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Viruses: little genomes, with big impacts

8th Feb 2011
Application of high-throughput genomics to Clostridium difficile transmission and evolution
Speaker: Dr Trevor Lawley

15th Feb 2011
The adventures of Superbug; tracking the global spread of MRSA
Speaker: Dr Matt Holden

1st Mar 2011
Malaria
Speaker: Dr Bronwyn McInnis

8th Mar 2011
More Malaria
Speaker: Dr Julian Rayner

15th Mar 2011
Parasitic Worms
Speaker: Dr Nancy Holroyd

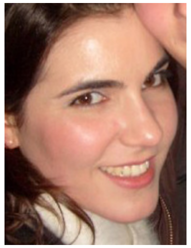
Astrid Gall

Simon Watson

Charlotte Houldcroft

Eve Coulter

Rachael Wash



Sabrina Calabressi

Nikolay Nikolov

Greg Baillie

Stephanie Franz

Matthew Cotton

Anne Palser

D. Farrer Marimon

Rachael Bashford-Rogers

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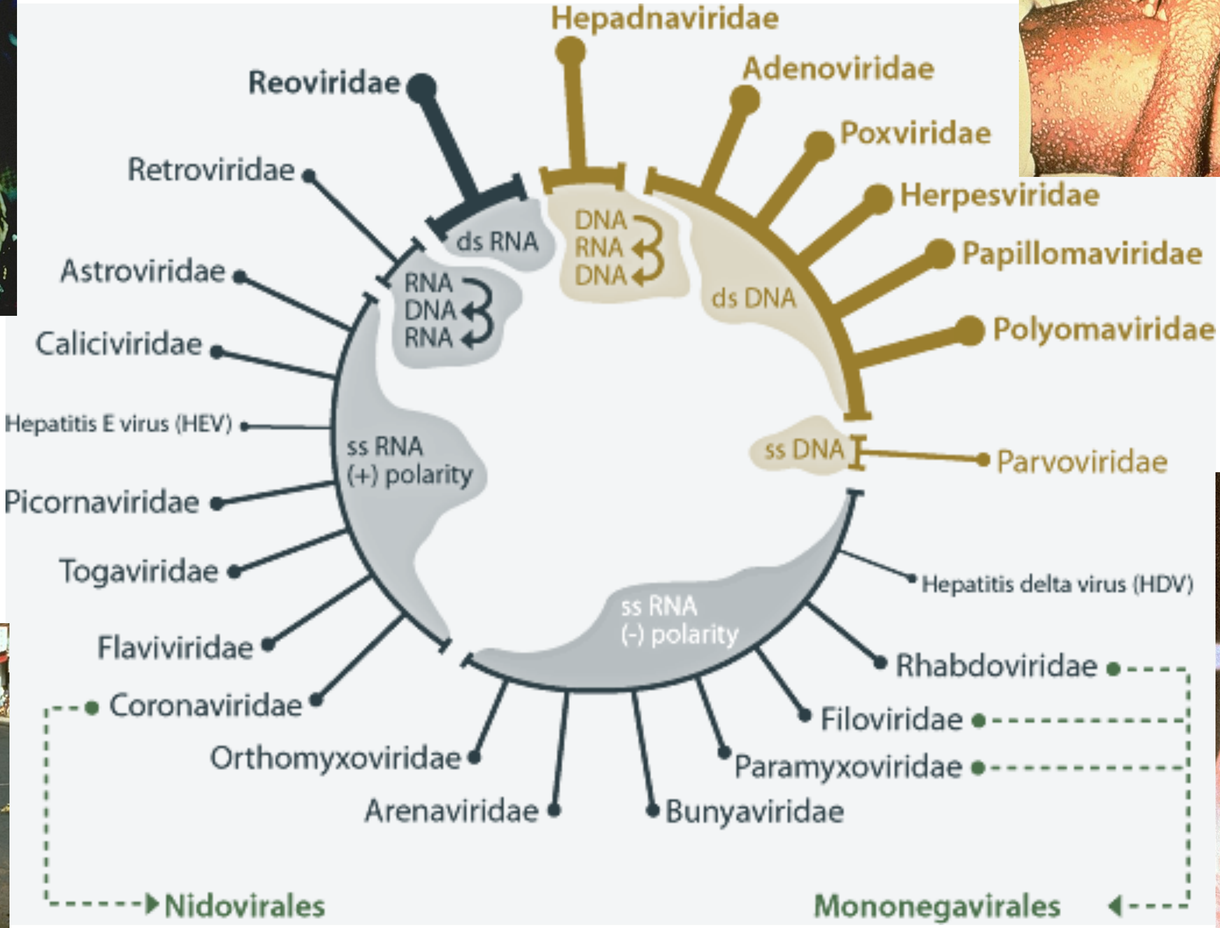
The virus world

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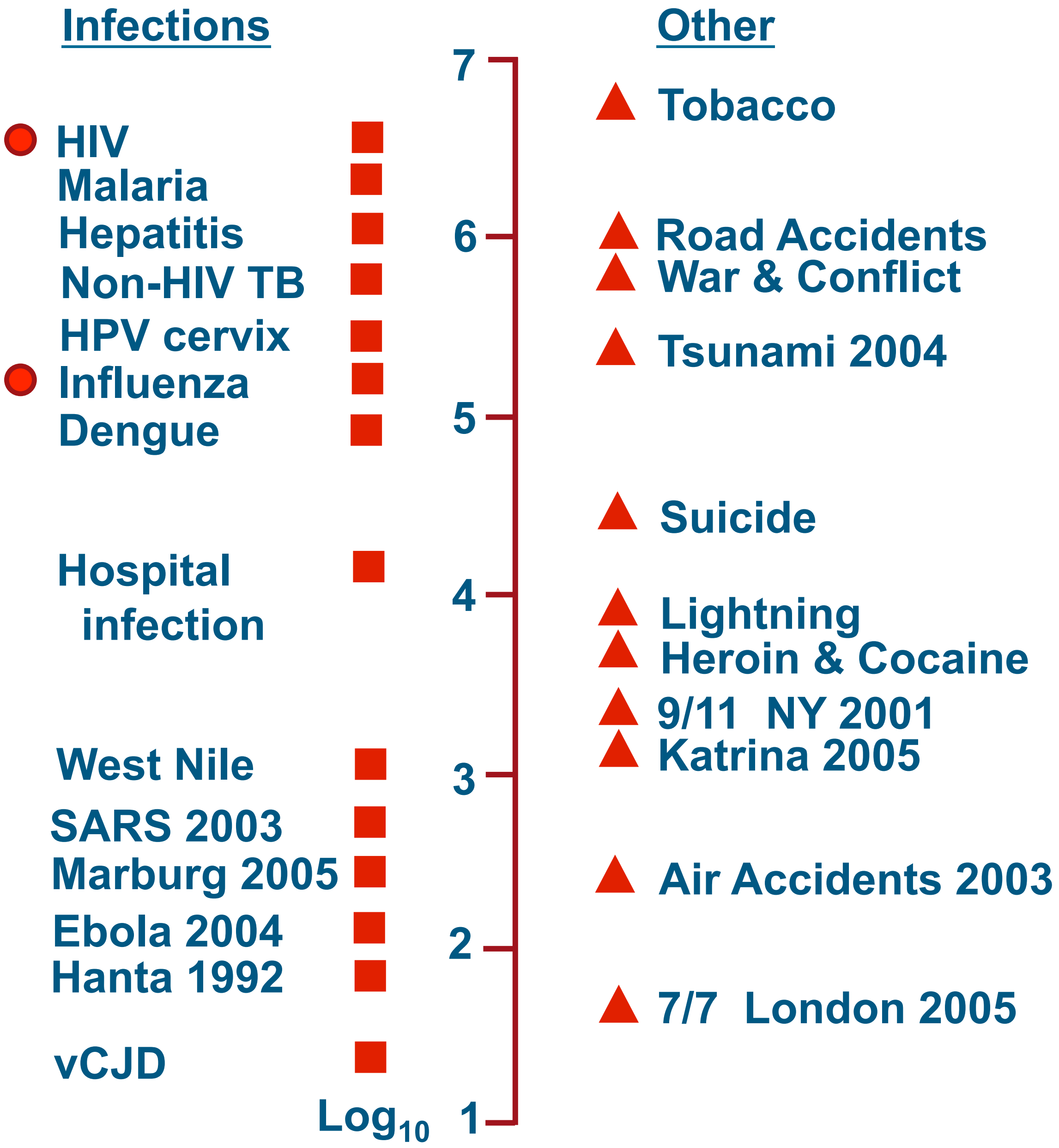
A 'Richter' scale of annual global mortality



Infections

- ● HIV ■
- Malaria ■
- Hepatitis ■
- Non-HIV TB ■
- HPV cervix ■
- ● Influenza ■
- Dengue ■
- Hospital infection ■
- West Nile ■
- SARS 2003 ■
- Marburg 2005 ■
- Ebola 2004 ■
- Hanta 1992 ■
- vCJD ■

Log_{10} 7 6 5 4 3 2 1

Other

- ▲ Tobacco
- ▲ Road Accidents
- ▲ War & Conflict
- ▲ Tsunami 2004
- ▲ Suicide
- ▲ Lightning
- ▲ Heroin & Cocaine
- ▲ 9/11 NY 2001
- ▲ Katrina 2005
- ▲ Air Accidents 2003
- ▲ 7/7 London 2005

Vaccines - weapons of mass protection - led to the eradication or reduction of:

Smallpox
Yellow Fever
Polio
MMR

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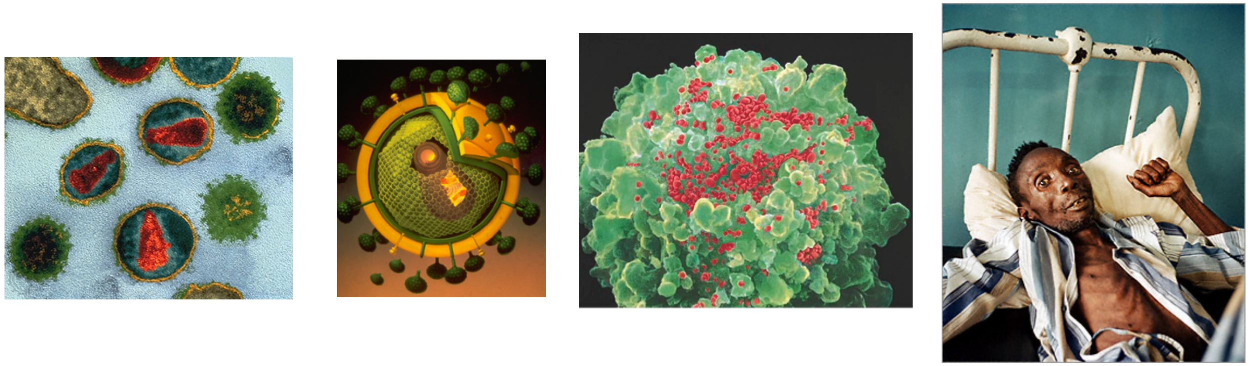
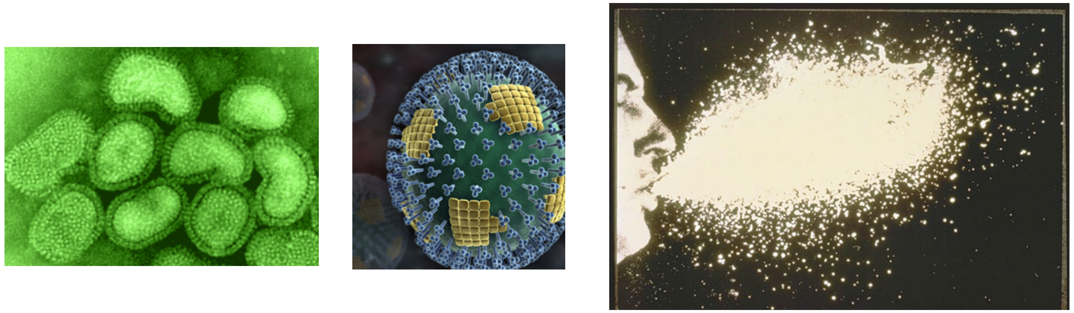
Kindly provided by Robin Weiss

