

Université de Strasbourg,
8 décembre 2023

UNIVERSITÉ
— PARIS-EST

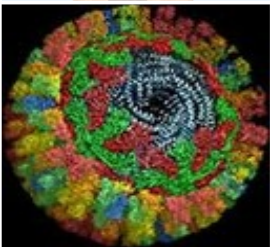
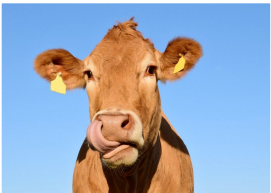
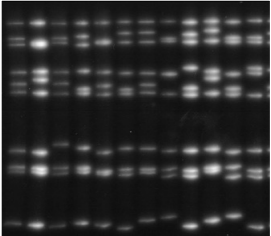
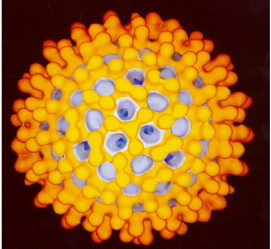
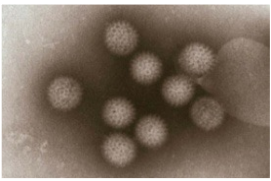
MASTER Virologie

Damien VITOUR



Les z'orbis : des z'arbos z'arbis des z'animaux

Laboratory for animal health,
UMR1161 Virology
Maisons-Alfort



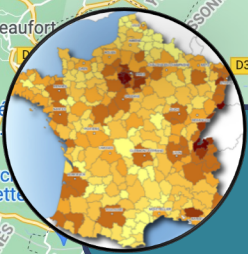
Laboratory for Animal Health, Maisons-Alfort

• Research

• Reference

• Expertise

• Surveillance



Virology Unit



UMR 1161 VIROLOGIE



Applicable immédiatement
14/02/2022

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Qualité / métrologie : Loeffler & Icube : ROMEY Aurore/ DUMAREST Marine **Bressou :** PIUMI François / FABLET Aurore & WATIER Fleur



Pascal PICCHIRALLO

Anses LSAn	FORMULAIRE LSA-NO-0046	Révision	09	1/1
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Many national and international mandates

Biology of Orbiviruses (BIOR) group

Damien Vitour



Grégory Caignard



Juliette Dupré



Marine Lemesle



Aurore Fablet



Pascal Dujardin

National Reference Laboratory



World Organisation
for Animal Health
Founded as OIE



Corinne Sailleau



Emmanuel Bréard



Stéphane Zientara



Mathilde Gondard



Lydie Postic



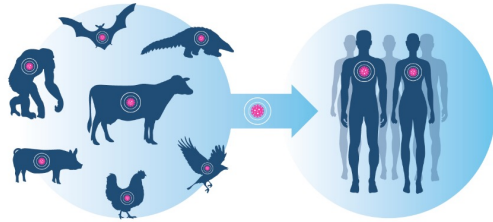
Mathilde Turpaud



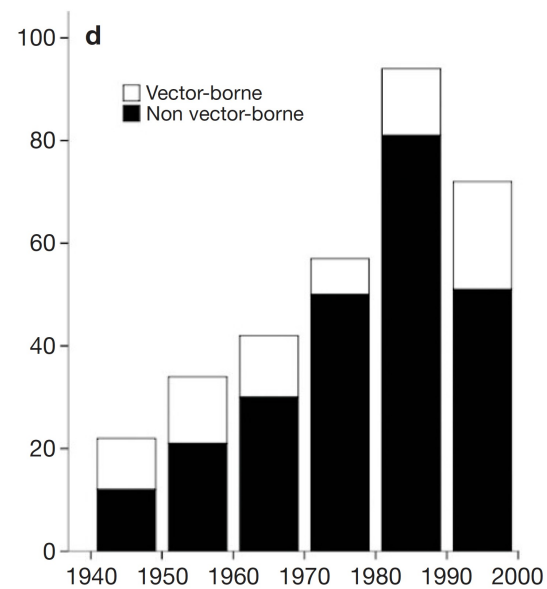
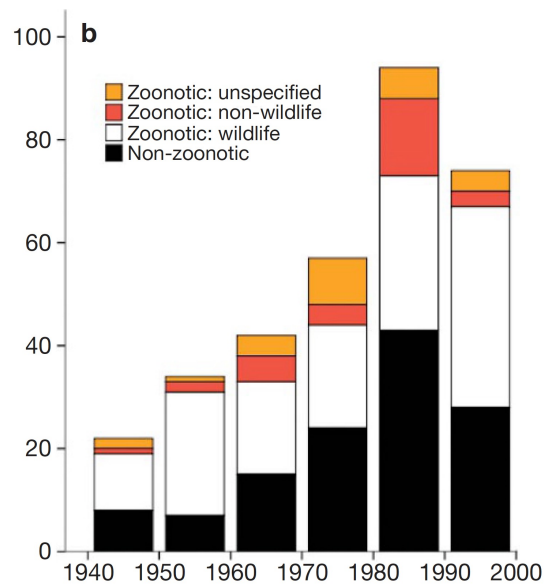
Philippine Toneatti



