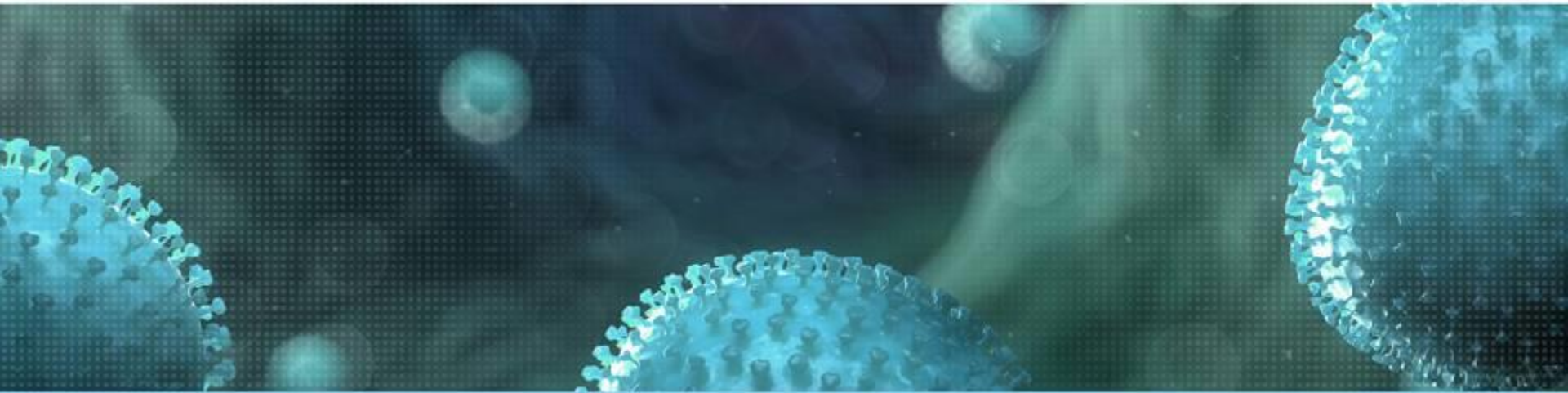


Erasmus MC



Viroscience lab

WHERE SKILLS MEET TO STUDY & PROTECT



Influenza virus surveillance strategy in the Netherlands

Ron A.M. Fouchier, PhD

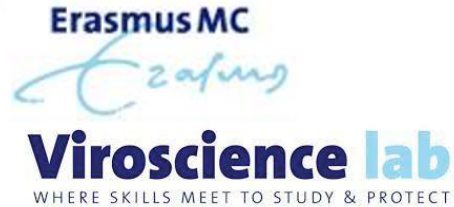
Dutch National Influenza Centre

- Organisation -



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Adam Meijer
Marit de Lange
Anne Teirlinck
Daphne Reukers
Dirk Eggink
Rianne van Gageldonk-Lafeber
et al.



Marion Koopmans
Ron Fouchier
Pascal Lexmond
Mark Pronk
et al.



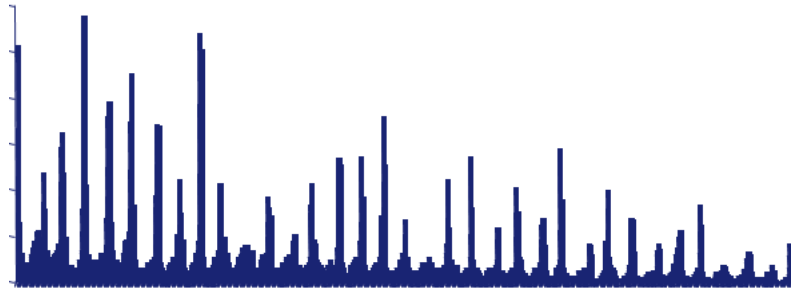
NIVEL
Kennis voor betere zorg

Mariëtte Hooiveld
et al.



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Erasmus

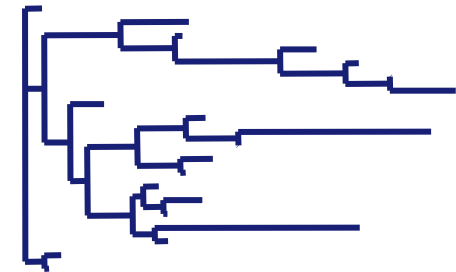
WHO global influenza surveillance - GISRS datasets -



Epidemiological

	F1968	F1973	F1979	F1987	F1989	F1992
V1968	<u>1280</u>	640	40	<20	<20	<20
V1973	320	<u>1280</u>	320	80	<40	<20
V1979	160	320	<u>1280</u>	160	160	20
V1987	40	80	160	<u>1280</u>	640	80
V1989	<20	<20	20	320	<u>2560</u>	640
V1992	<20	<20	<20	20	320	<u>1280</u>