Our villains

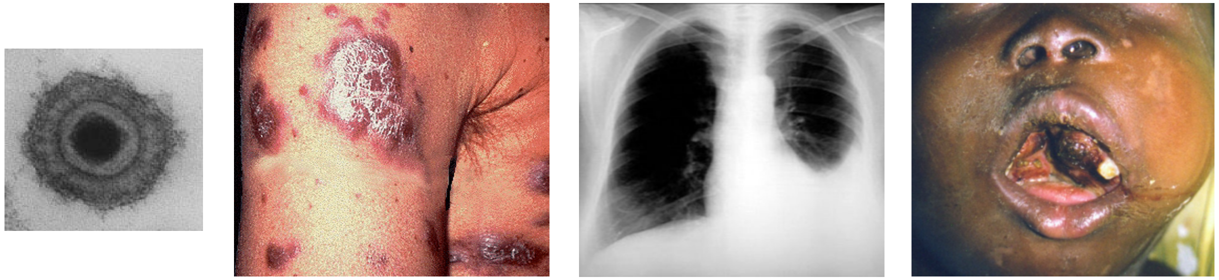
Human Immunodeficiency Virus (HIV)



Influenza virus



EBV & KSHV



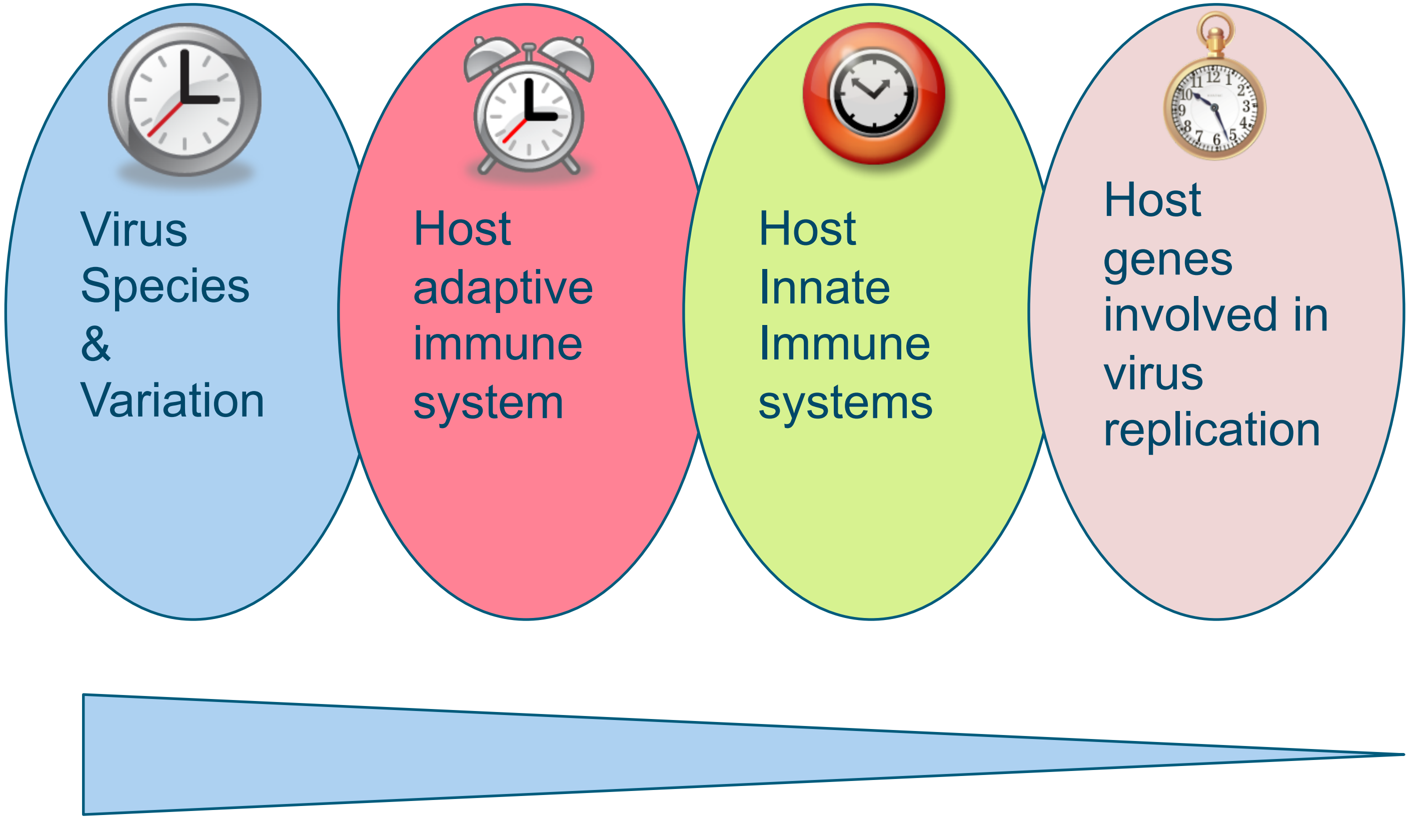
More than a human

The Human Metagenome

- ~ 2 x 10^{13} human genome copies
- ~ 10^{14} bacteria of > 1000 species
- ~ 10^{15} viral copies of DNA + RNA

1. As an ecosystem we are <50% human
2. Most of our microbes are commensal
3. A few are pathogens
4. Some are only pathogenic in susceptible individuals

Infection, genetics and evolution



Virus Species & Variation

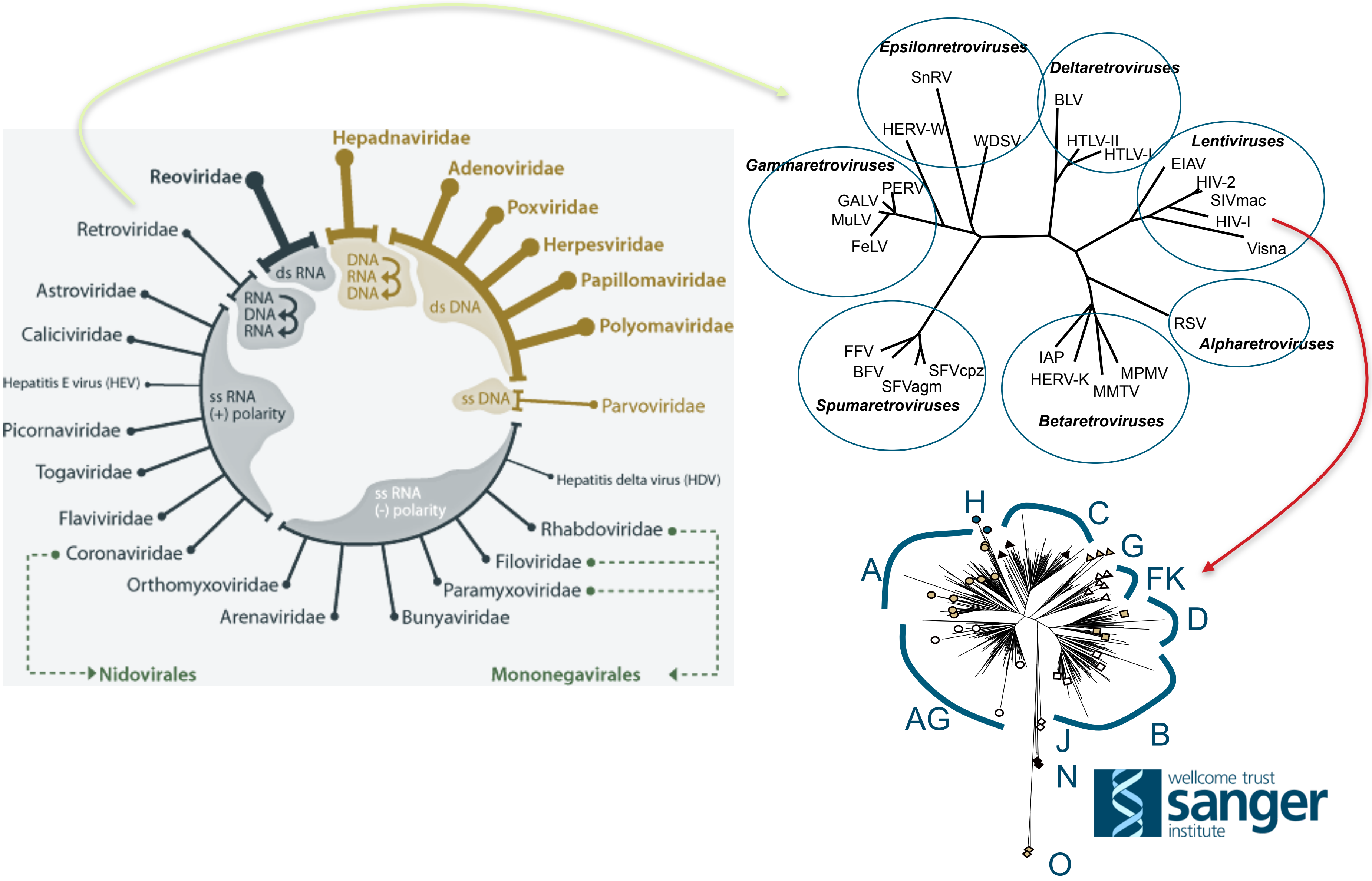
Host adaptive immune system

Host Innate Immune systems

Host genes involved in virus replication

Rate of evolution

Where does this end!