Emerging infectious diseases: a One Health issue



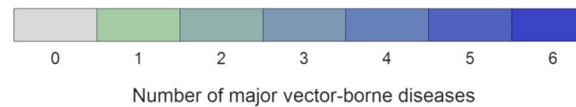
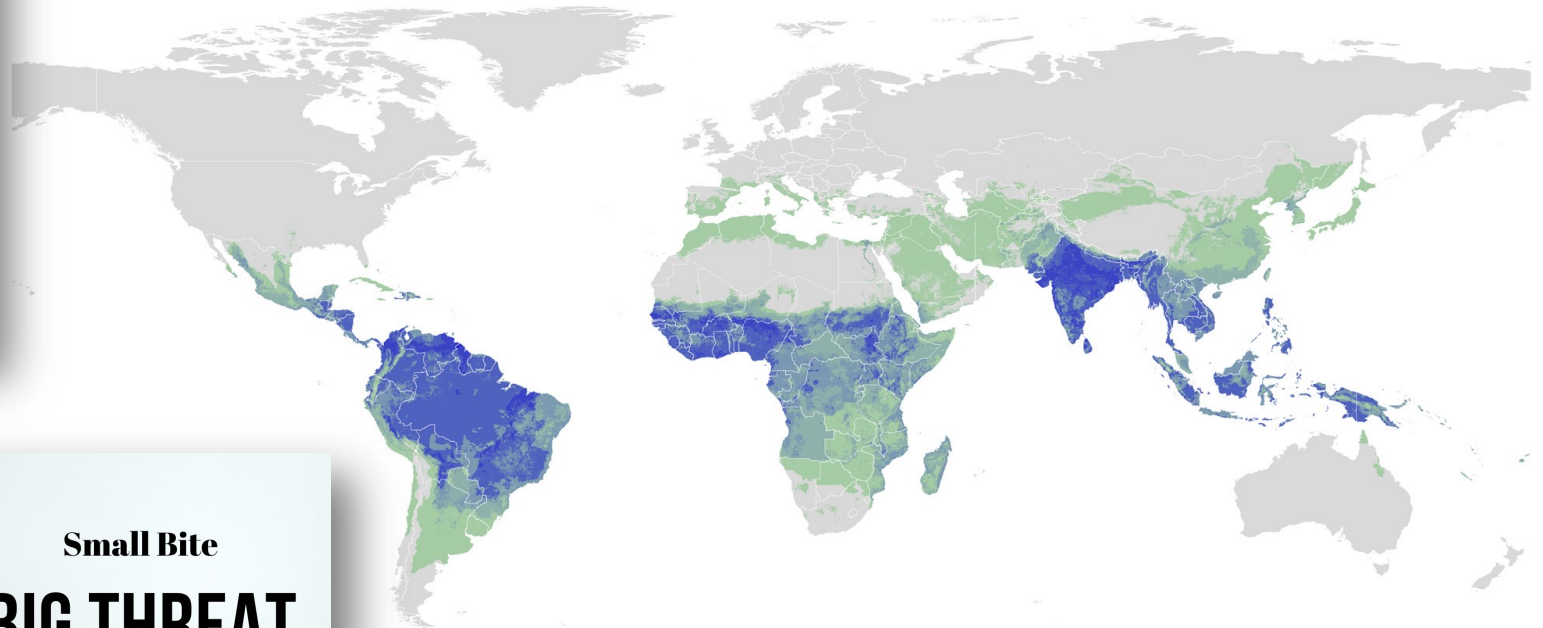
- **60%** of ID in humans are spread from **animals**.
- **VBD** account for $\geq 1/5$ of all ID.



