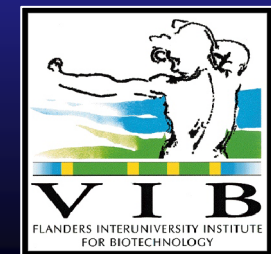
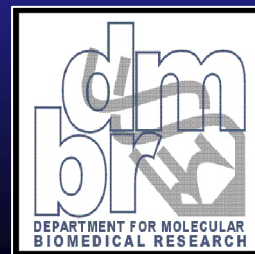


# ***Immunization with a novel, M2e-based vaccine protects against influenza***

Xavier Saelens  
VIB-UGent

*EU-funded Research on Pandemic and Avian Influenza*

DMBR, Ghent, February 7, 2006.



# The flu and influenza virus

## Family Orthomyxoviridae

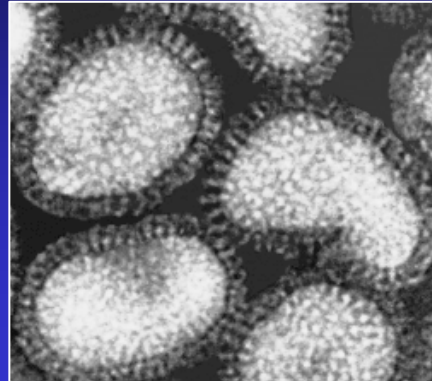
00.046.0.01. **Influenzavirus A**

00.046.0.04. **Influenzavirus B**

00.046.0.02. *Influenzavirus C*

00.046.0.03. *Thogotovirus*

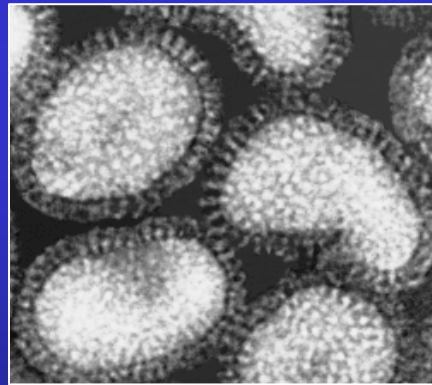
00.046.0.05. *Isavirus*



USA	world
25 million cases	0.5 billion cases
20.000-40.000 deaths	250.000-500.000 deaths