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Population biology

The consensus sequence

The minority species

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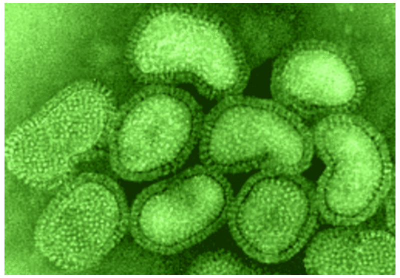
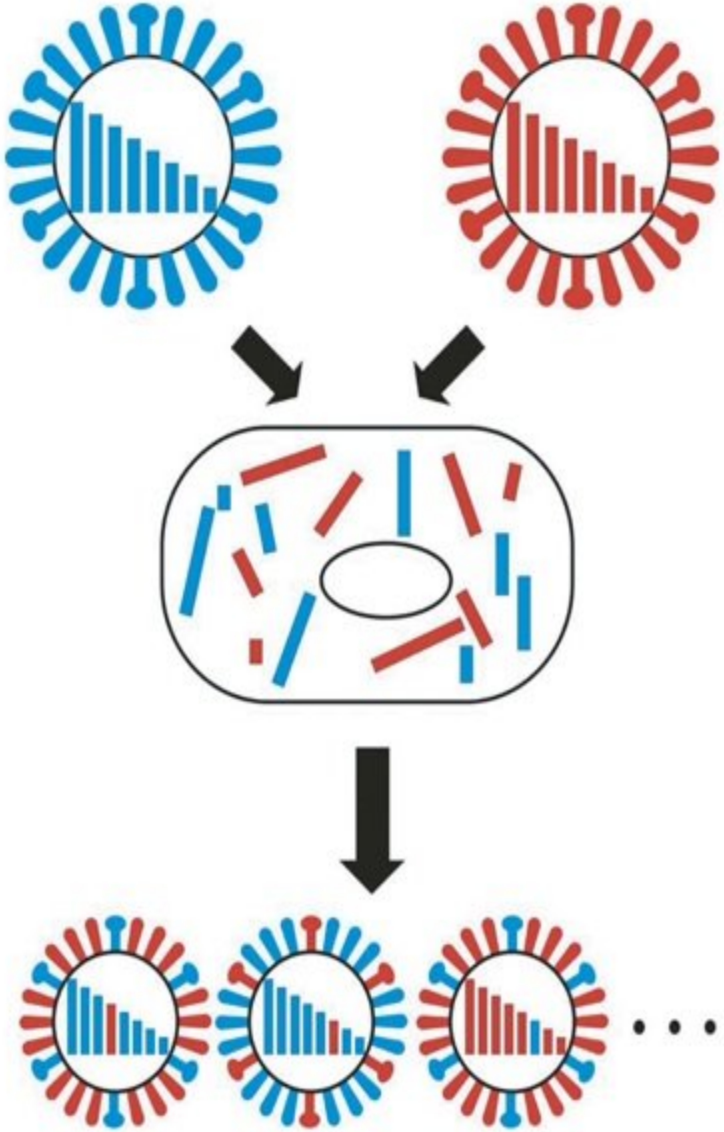
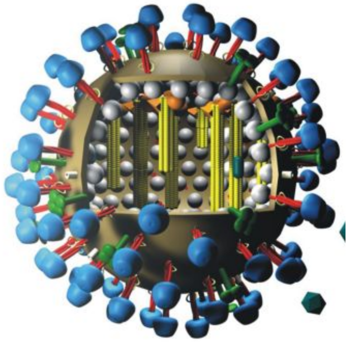
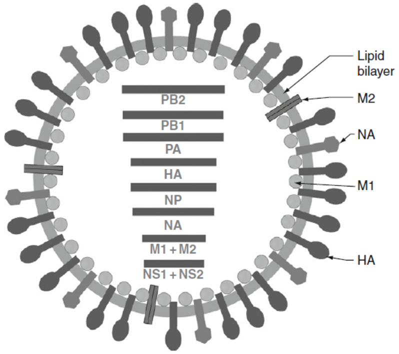
Influenza – swapping parts of your genome (Reassortment)

