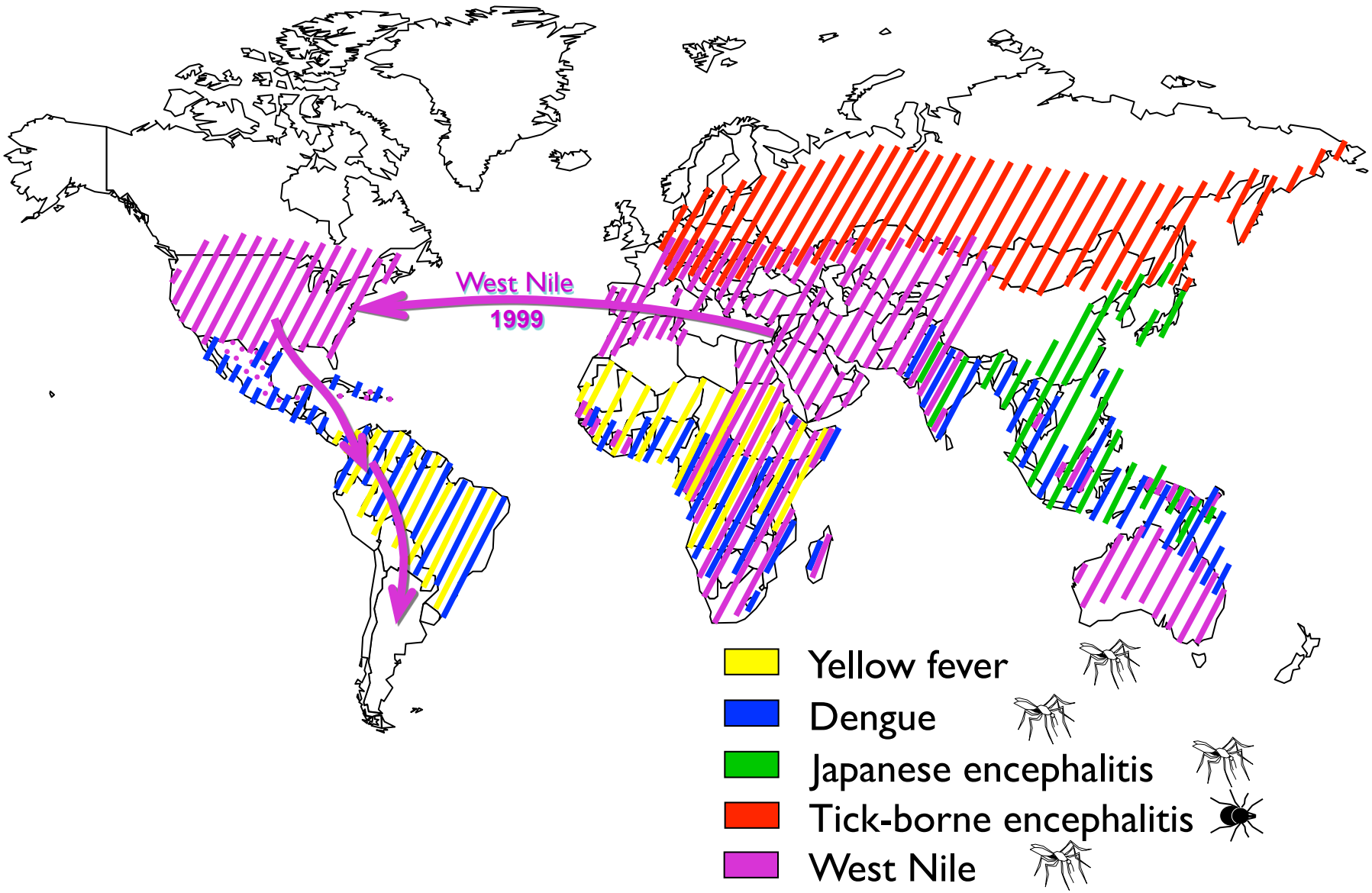
ICGEB: an intergovernmental organization

82 Signatory States
60 Member States
3 Components
39 Affiliated Centres

The Mandate
To provide a Centre of excellence for research and training in genetic engineering and biotechnology addressed to developing countries and economies in transition