Average morbidity and mortality in an interpandemic influenza season

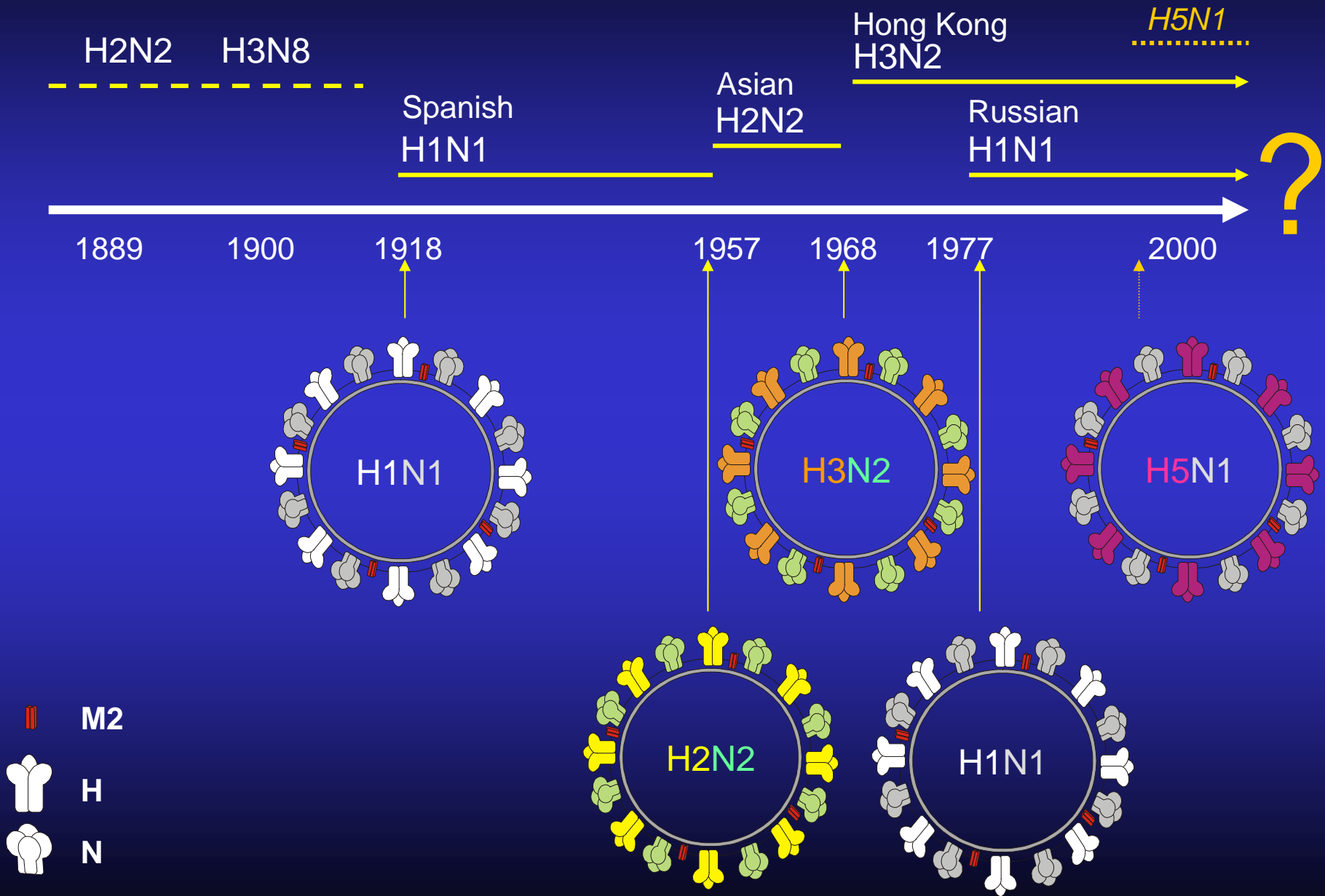
# *Influenza A: a zoonotic infection*



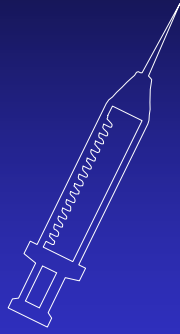
H: 16 subtypes  
N: 9 subtypes



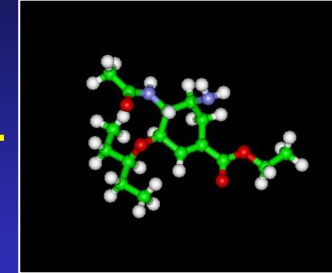
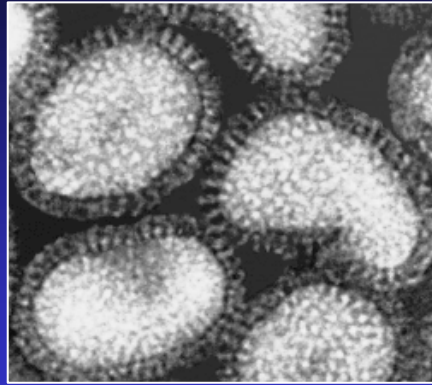
# Influenza A pandemics



