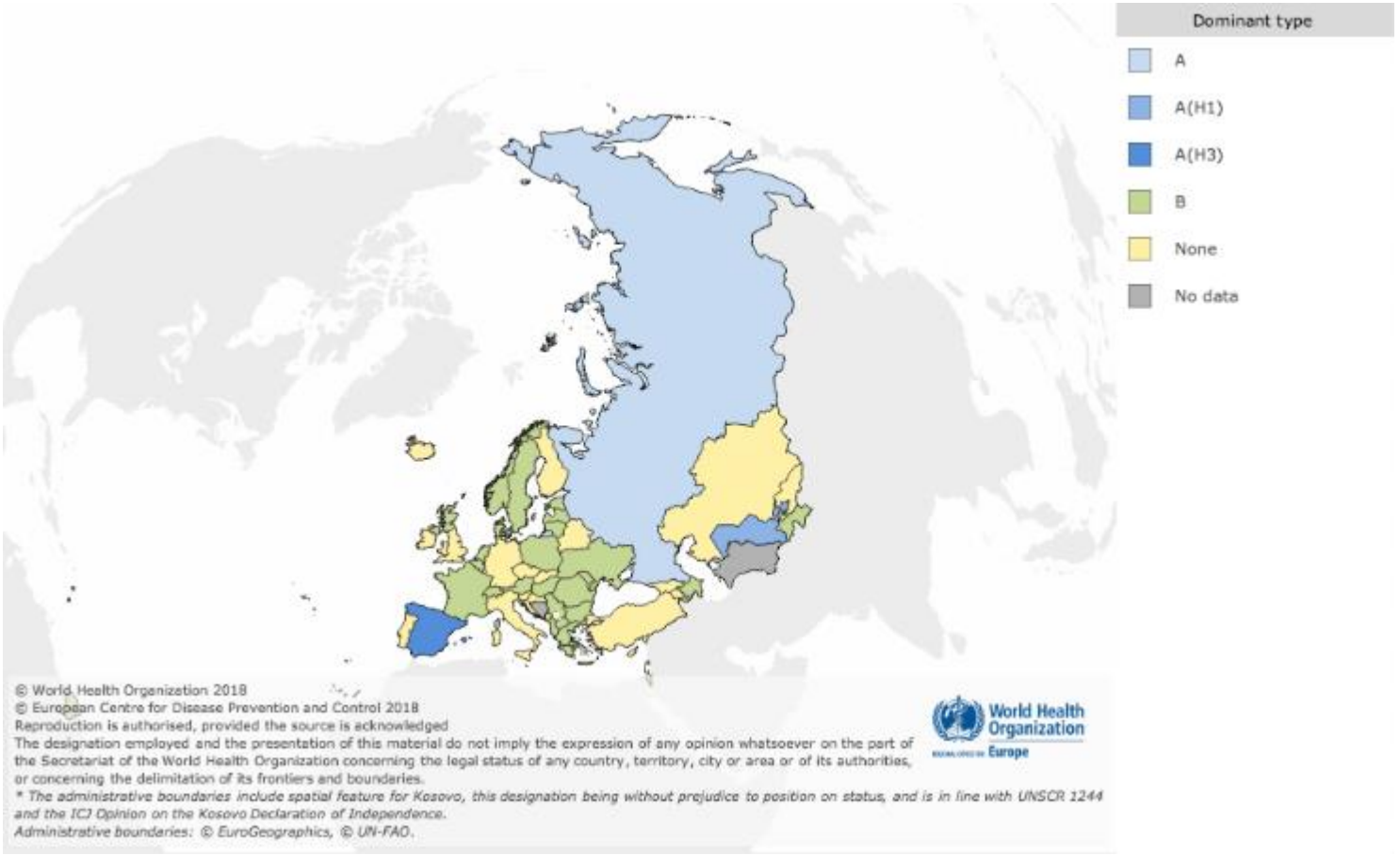
Week 7


Dominant type
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A(H3)
B
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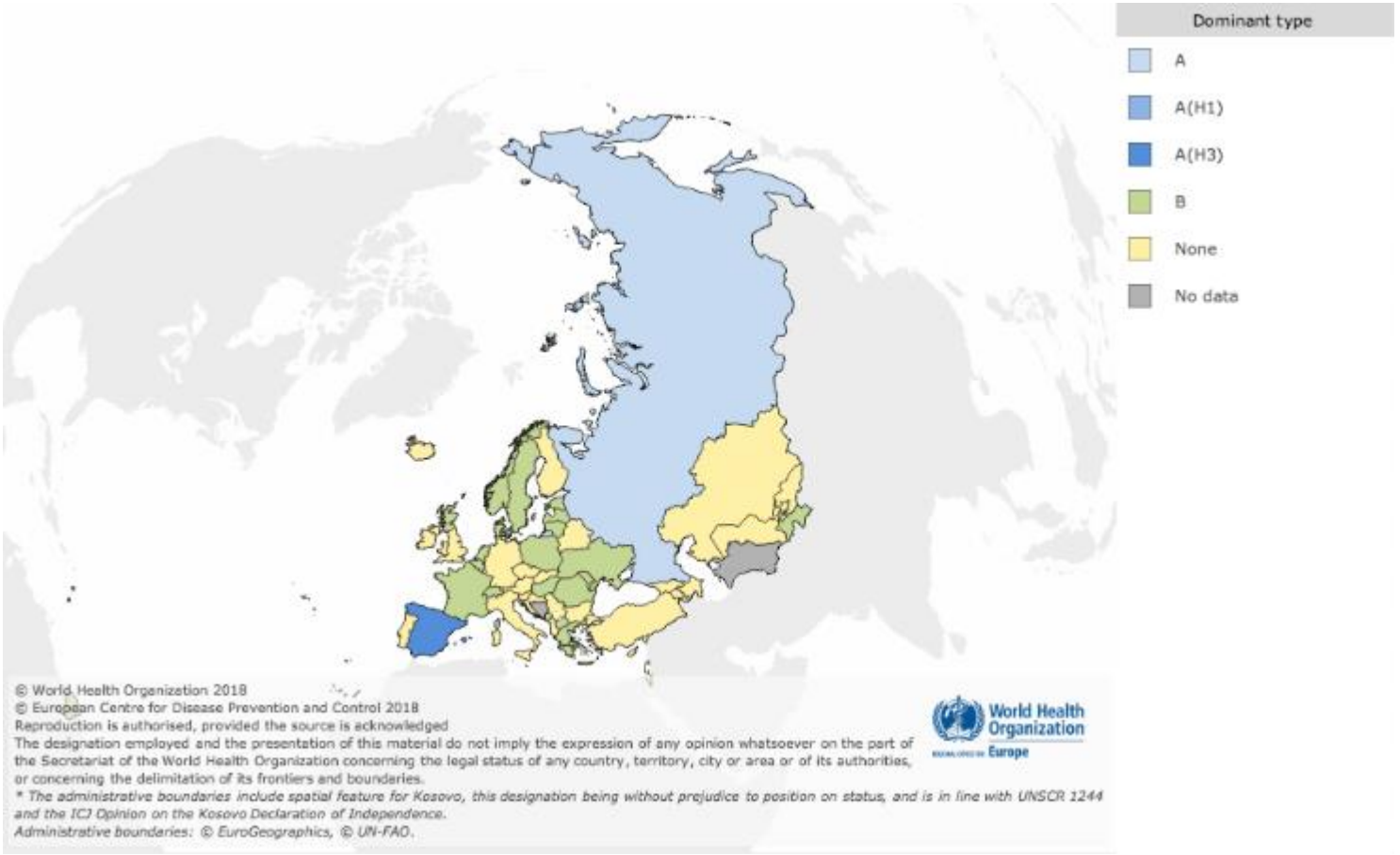
Week 9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A(H3)
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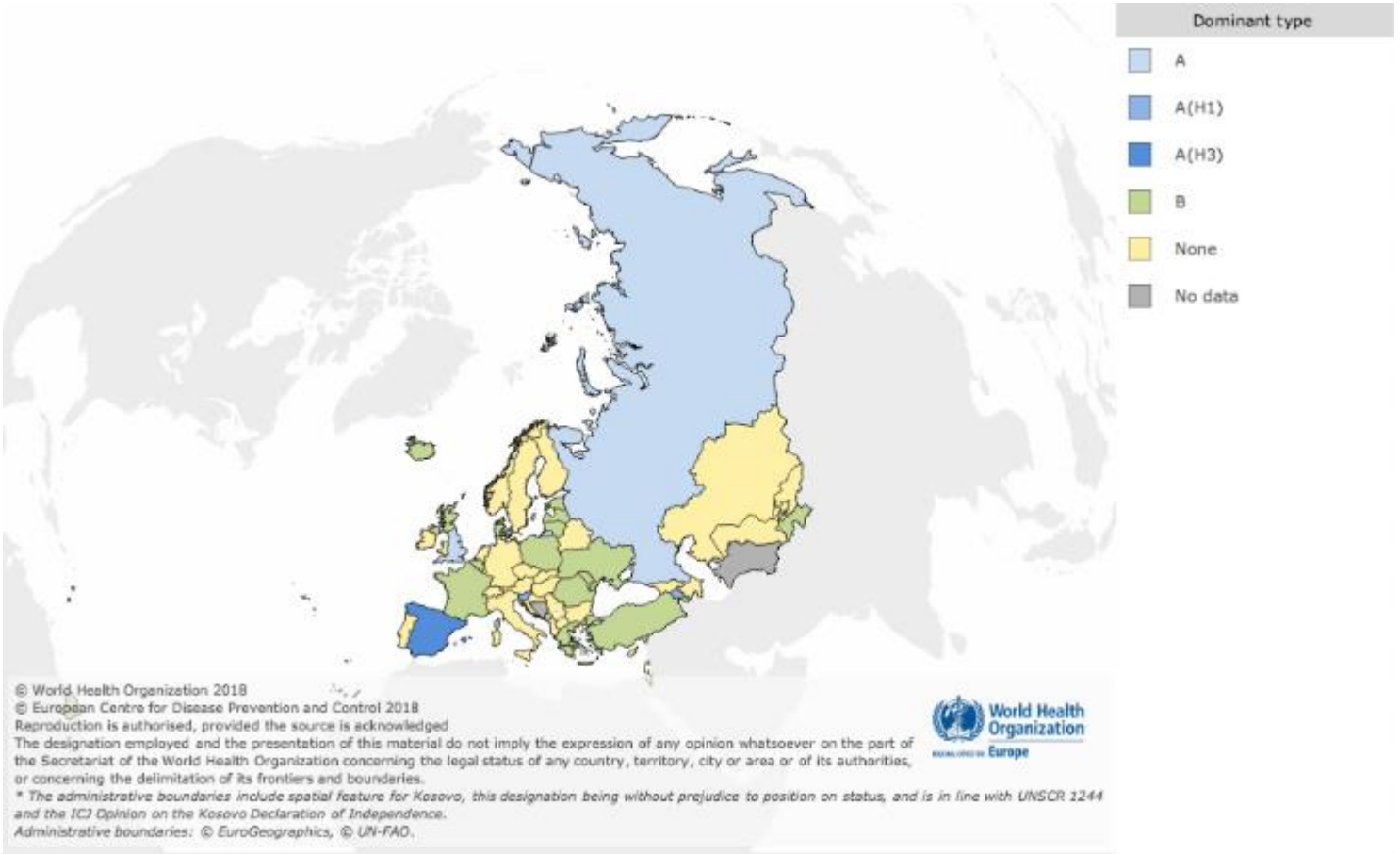
Week 11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A(H3)
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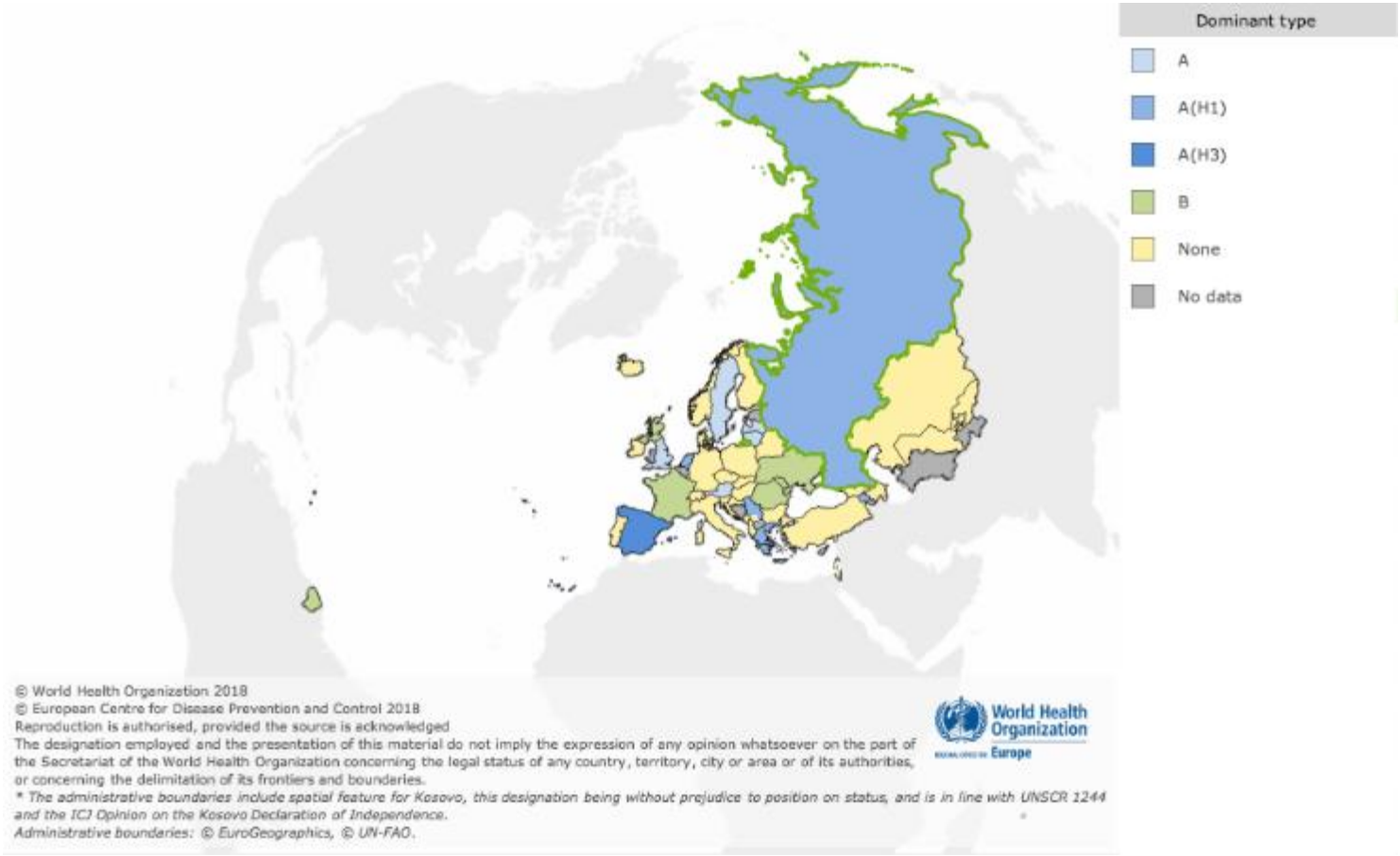
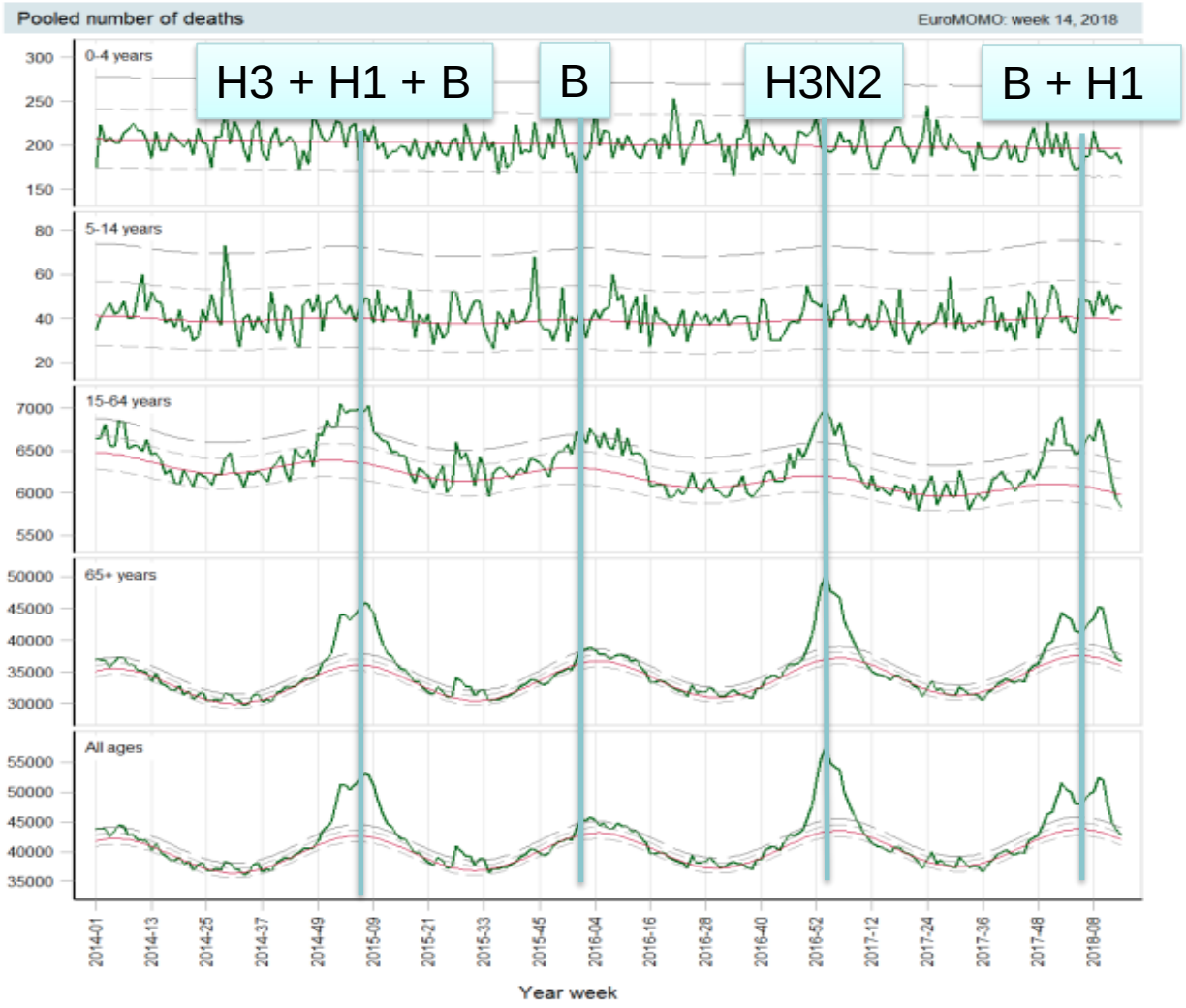
Week 13



