Neuraminidase (N)

Hemagglutininine (H)

Genome

Replication enzymes
Influenza A viruses in nature

http://www.brown.edu/Courses/Bio_160/Projects1999/flu/mechanism.html
Influenza B
- Mild epidemics
- Only man

Influenza A
- Epidemics and pandemics
- Man and animal

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

Amantadine, Symmetrel®

Only active against Influenza A.

Not potent.

Virus becomes rapidly insensitive (resistant)

Rimantadine, Flumadine®
Chinese farmer have used an anti-viral made (amantadine) for humans on chickens. (China Photos Via Getty Images)
Second Generation Influenza Drugs
With Tamiflu

Neuraminidase inhibition prevents the virus from escaping and spreading to other cells

Source: Roche
Oseltamivir Resistance during Treatment of Influenza A (H5N1) Infection

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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?
1. Binding/penetration

2. Replication of genome

3. Assembly of particle

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.

- Monitoring & collecting resistant viruses in Europe.
- Developing laboratory models to understand drug resistance.
- Designing novel drugs and preparing them for use in models.
- Characterizing resistant patient strains.
- Understanding host factors involved in drug resistance.
- Designing high-tech drug test and bioinformatic tools.
- Societal impact of drug resistance & information of doctors.

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