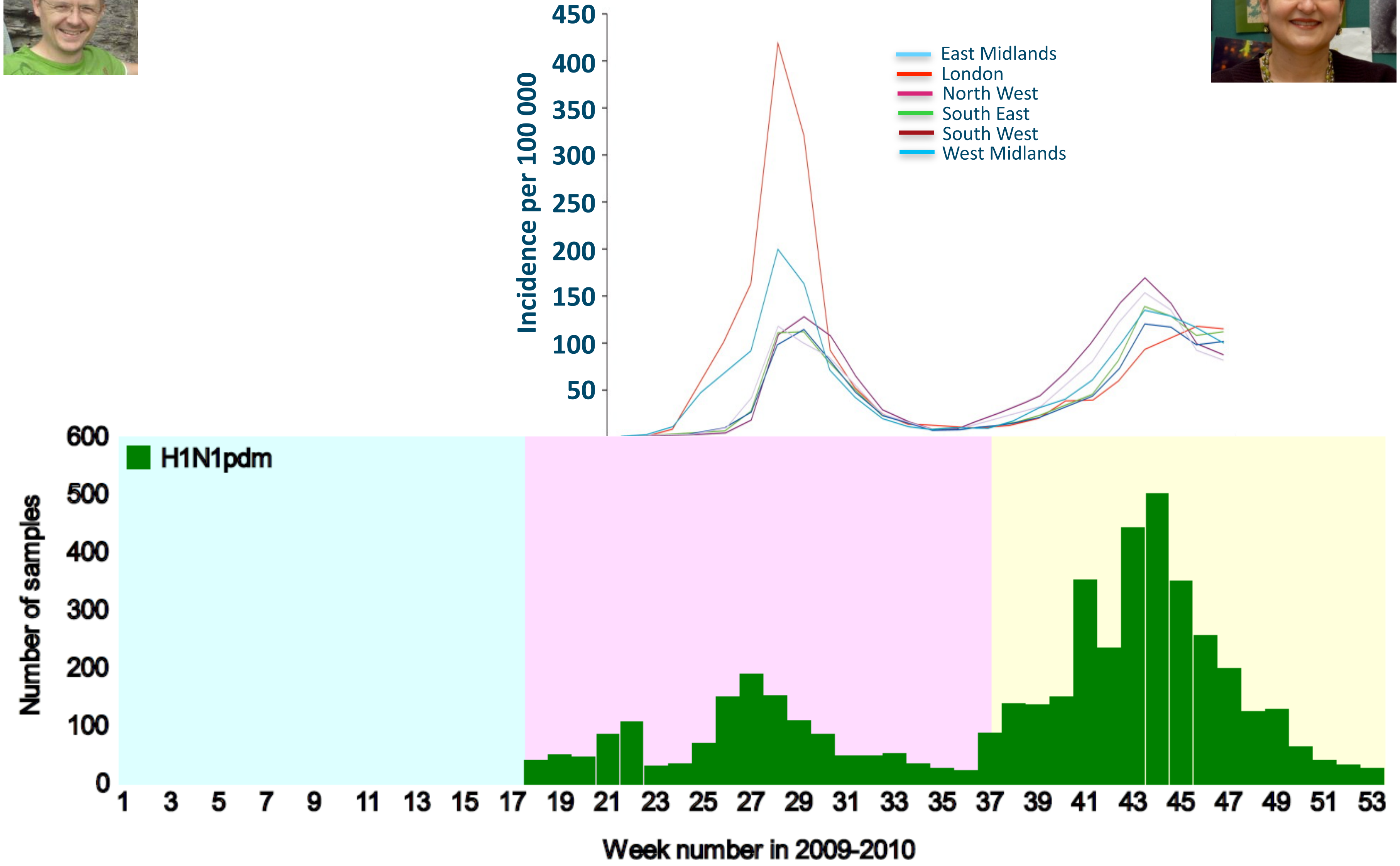




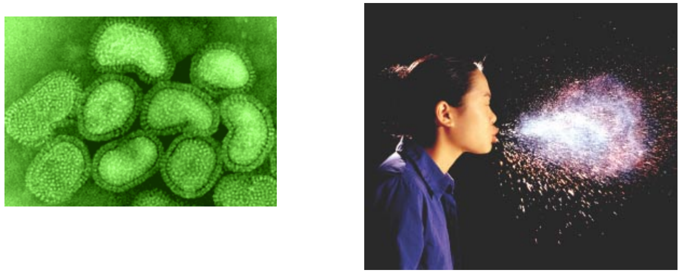




A pandemic finally arrives



Influenza

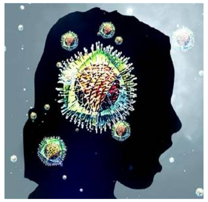


Molecular epidemiology

Pathogen Biology

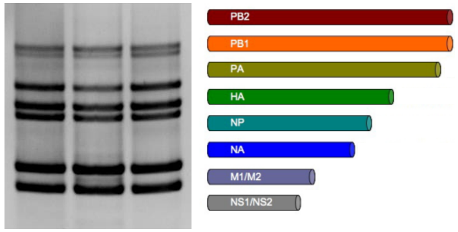
ACCGTAATGC

Virus genome sequencing 2011

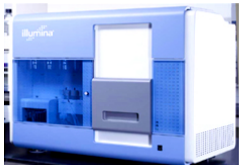


1. Samples

2. RNA



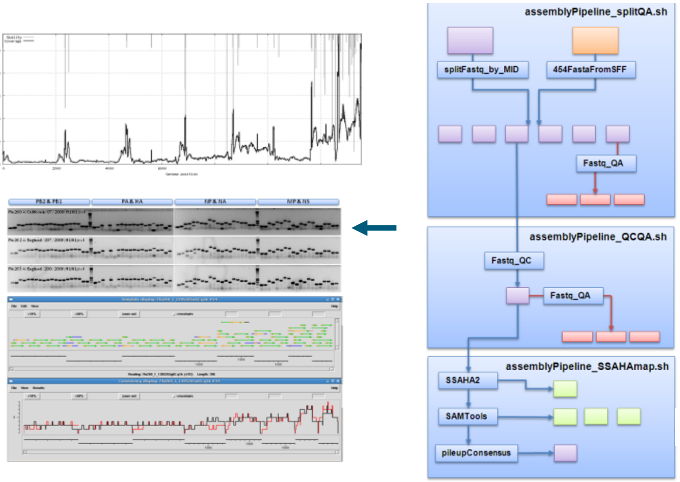
3. One Tube Genome Amplification



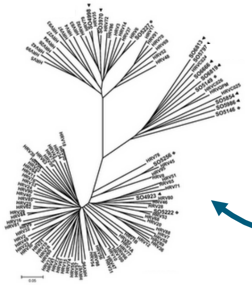
4. Illumina

4. ABI3730

4. 454



