

Antiviral Drugs Against Influenza

Johan Neyts

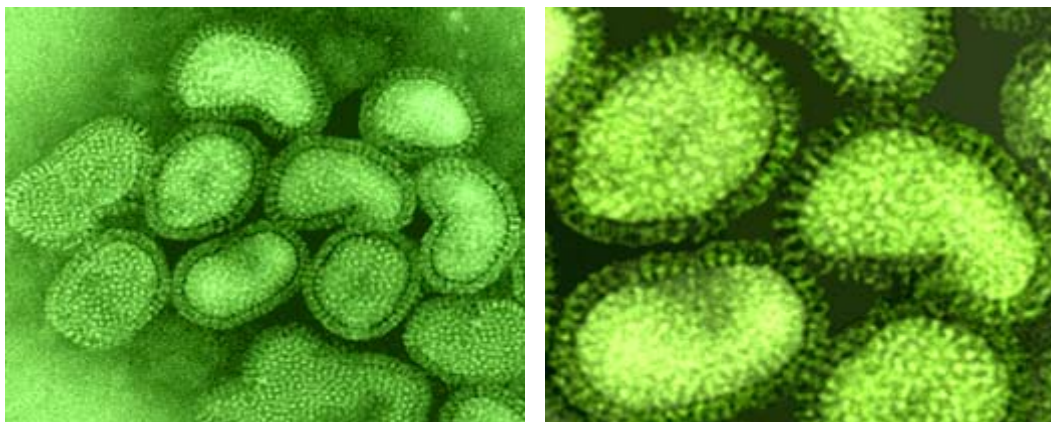
Rega Instituut, KULeuven

Lieve Naesens



Jan Balzarini





Hemagglutinine

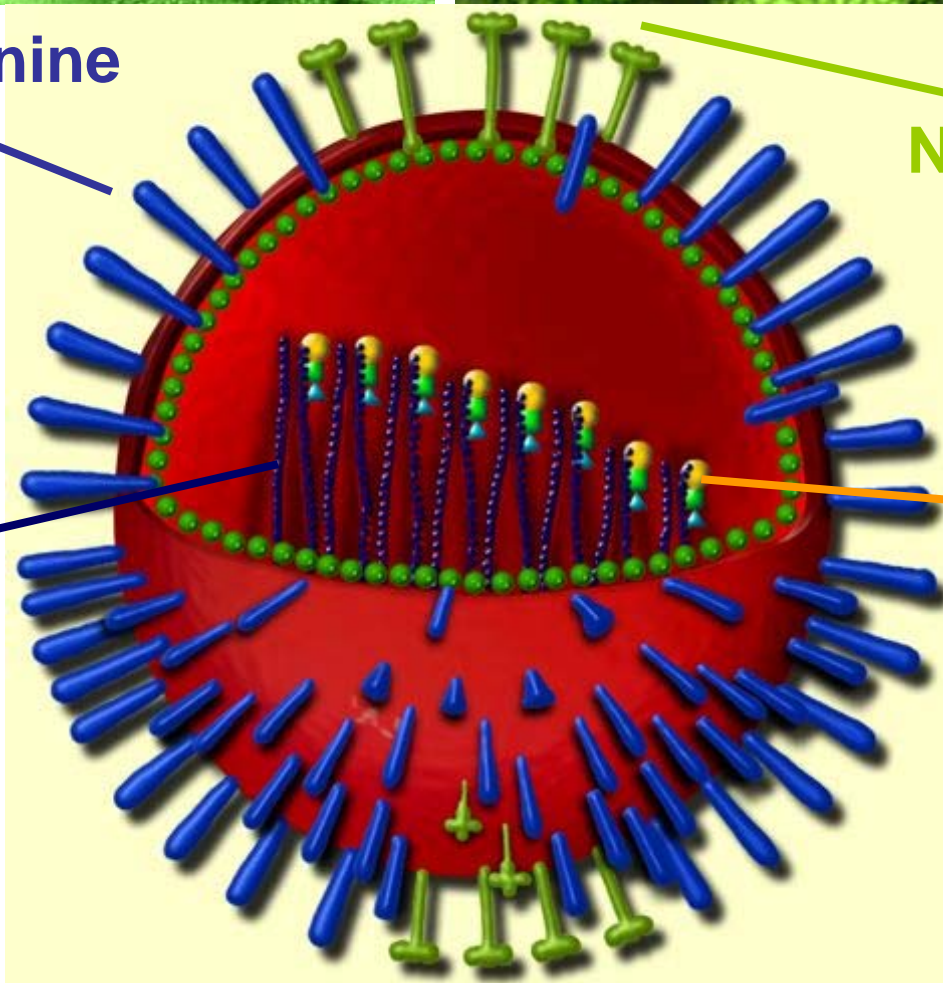
(H)