# Protection against influenza?



Vaccine



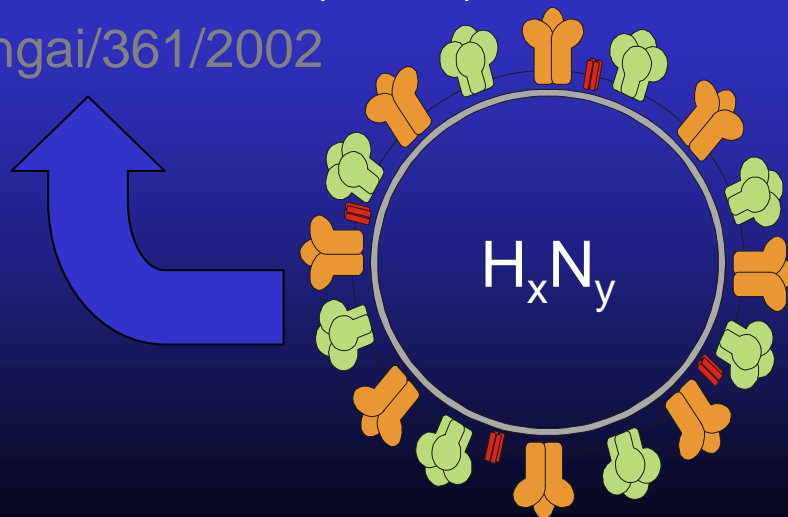
Antivirals: ex. oseltamivir

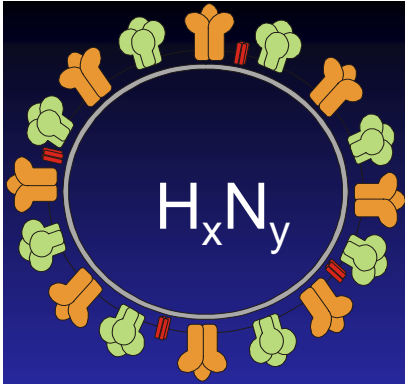
2005-2006 Influenza vaccine:

A/New Caledonia20/99 (H1N1)

A/California/7/2004 (H3N2)

B/Shanghai/361/2002



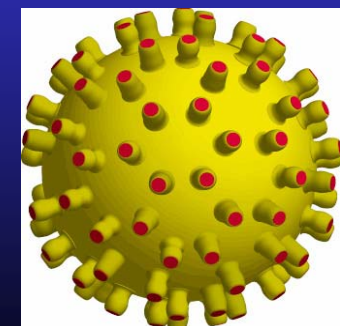
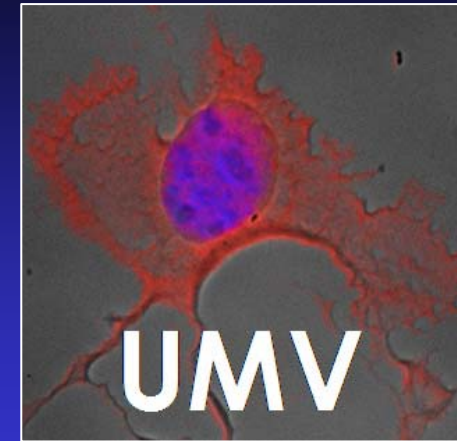
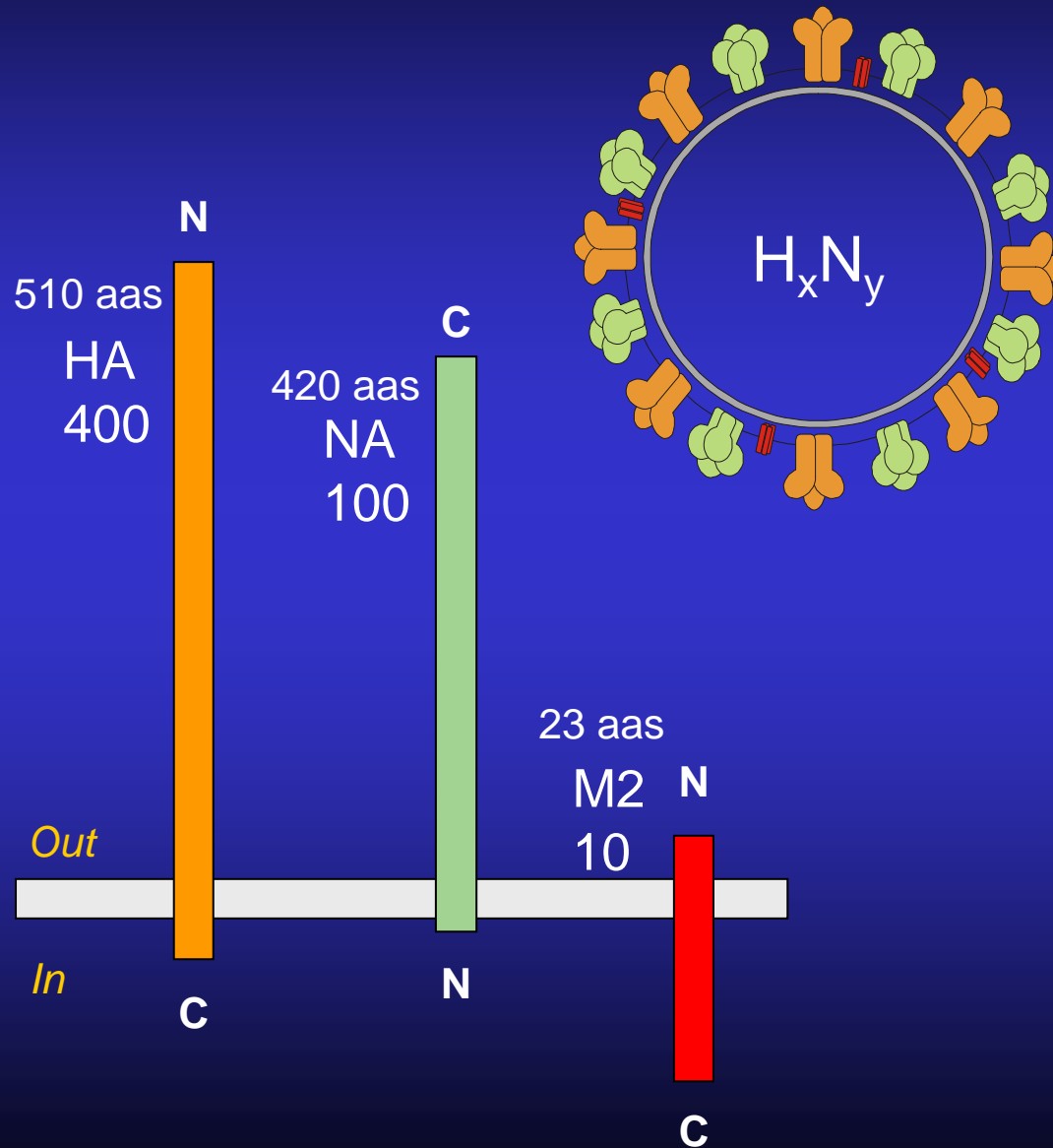