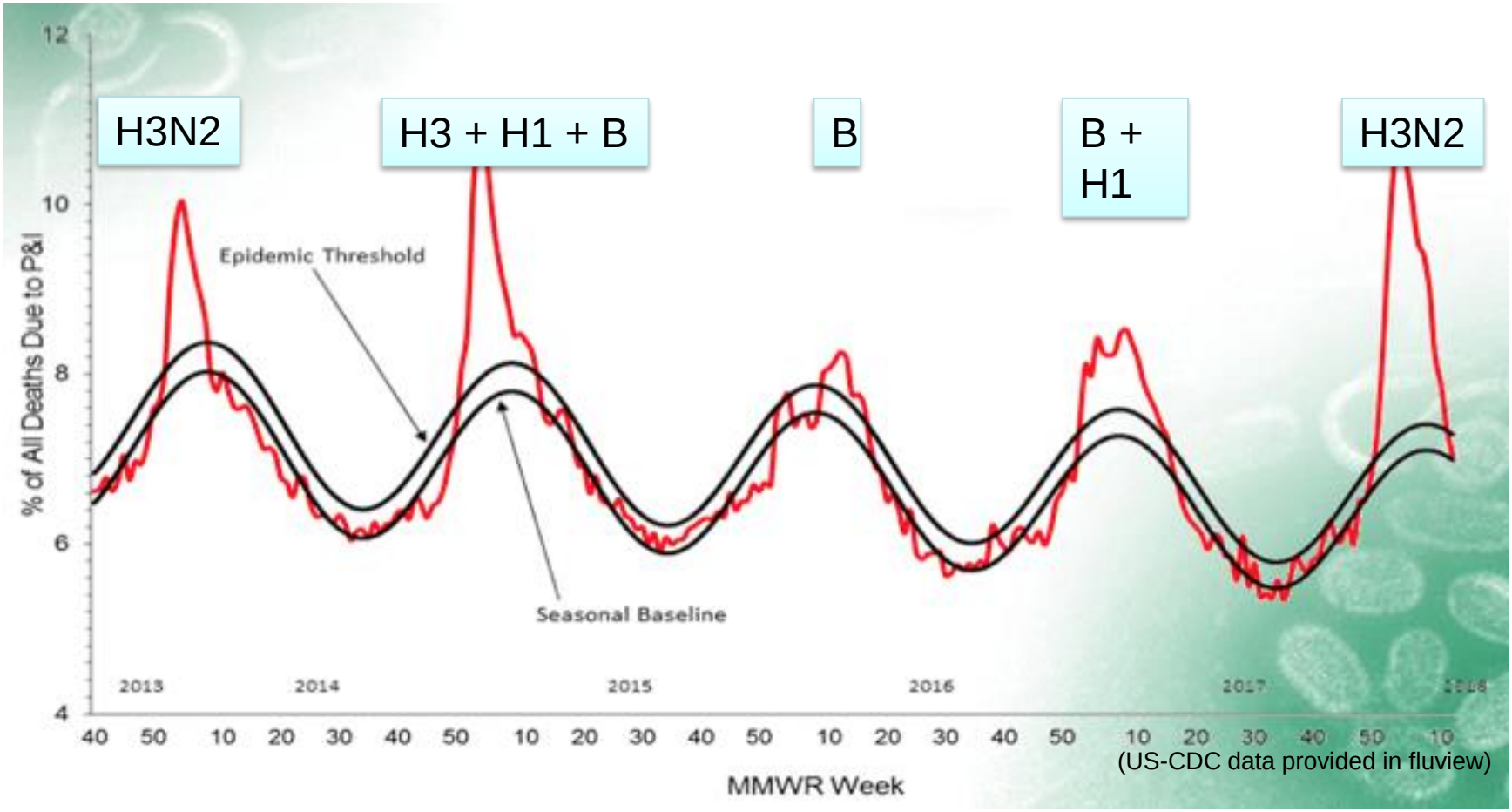
Les caractéristiques de cette saison

- Début précoce
- Plusieurs virus
- Une ile de H1N1pdm09 dans un ocean de B
- Une bascule en milieu de saison
- La réapparition du of H3N2 en finde saison
- Une fin tardive

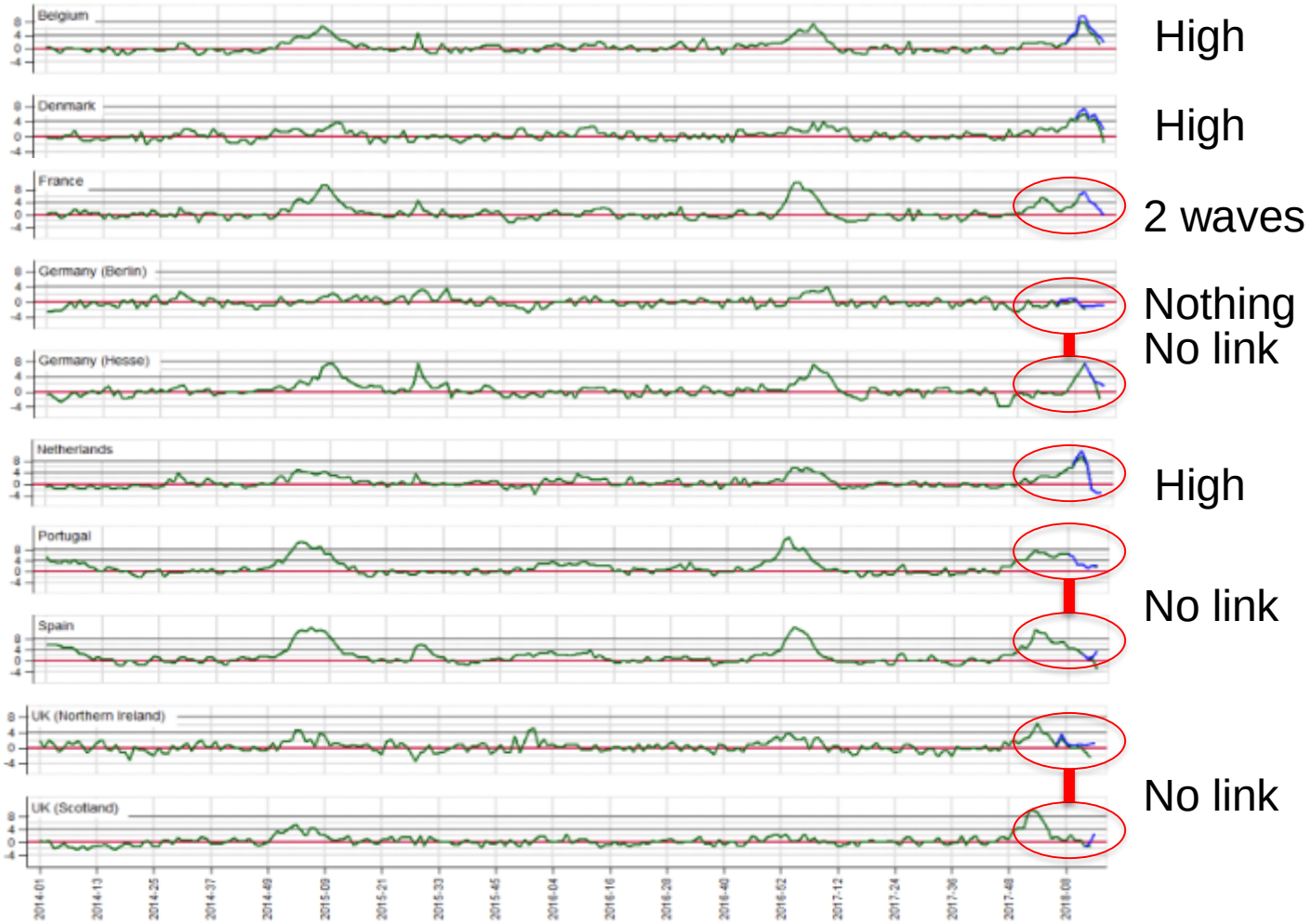
Données de mortalité globale mesurée en Europe



