



3rd GRF One Health Summit

The One Health Approach for Communicable Diseases

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Davos, Switzerland

PREDEMICS

***Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses
with Pandemic Potential using Multidisciplinary Approaches***

**Sylvie van der WERF
On behalf of the
PREDEMICS consortium
Institut Pasteur**



FP7-HEALTH.2011.2.3.3-1:

Identification of factors promoting the emergence of pathogens with human pandemic potential from pathogens with a zoonotic background and related prevention strategies

Project N° 278433 11.75 M€

Dates: 01/11/2011-30/10/2016 (60 months)

17 partners (23 teams)

8 countries

Multidisciplinary, One Health approach

Coordinator: Sylvie van der Werf (IP)

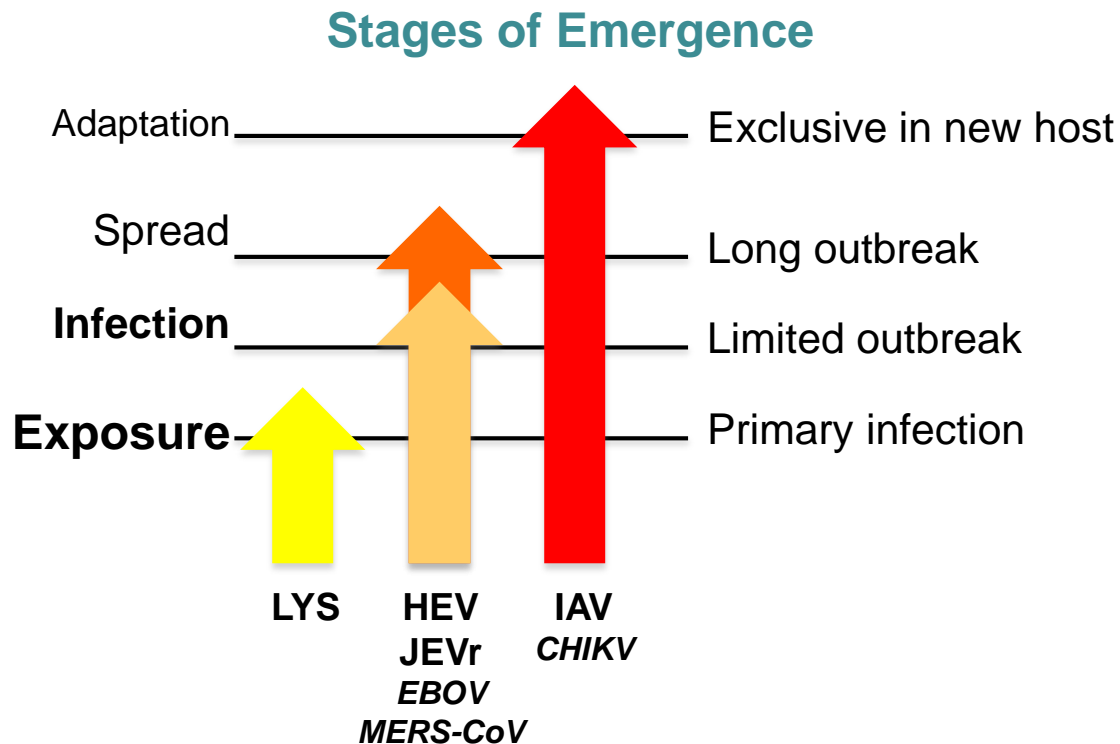
Co-coordinator: Hervé Bourhy (IP)

Project manager: Sophie Ablott (IP)

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Unravel the complex interactions between the factors involved in the four stages of emergence