Phenotype



Genotype

- Phenotypes
- antigenic drift (vaccine strain selection)
 - zoonotic/emerging strains
 - antiviral resistance
 - diagnostic methods

The era of next generation sequencing - SARS-CoV-2 and influenza -



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Search | Back to results | Worksets | Upload | Batch Upload | Settings | Analysis

Count **387,060 viruses** | GISAID published | 223,932 viruses (1,092,987 sequences) | Total count | 387,060 viruses (1,743,534 sequences)

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EpiCoV™ | Search | Downloads | Upload

Search ▼ Reset filters

EPI_ISL ID Virus name EPI_SET ID Complete [?]

Location Host High coverage [?]

Collection to Submission to Low coverage excluded [?]

Clade Lineage Substitutions [?] Variant With patient status [?]

Collection date complete [?]

Under investigation

<input type="checkbox"/>	Virus name	Passage de	Accession ID	Collection da	Submission C	Length	Host	Location	Originating
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2680/2022	Original	EPI_ISL_15204508	2022-08-28	2022-10-01	29,574	Human	Asia / Malaysia /	MKAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2613/2022	Original	EPI_ISL_15204507	2022-08-27	2022-10-01	29,436	Human	Asia / Malaysia /	HSAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2650/2022	Original	EPI_ISL_15204506	2022-08-30	2022-10-01	29,739	Human	Asia / Malaysia /	HSAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2676/2022	Original	EPI_ISL_15204505	2022-08-30	2022-10-01	29,759	Human	Asia / Malaysia /	MKAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2657/2022	Original	EPI_ISL_15204504	2022-08-29	2022-10-01	29,752	Human	Asia / Malaysia /	HSAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2482/2022	Original	EPI_ISL_15204503	2022-08-12	2022-10-01	29,438	Human	Asia / Malaysia /	HSAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2659/2022	Original	EPI_ISL_15204502	2022-09-03	2022-10-01	29,728	Human	Asia / Malaysia /	HSAJB
<input type="checkbox"/>	hCoV-19/Malaysia/C19UMB2612/2022	Original	EPI_ISL_15204501	2022-08-18	2022-10-01	29,725	Human	Asia / Malaysia /	Hospital M

Total: 13,341,239 viruses

EPI_SET Select Analysis Download

- Contact tracing
- Epidemiology
- Variant tracing
- New variants
- Spill-overs (e.g. mink)
- (Antigenic?) evolution
- Basic science

Sequencing platforms

- Plenty to choose from-



ABI 3730xl



454 GS FLX



Illumina HiSeq 2000



Illumina MiSeq

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Ion Torrent PGM



PacBio



Minlon



GridION

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Transforming the surveillance paradigm

- "Sequence first surveillance" -



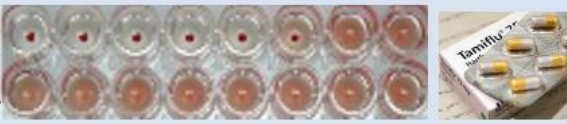
Phenotype First

Isolate and propagate all




Phenotypically analyze all

HI
HA




Genetic analysis: a subset




Genotype First

Genetically analyze all (+)