Neuraminidase

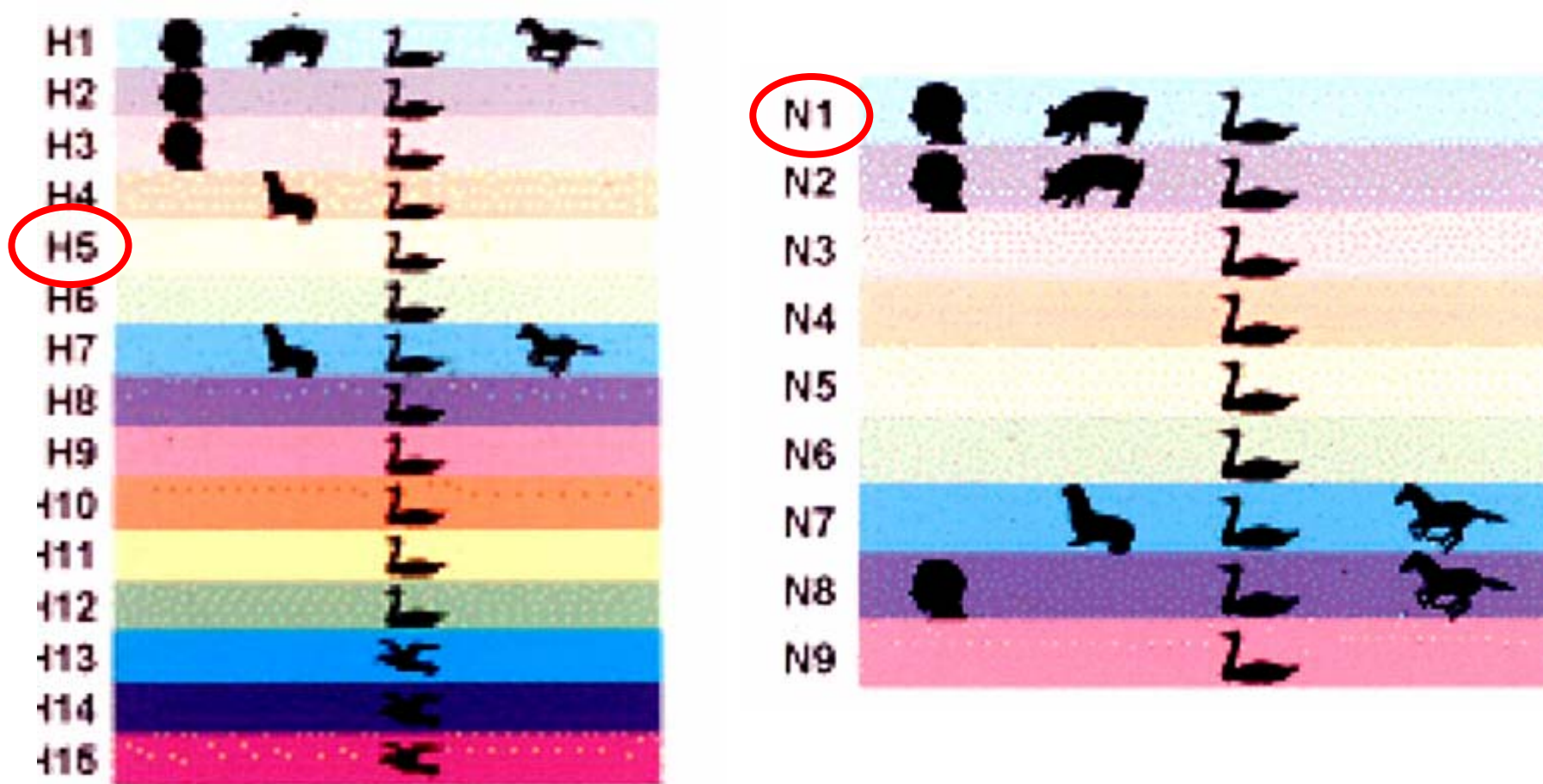
(N)