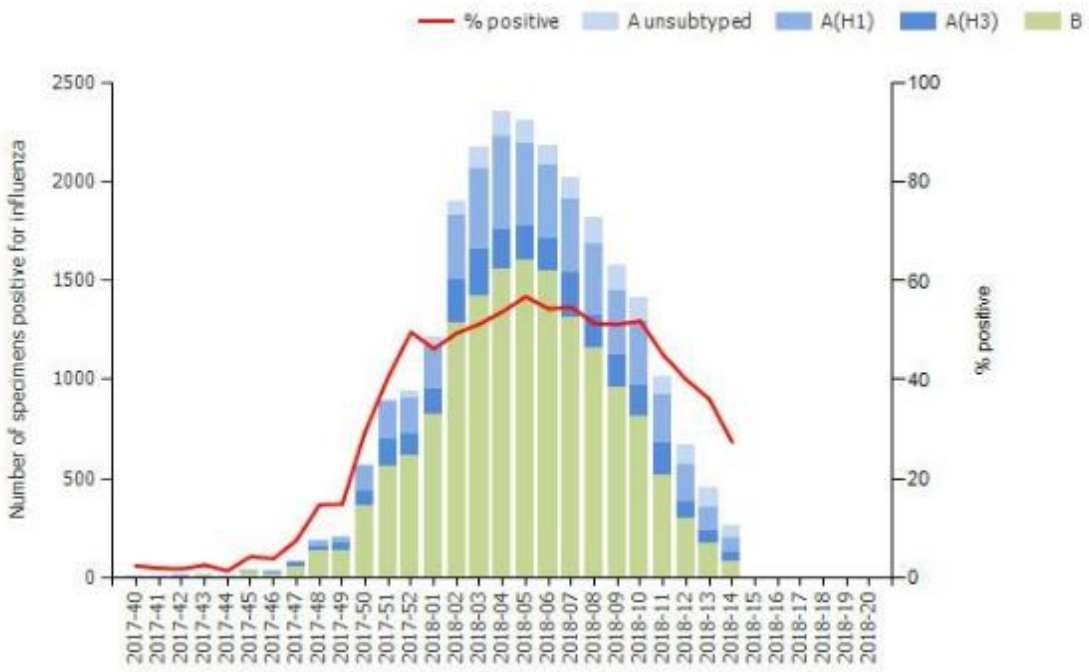
Pooled mortality data in the USA

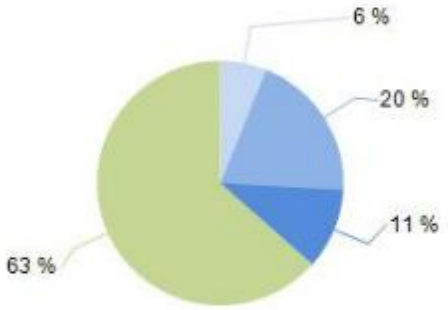


(US-CDC data provided in fluview)

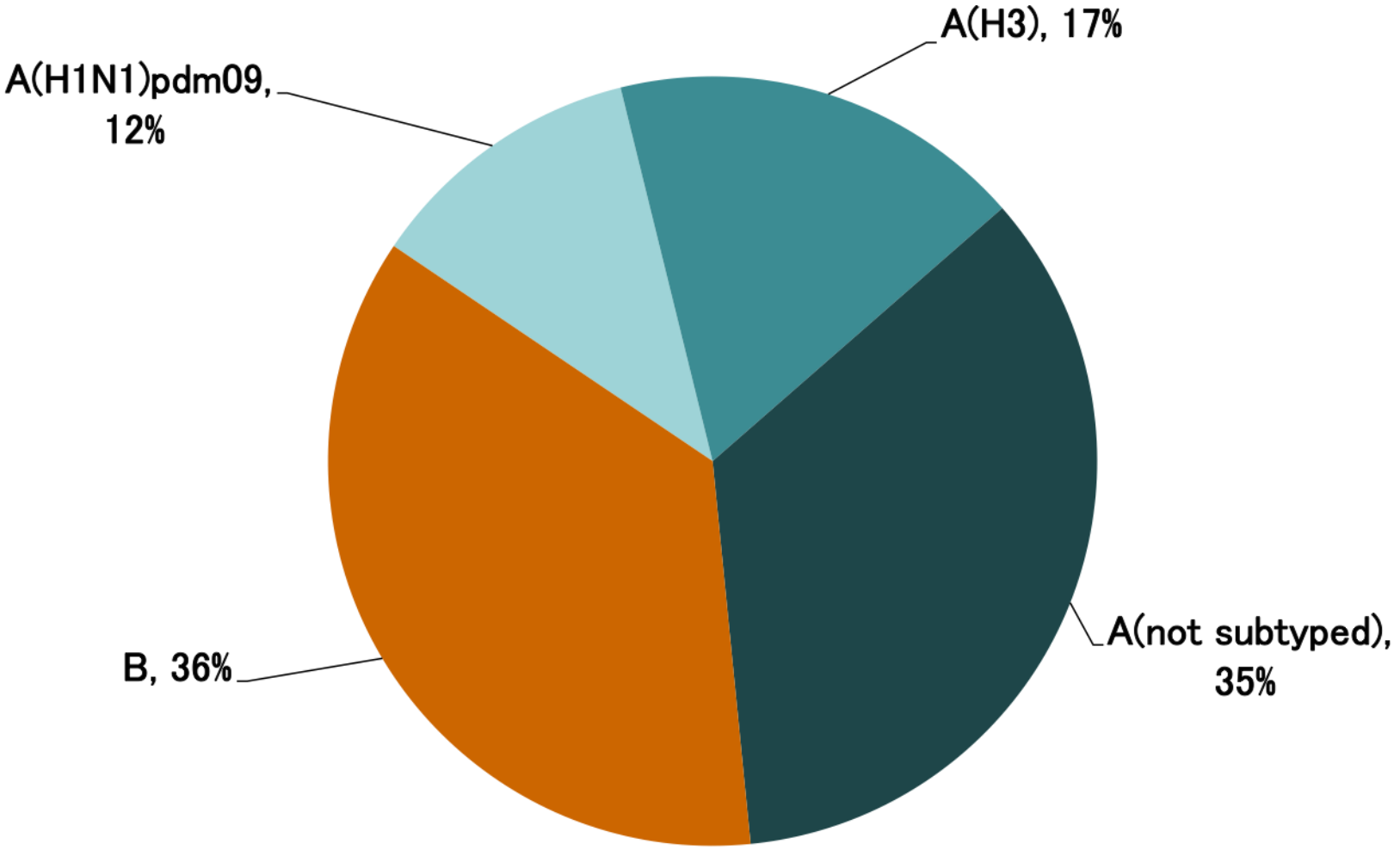

Belgium
Denmark
France
Germany (Berlin)
Germany (Hesse)
Netherlands
Portugal
Spain
UK (Northern Ireland)
UK (Scotland)
2014-01
2014-13
2014-25
2014-37
2014-49
2015-09
2015-21
2015-33
2015-45
2016-04
2016-16
2016-28
2016-40
2016-52
2017-12
2017-24
2017-36
2017-48
2018-08
High
High
2 waves
Nothing
No link
High
No link
No link

Influenza in Europe, the global picture





Répartition des virus influenza par soustypes
(du 4 Septembre 2017 au 28 Janvier 2018)



Data source: FluNet, (www.who.int/flunet), Global Influenza Surveillance and Response System (13 February 2018)

Circulation des virus

World Health Organization

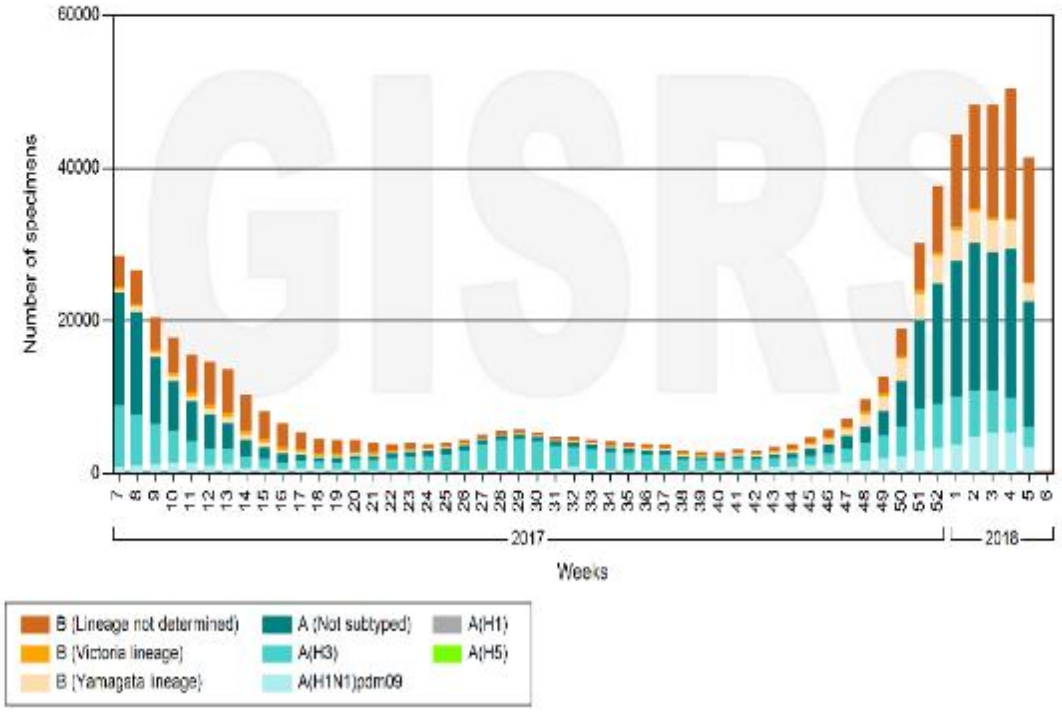
Influenza Laboratory Surveillance Information

by the Global Influenza Surveillance and Response System (GISRS)