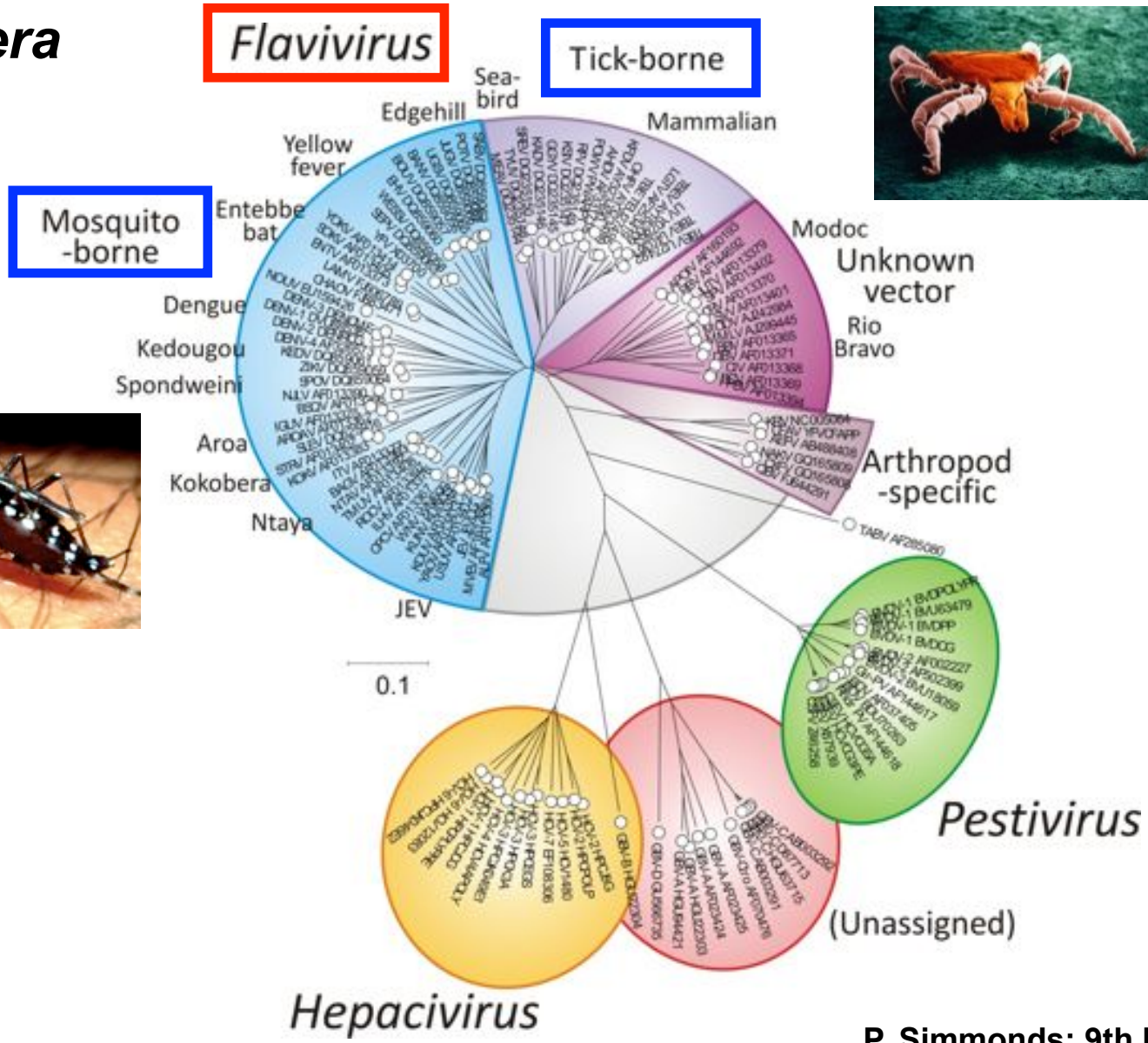
Developing knowledge

Flaviviruses



Family Flaviviridae

3 genera



P. Simmonds; 9th ICTV Report

Basic and translational research in virology @ICGEB

HIV-1
Flavivirus (Dengue, TBEV)
Papillomavirus
Rotavirus
Viral hepatitis (HCV, HBV, HEV)