Genome

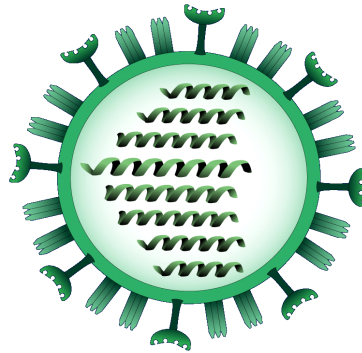
**Replication
enzymes**



Influenza A viruses in nature



Type B



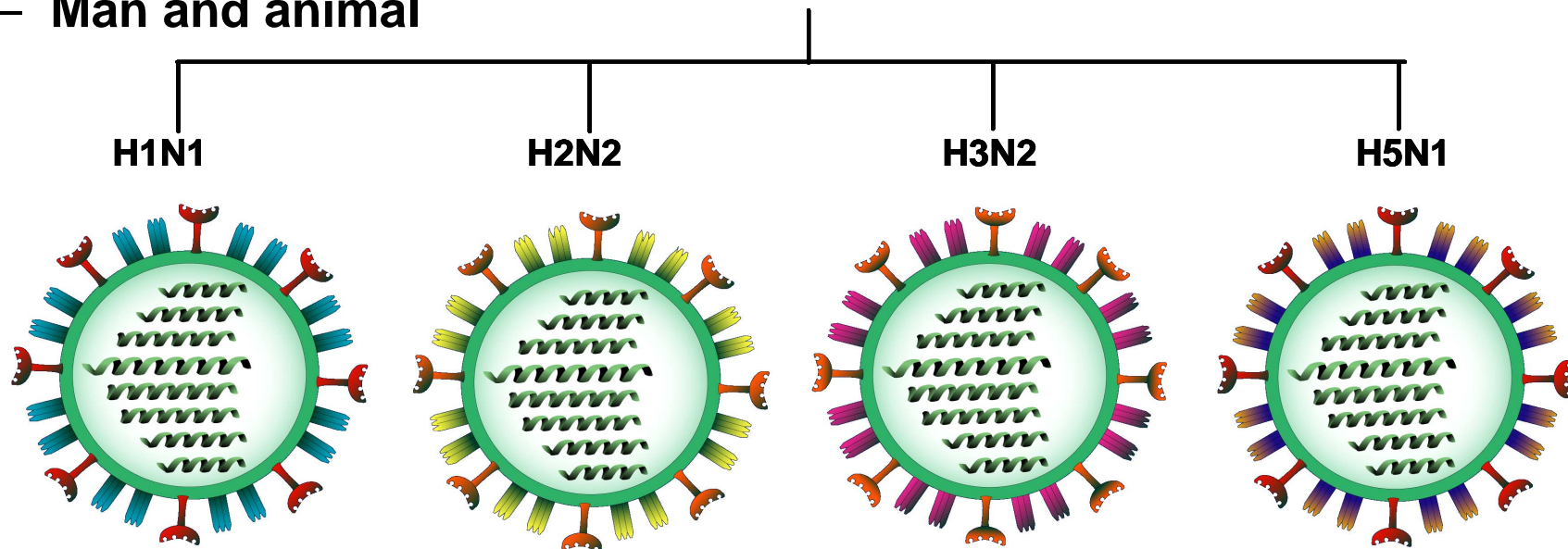
Influenza B

- Mild epidemics
- Only man

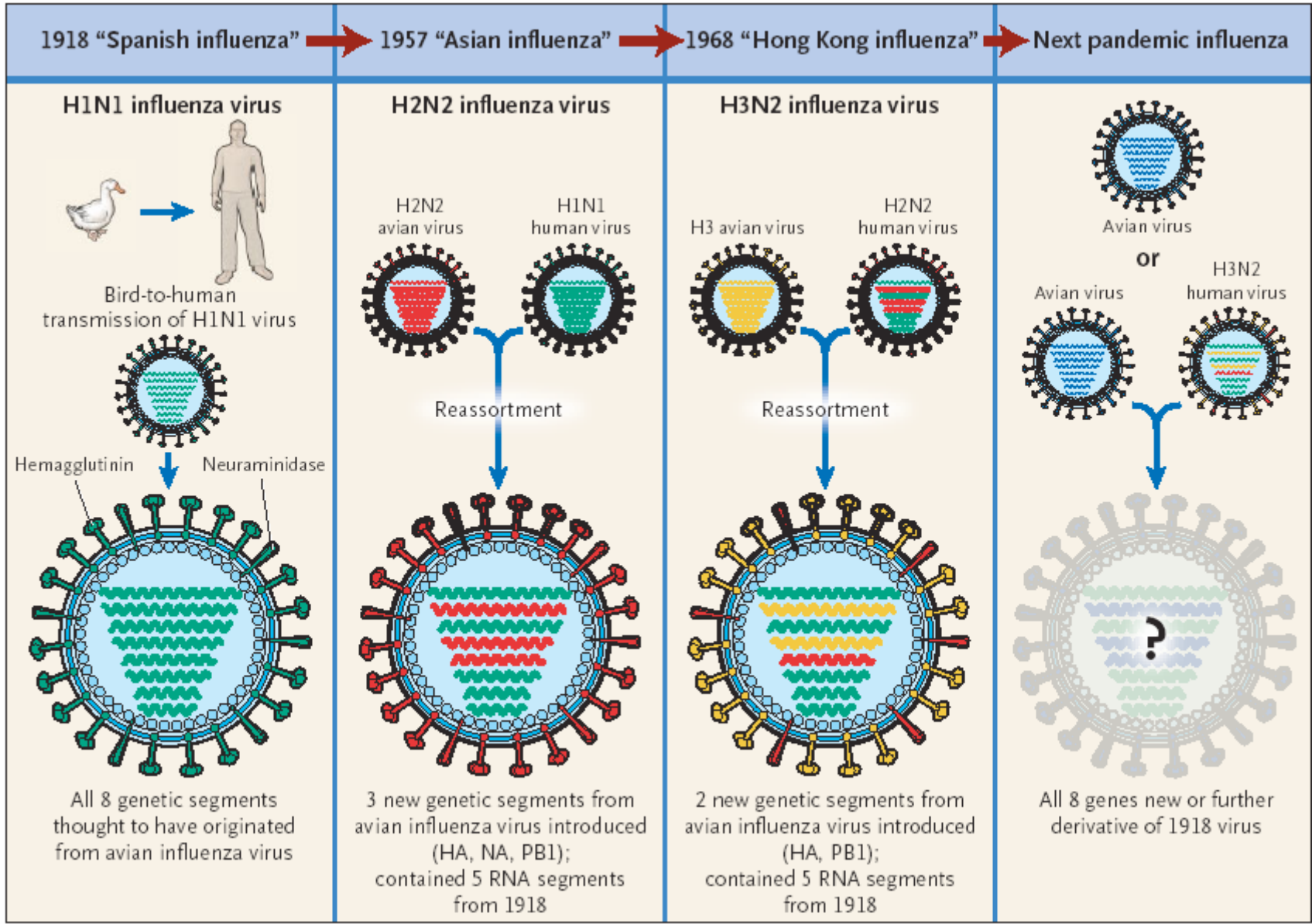
Influenza A

- Epidemics and pandemics
- Man and animal

Type A



Source : Roche



Reference to be added.

Why do we need anti-influenza drugs?

Winter flu

Each year an estimated 400.000 people die of influenza (likely twice as many).

Vaccination is not always effective (e.g. in elderly).

Pandemic flu

As long as birds and man exist, flu pandemics will occur.

If a (potential) pandemic strain emerges, it may take months before a vaccine will be available.

During this time-span, but also later, the use of antivirals will be essential to help contain an outbreak.

Antiviral drugs will also be essential to prevent infection in selected groups, for example health care workers.

First Generation Influenza Drugs



Rimantadine, Flumadine®

Amantadine, Symmetrel®

Only active against Influenza A.

Not potent.