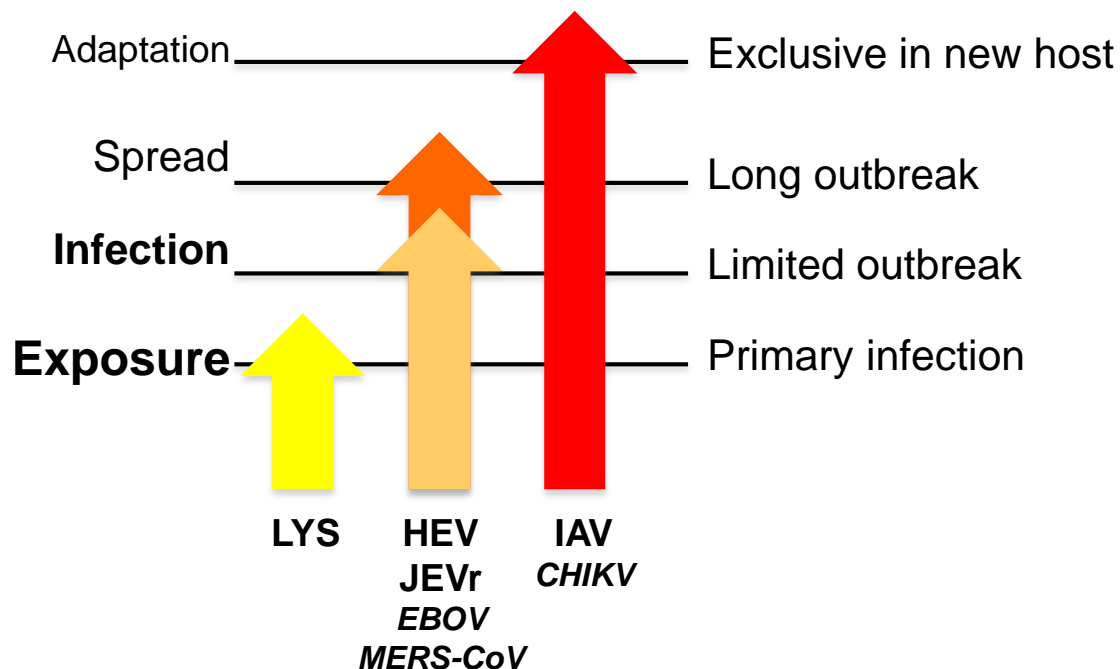
Unravel the complex interactions between the factors involved in the four stages of emergence

For selected zoonotic RNA viruses w/ epidemic potential representing main transmission routes

Transmission Routes

- Respiratory (IAV, *MERS-CoV*)
- Faecal-oral (HEV)
- Contact (LYS, *EBOV*)
- Vector-borne (JEVr, *CHIKV*)

Stages of Emergence



Unravel the complex interactions between the factors involved in the four stages of emergence

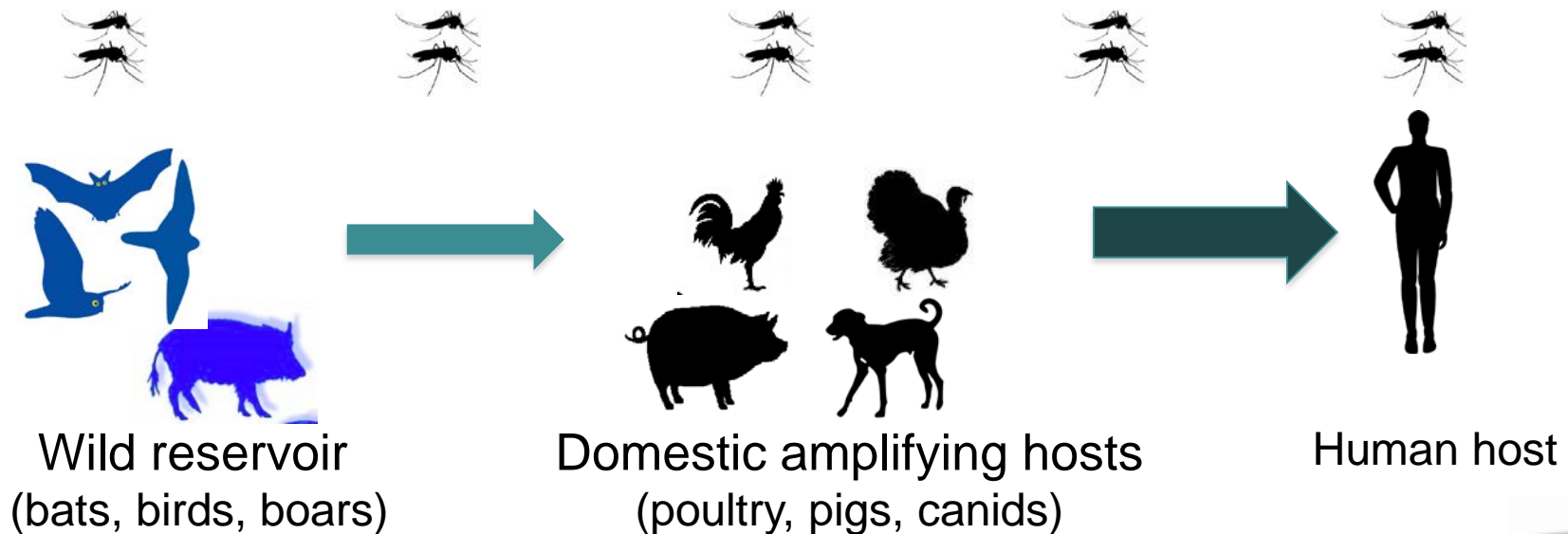
For selected zoonotic RNA viruses w/ epidemic potential representing main transmission routes