5. Assembly + QA/QC



6. Analysis

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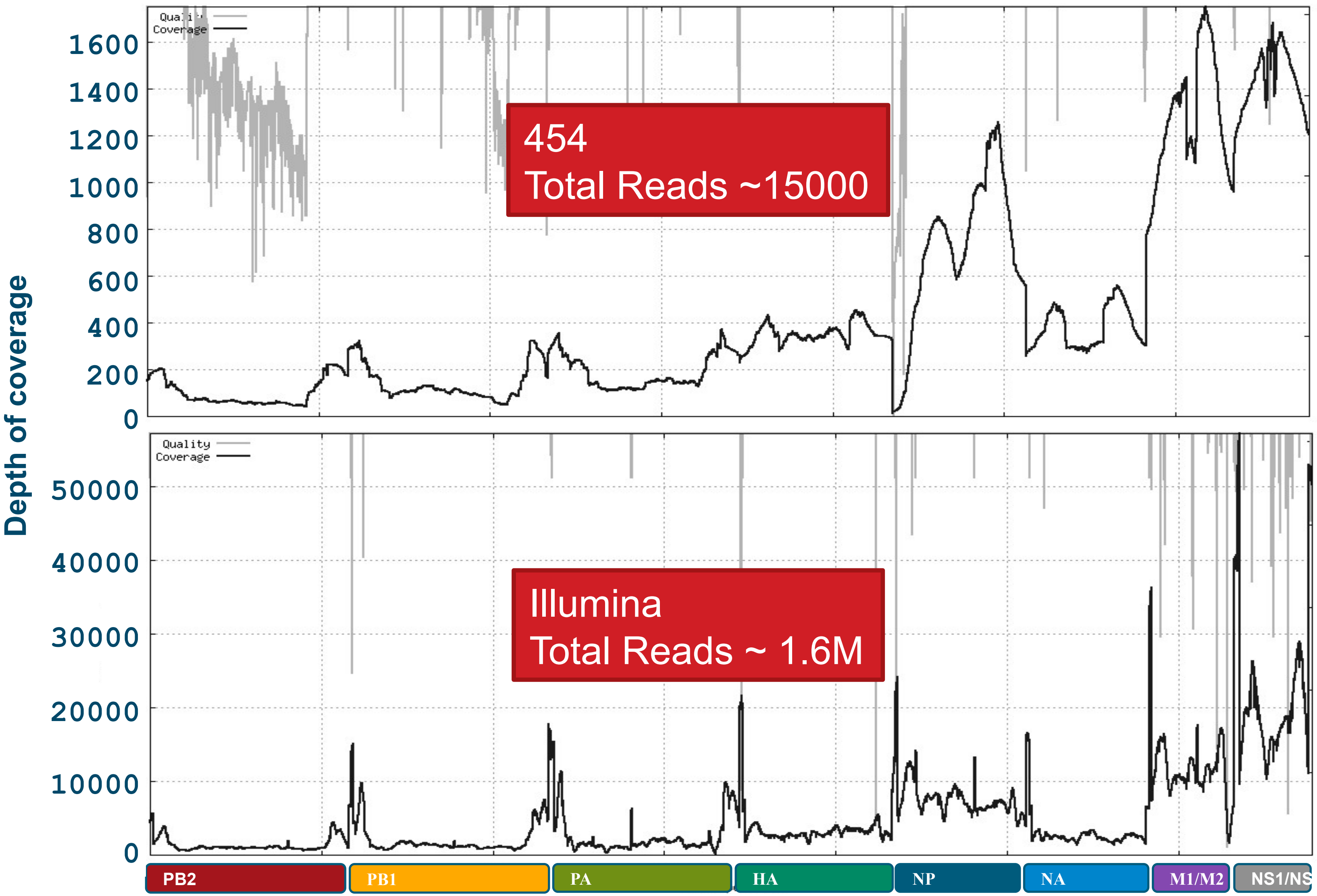
2nd Generation Influenza sequencing



454
Total Reads ~15000

Illumina
Total Reads ~ 1.6M

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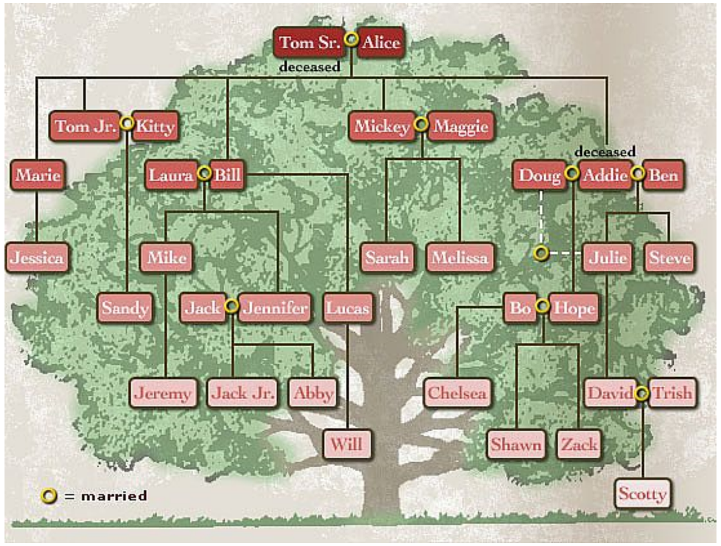
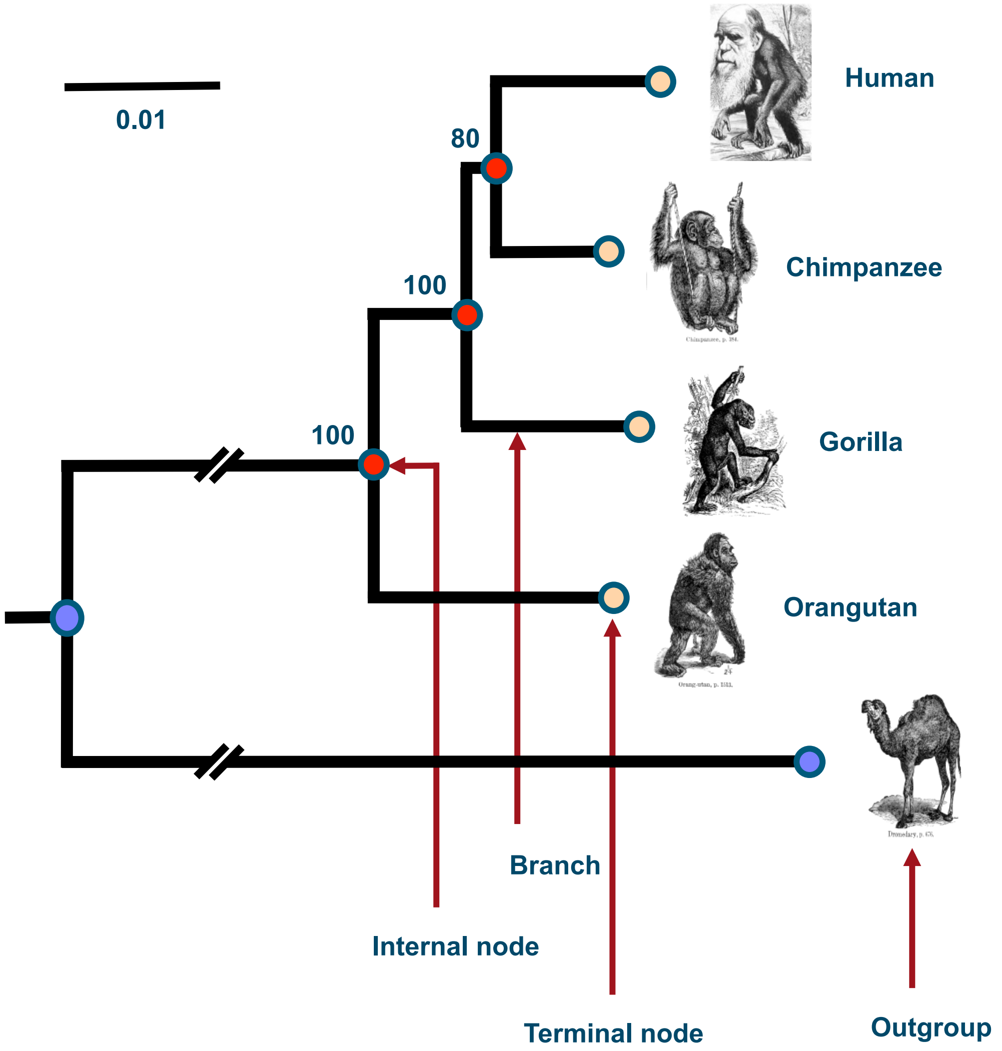
Family trees, heredity and Phylogenetics





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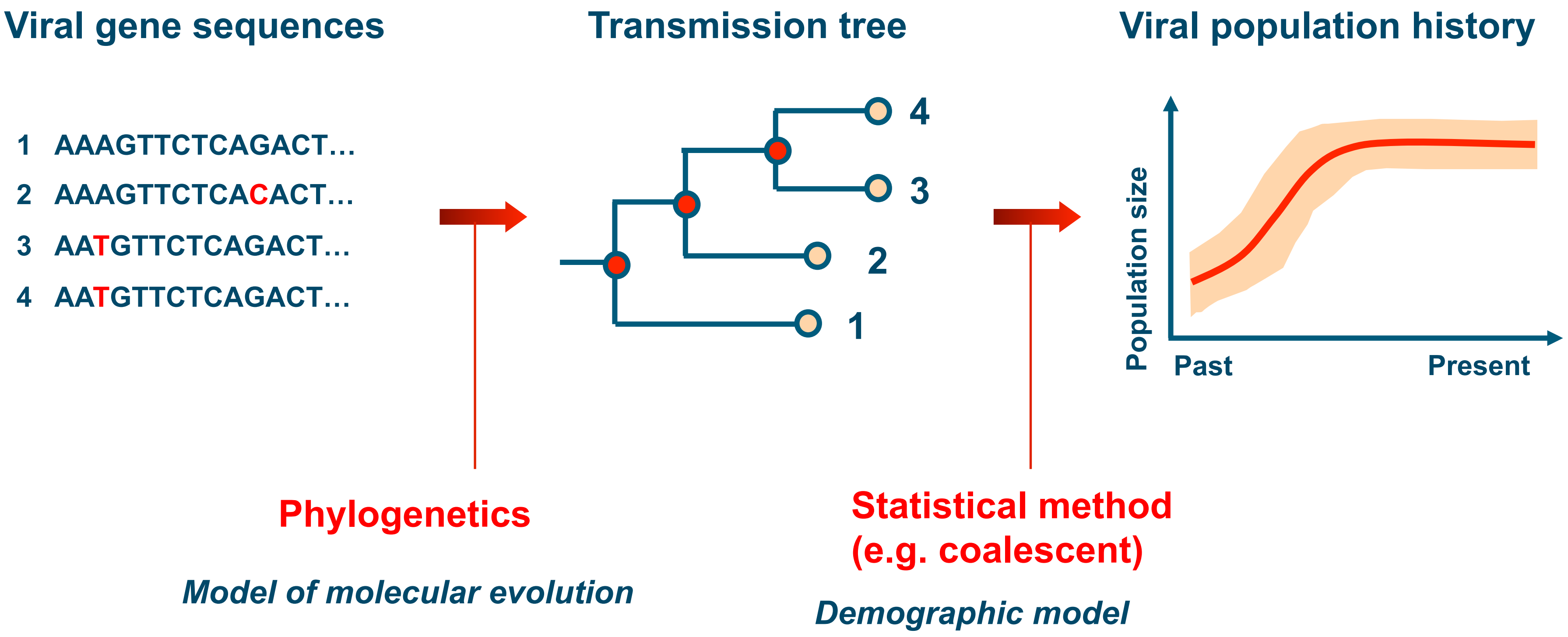
Kindly provided by Stephane Hue