## *M2e: a conserved IVA antigen*

### Human Influenza A strains

<u>consensus M2e sequence</u>		<u>SLLTEVET PIRNEWGCRCNDSS D</u>
A/Brevig_Mission/1/1918	H1N1	SLLTEVET <b>P</b> TRNEWGCRCNDSS D
A/Puerto Rico/8/1934	H1N1	SLLTEVET PIRNEWGCRCN <b>G</b> SS D
A/Chile/13/1957	H2N2	SLLTEVET PIRNEWGCRCNDSS D
A/Japan/170/1962	H2N2	SLLTEVET PIR <b>S</b> EWGCRCNDSS D
A/An Arbor/7/1967	H2N2	SLLTEVET PIRNEWGCRCNDSS <b>N</b>
A/Aichi/2/68	H3N2	SLLTEVET PIRNEWGCRCNDSS D
A/England/878/1969	H3N2	SLLTEVET PIRNEWGCRCNDSS <b>N</b>
A/Caracas/1/1971	H3N2	SLLTEVET PIR <b>K</b> EWGCRCNDSS D
A/Taiwan/3/71	H3N2	<b>S</b> FLTEVET PIRNEWGCRCNDSS D
A/Aichi/69/1994	H3N2	SLLTEVET PIRNEW <b>E</b> CRCN <b>G</b> SS D
A/Wuhan/359/95	H3N2	SL <b>P</b> TEVET PIR <b>S</b> EWGCRCNDSS D
A/Wisconsin/10/98	H1N1	SLLTEVET PIRN <b>G</b> <b>W</b> <b>E</b> <b>C</b> KNDSS D
A/New York/497/2003	H1N1	SLLTEVET PIRNEWGCRCNDSS D
A/New York/378/2005	H3N2	SLLTEVET PIRNEWGCRCNDSS D