Virus becomes rapidly insensitive (resistant)

Bird Flu Drug Rendered Useless

Chinese Chickens Given Medication Made for Humans

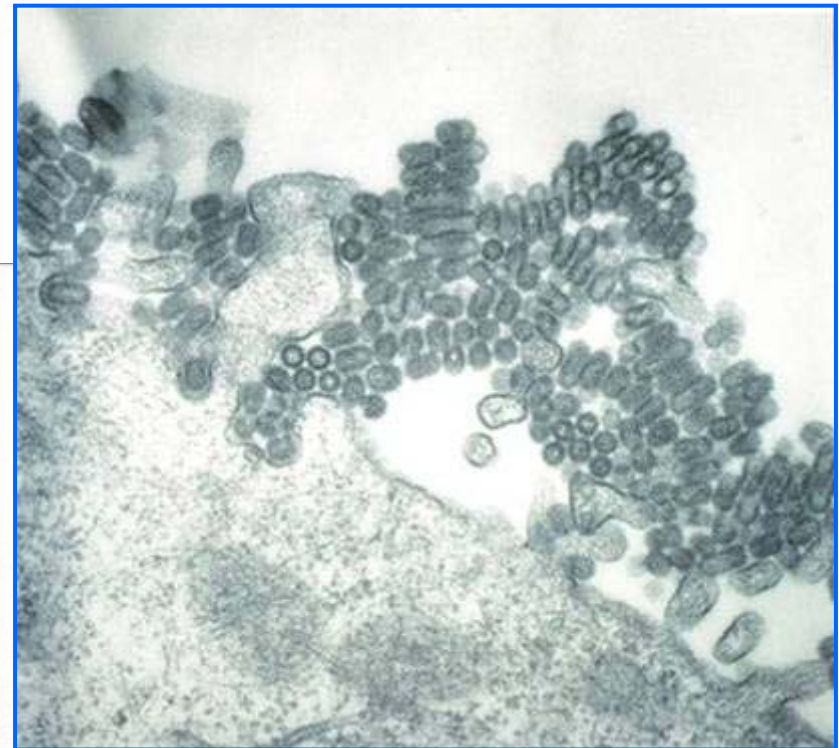
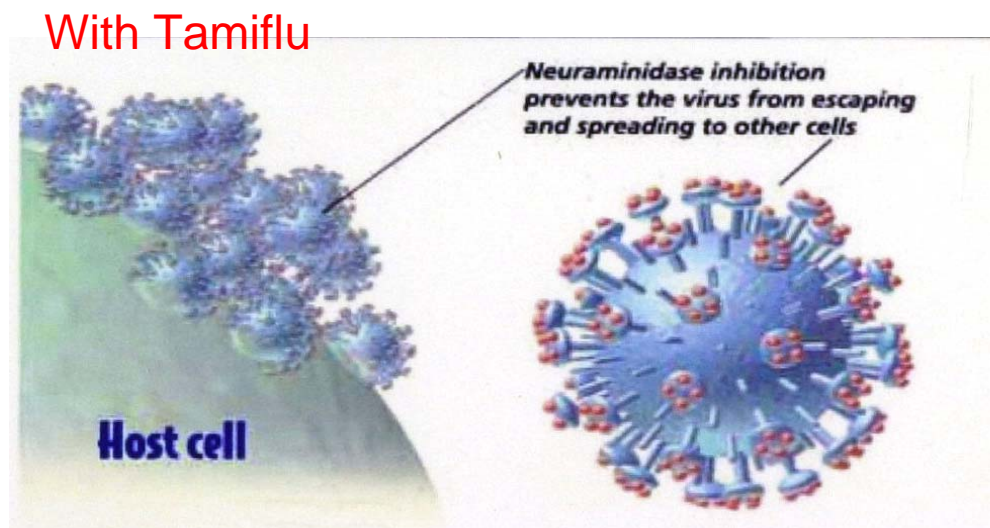
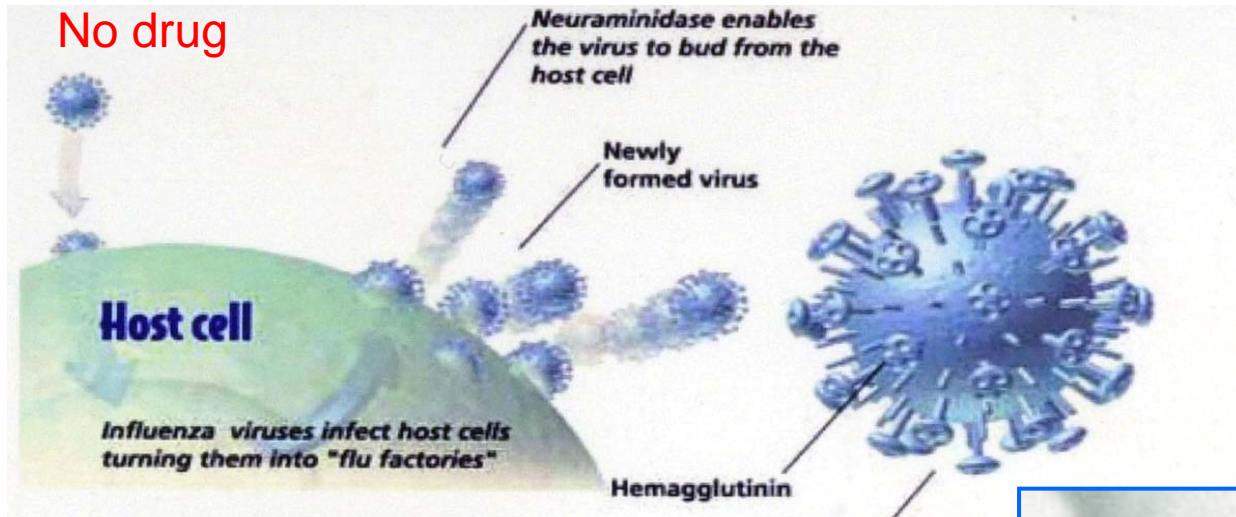
Washington Post Saturday, June 18, 2005