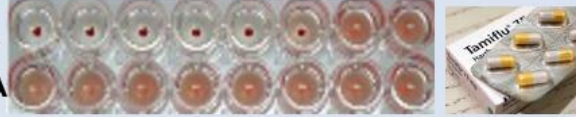


Isolate and propagate subset



Phenotypically analyze

HI
HA



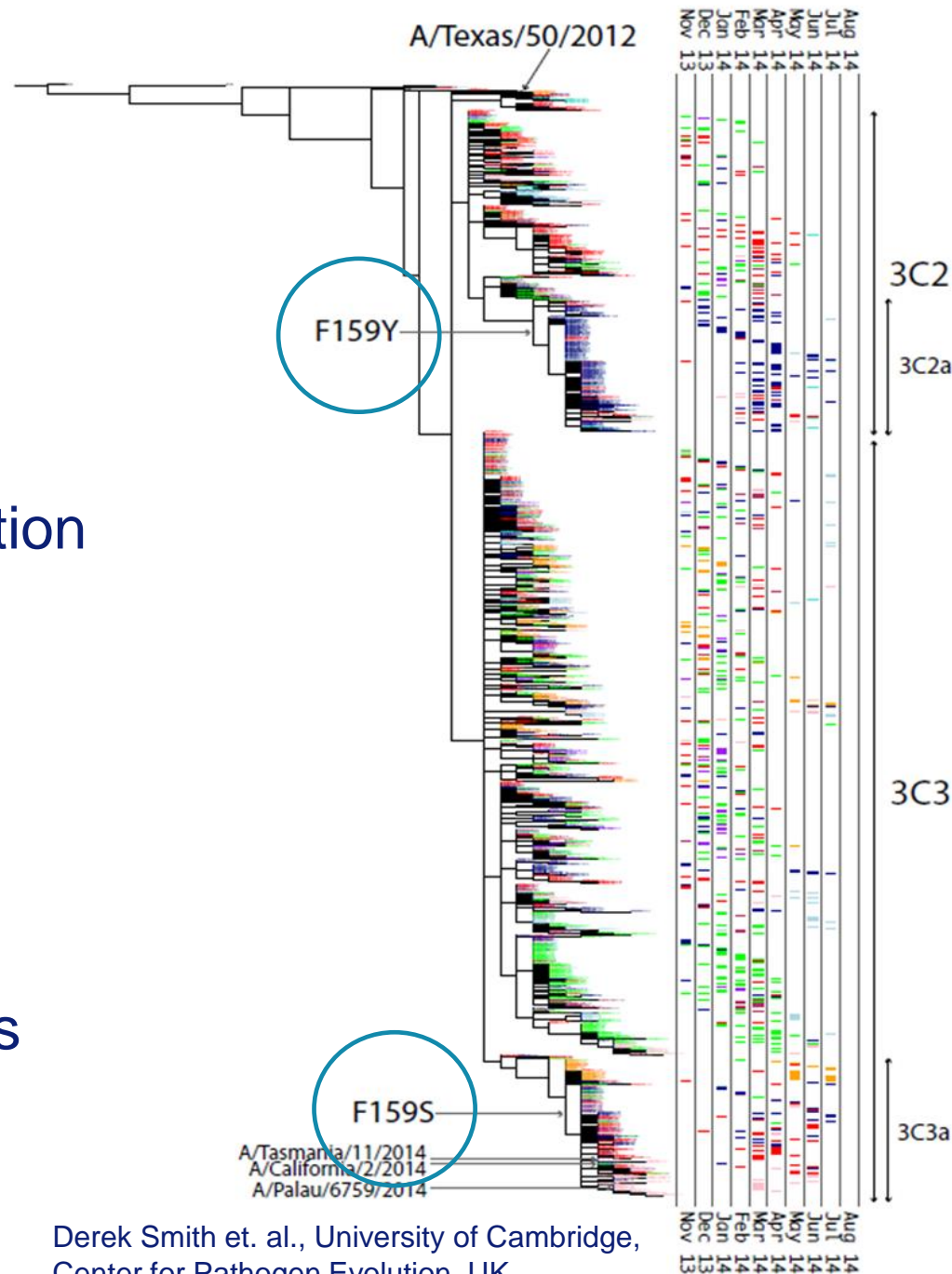
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Sequence data

- Purpose? -

- Genomic analysis
 - Vaccines
 - Drift/shift characterization
 - Forecast fitness
 - Antiviral drug resistance
 - Diagnostics
- Synthetic virology
 - Combat emerging viruses