generated on 13/02/2018 10:35:26 UTC

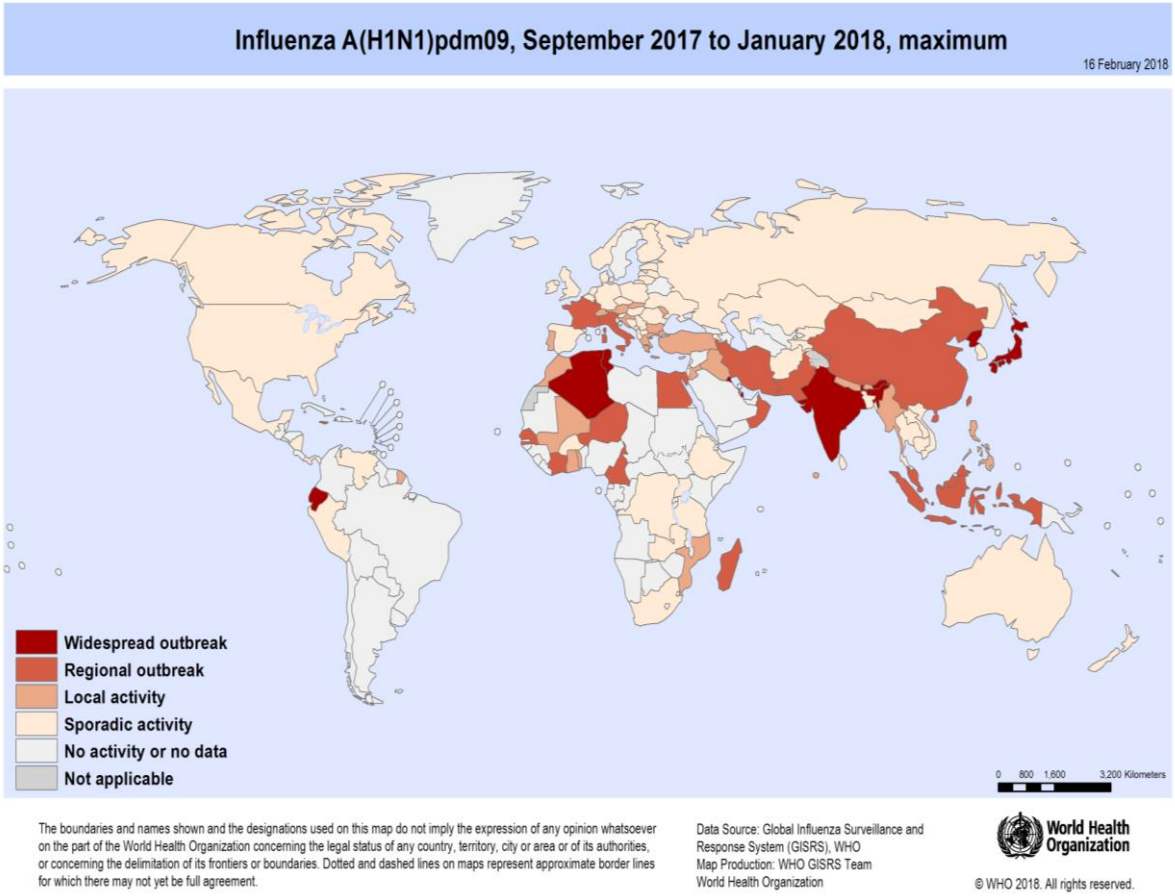
Global circulation of influenza viruses

Number of specimens positive for influenza by subtype

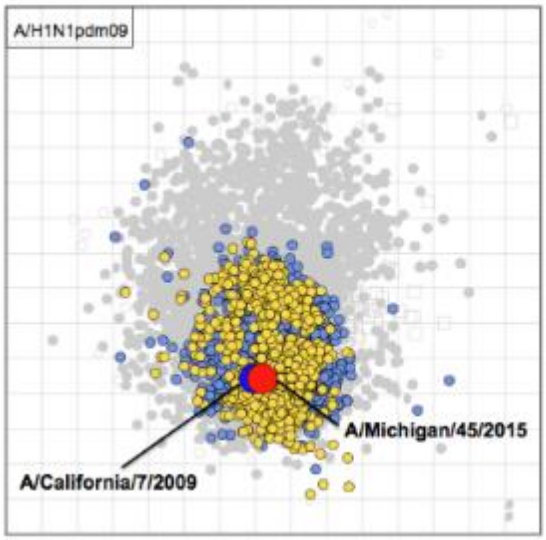


Data source: FluNet (www.who.int/flunet), GISRS

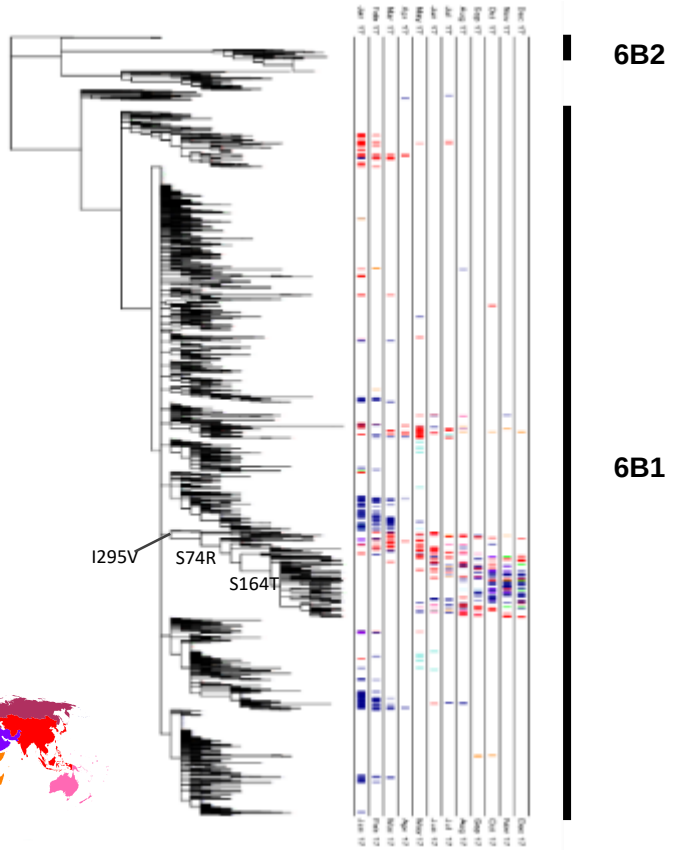
Zones de prédominance de A(H1N1)pdm09



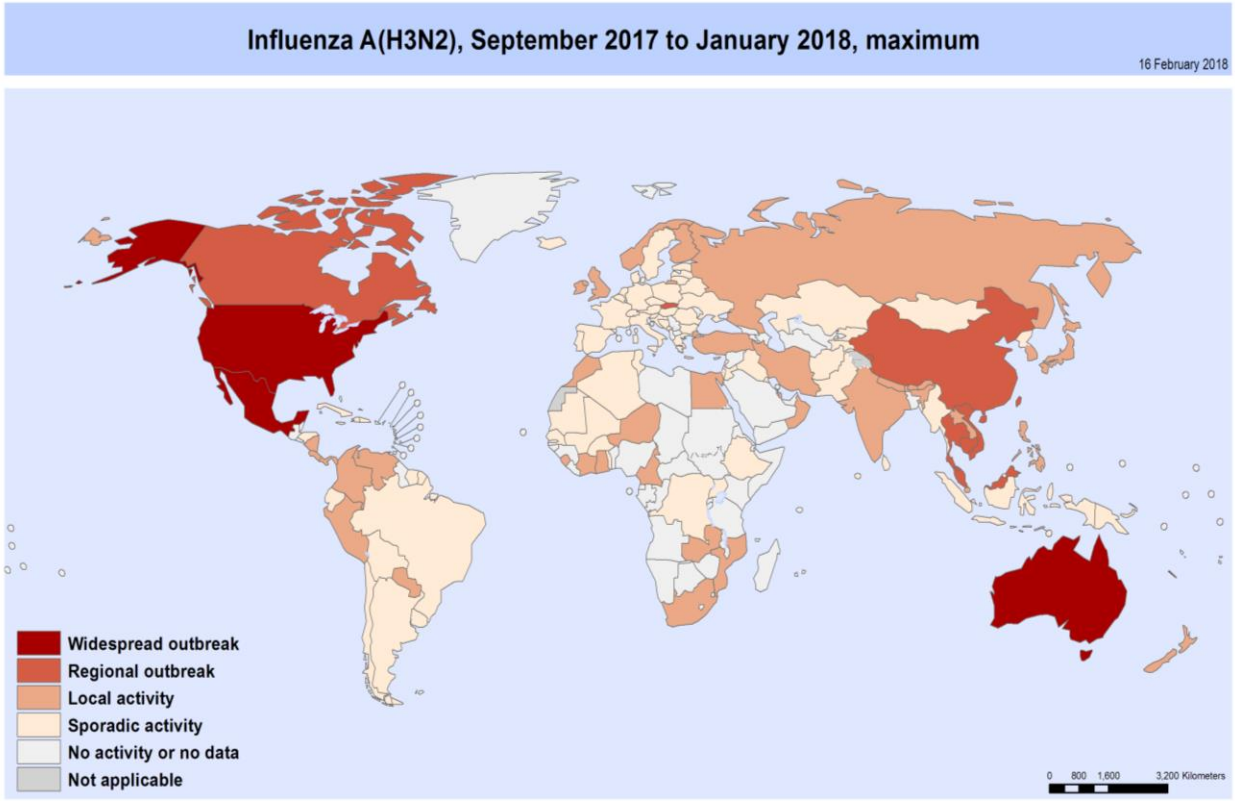
A(H1N1)pdm09: HA characterization



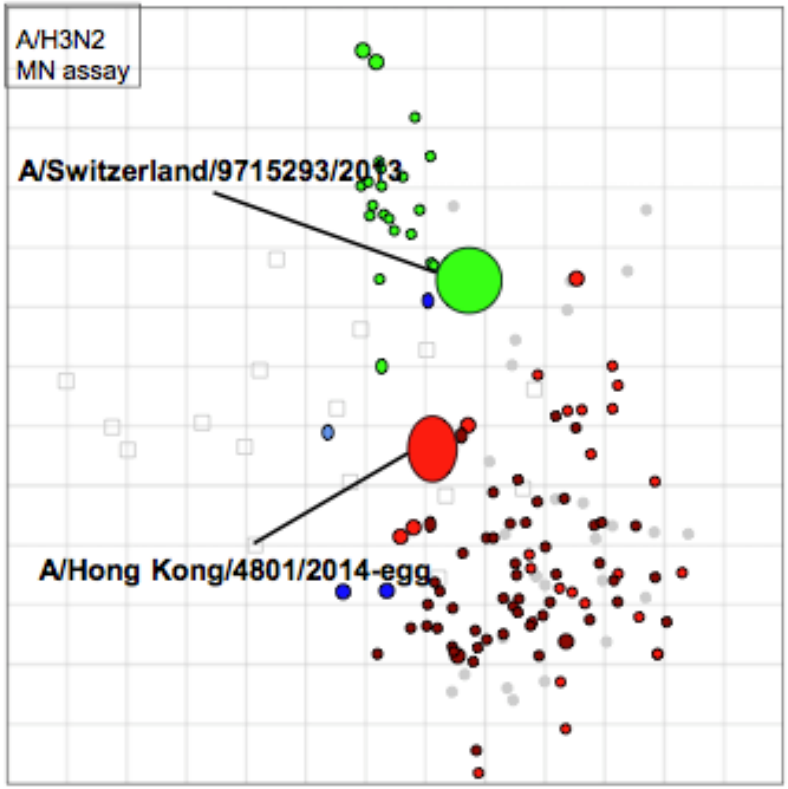
North America
South America
Europe
Africa
Middle East
Russia
E SE Asia
Oceania

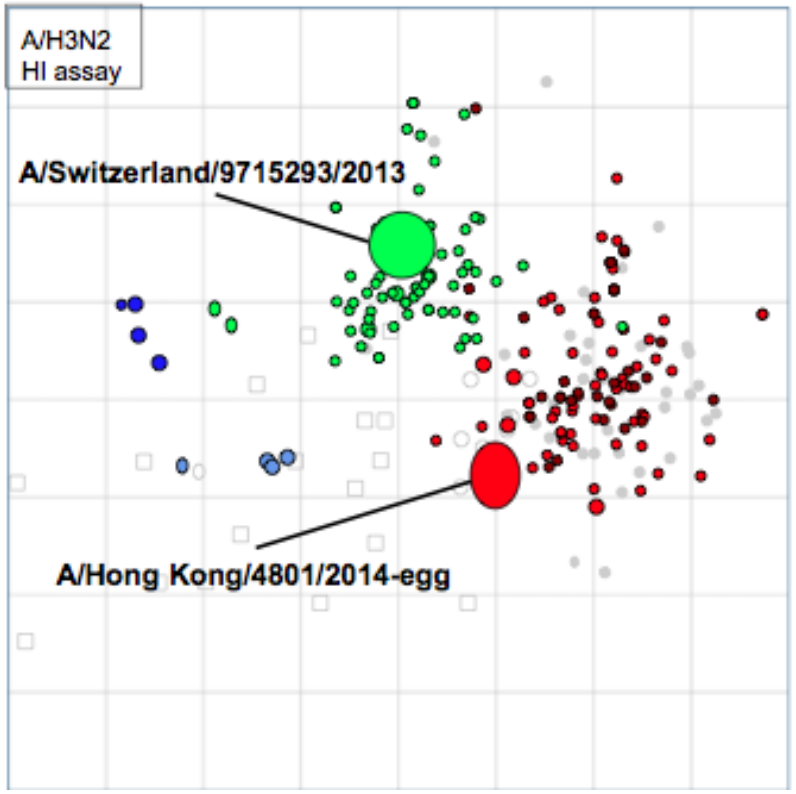


Zone de predominance de A(H3N2)



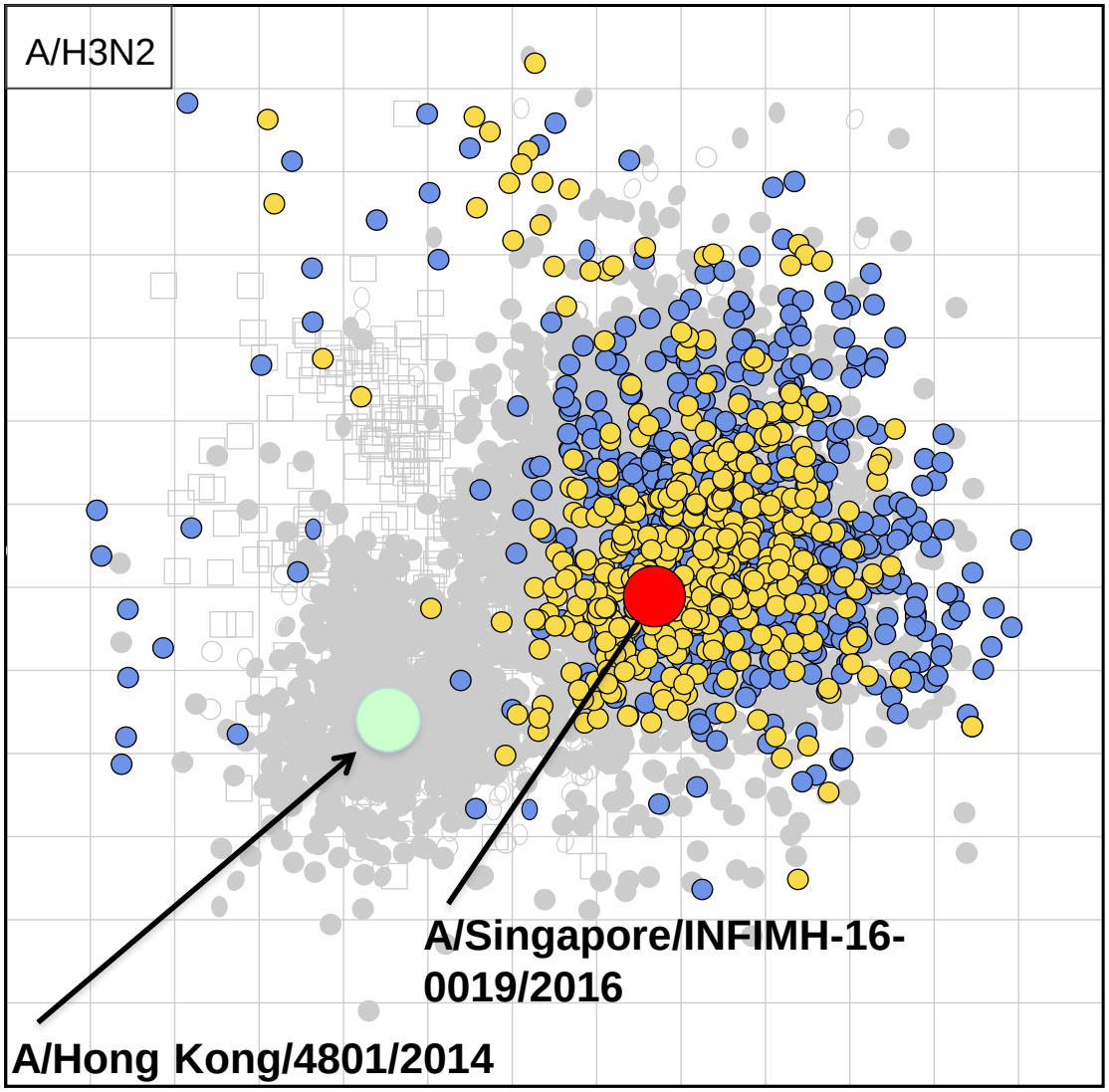
Analyses des différences antigéniques en les virus des clades,3C.3a, 3C.2a et 3C.2a1 (2016-2017)