# An Influenza A vaccine based on the extracellular domain of the M2-protein

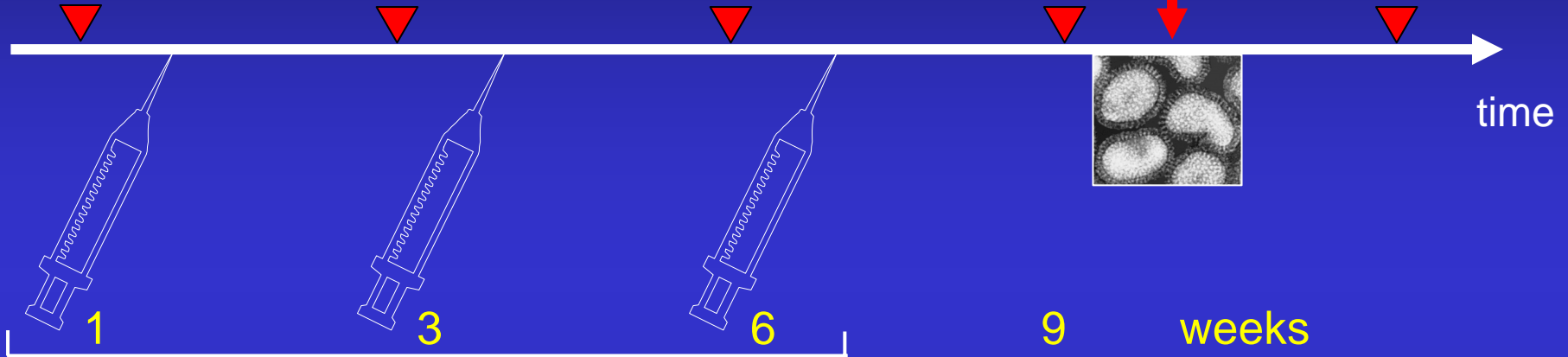


M2e-VLP

# Immunization with M2e-HBc protects mice



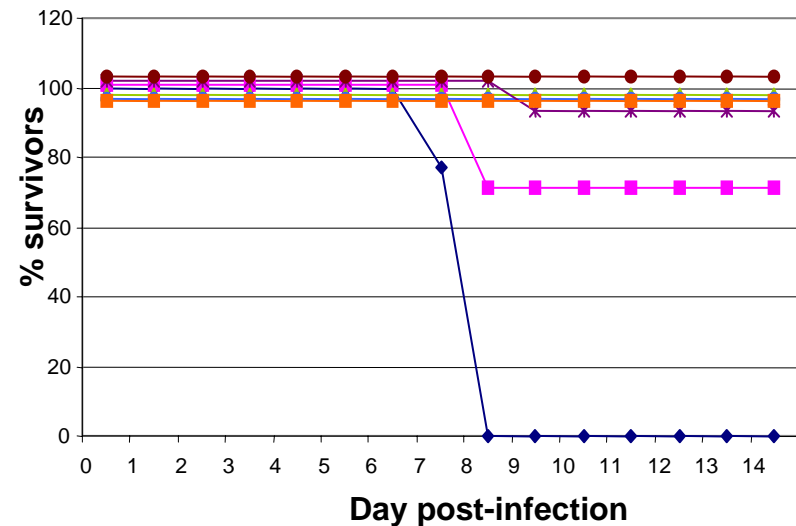
Challenge  
(4 LD<sub>50</sub>)



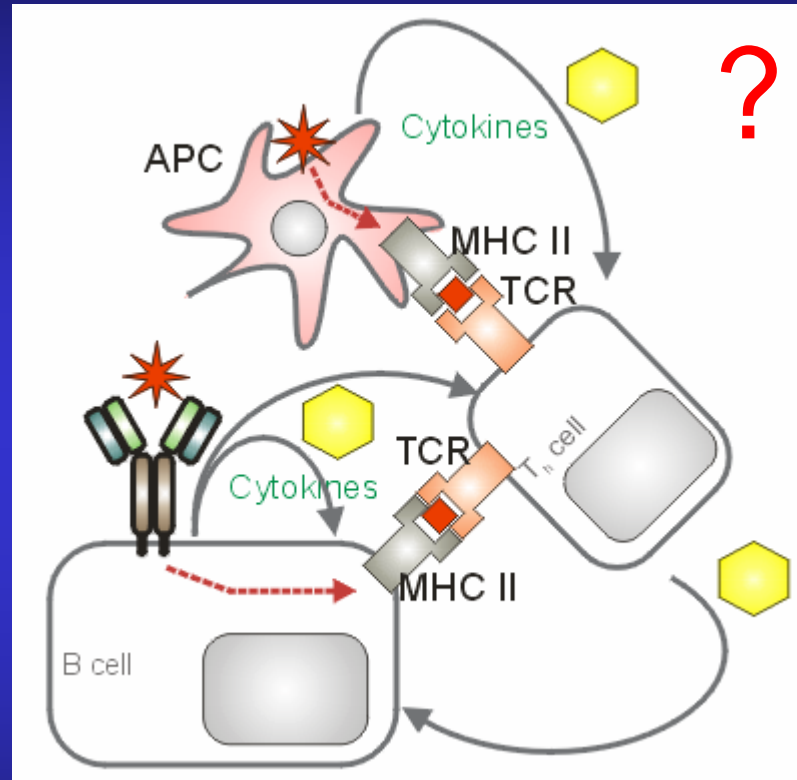
immunizations

▼ = serum samples

Adjuvant!