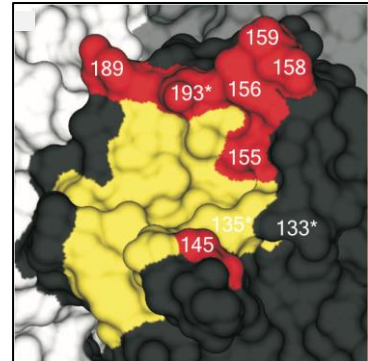


Molecular basis of antigenic drift

- Changes around RBS -

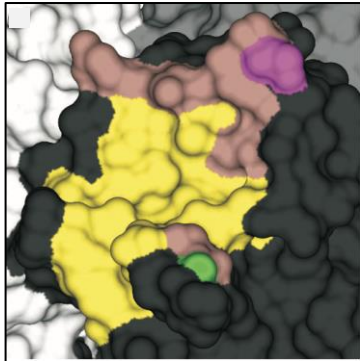


H3 1968-2003

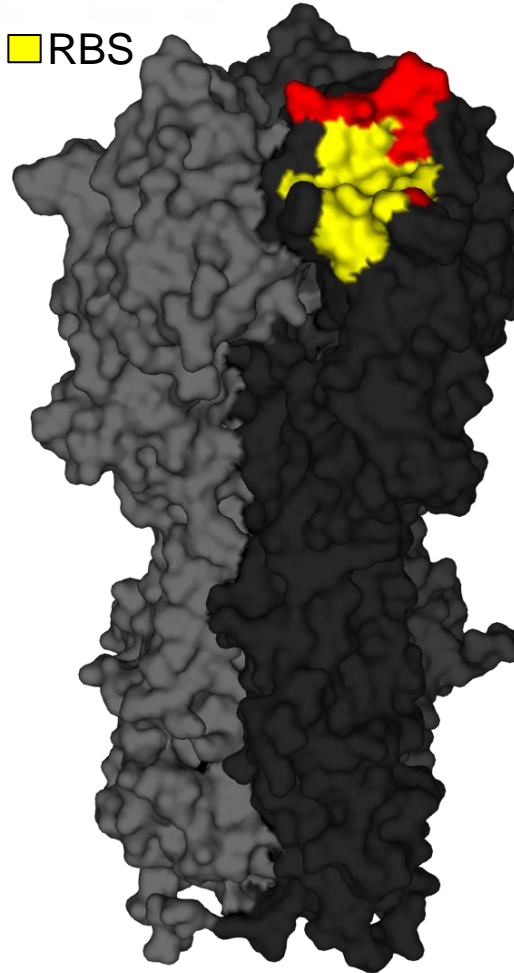


Koel et al., Science 2013

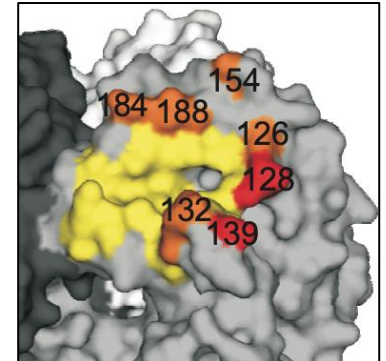
B 2008/2010



■ RBS

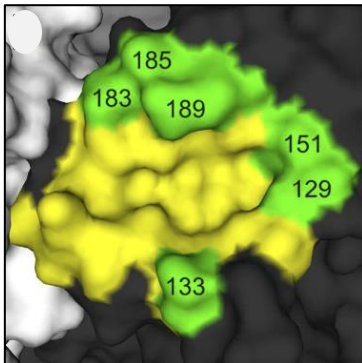


H2N2 1957-1968



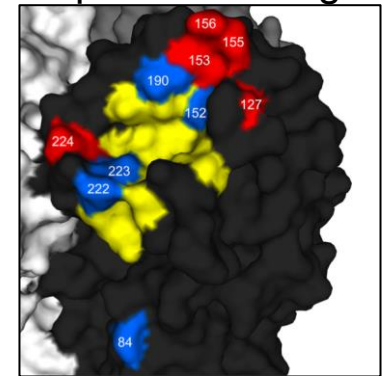
Linster et al., JVI 2019

H5 Clade 2.1



Koel et al., MBio 2014

H1pdm scanning



Koel et al., JVI 2015

Influenza virus resistance mutations - Adamantanes, NAI, baloxavir-



Updated frequently

Antiviral Research 175 (2020) 104718



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Contents lists available at [ScienceDirect](#)

Antiviral Research

journal homepage: www.elsevier.com/locate/antiviral



Global update on the susceptibilities of human influenza viruses to neuraminidase inhibitors and the cap-dependent endonuclease inhibitor baloxavir, 2017–2018



Emi Takashita^{a,*}, Rod S. Daniels^b, Seiichiro Fujisaki^a, Vicki Gregory^b, Larisa V. Gubareva^c, Weijuan Huang^d, Aeron C. Hurt^e, Angie Lackenby^f, Ha T. Nguyen^c, Dmitriy Pereyaslov^g, Merryn Roe^e, Magdi Samaan^h, Kanta Subbarao^e, Herman Tseⁱ, Dayan Wang^d, Hui-Ling Yen^j, Wenqing Zhang^h, Adam Meijer^k

<https://gisa>

NGS-based surveillance

- MinIon/GridIon, real-time -



- RNA Isolation (1 hour)
- Multi-segment RT/PCR (4 hours)
- PCR purification (30 minutes)
- Library prep (1 hour)
- Start sequence run (5 min)
- Real time base calling (20.000 bp read in 10 min)
- Max run 16-48 hours
- Analyses



Influenza surveillance

- Erasmus approach: sequence first -



Previous:	Now:	sample size	
1. Culture	1. Sequence	~1000	Sentinel GPs Hospitals
2. HI/VN, resistance	2. Culture	100s	
3. Sequence	3. HI/VN, resistance	10s	

Similar numbers, similar output of totally characterized samples

Last year: ~1800 (overshoot)



Email: viroscience@erasmusmc.nl
Website: www.viroscience.nl