Données OMS

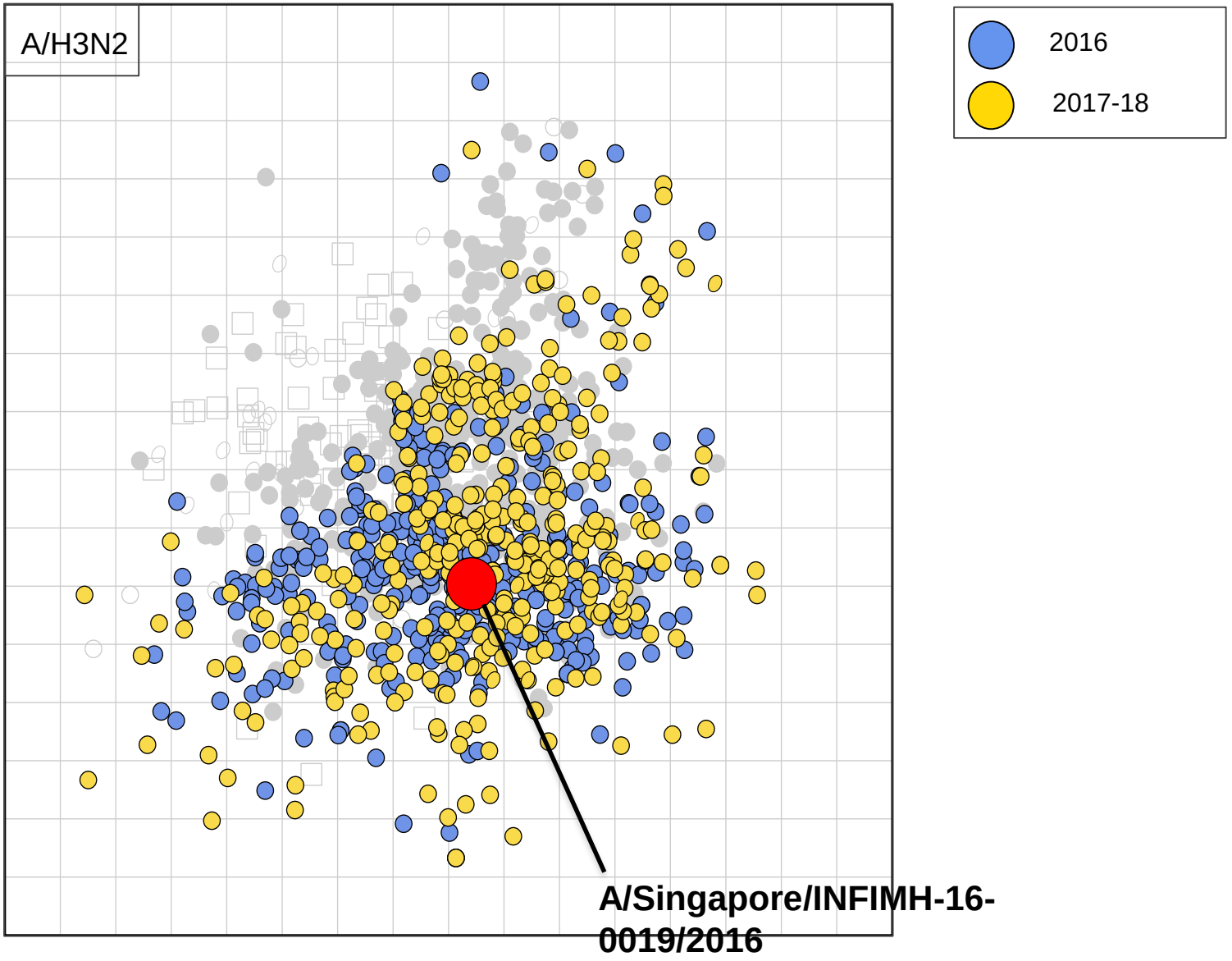
Antigenic cartography from Univ. Cambridge

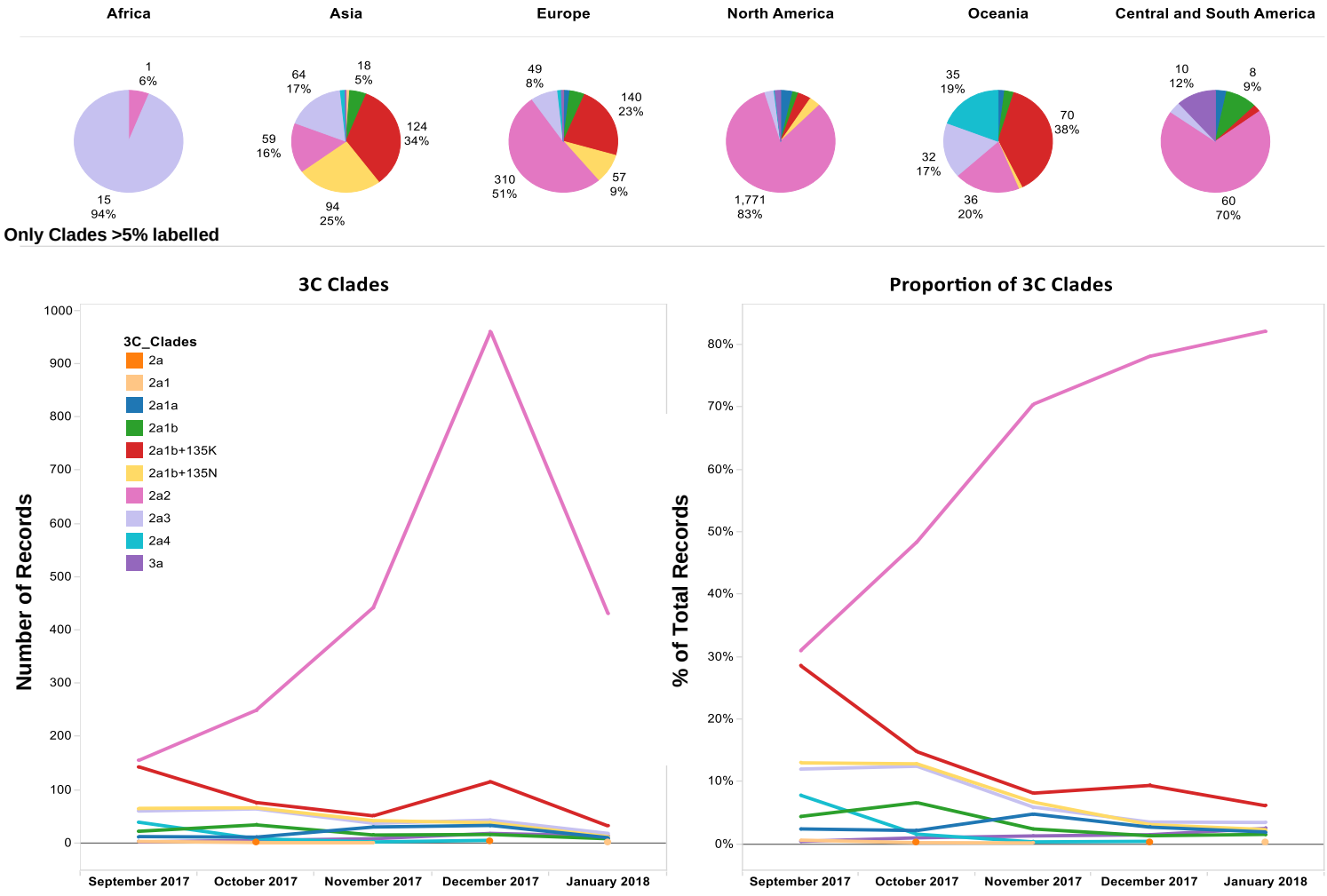


February 2017-August 2017

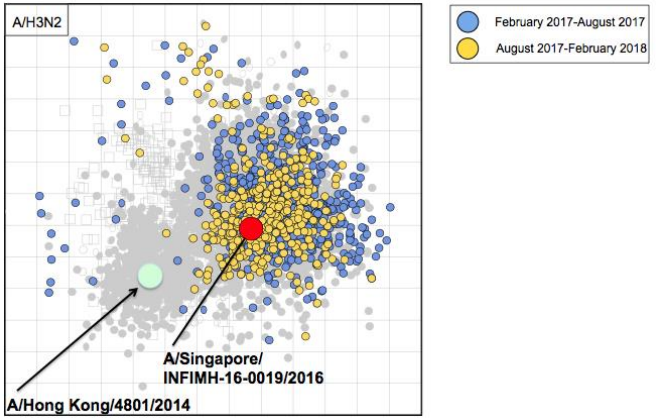
August 2017-February 2018

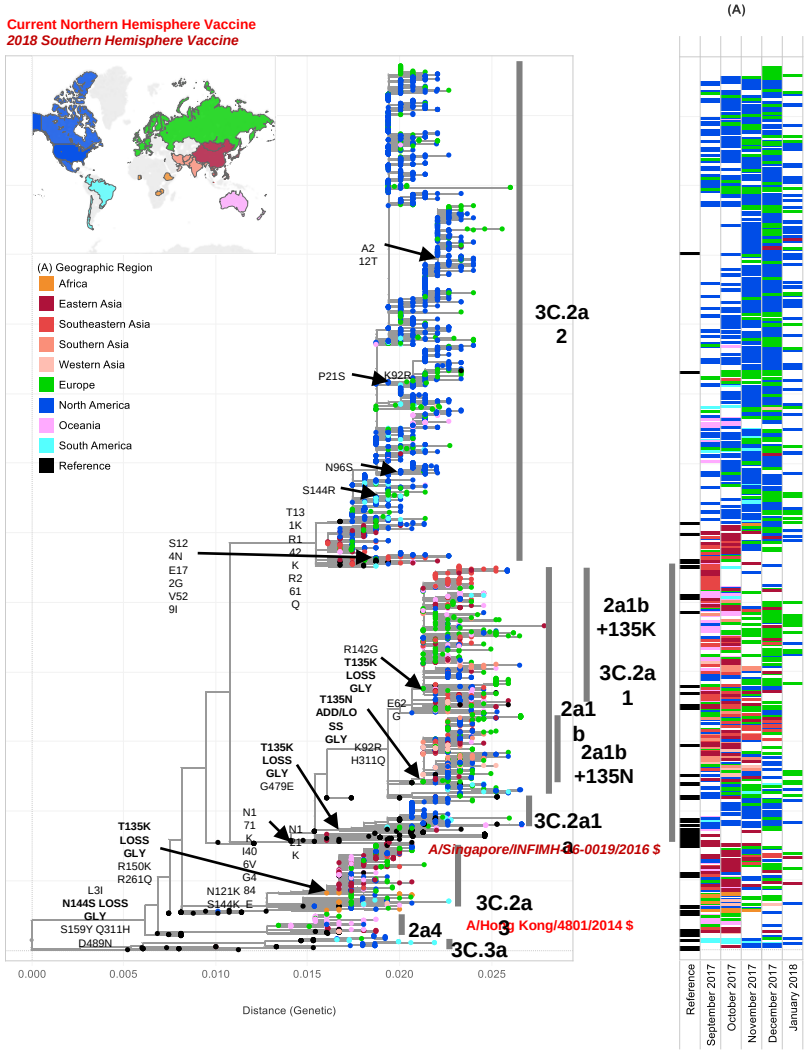
Antigenic cartography from Univ. Cambridge