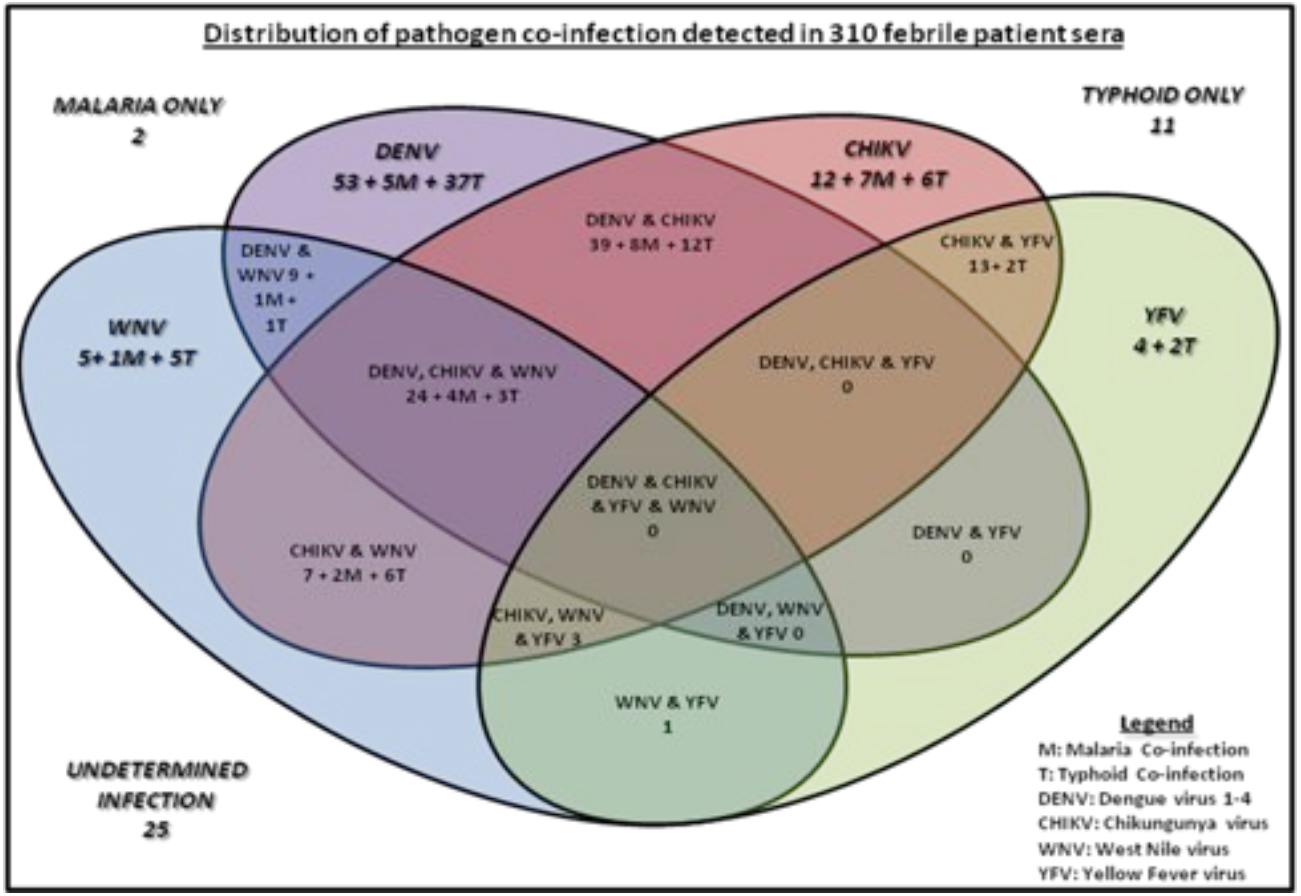
Translational:

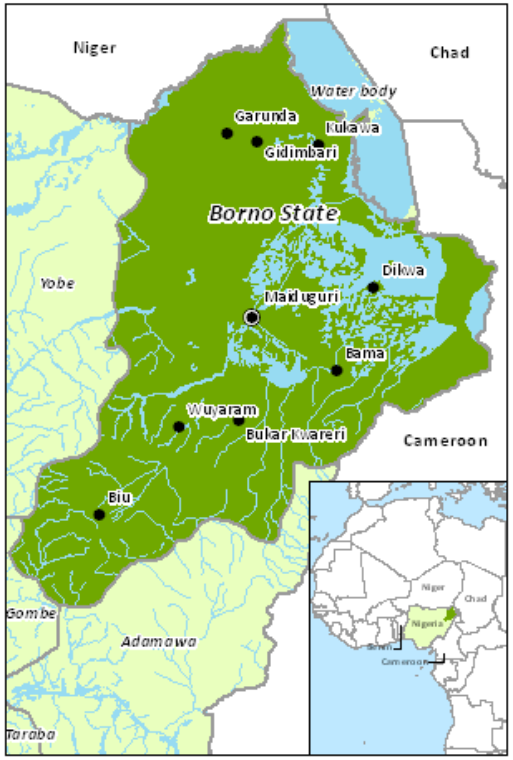
- Biotechnology transfer of biosilmilars's production knowhow to ICGEB Member States following patent and exclusivity expiry (i.e. EPO, IFN, G-CSF, Insulin).
- Development of novel recombinant proteins as inexpensive, highly sensitive and specific diagnostic intermediates for viral infections (i.e. Dengue, HIV, HCV).
- Vaccine development (i.e. Dengue, Malaria).

North-South Collaboration

ICGEB, Laboratory of Molecular Virology, Trieste ITALY
&
WHO National Polio /ITD Laboratory,
University of Maiduguri Teaching Hospital,
Borno State, NIGERIA