Vector-borne diseases: the new threat ?



● **VBD** cause more than **700,000 deaths** annually.



Vector-borne diseases: the new threat ?

Le Parisien

À la une Île-de-France & Oise En continu Faits divers Politique Économie Société Sports Culture Étudiant Vidéos Guide Shopping Codes

Dengue : cinq minutes pour comprendre le nombre de cas particulièrement élevé cette année

Santé publique France recense à ce jour en France métropolitaine 41 cas autochtones de dengue, c'est-à-dire des personnes n'ayant pas voyagé récemment dans une zone de circulation du virus.



Le moustique-tigre est reconnaissable à ses rayures blanches et noires. DR

Midi Libre

Accueil > Santé

Alerte à la dengue : le nombre de cas explose en France, ce que l'on sait sur la situation



Les cas de dengue explosent en France. // ILLUSTRATION PIXABAY

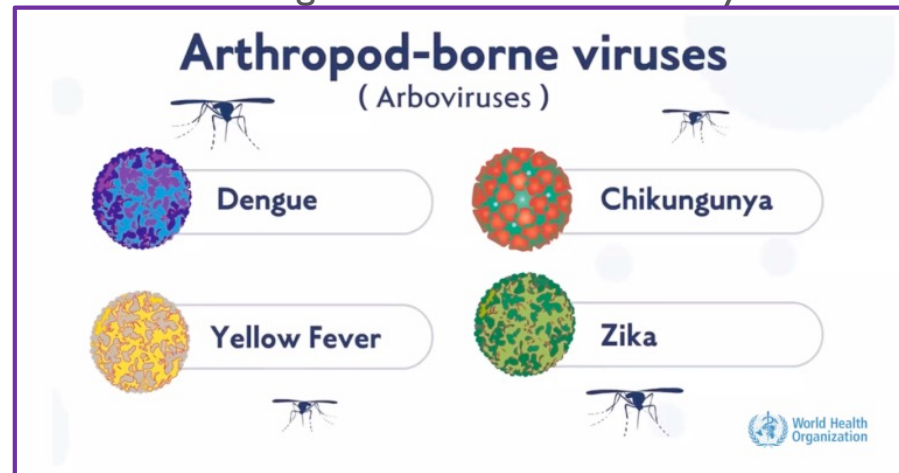
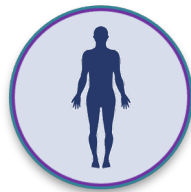


Aedes albopictus in France



Arthropod-borne viruses

Leading arbovirus diseases today



World Organisation
for Animal Health
Founded as OIE

- ✓ **Asfarviridae:** African swine fever
- ✓ **Togaviridae:** Equine encephalitis (EEE, WEE, VEE)
- ✓ **Flaviviridae:** West Nile
- ✓ **Nairoviridae:** Nairobi sheep disease
- ✓ **Phenuiviridae:** Rift Valley fever
- ✓ **Peribunyaviridae:** Schmallenberg
- ✓ **Rhabdoviridae:** Vesicular stomatitis
- ✓ **Sedoreoviridae:** Bluetongue, African horse sickness