Phylogenetics & Statistics

BEAST: Bayesian evolutionary analysis by sampling trees



Viral gene sequences

1 AAAGTTCTCAGACT…
2 AAAGTTCTCACACT…
3 AATGTTCTCAGACT…
4 AATGTTCTCAGACT…

Transmission tree

Viral population history

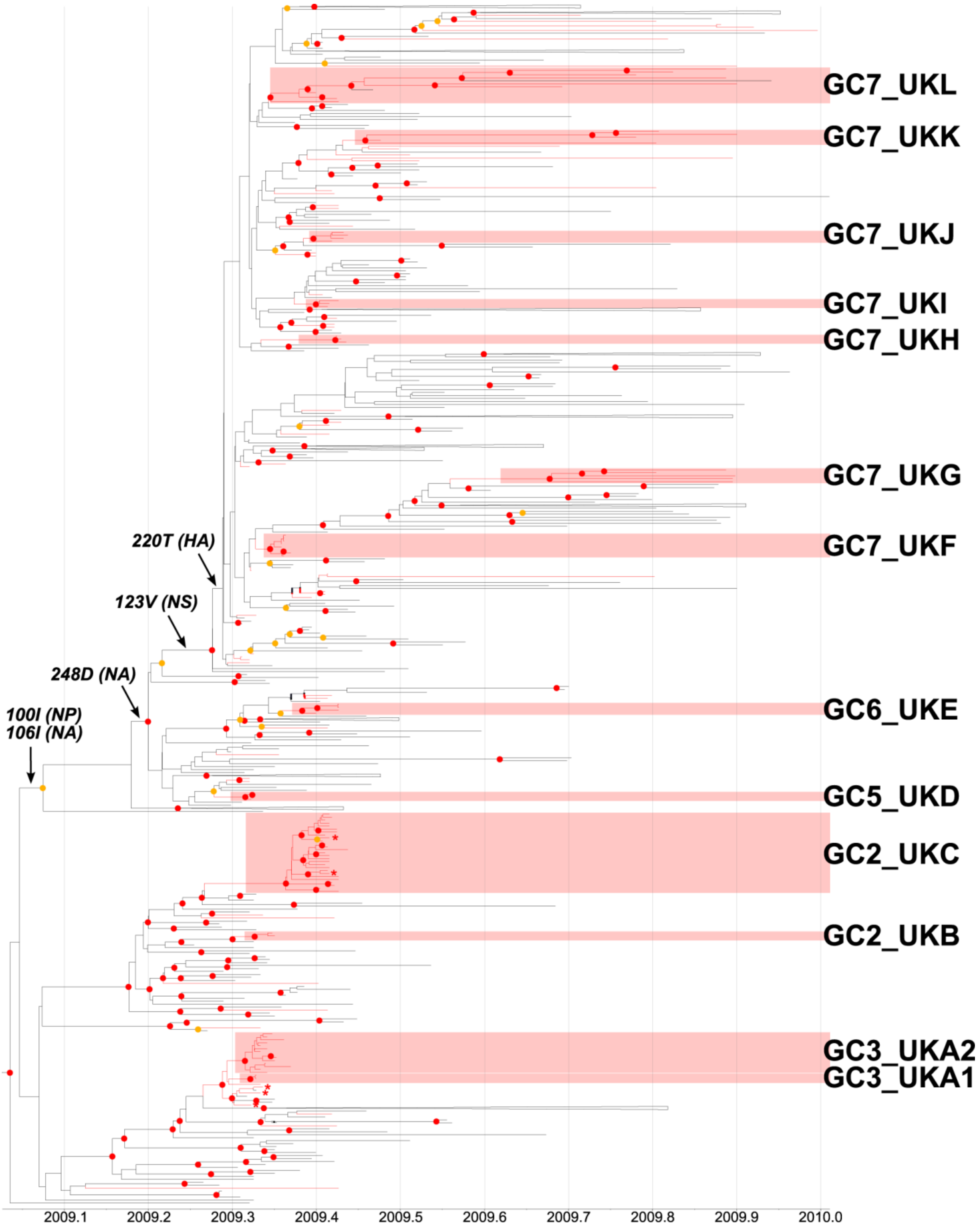
Phylogenetics

Model of molecular evolution

Statistical method (e.g. coalescent)

Demographic model

Thanks to Stephane Hue



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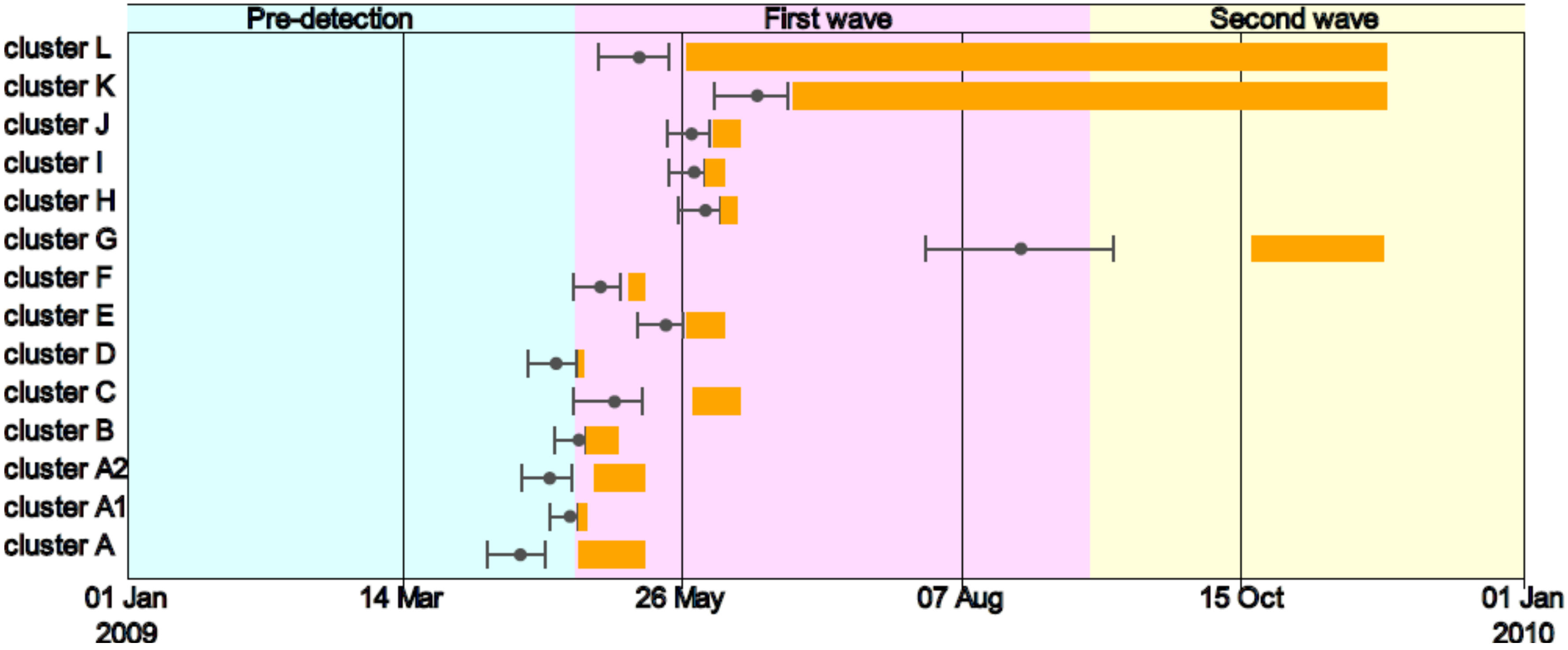
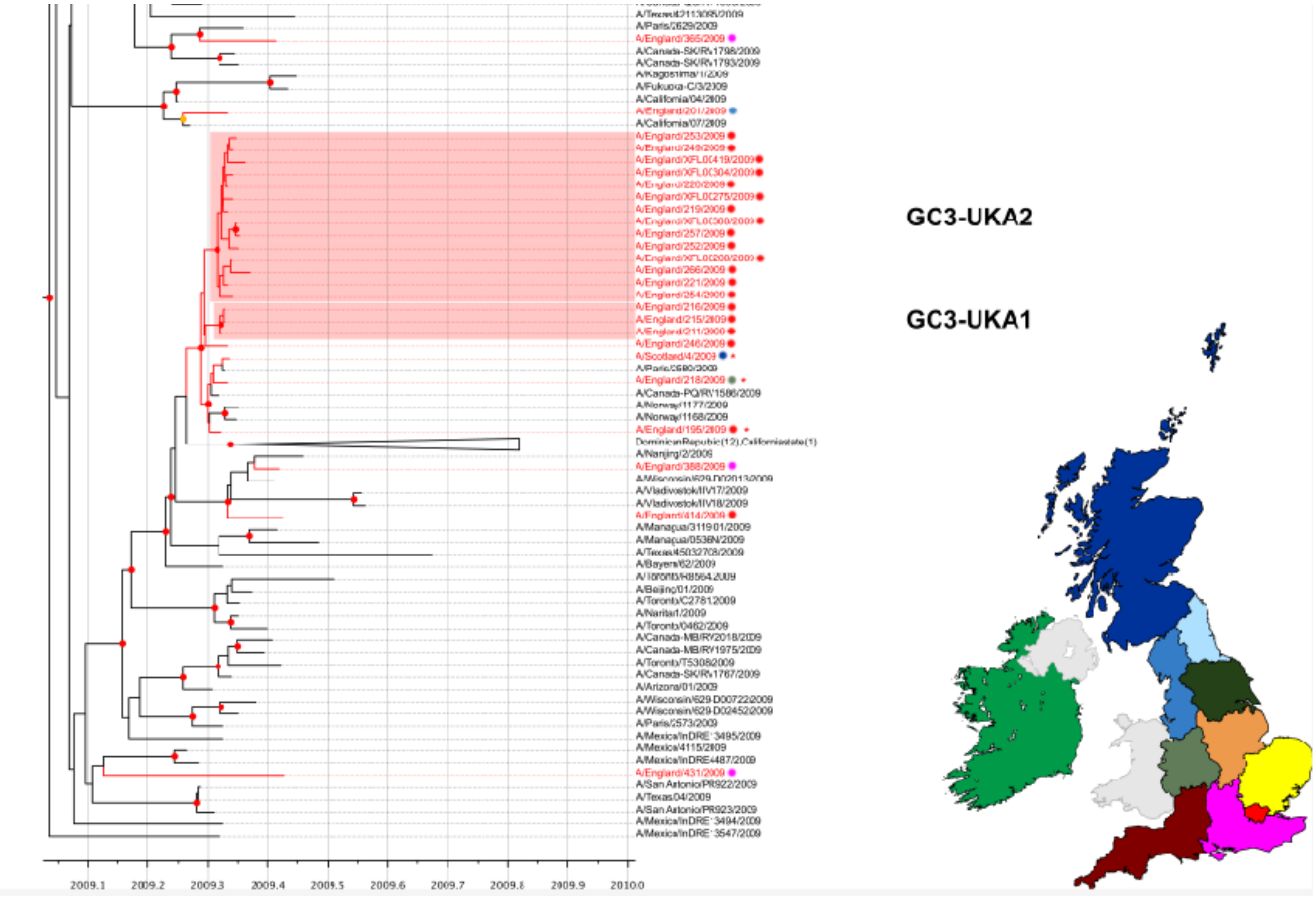
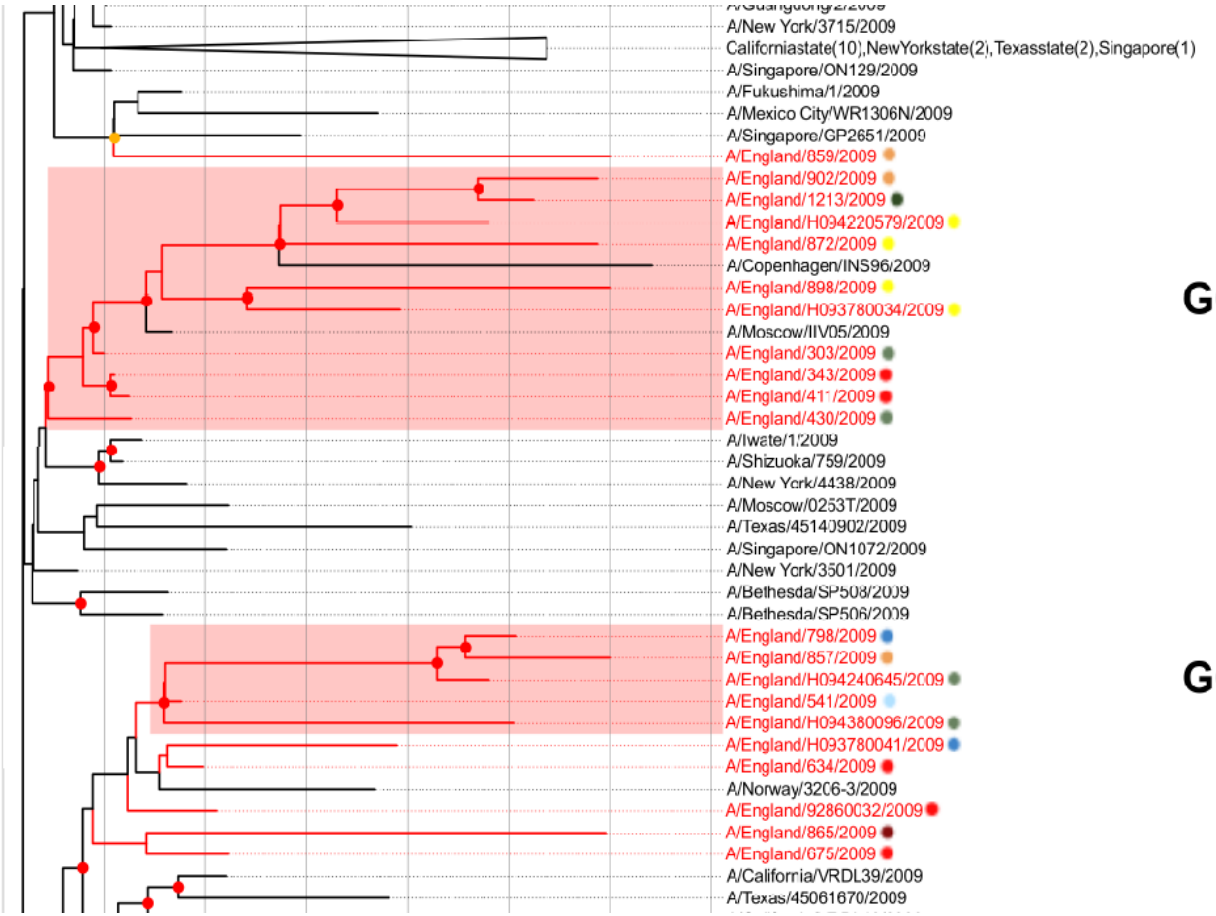