Establishment of a reference laboratory for Arbovirus infection surveillance

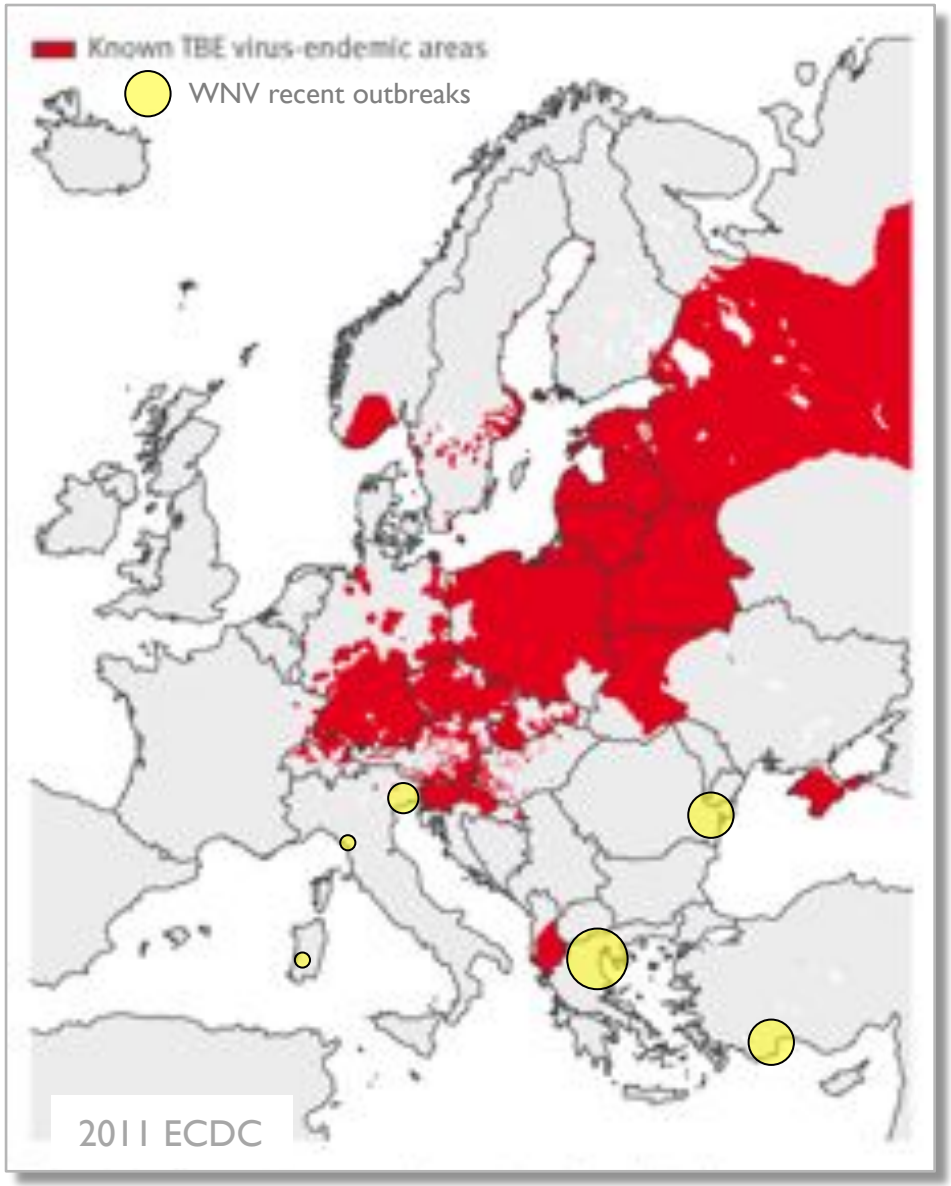




ACHIEVEMENTS

- Implementation of virological assays (IgM/ IgG ELISA, RT-PCR, PRNT);
- Exchange of knowhow and researchers;
- Survey of Arbovirus seroprevalence in 310 suspected febrile Malaria and Typhoid patients in Nigeria;

FLAVIVIRUS INFECTION IN EUROPE



TBEV

•Endemic Central Europe and Asia. In Italy present in Friuli Venezia Giulia and Trentino Alto Adige.

• The most important arthropod-borne viral disease in Europe. TBEV causes >2000 cases every year.