Chinese farmer have used an anti-viral made (amantadine) for humans on chickens. (China Photos Via Getty Images)

Second Generation Influenza Drugs





Source: Roche

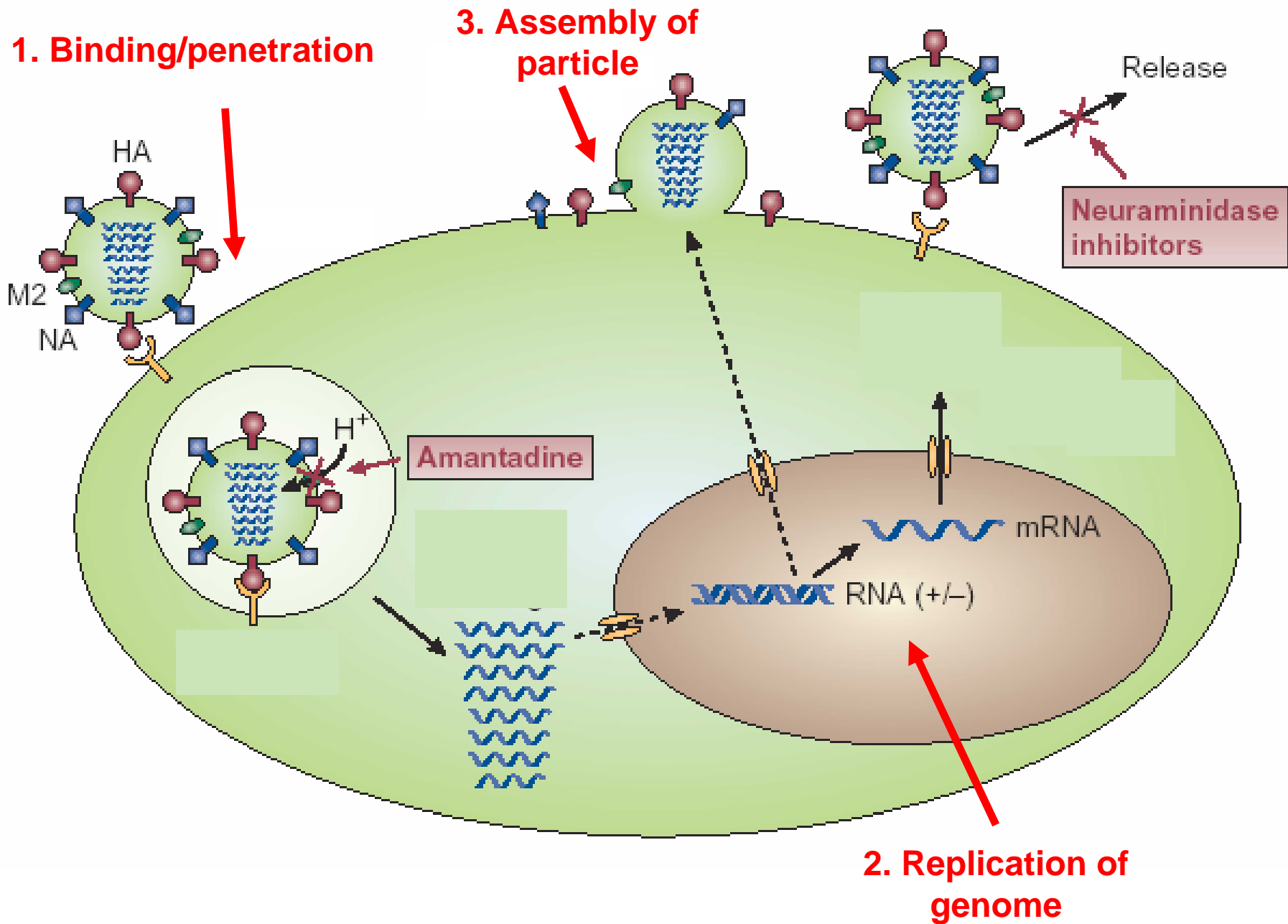
Oseltamivir Resistance during Treatment of Influenza A (H5N1) Infection