From the main reservoirs, intermediate amplifying hosts and vectors

Transmission Routes

- Respiratory (IAV, *MERS-CoV*)
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Reservoirs and Vectors



- 1) Which key factors (considering environment, ecology, anthropology, virus evolution and virus-host interplay) are associated with the highest risk of virus emergence?**
- 2) What is the impact of the transmission route on viral evolutionary trajectories and cross-species transmission?**
- 3) How do viral and host determinants interact to favour/limit the potential for cross-species transmission and adaptation to a new host?**
- 4) Which intervention strategies limit most effectively cross-species transmission and spread in the new host?**

Stability in the environment

Role of environmental compartment for **IAV** transmission

(Breban *J Math Biol* 2012)

IAV survival influenced by host cell origin and nature of the HA

(Shigematsu *et al. Influenza Other Respir Viruses*, 2014; Sawwo *et al PLoS ONE* 2014)

Environment, wild, domestic animals and food-chain

Screening of environment, wild hosts, domestic pigs for **HEV**

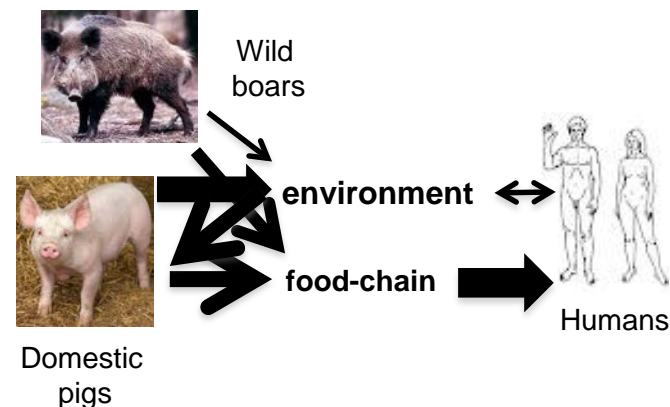
in Sweden, Italy and France and comparison w/ human data

Insights into HEV spatio-temporal spread, and transmission

Importance of anthropological factors (role of food chain)

(Lin *et al J Gen Virol* 2014; Monne *et al Epidemiol Infect* 2014;

Garbuglia *et al EID* 2013; Pavio *et al EID* 2014)



Animal density and movement

LYS in bat colonies affected by colony size, species number

Bat species *M. schreibersii* serves as a regional reservoir

Inter-annual variations in EBLV-1 seroprevalence explained by differences in behavior ecology and population dynamics

Incubation- and immune-period durations, most relevant drivers of virus persistence.

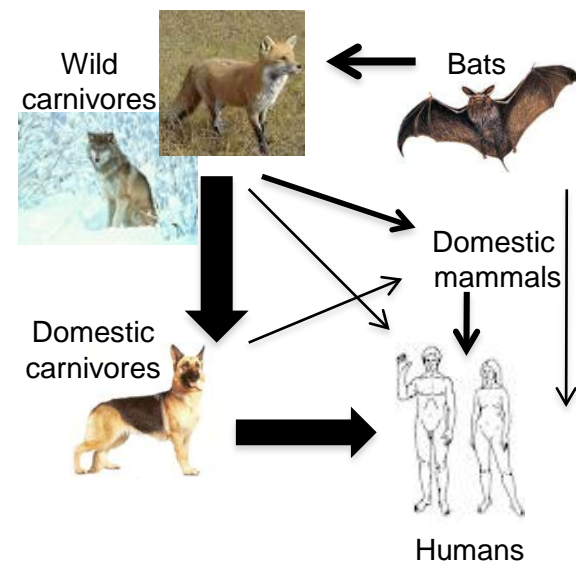
(Serra-Cobo et al PLoS One. 2013 ; Pons-Salort et al. PLoS ONE 2014)

Genetic structure of animal populations

Genetic structure of Red fox subpopulations in Northern Italy and partial segregation influenced geographical spread of CDV and rabies.