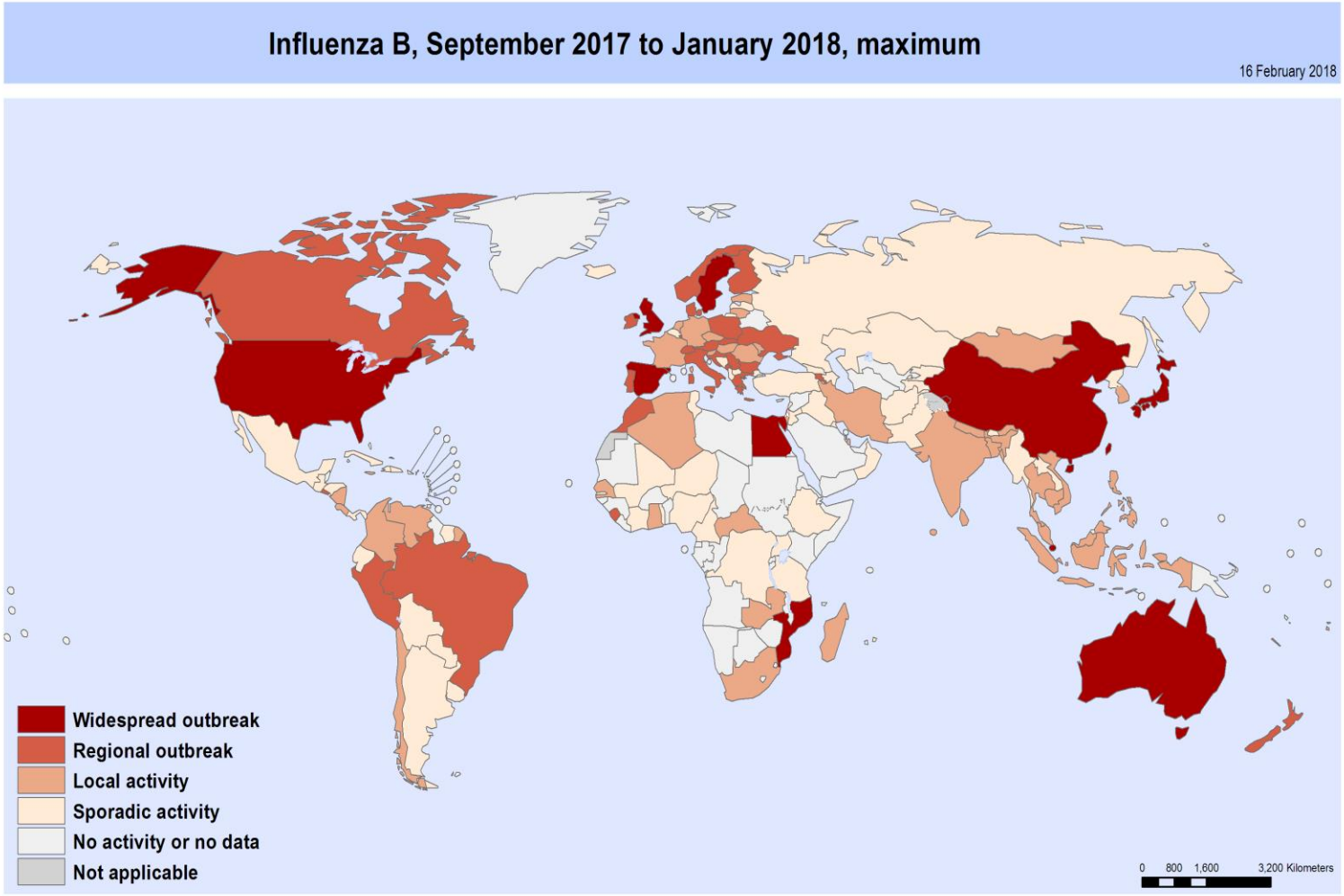

Africa
1
6%
15
94%
Asia
64
17%
18
5%
59
16%
124
34%
94
25%
Europe
49
8%
140
23%
310
51%
57
9%
North America
1,771
83%
Oceania
35
19%
70
38%
32
17%
36
20%
Central and South America
10
12%
8
9%
60
70%
Only Clades >5% labelled
3C Clades
Number of Records
3C_Clades
2a
2a1
2a1a
2a1b
2a1b+135K
2a1b+135N
2a2
2a3
2a4
3a
September 2017
October 2017
November 2017
December 2017
January 2018
Proportion of 3C Clades
% of Total Records

A/H3N2:
HA characterization





Influenza B viruses



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), WHO
Map Production: WHO GISRS Team
World Health Organization

World Health Organization

Lignages Influenza B détectés par GISRS

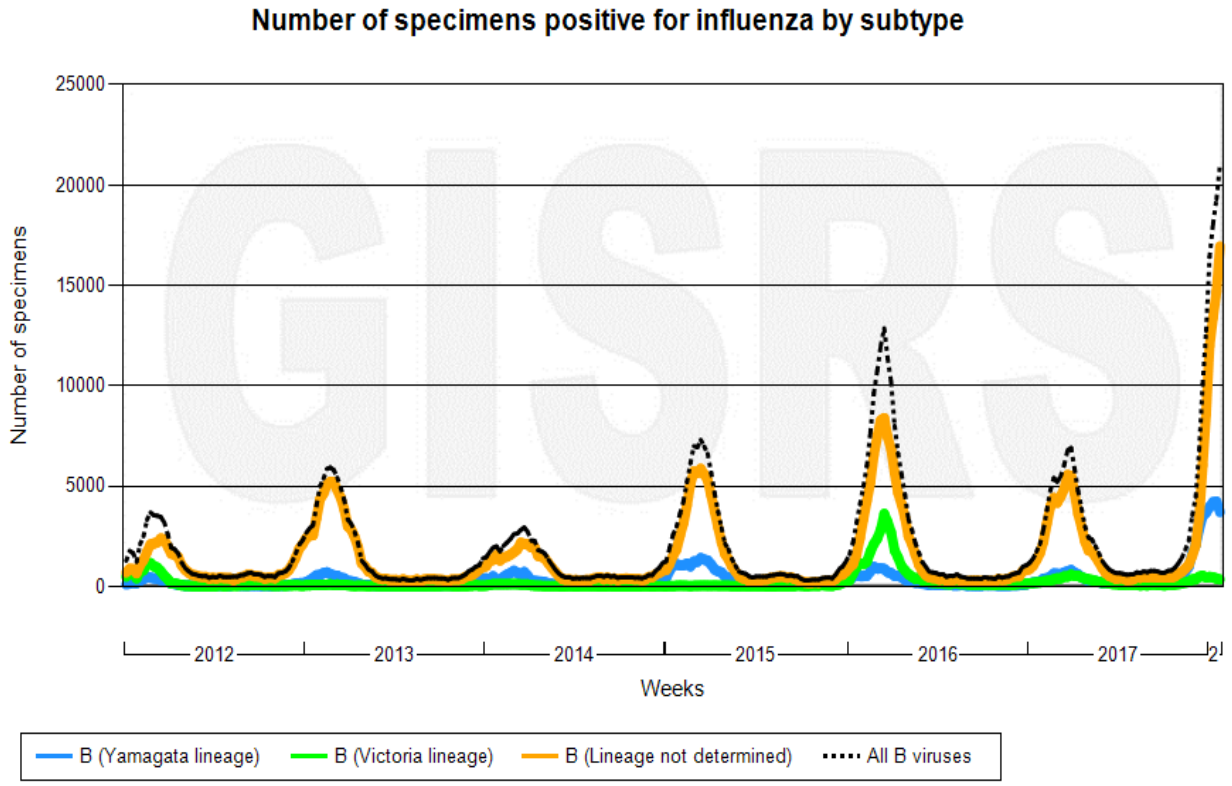
World Health Organization

Influenza Laboratory Surveillance Information

by the Global Influenza Surveillance and Response System (GISRS)

13/02/2018

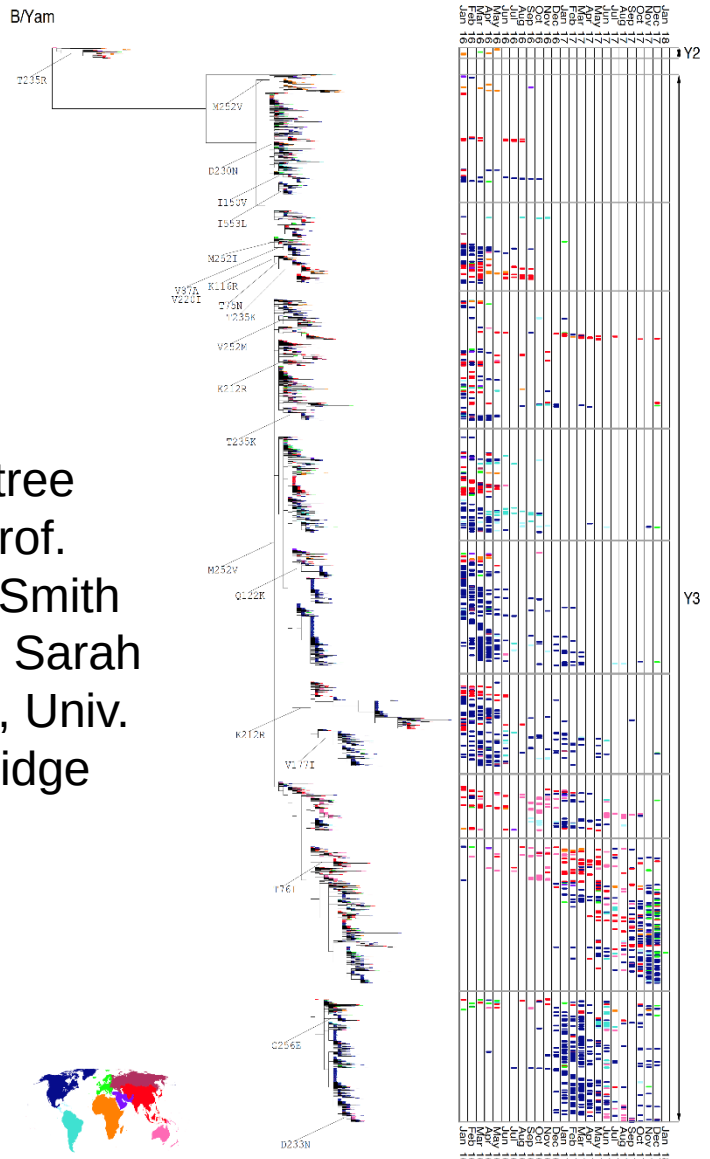
Global circulation of influenza B viruses

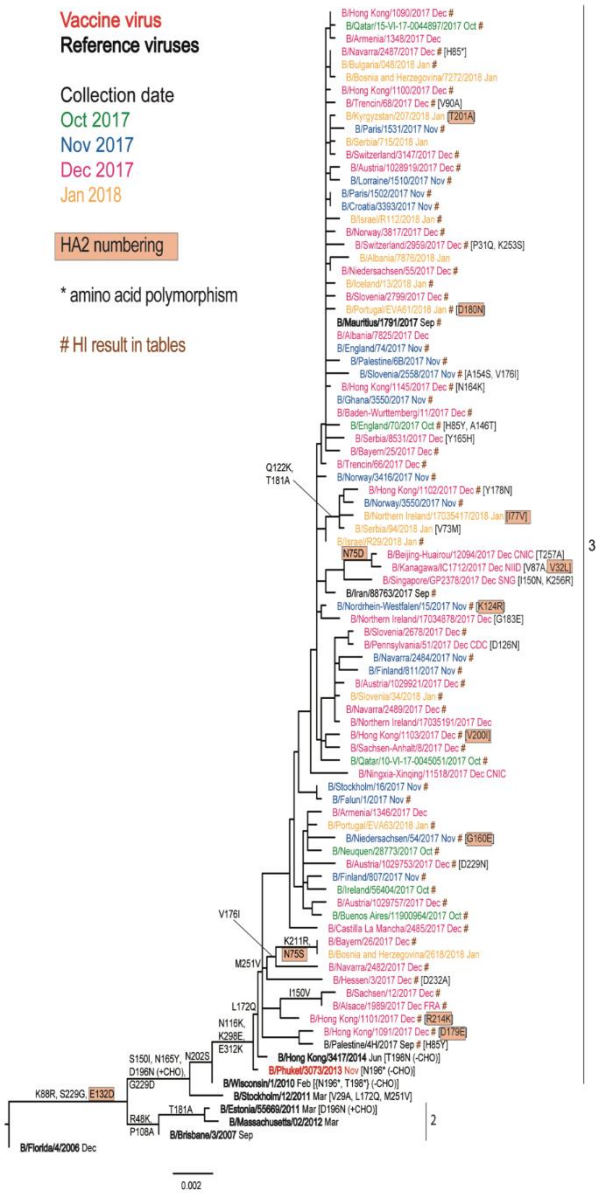


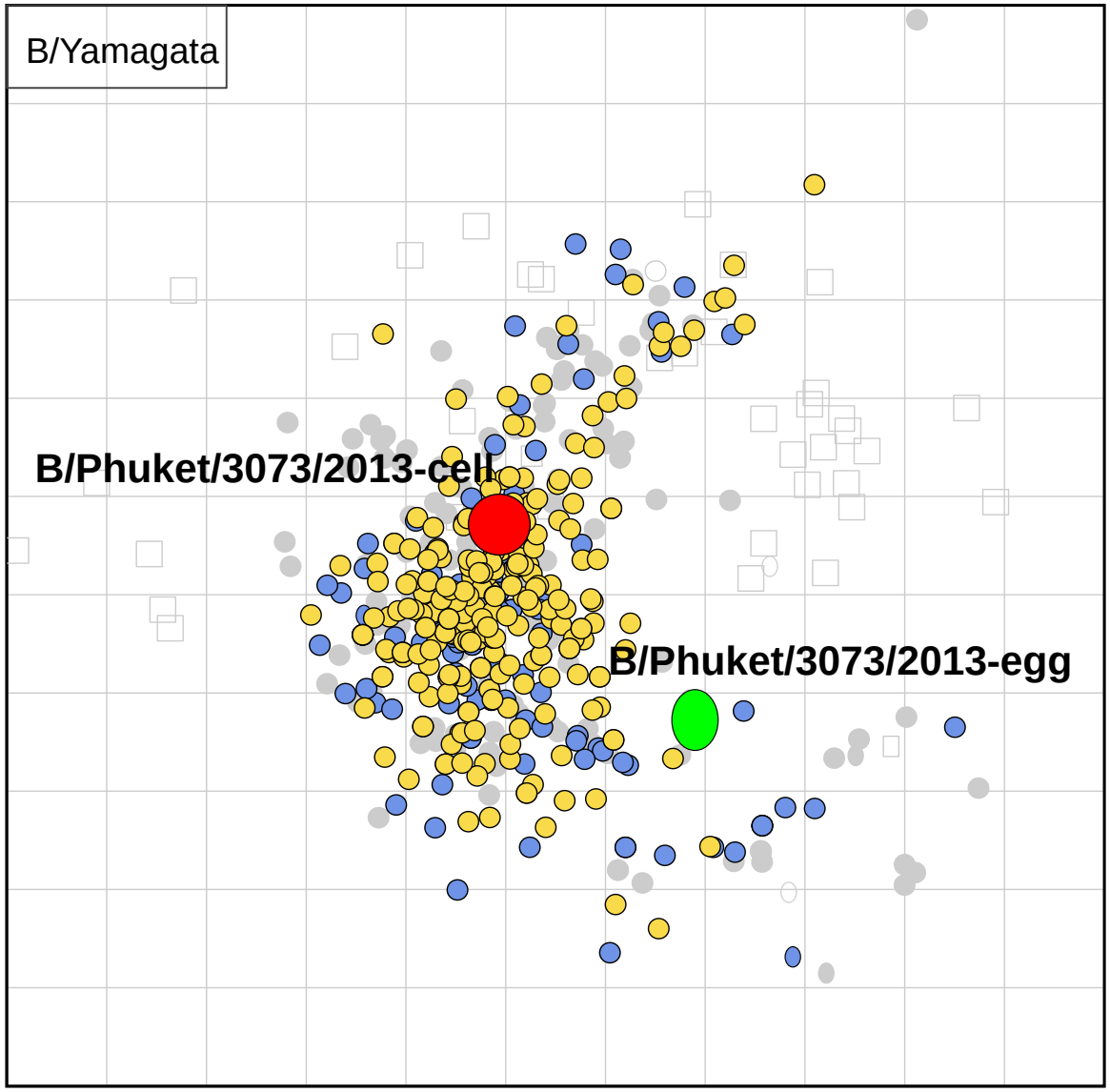
Data source: FluNet (www.who.int/flunet), GISRS