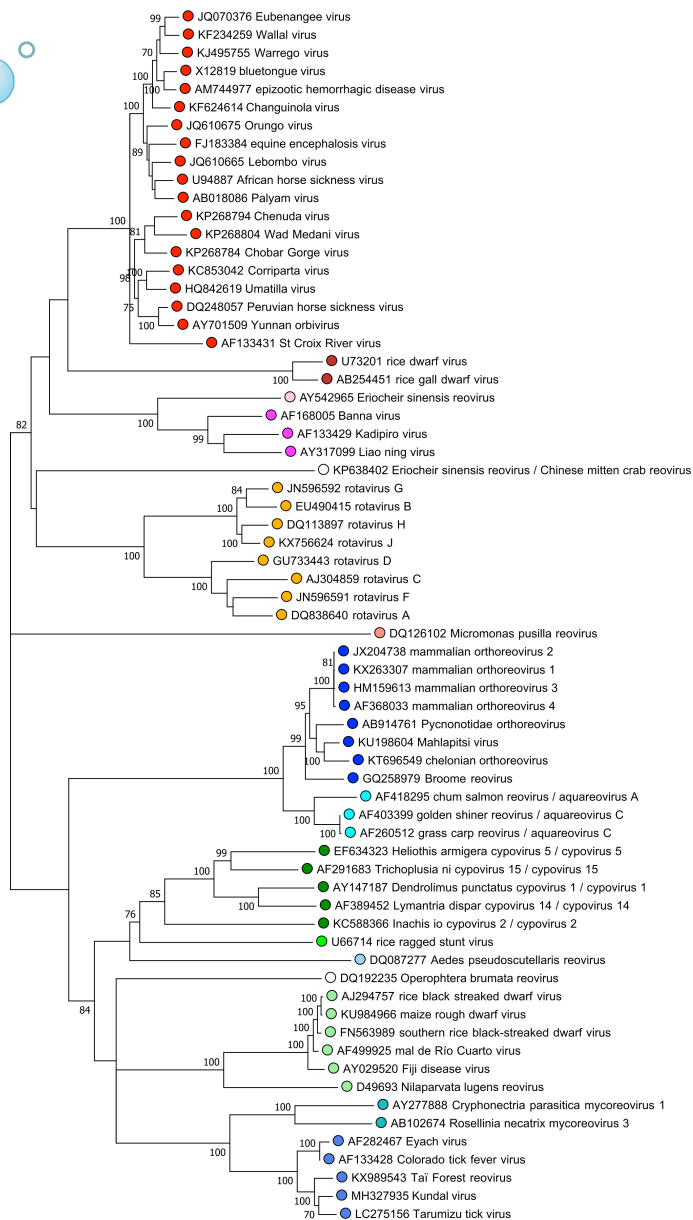
dsDNA

(+) ssRNA

(-) ssRNA

dsRNA

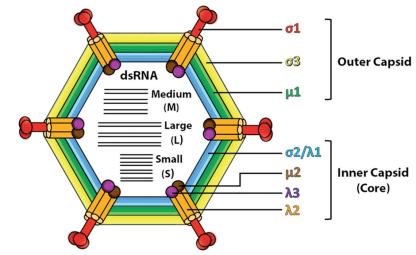
Reovirales order



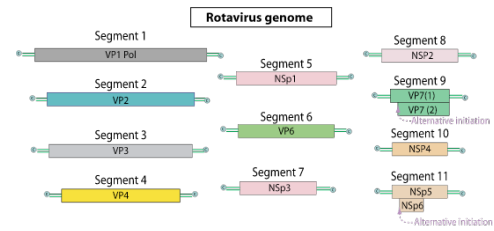
genus	family
<i>Orbivirus</i>	<i>Sedoreoviridae</i>
<i>Phytoreovirus</i>	<i>Sedoreoviridae</i>
<i>Cardoreovirus</i>	
<i>Seadornavirus</i>	
<i>Rotavirus</i>	<i>Rotaviridae</i>
<i>Mimoreovirus</i>	<i>Mimoreoviridae</i>
<i>Orthoreovirus</i>	<i>Orthoreoviridae</i>
<i>Aquareovirus</i>	<i>Aquareoviridae</i>
<i>Cypovirus</i>	<i>Cypoviridae</i>
<i>Oryzavirus</i>	<i>Spinareoviridae</i>
<i>Dinovernavirus</i>	
<i>Idnoreovirus</i>	
<i>Fijivirus</i>	<i>Fijiviridae</i>
<i>Mycoreovirus</i>	<i>Mycoreoviridae</i>
<i>Coltivirus</i>	<i>Coltivirus</i>