Importance of migrant individuals and ecological and physical corridors in disease dynamics

(Fusaro A et al Infect Genet Evol. 2013 ; Nouvellet P et al 2013 PLoS One)



Computational methods for viral evolutionary inference for phylogeographic applications.

Inform source and spread of the viruses

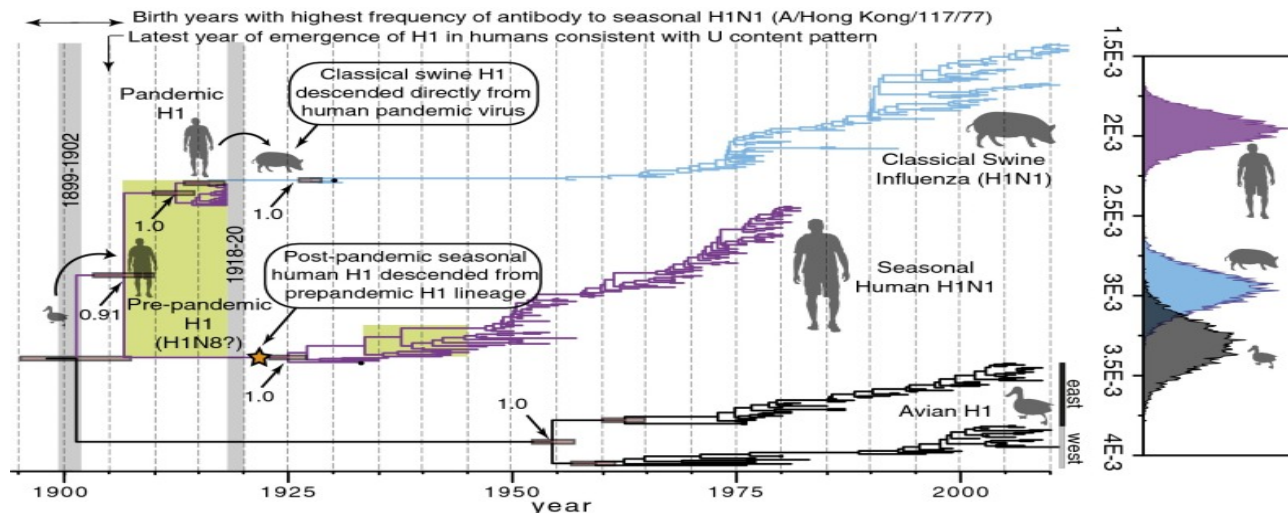
Source and spread of **HP avian IAV** H7N1 and H7N3 in Northern Italy (199-2001) – role of mutations conferring fitness advantage (*Monne et al JVI 2014*)

Genesis and source of Influenza A(H7N9) in China (*Lam et al Nature 2013*)

Times of divergence of **JEVr** ancestral lineages and dispersal from the Old to the New World or, northward or eastward across the Old World (*Moureau et al. PLoS ONE 2015*)

Trace cross-species transmission and emergence

1918 IAV arose via reassortment between a preexisting human H1 lineage and an avian virus (*Worobey et al PNAS 2014*)



Computational methods for viral evolutionary inference for phylogeographic applications.

Simulate real-time estimates of evolutionary rate, date of emergence
and intrinsic growth rate (R_0)

MERS-CoV (*Cotten et al. Lancet 2013; Cauchemez et al Lancet ID 2014*)