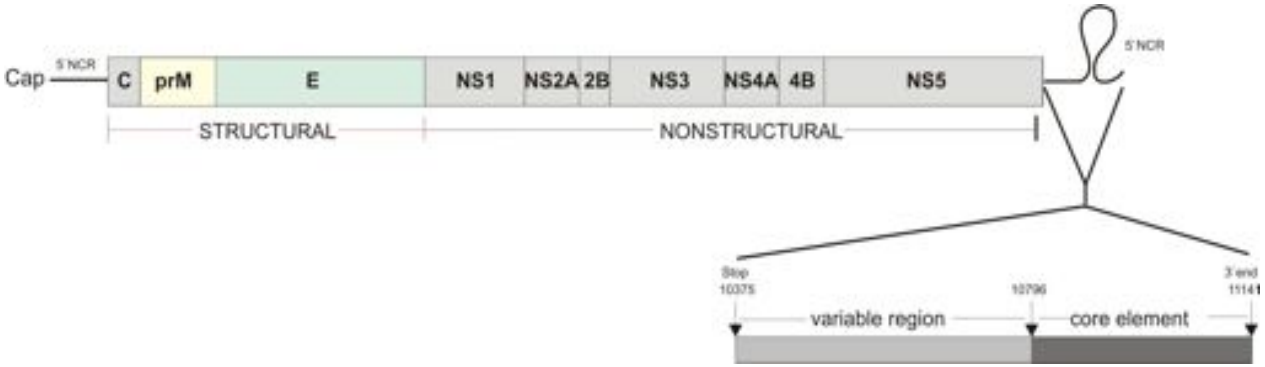
WNV

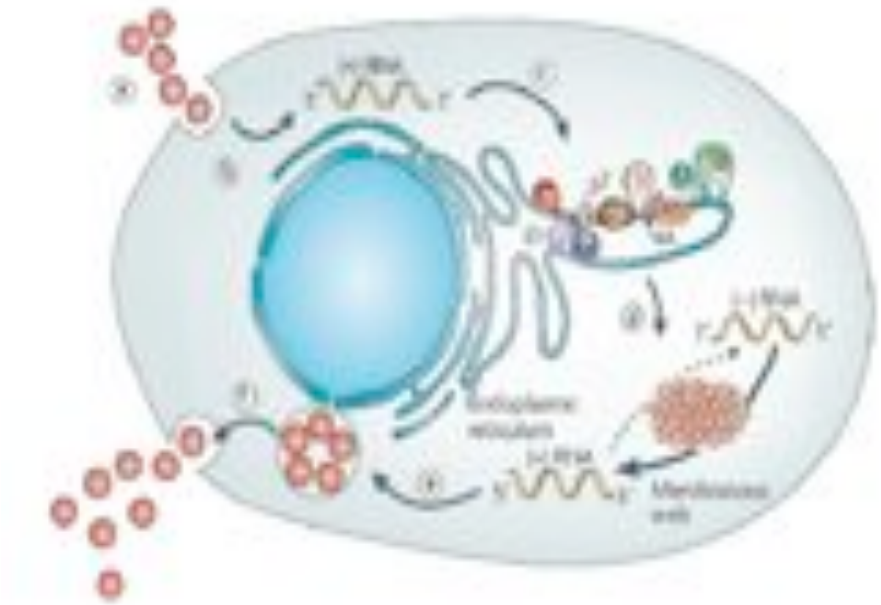
•Endemic in EU with seasonal outbreaks in horses and humans. Since 2008 increased WNV activity was reported in Southern EU, including human cases of WNV in Italy (Veneto/FVG), Hungary and Romania. During 2010, an outbreak of WNV was reported in Greece with over 260 human cases.

TBEV and WNV geographical distribution are expanding due to climatic, ecological and socio-political changes.

Numerosi casi importati di **DENV**.

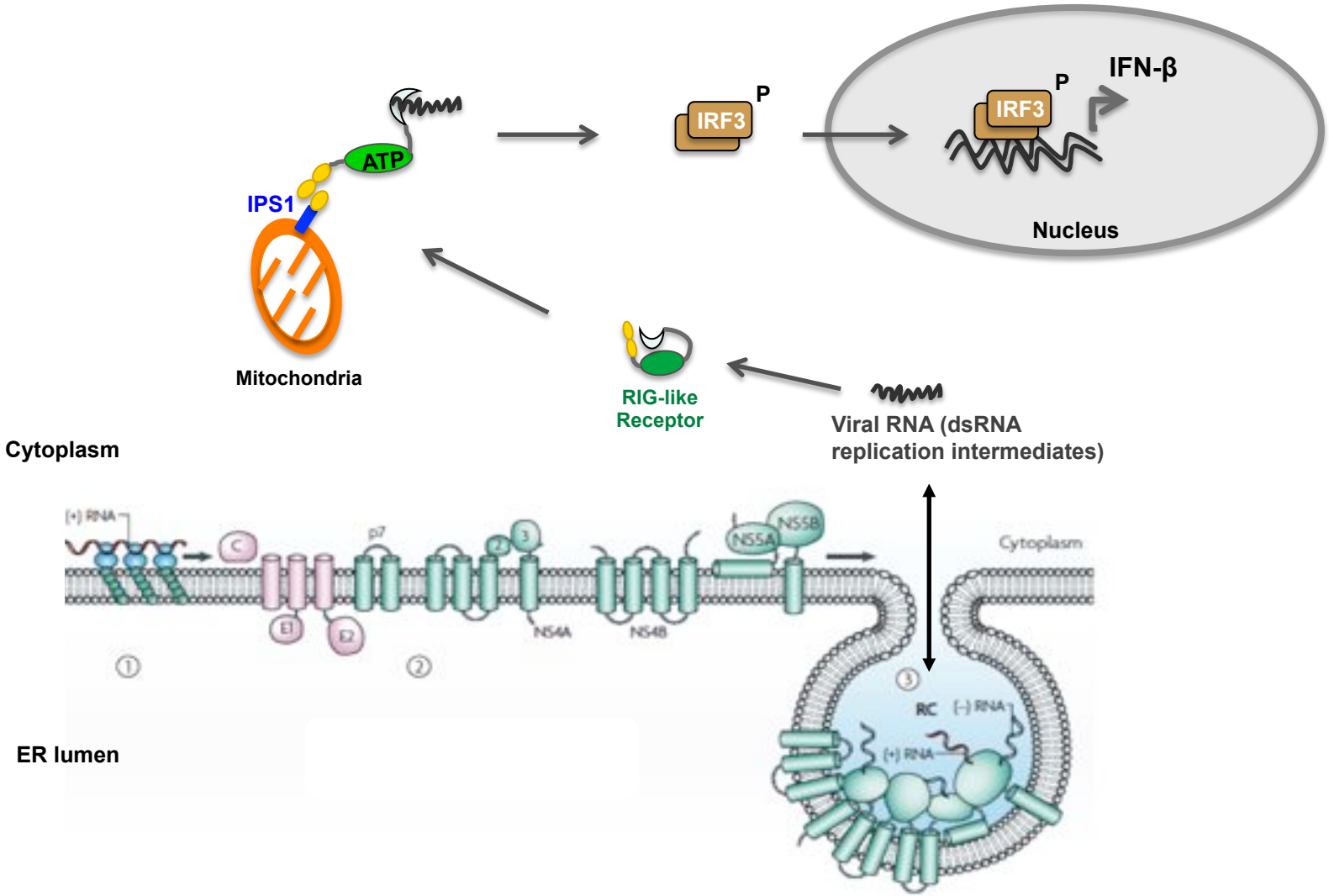
Flavivirus genome structure & life cycle