Pre-detection
First wave
Second wave
cluster L
cluster K
cluster J
cluster I
cluster H
cluster G
cluster F
cluster E
cluster D
cluster C
cluster B
cluster A2
cluster A1
cluster A
01 Jan 2009
14 Mar
26 May
07 Aug
15 Oct
01 Jan 2010

Phylogeography

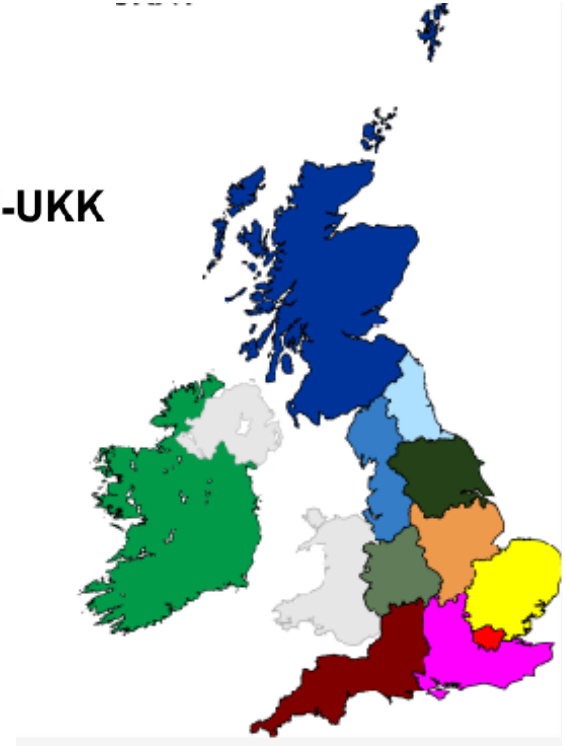


Phylogeography

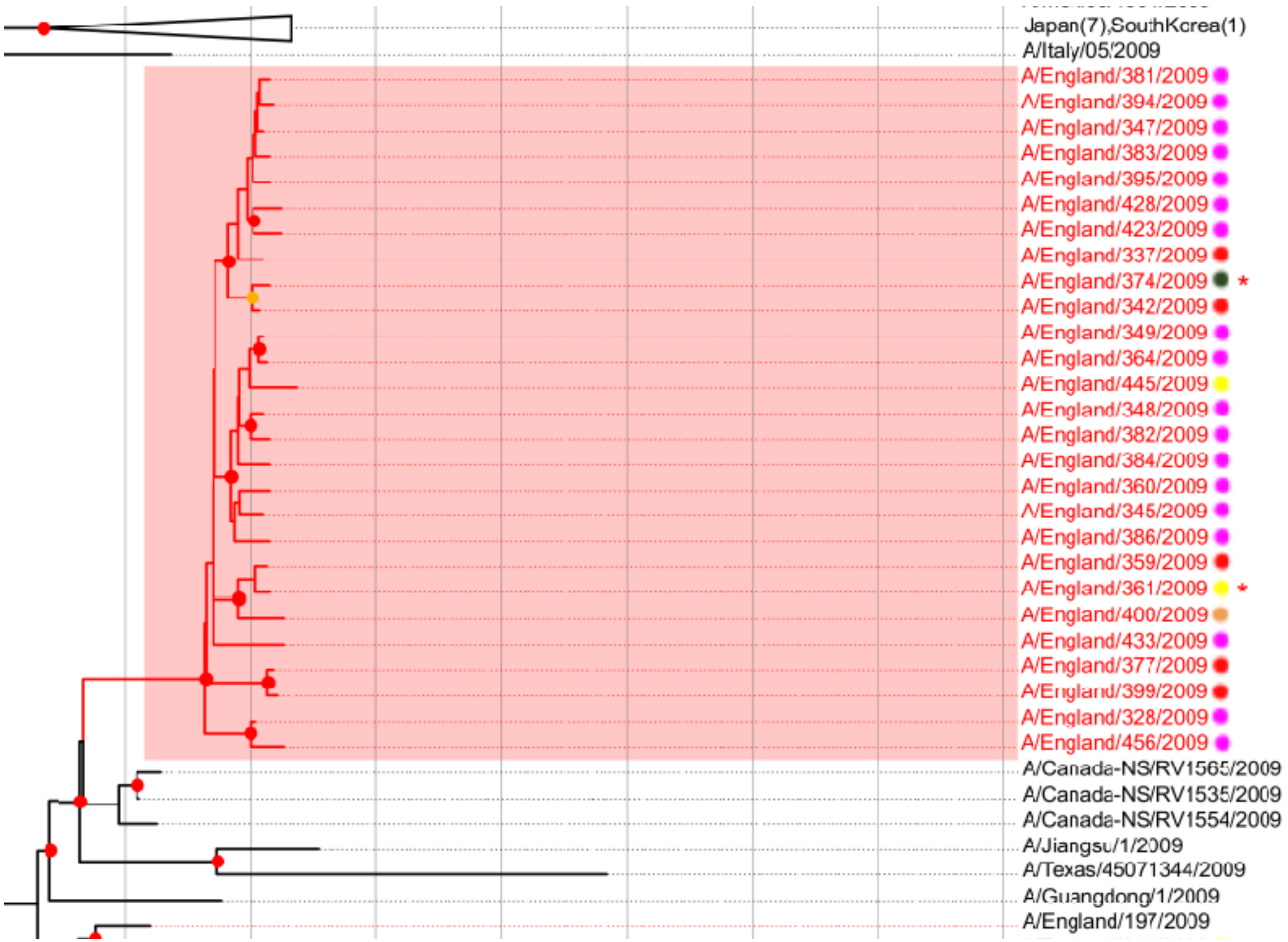


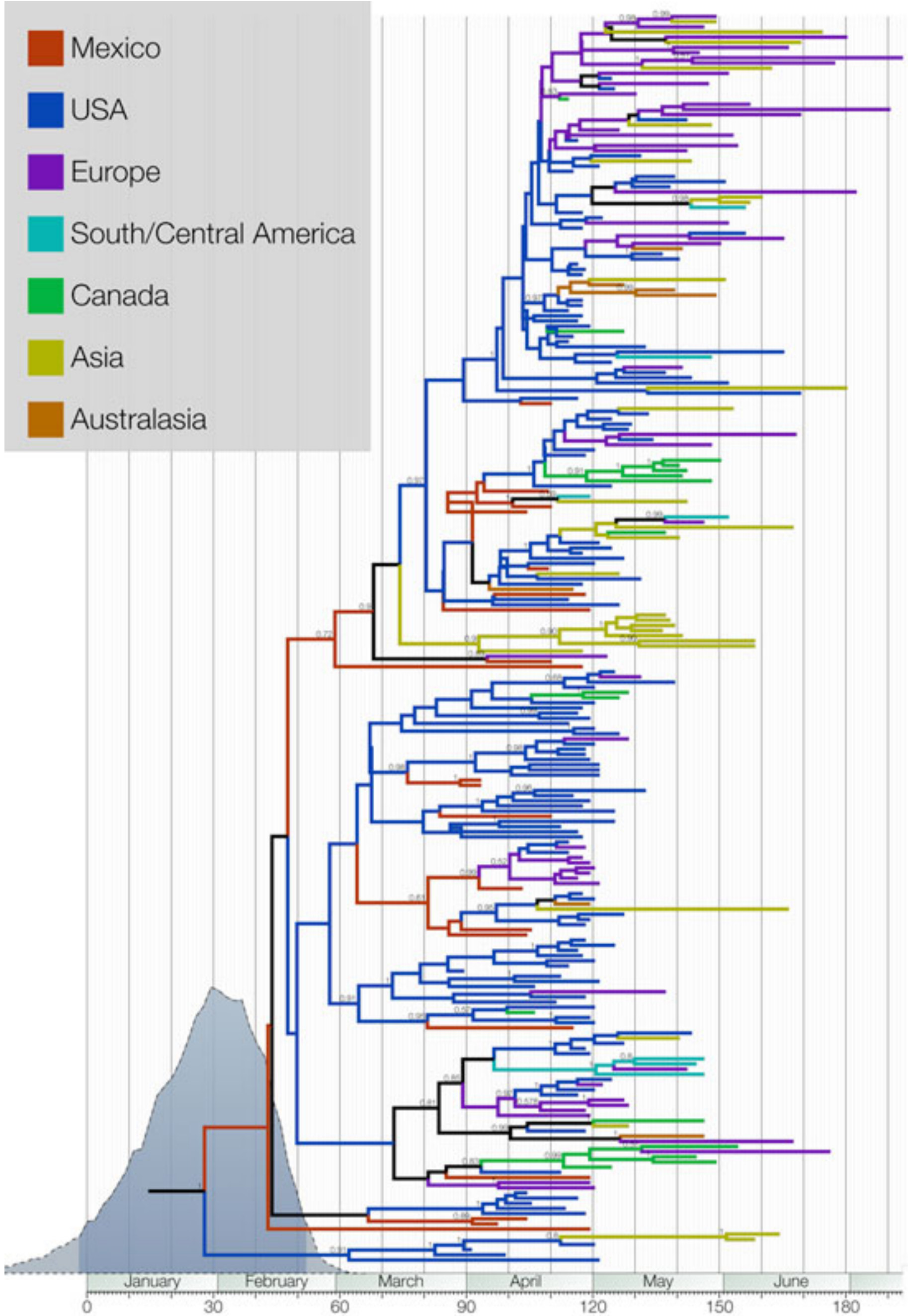
GC7-UKL

GC7-UKK



Phylogeography





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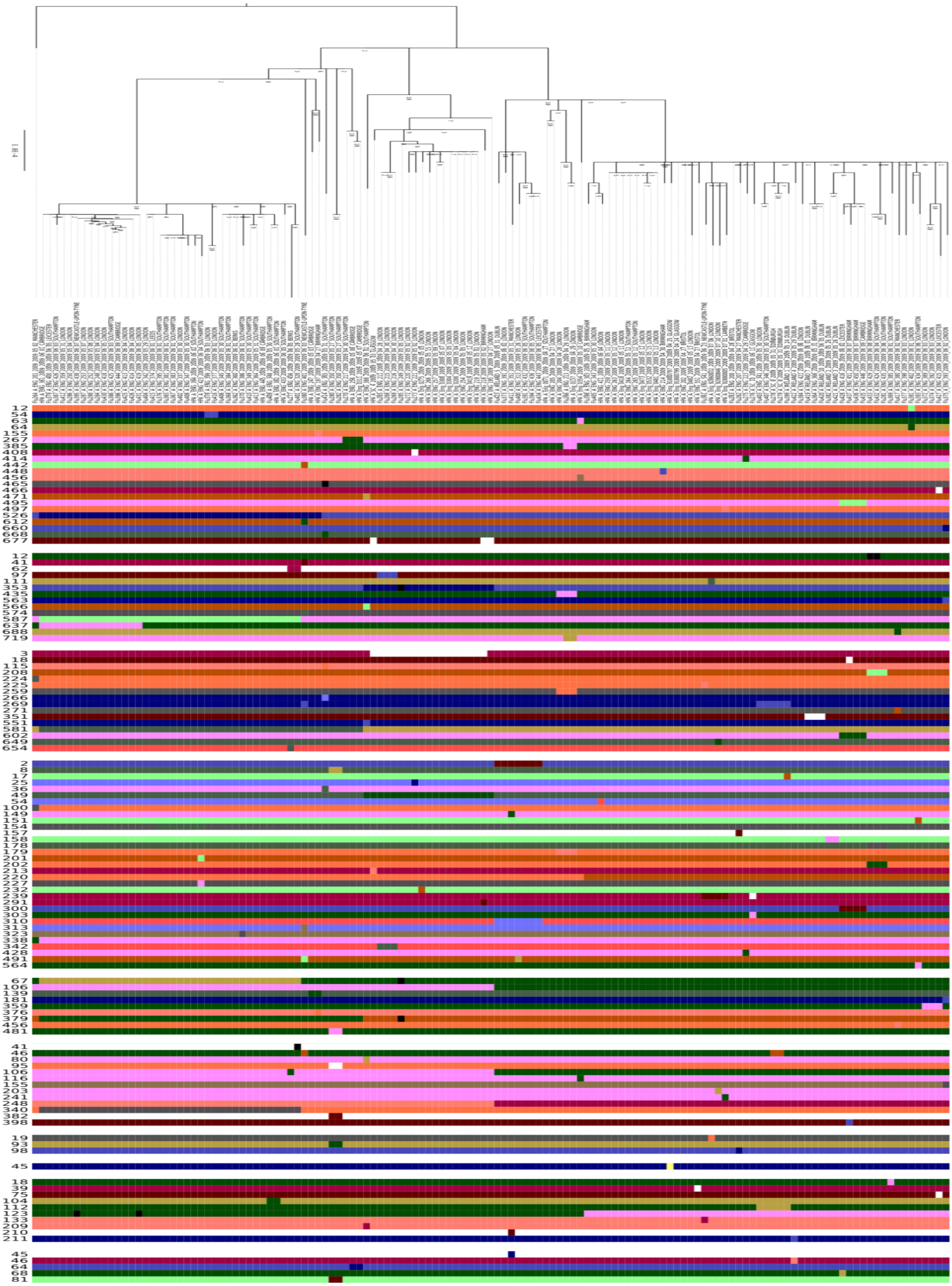
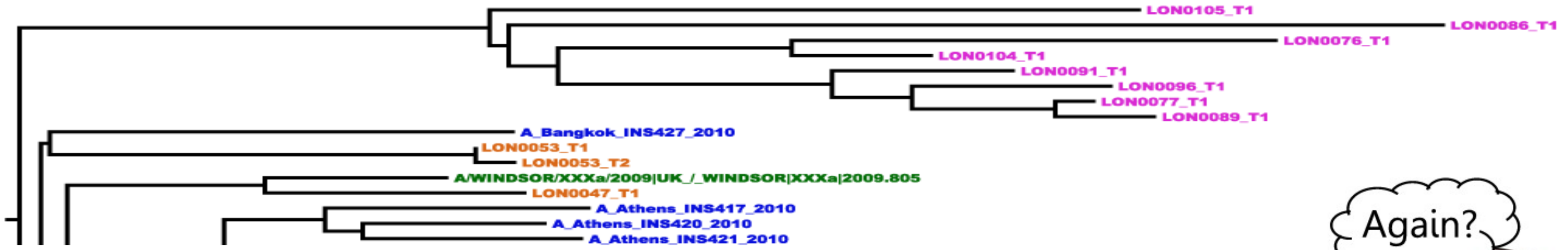
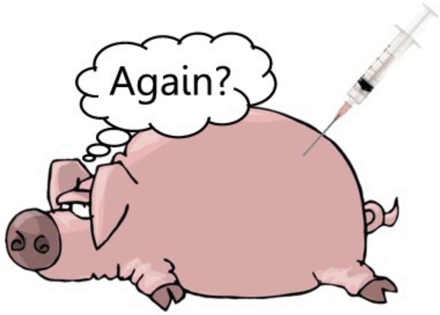
Andrew Rambaut[*] and Edward Holmes. PLoS Curr Influenza. 2009 August 18: RRN1003.


3.0E-4
PB2
12 54 63 64 155 267 385 408 414 442 448 456 465 466 471 495 497 526 612 660 668 677
PB1
12 41 62 97 111 353 435 563 566 574 587 637 688 719
PA
3 18 115 208 224 225 259 266 269 271 351 551 581 602 649 654
HA
2 8 17 25 36 49 54 100 149 151 154 157 158 178 179 201 202 213 220 227 232 239 291 300 303 310 313 323 338 342 428 491 564
NP
67 106 139 181 359 376 379 456 481
NA
41 46 80 95 106 116 155 203 241 248 340 382 398
M1
19 93 98
M2
45
NS1
18 39 75 104 112 123 133 209 210 211
NS2
45 46 64 68 81





Tuesday, 1 February 2011

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Flu: 300 in intensive care fight

Outbreak fear ... flu virus

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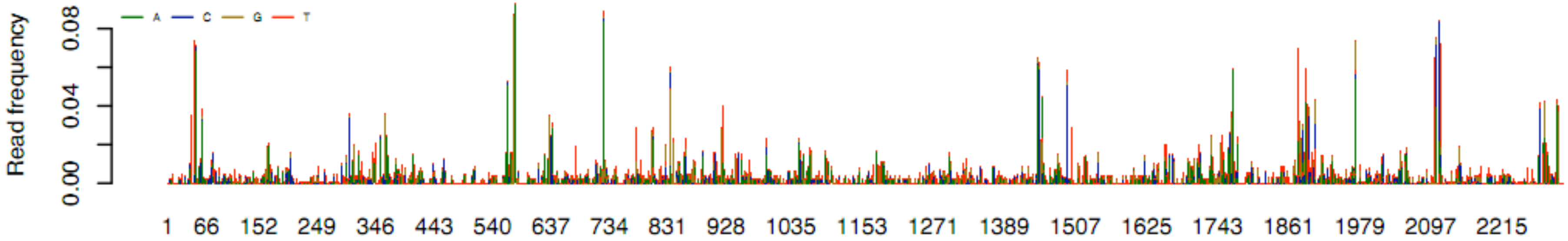
Population biology