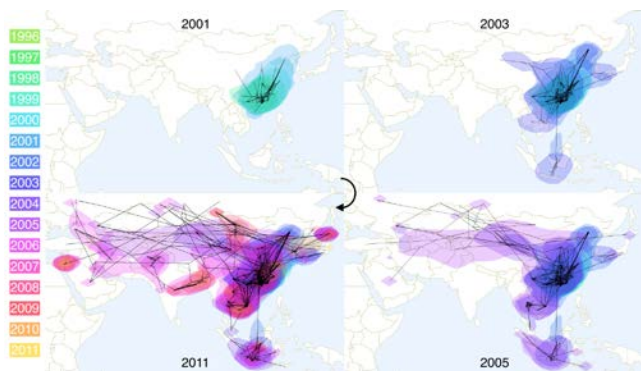
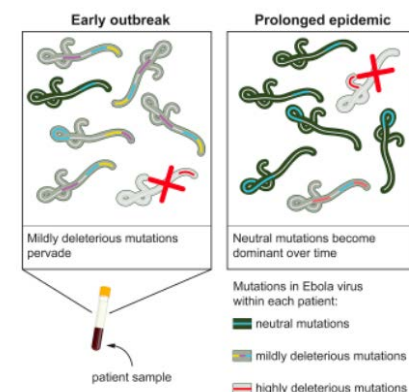
EBOV (*Dudas & Rambaut Plos Curr 2014; Gire et al. Science 2014; Park et al. Cell 2015*)

Examine drivers of global spread

Avian influenza A(H5N1) (*Trovao et al Mol Biol Evol 2015*)

Pandemic influenza A(H1N1)pdm09

Seasonal influenza A(H3N2) (*Bedford et al eLife 2014; Lemey et al PLoS Path 2014*)



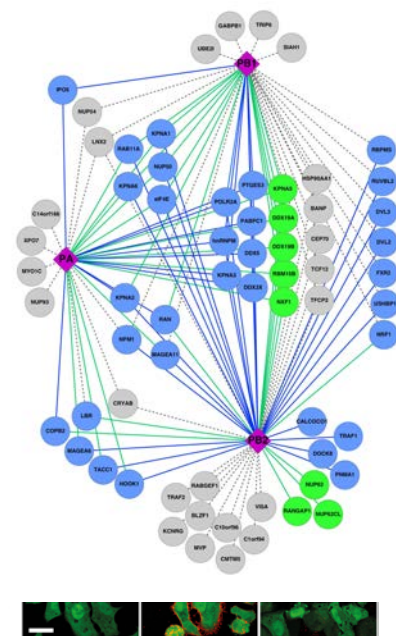
Molecular determinants of replication efficiency, pathogenesis and transmissibility

Intrinsic within host variability of **IAV** and link w/ pathogenesis (Selleri et al. CMI 2012)

Molecular determinants for **IAV** cross-species transmission, adaptation from avian to mammalian hosts, and airborne *transmission* (Wendel et al. JVI 2015; Czudai-Matvich et al JVI 2014; Linster et al Cell 2014)

Molecular determinants of virulence of **JEV** genotype 5 (de Wispelaere et al. JVI 2015)

Interactomics and proteomic approaches for the identification of host factors involved in viral infection (Munier et al Mol Cell Proteomics 2013; Rogee et al. JVI 2014)



Impact of innate immunity

Mechanisms of innate immune response and immune evasion

Rabies (Luco S et al PLoS Pathog. 2012; Wiltzer et al. J Virol 2012; Wiltzer et al. JID 2014)

WNV (Bordii et al J Biol Regul & Hom Agents 2014)

IAV (Ocana-Macchi et al. Virology 2012)

Impact of adaptive immunity

Cellular and humoral cross-immunity against **H3N2v IAV** (Agrati et al PLoS ONE 2014)

Protective properties of anti-NA antibodies (Halbherr et al JVI 2015)

Vaccine candidates

Recombinant vaccines (JEV) (*de Wispelaere et al. PLoS NTD 2015*)

Attenuated strains through random codon re-encoding

Mapping methods and modelling to identify high risk situations, dynamics of outbreaks and impact of intervention strategies