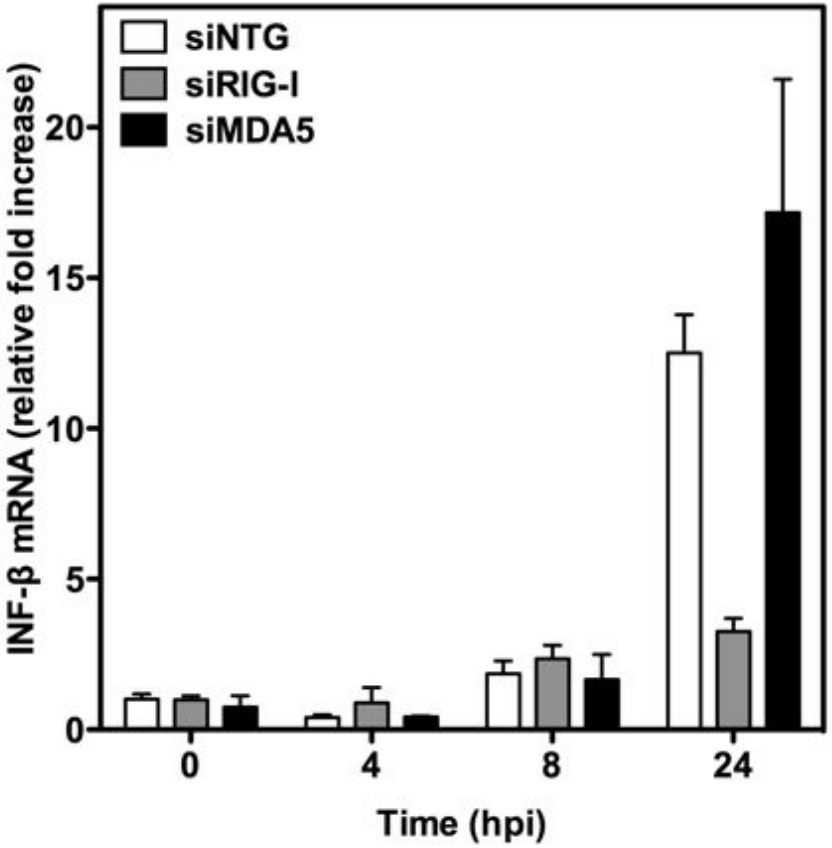


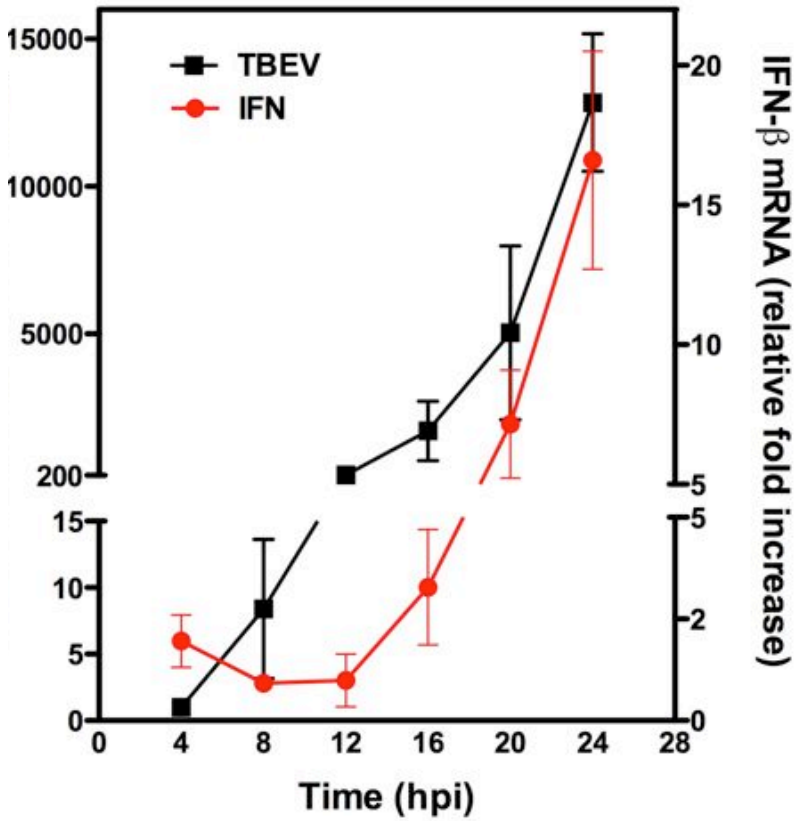
a) Virus binding and internalization
b) Uncoating
c) Translation and polyprotein processing
d) RNA replication is closely associated with rearranged and proliferated membranes
e) Packaging and assembly
f) Maturation and release