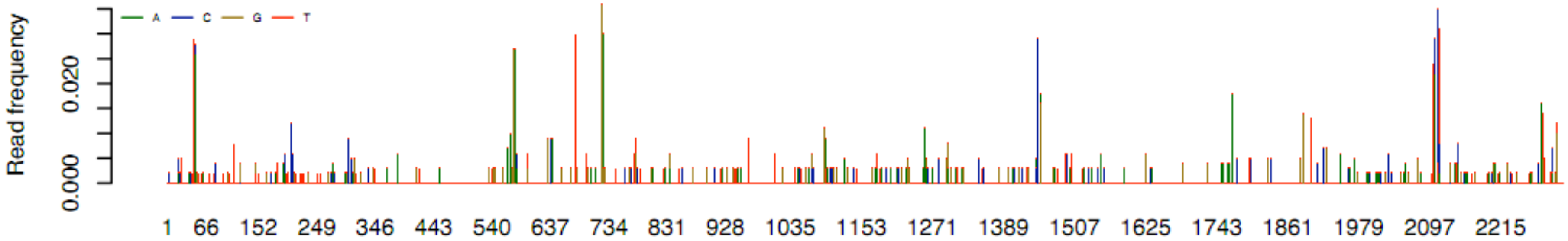
The consensus sequence

The minority species

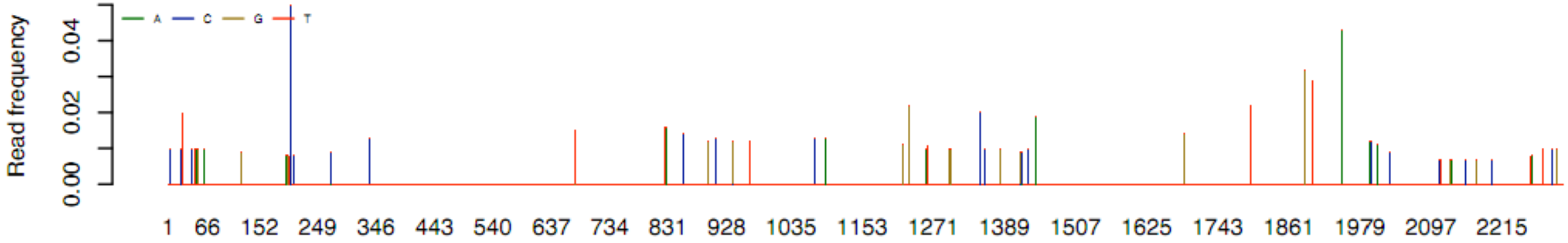
Full genome minority species



(a) PRQC0



(b) PRQC25



(c) PRQC40

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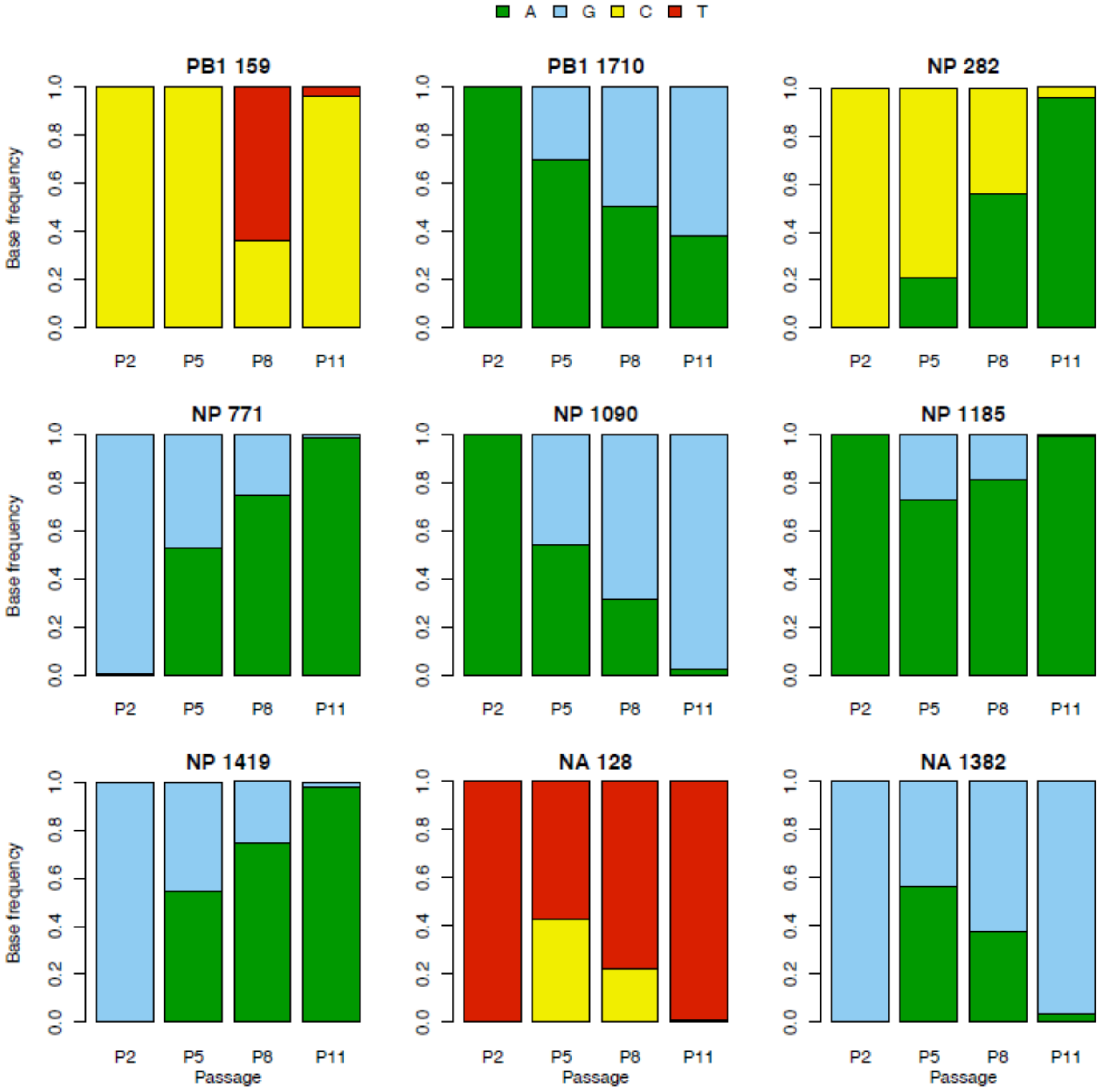
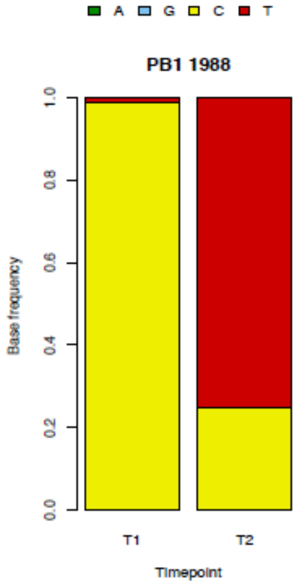
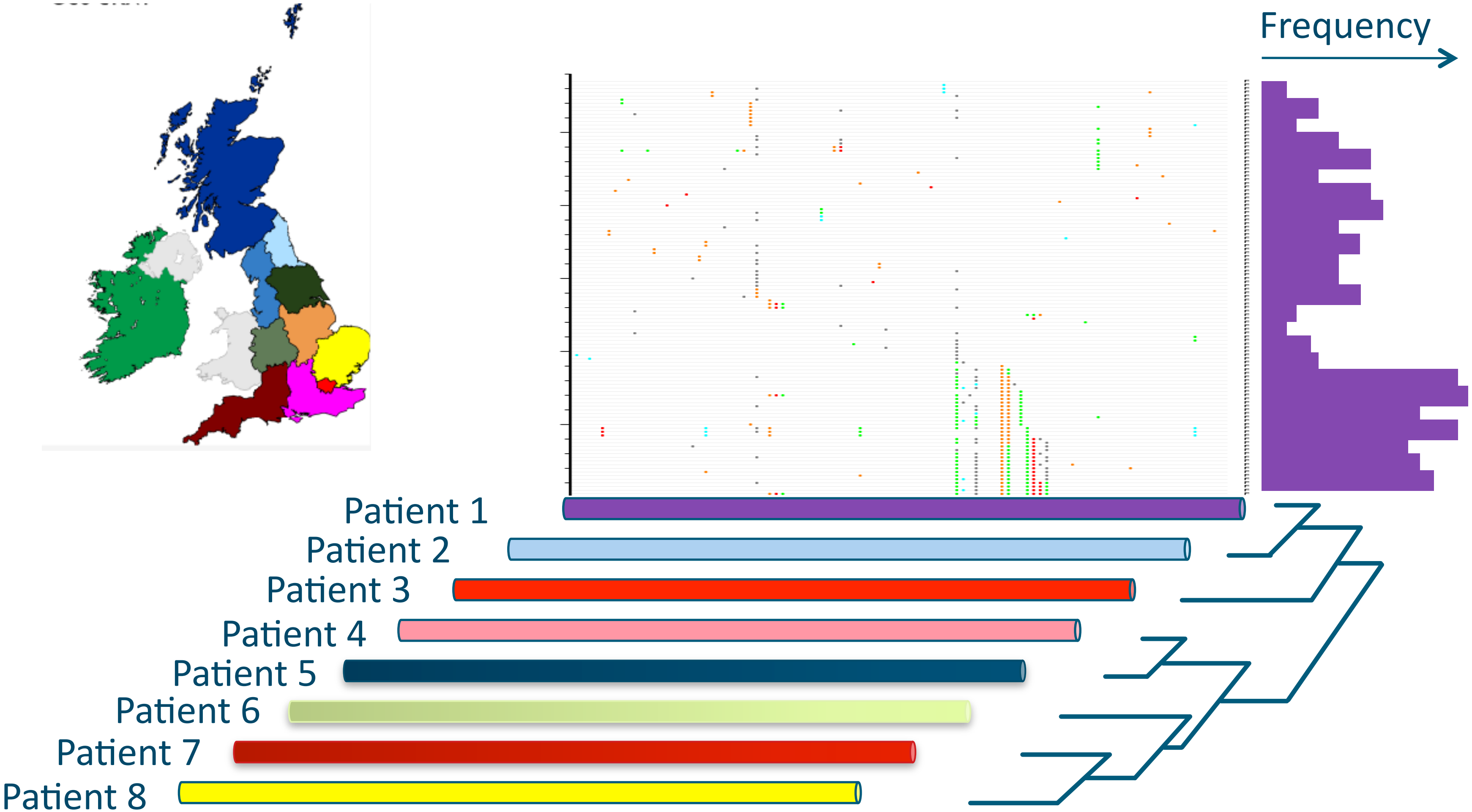
In tissue culture



In humans



Consensus and population structure



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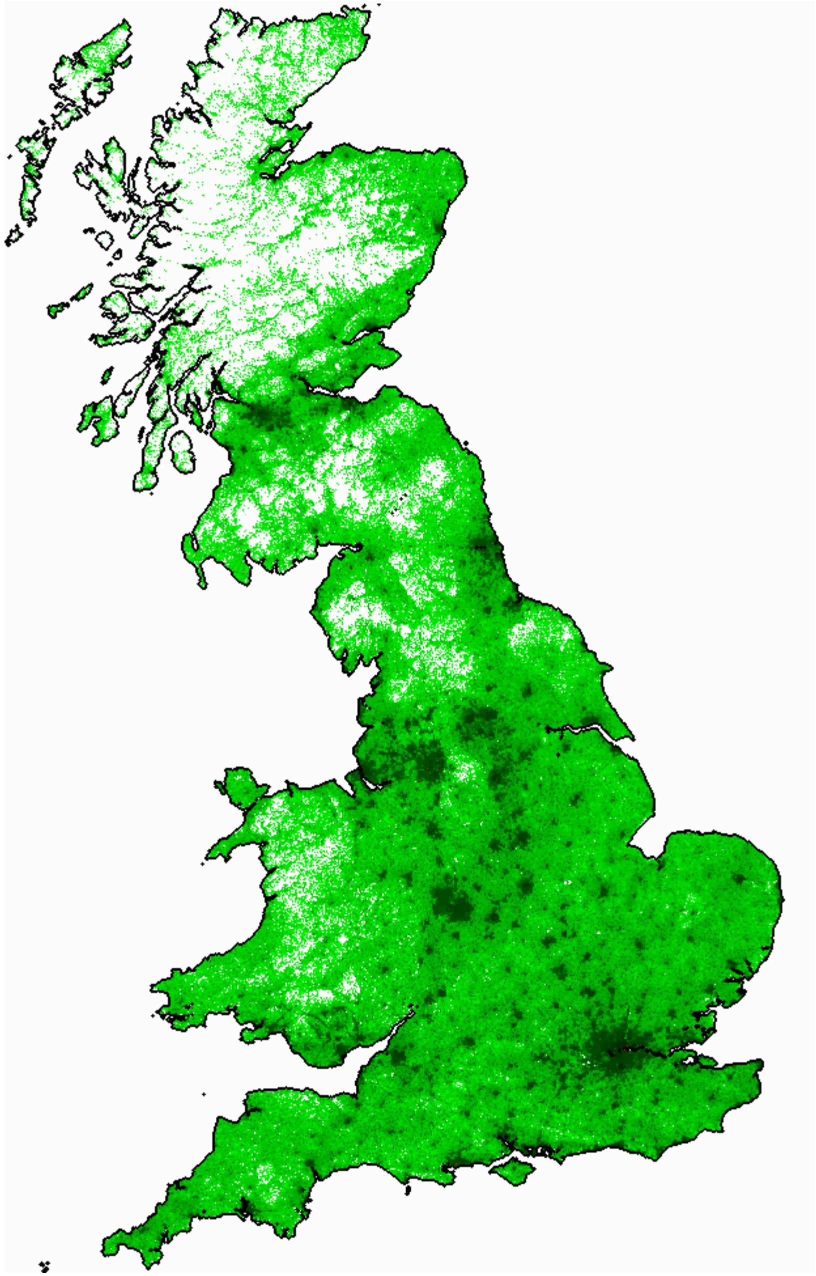
Modelling pandemic influenza -UK

A mathematical model of the spread of pandemic influenza following the introduction of a single infected individual into a UK airport.

I sec = 1day
Grey, population density
Red, infected individuals
Green, end of infection.



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Ferguson et al Nature 2006

The Red Queen Hypothesis

(Van Valen, 1973)

"Now, here, you see, it takes all the running you can do to keep in the same place"

Carrol, L. 1872. Through the looking glass and what Alice found there.