Rabies

IAV

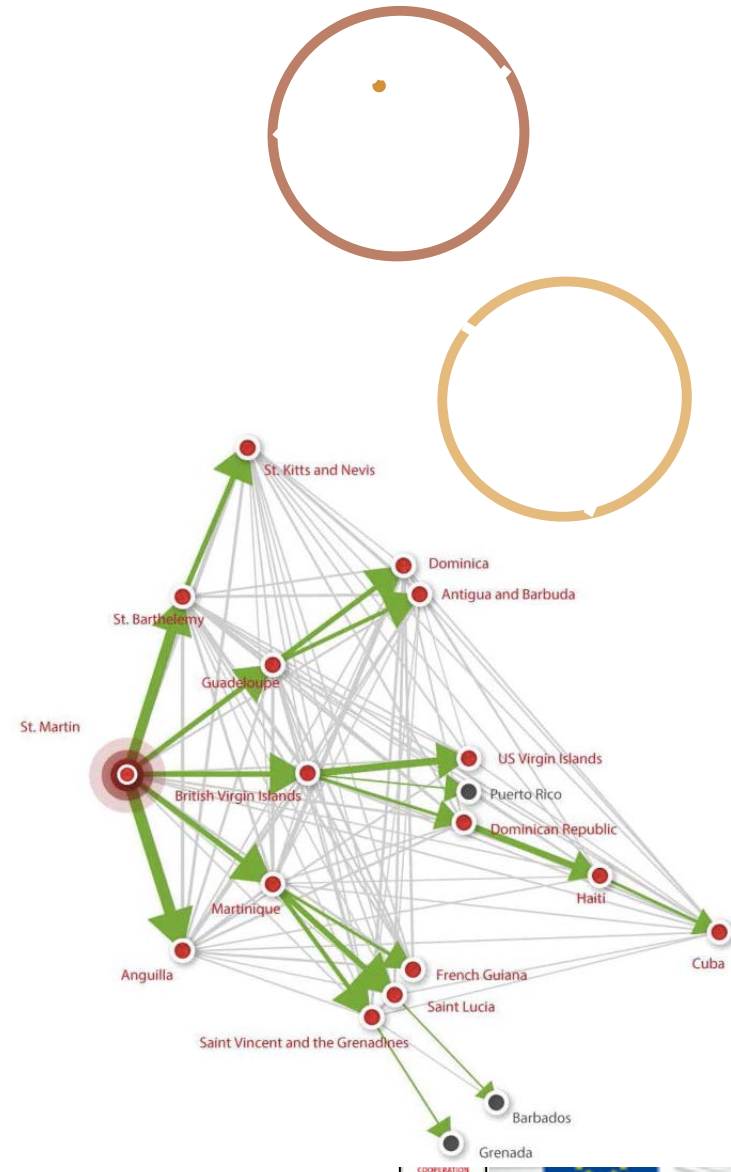
H1N1pdm09 (*Apolloni et al BMC Inf Dis 2013; Poletto et al. J Theor Biol 2013*)

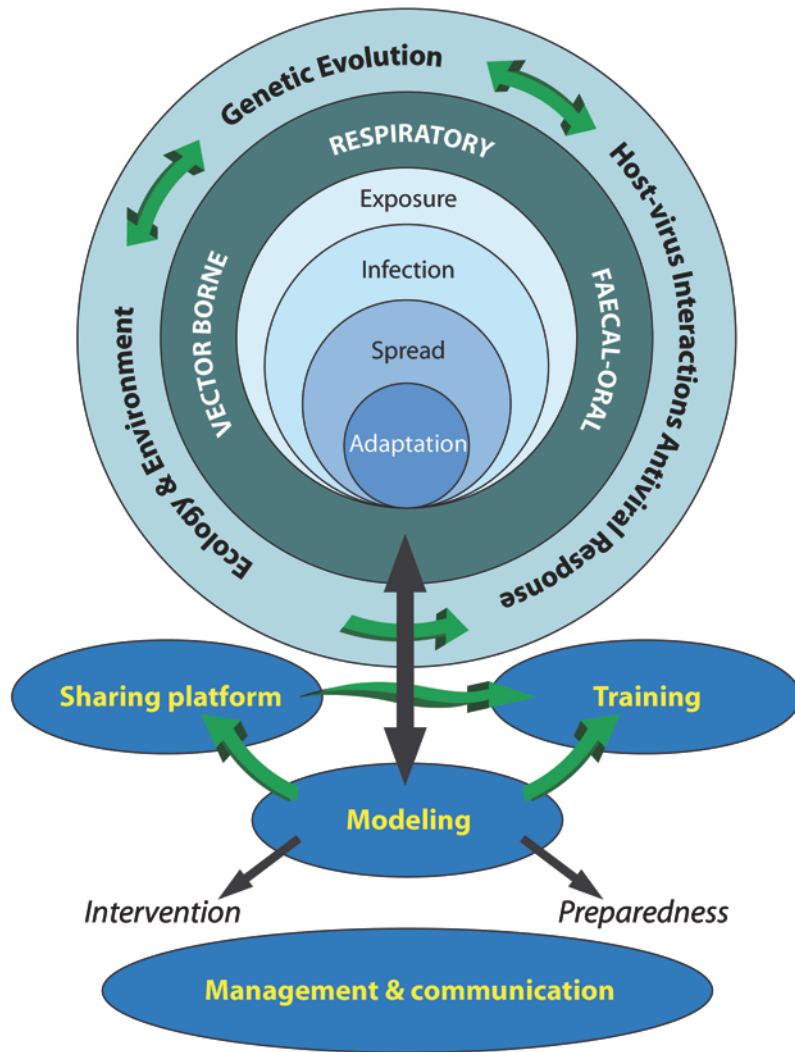
H3N2v ; H7N9 (*Cauchemez et al. PLoS Med 2013; Kucharski et al. EID 2015; Kucharski et al PLoS Curr 2014*)