Menno D. de Jong, M.D., Ph.D., Tran Tan Thanh, M.Sc.,
Truong Huu Khanh, M.D., Vo Minh Hien, M.D., Gavin J.D. Smith, Ph.D.,
Nguyen Vinh Chau, M.D., Bach Van Cam, M.D., Phan Tu Qui, M.D.,
Do Quang Ha, M.D., Ph.D., Yi Guan, M.D., Ph.D., J.S. Malik Peiris, D.Phil., M.D.,
Tran Tinh Hien, M.D., Ph.D., and Jeremy Farrar, D.Phil., F.R.C.P.

SUMMARY

Influenza A (H5N1) virus with an amino acid substitution in neuraminidase conferring high-level resistance to oseltamivir was isolated from two of eight Vietnamese patients during oseltamivir treatment. Both patients died of influenza A (H5N1) virus infection, despite early initiation of treatment in one patient. Surviving patients had rapid declines in the viral load to undetectable levels during treatment. These observations suggest that resistance can emerge during the currently recommended regimen of oseltamivir therapy and may be associated with clinical deterioration and that the strategy for the treatment of influenza A (H5N1) virus infection should include additional antiviral agents.

Can we design novel influenza drugs
with a resistance profile different from
that of Tamiflu & Relenza ?



Modified from Palese (2004) Nat. Med. 10(12 Suppl):S82-7.



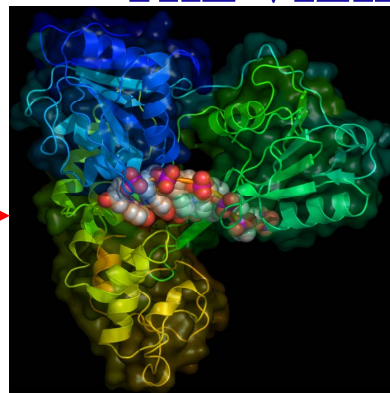
Deciphering the viral world

Structure & Genome of Viral Enzymes Involved in Replication

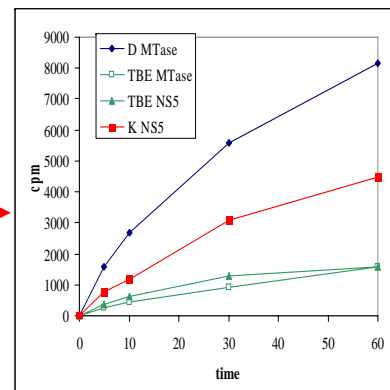
THE VIZIER PIPELINE



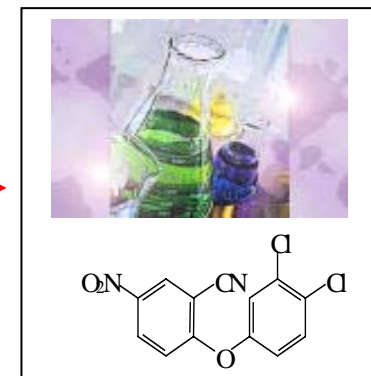
Collect and culture viruses and analyze their genome.



Produce viral proteins and determine their structure.



Determine and study the function of the viral proteins.