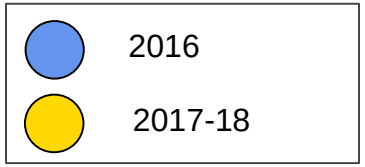
B/Yamagata arbre phylogénétique des HA

Large tree from Prof. Derek Smith and Dr Sarah James, Univ. Cambridge





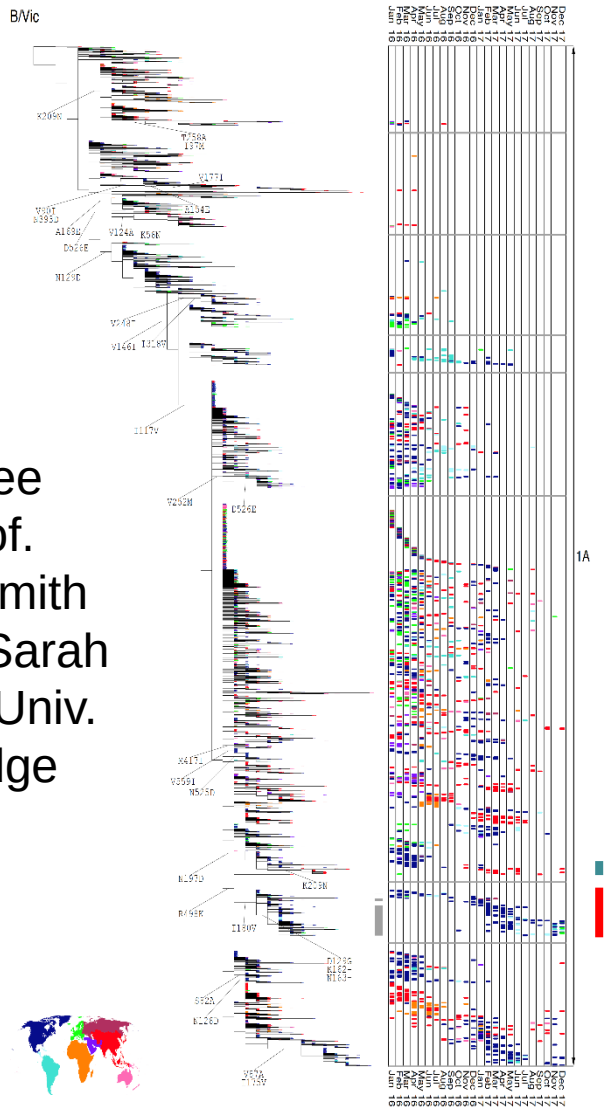




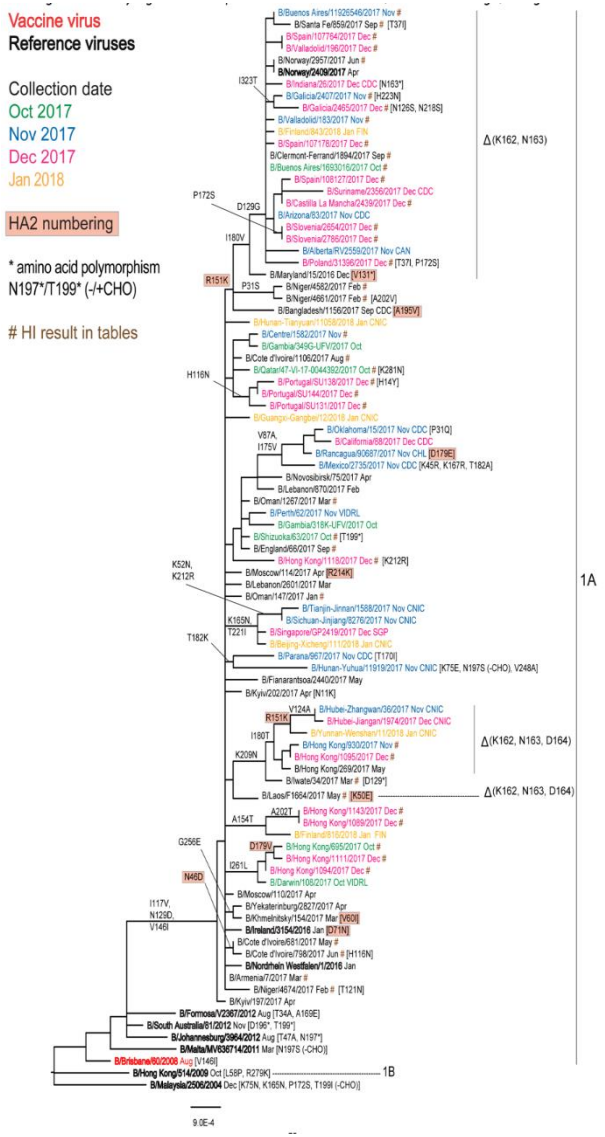
Antigenic cartography from Prof. Derek Smith and Dr Sarah James, Univ. Cambridge

B/Victoria arbre phylogénétique des HA

Large tree from Prof. Derek Smith and Dr Sarah James, Univ. Cambridge



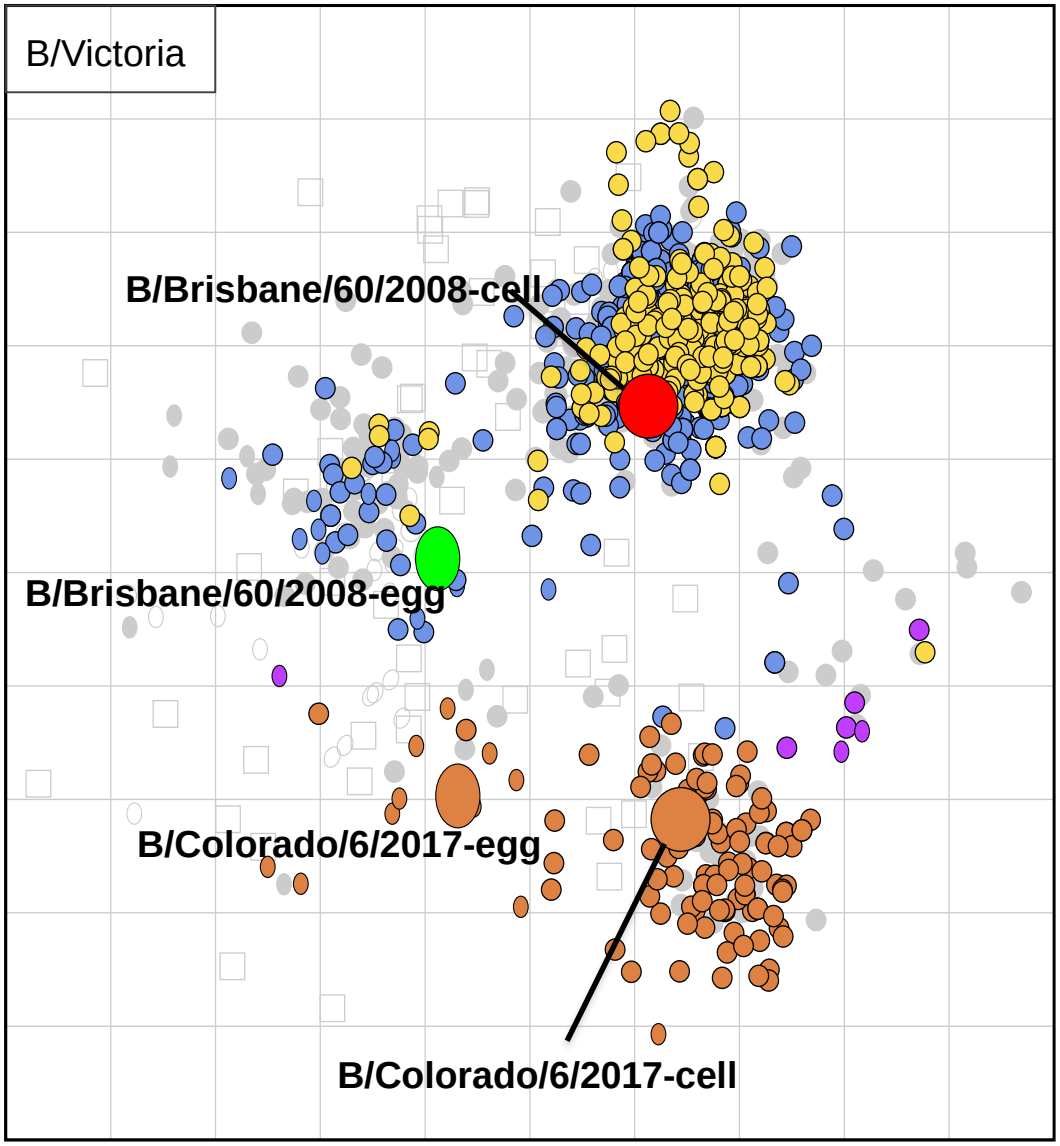
Δ162-164
Δ162-163

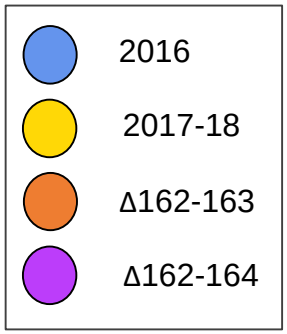


Influenza B/Victoria virus avec deletion

V1A-2 DEL = 109 virus

V1A-3 DEL = 9 virus





Antigenic cartography from Prof. Derek Smith and Dr Sarah James, Univ. Cambridge

Les alternatives en développement

To try to do better than nature

Liste des vaccins disponibles

- Vaccins sur oeuf
- Vaccins sur cellule
- Vaccins atténués (Fluenz)
- Vaccin avec adjuvants type squalènes
- Vaccin haute dose
- Vaccins recombinants (Flublock)

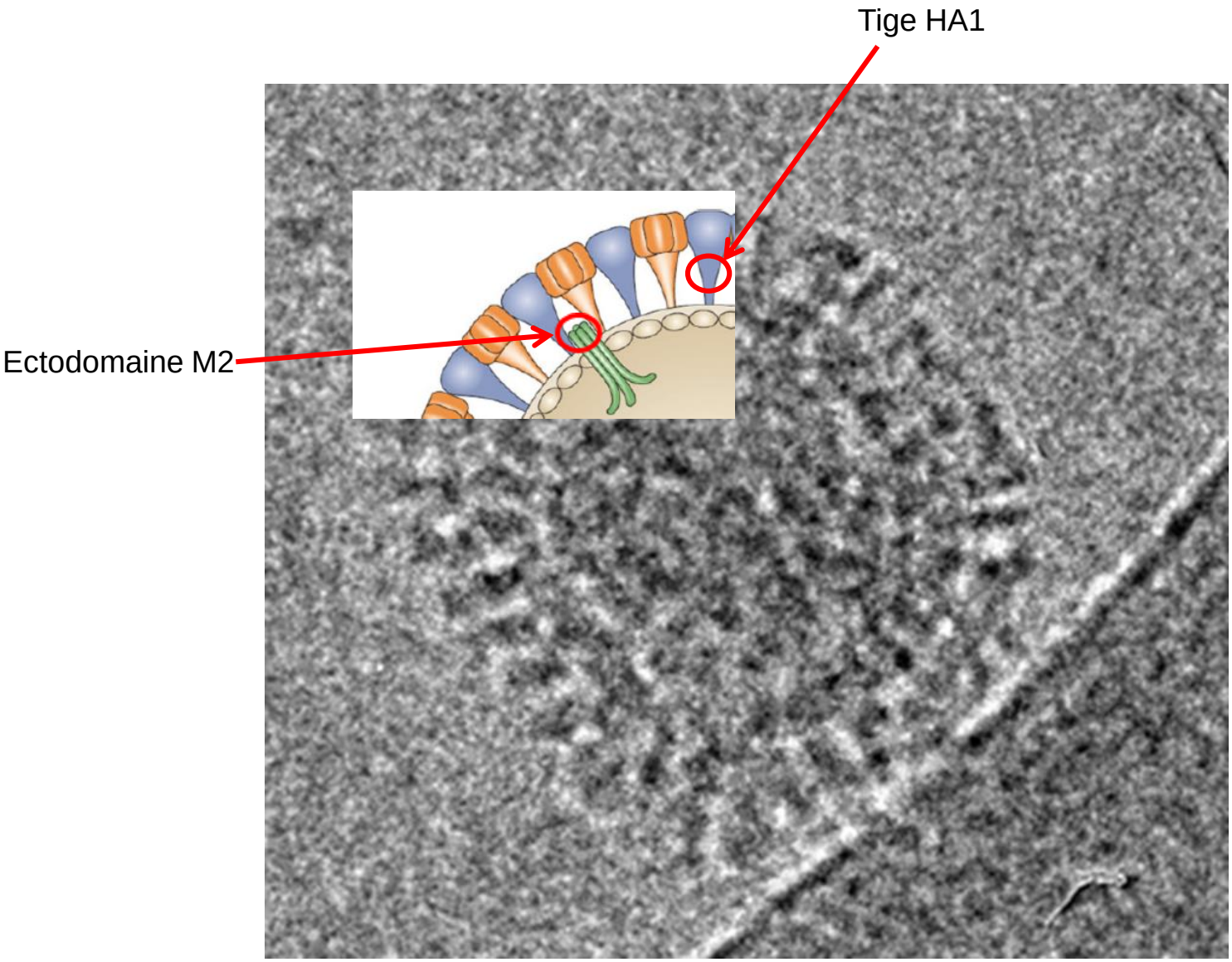
Liste des vaccins disponibles et en cours de développement