MERS-CoV (*Breban et al. Lancet. 2013; Cauchemez S et al.. Euro Surveill. 2013; Lessler et al PLoS Curr 2014*)

EBOV (*WHO Ebola Response Team N Engl J Med 2014; WHO Ebola Response Team N Engl J Med 2014; Faye et al. Lancet ID 2015*)

CHIKV (*Cauchemez et al. EuroSurv 2014*)





Data sharing platform

Based on model and accession rules of EpiFlu2 database



Collaborations



Isabel Minguez-Tudela
(1956-2011)



Isabel was a senior scientific officer at DG Research and Innovation at the European Commission and throughout the years has supported research with a “One Health” vision, with special attention to training young scientists operating with an interdisciplinary approach

Training courses

- *Zoonotic features of IAV, HEV, JEVr, LYS*

Workshops and hands-on

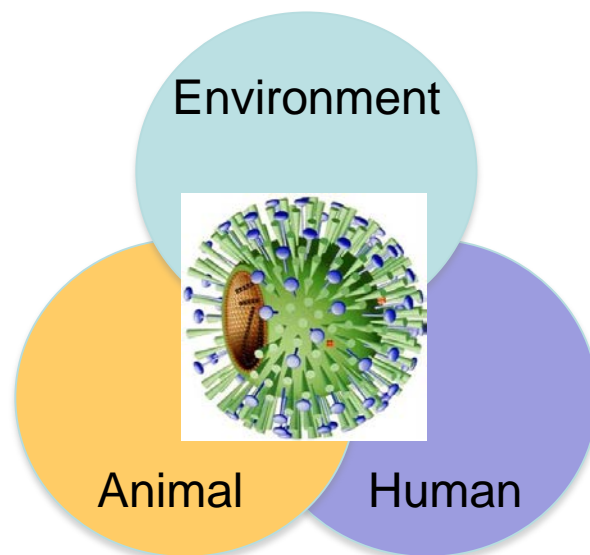
- *Virus evolution and phylogeny*
- *Rabies hands-on course (WHO, IP int network)*

e-learning activities

- *(Bourhy et al. Bull WHO 2015)*
- **Scientist exchange program**

- Ecologic, epidemiologic, virologic or host factors that condition virus maintenance and spread in local ecosystems - Mapping methods for animal densities & behaviours
- Extent and drivers of viral diversity in Europe and globally
- Impact of viral population (quasispecies) structure on cross-species transmission potential and pathogenicity
- Factors that determine cross-species transmission and adaptation from animal reservoirs to domestic hosts and humans
- Viral/host determinants of change of vector, host susceptibility and/or pathogenicity
- Evolutionary epidemic and transmission models for risk assessment and contingency planning

ONE HEALTH Approach



Aknowledgments Consortium Partners

Partner	Institution	PIs	Country
1 (coordinator)	IP	<u>S.van der Werf</u> H. Bourhy JC.Manuguerra S. Cauchemez R. Breban	France
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11	UNIMAR	M. Matrosovich	Germany
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16	ISS	F. Ruggeri	Italy
17	UNIBO	V. Zambri	Italy
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19	GISAID	A. Hay	Germany



Thank you
for your attention

Kick-off Meeting – 22-23/11/2011 – Institut Pasteur