# What is an adjuvant doing?



 adjuvant

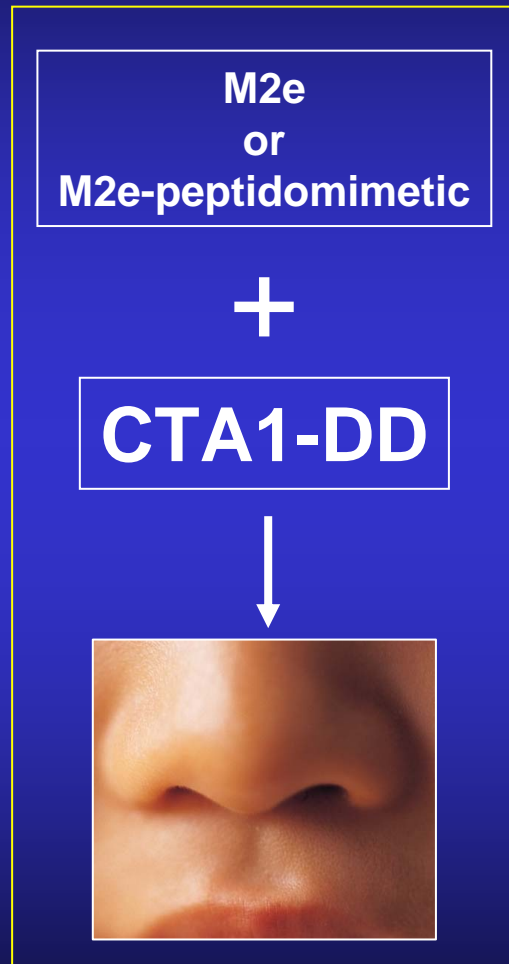
 antigen



[www.universolvaccine.org](http://www.universolvaccine.org)