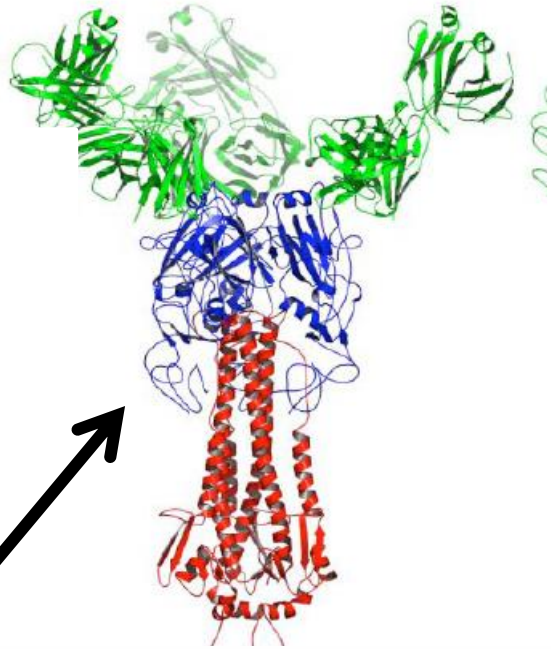
- Vaccins sur oeuf
- Vaccins sur cellule
- Vaccins atténués (Fluenz)
- Vaccin avec adjuvants type squalènes
- Vaccin haute dose
- Vaccins recombinants (Flublock)

- Vaccin dit add-on (réponse cellulaire et humorale)
- Vaccins universels (réponse longue durée et élargie)
  - Classiques
  - Vectorisés (MVA)

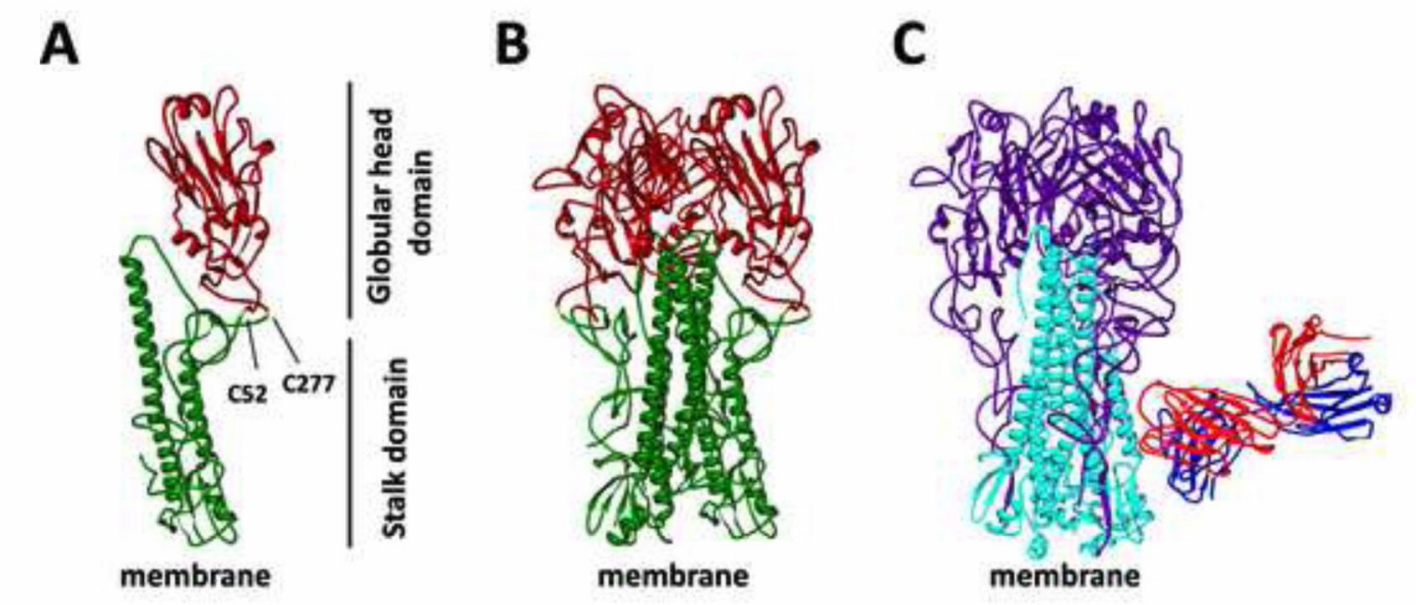
- Vaccin ADN

La vaccination « universelle »





Anti-Ha1
(variable)

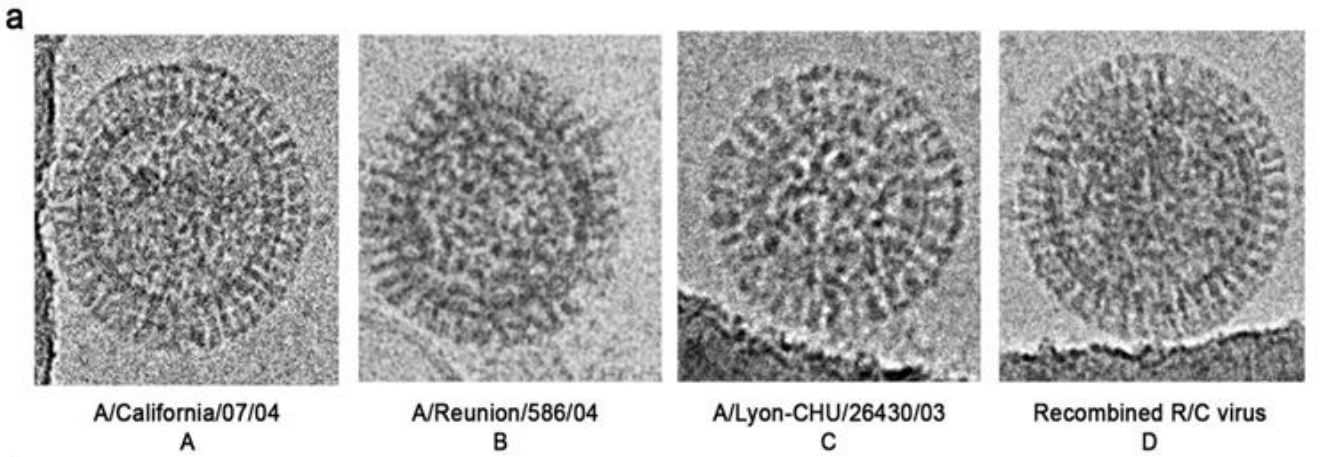


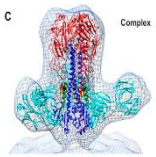
Anti-Ha2
(stable)

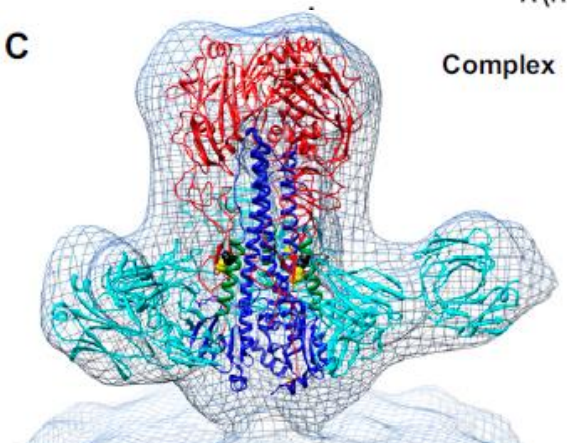
Skehel & Whiley, 2000

Harris et al, PNAS 2013

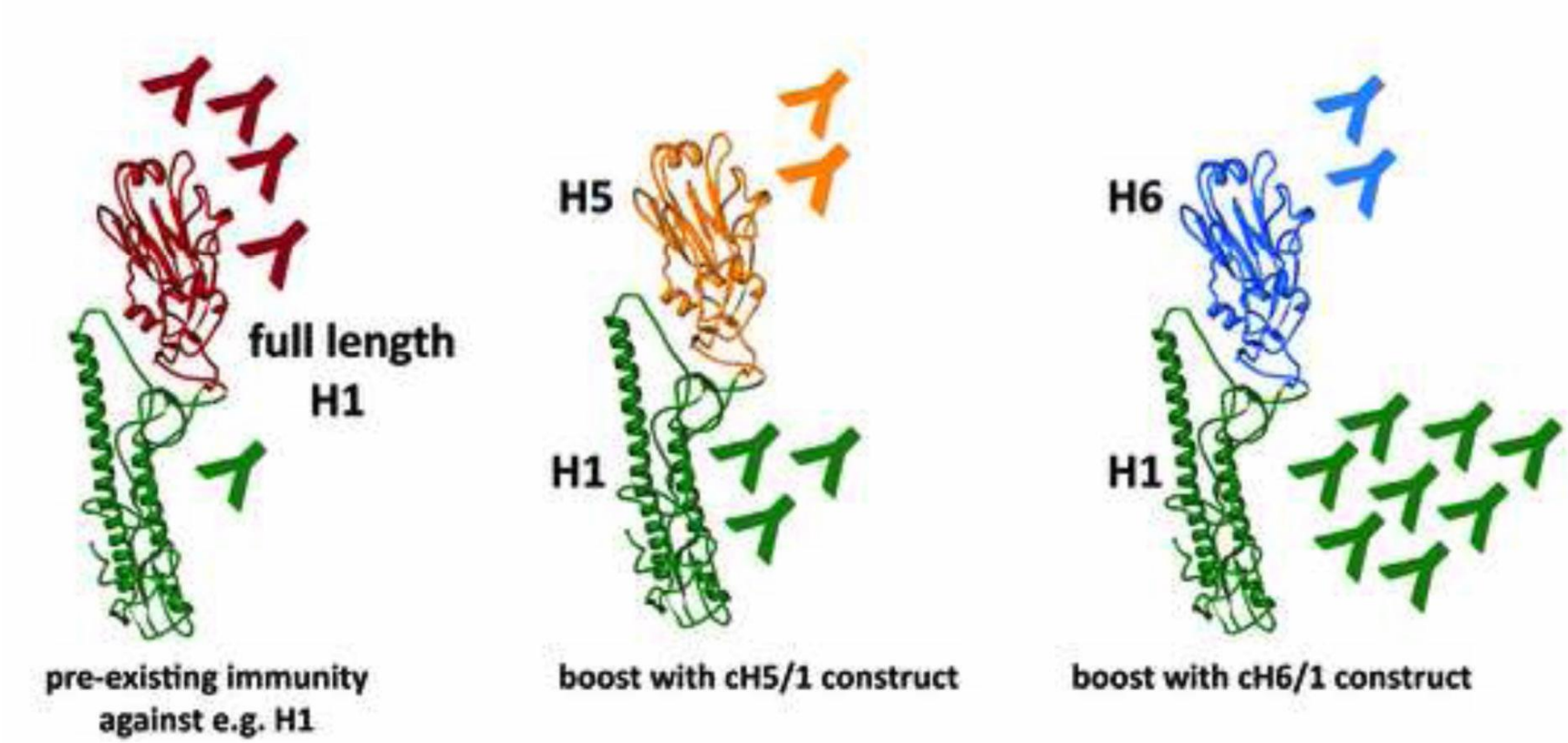
Do anti Ha2 antibodies exist?







Stratégie basée sur la construction de vaccins chimériques portant des épitopes communs H1 – H5



Au total

- La vaccination contre la grippe est indispensable (fardeau +++)
- Cette vaccination est difficile a réaliser
  - Vaccins aux performances inégales
  - Revaccination annuelle
  - Cible ayant une réponse immunitaire défaillante
- Le vaccin quadrivalent était une évolution indispensable
- Tel que préparé
  - Le choix de la composition est OK
  - La technique de production est perfectible
- De nouveaux vaccins sont indispensables
- Une vaccination plus personnalisée devrait être proposée

Acknowledgements

- NIC & Hospital Lyon :
  - Maxime Pichon
  - Rolf Kramer
  - Alexandre Gaymard
  - Antonin Bal
  - Vanessa Escuret
  - Maude Bouscambert
  - Jean Sebastien Casalegno
  - Emilie Frobert
  - Martine Valette
  - Laurence Josset
  - Florence Morfin

- WHOcc
  - -John McCauley
  - - Rod Daniels
  - - Jackie Katz
  - - Takato Odagiri