<u>Hypothesis</u>: Flaviviruses replicate in vesicles that protect viral RNA from intracellular innate immunity recognition

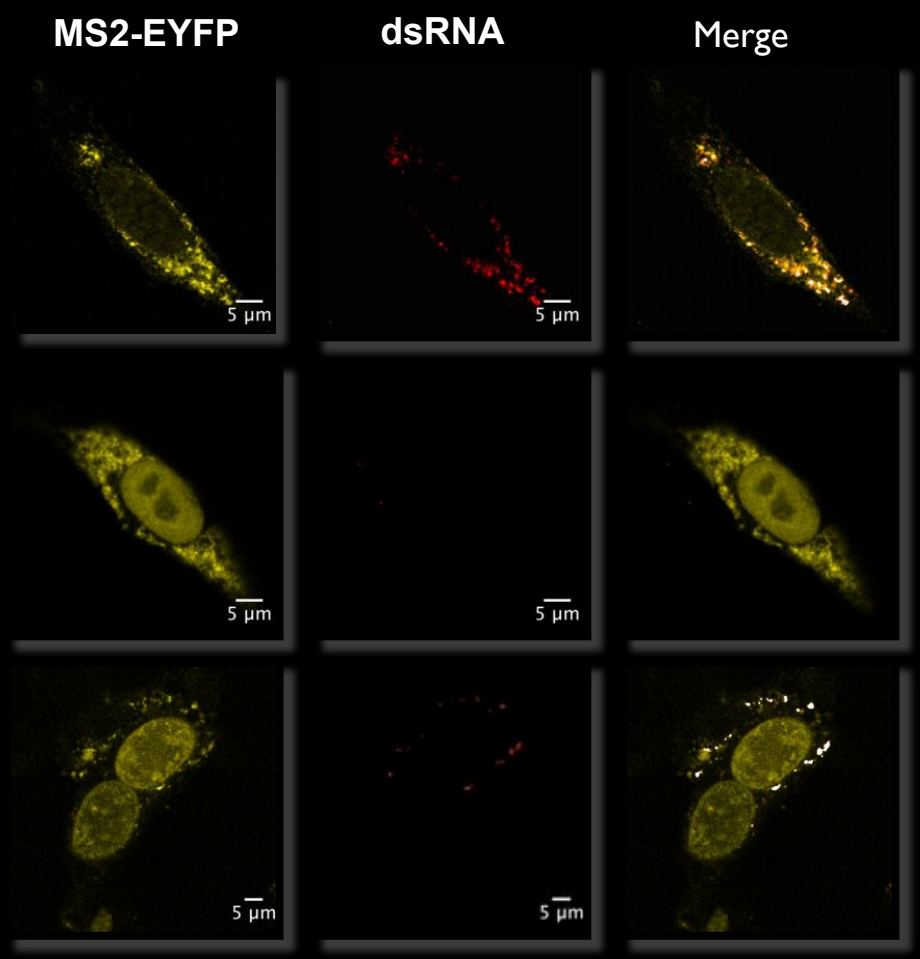


RIG-I dependent Induction of IFNβ by TBEV is delayed





TBEV RNA is protected by intracellular membranes



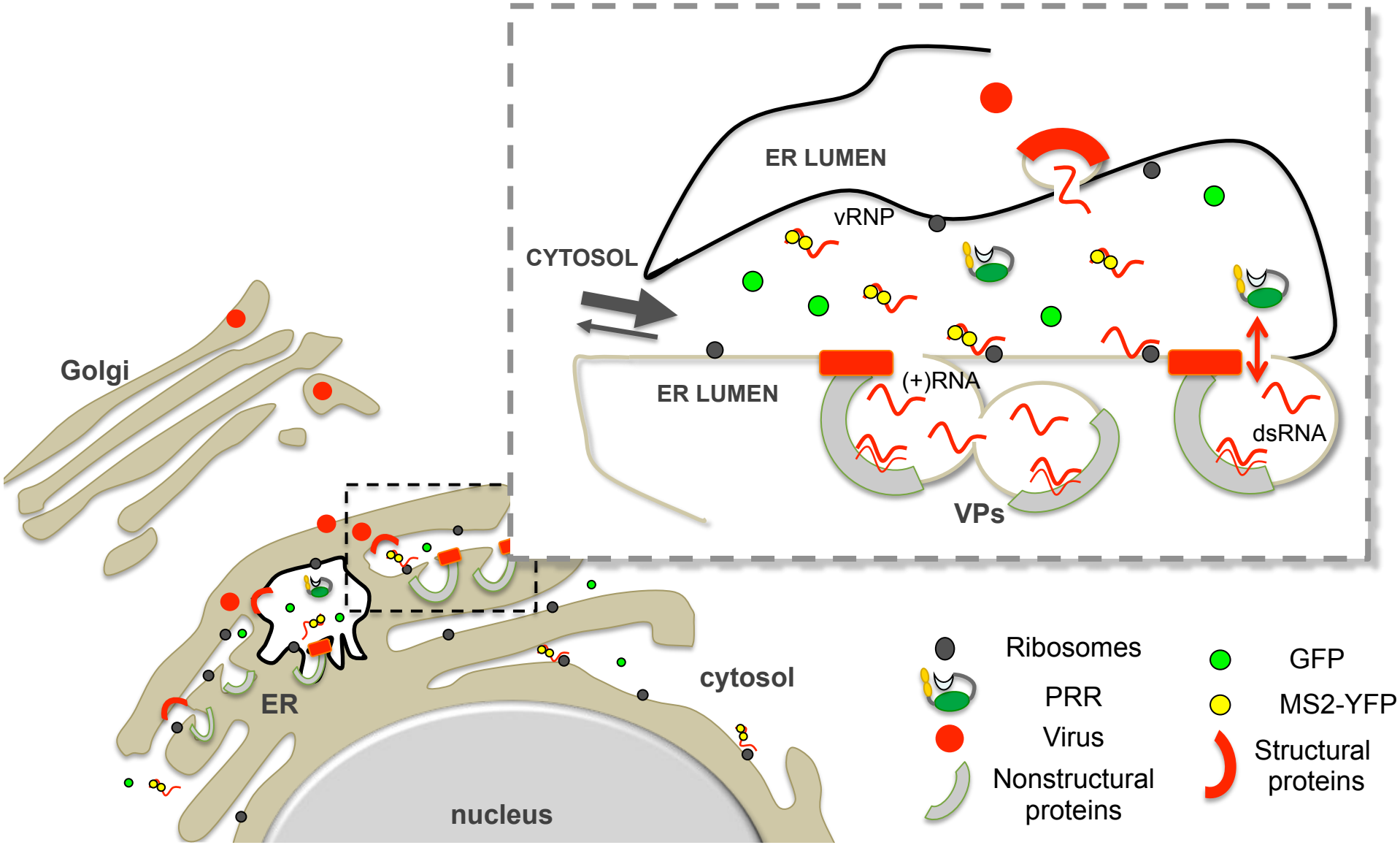
EYFP-MS2
TNd/ΔME_24xMS2
Digitonin>fix>Triton

EYFP-MS2
TNd/ΔME_24xMS2
Digitonin (no Triton)

EYFP-MS2
TNd/ΔME_24xMS2
Digitonin>RNAse>fix>Triton

SELECTIVE PERMEABILIZATION OF THE PLASMA MEMBRANE BY DIGITONIN TREATMENT

Compartment organization in Flavivirus infection: a working model



The Molecular Virology lab at the ICGEB

http://www.icgeb.org/molecular-virology.html

Current members:

A. Kula, postdoc
M. Bardina, postdoc
L. Miorin, postdoc
A. Albornoz, PhD
E. Cevik, PhD
R. Ellersich, undergrad

Past members:

A. Knezevich (Ospedali Riuniti, Trieste)
P. Maiuri (Curie, Paris)
G. Bartolomei (University of Zurich)
I. Vacca (Novartis, Siena)
M. Dieudonnè (Venezuela)
J. Guerra (University of Geneva)
C. Biancotto (IEO, Milan)
A. De Marco (EMBL, Heidelberg)
A. Nowordworska (ELETTRA, Trieste)
M.V. Falzacappa (IEO, Milan)
M. Baba (University of Maiduguri, Nigeria)

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ISS-AIDS, Italy
Beneficentia Stiftung, Lichtenstein
Fondo TS

ICGEB core facilities:

Fluorescence microscopy and related techniques (http://www.icgeb.org/fluorescence-microscopy.html)
Biosafety laboratory level 3 (http://www.icgeb.org/biosafety-level-3-laboratory-40bl341.html)

The 3rd ICGEB Workshop on Human RNA Viruses, Buenos Aires 3-5 April 2012