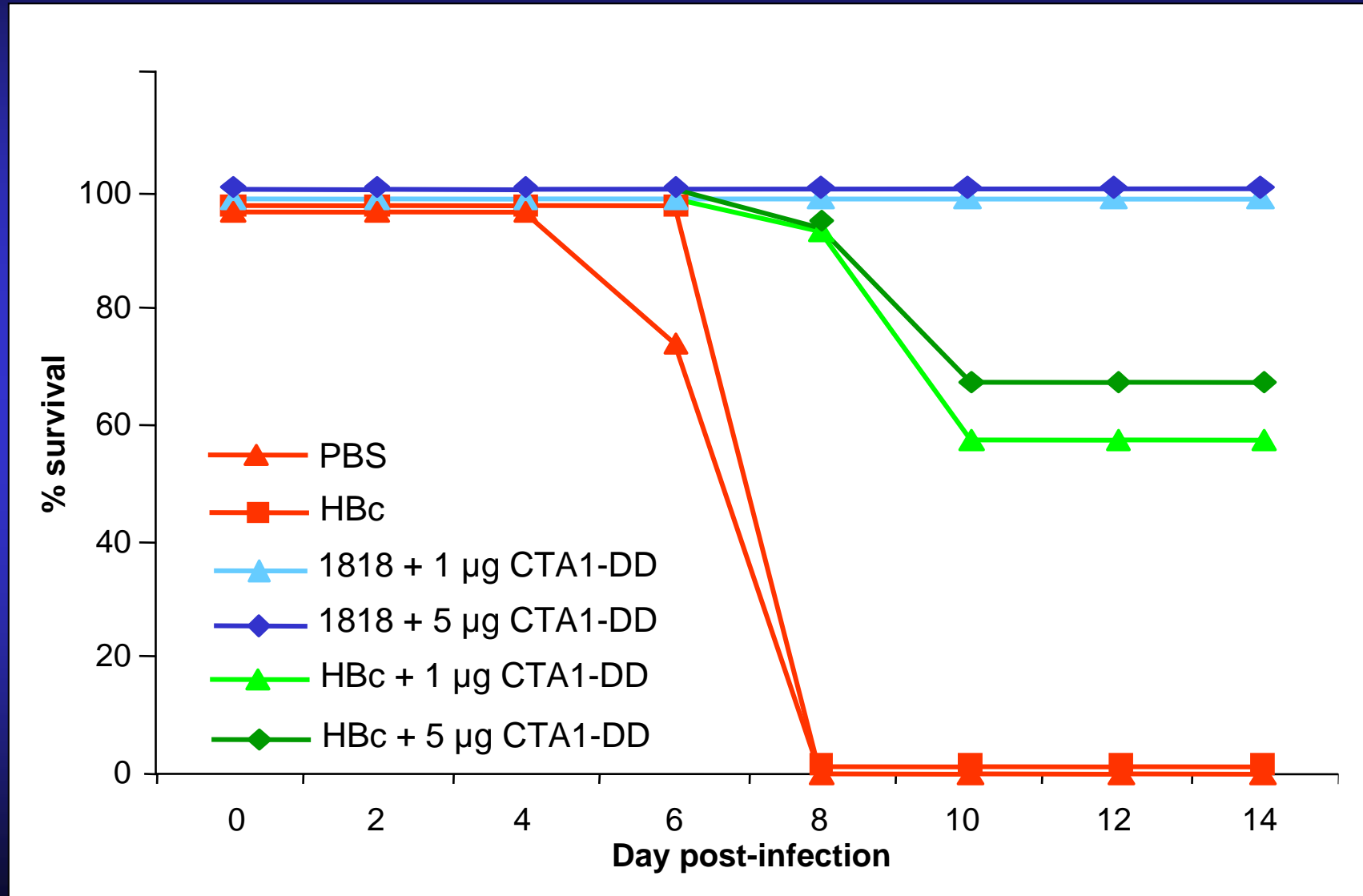
**Arexis**  
coordinator



## Summary CTA1-DD toxicity data

- CTA1-DD is a potent non-toxic adjuvant that, contrary to CT, exhibits the following properties:
  - Does not induce fluid loss in the small intestine
  - Does not induce thymocyte cAMP
  - Does not elicit foot edema
  - Does not promote inflammation
  - Does not bind or accumulate in the CNS
  - Does not promote increases in total serum IgE
  - Does not reduce survival

## *Intranasal immunization with M2e-HBc + CTA1-DD protects*



## *Improvements and preparation for clinical studies?*

M2e coupled a different carrier

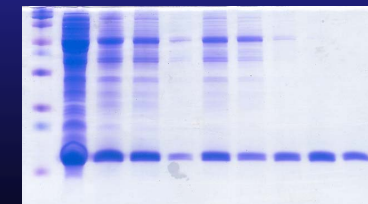
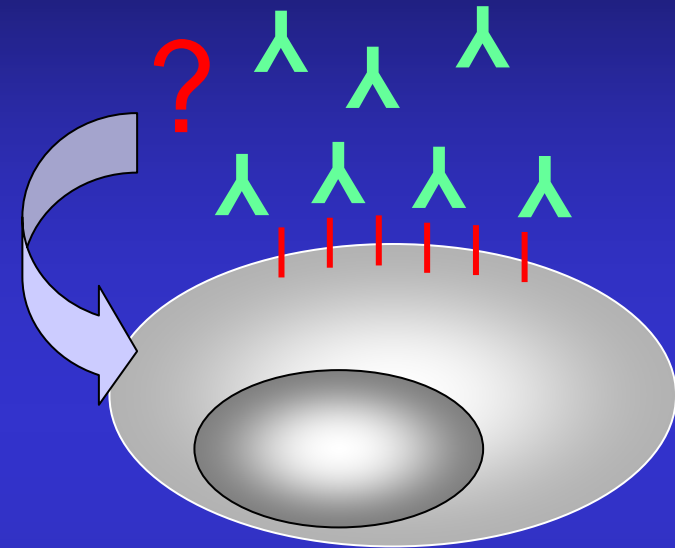
M2e peptidomimetics

Correlates of protection?

Mechanism of action?

GLP production?

*In vivo* delivery vehicle



## Conclusions

- Vaccination with **M2e-VLPs** protects mice against a potentially lethal influenza challenge.
- Protection is mediated by **antibodies**
- Protection is enhanced by adjuvants acceptable for human use
- Intranasal immunization with **CTA1-DD** adjuvanted M2e-VLPs improves protection against a lethal influenza challenge
- The co-operative “universal vaccine” research project aims to produce an M2e-based influenza A vaccine applicable for **intranasal use** in humans.



# Acknowledgements

UMV

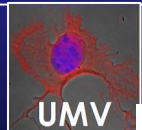
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Schotsaert

Kenny Roose  
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Koen Van Laer

Willy Min Jou  
Walter Fiers



Acambis



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