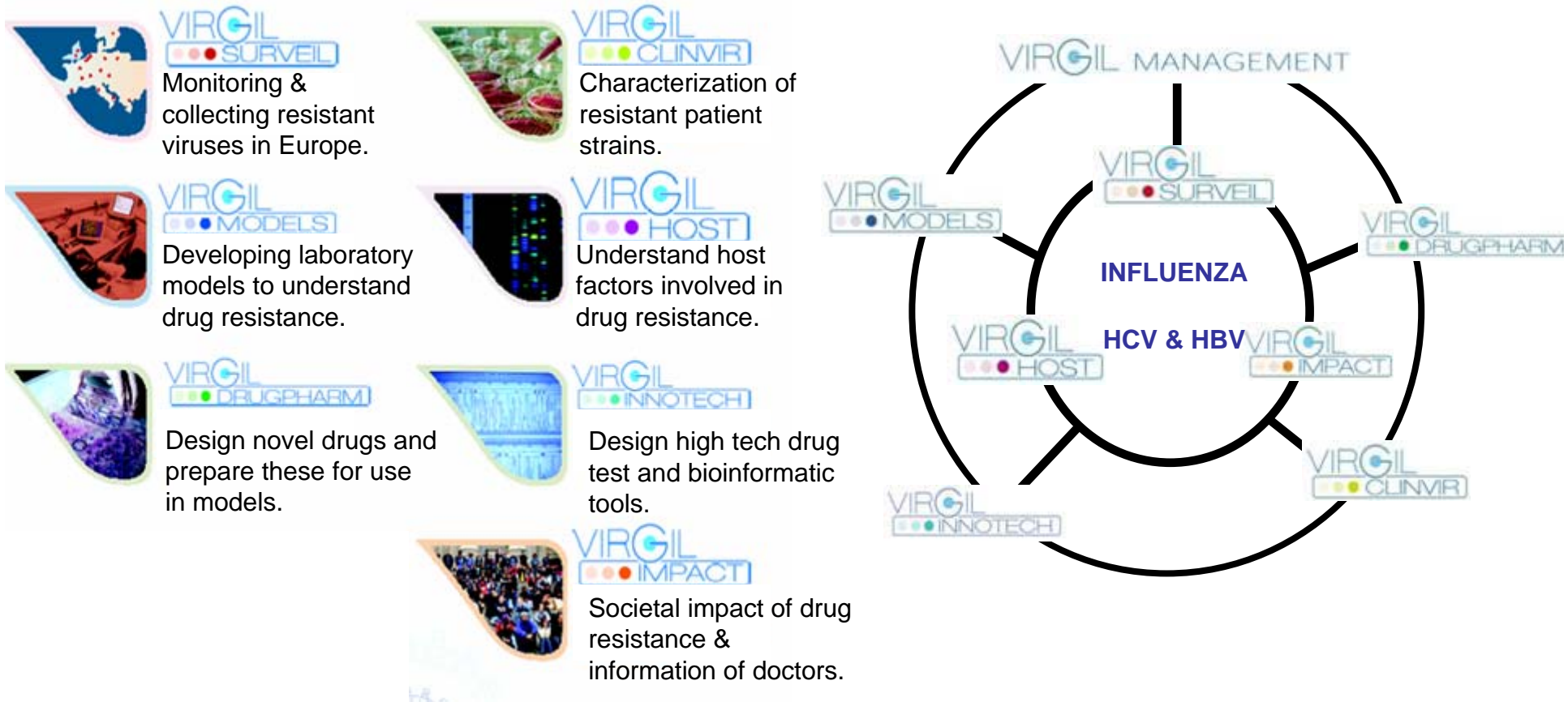


Design inhibitors that inhibit the function of the viral replication machinery.

Coordinator: Dr. B. Canard, AFMB, University of Marseille
EU Officer : Dr. J. Enfedaque

COMBATING RESISTANCE TO ANTIVIRAL TREATMENTS

The first-ever European Vigilance Network capable of addressing antiviral drug resistance.



Coordinator: Prof. Dr. F. Zoulim, Lyon
EU Officer : Dr. A. Lonroth

CONCLUSION

The pandemic clock is ticking, but
we have no idea what time it is.



**However, for the first time in history we have the
chance to prepare for a pandemic and have the
responsability to do so!**

**The activities supported by the UE form an essential contribution
towards this goal.**