○ 2 families ; 15 genus

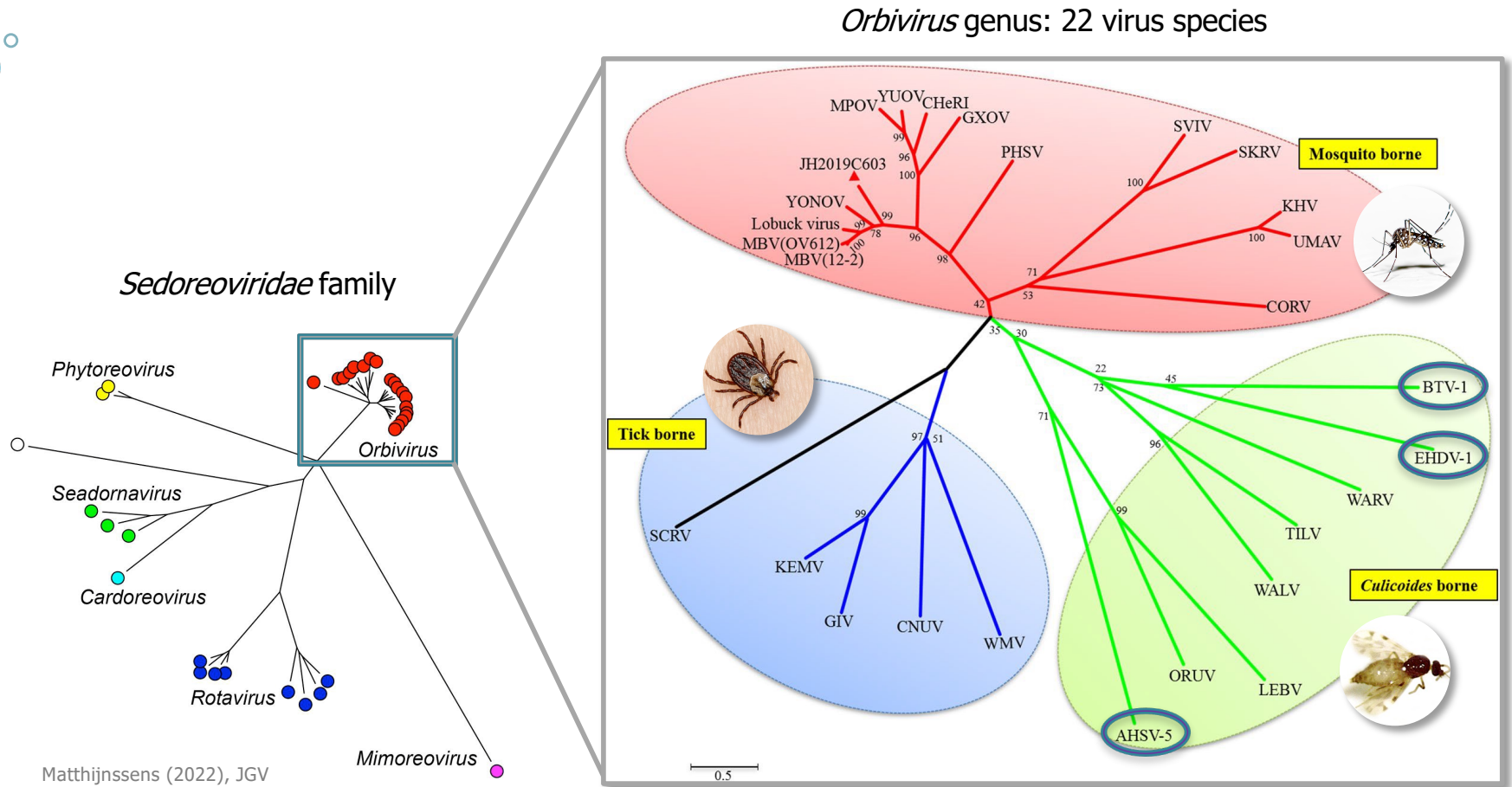
○ Unenveloped (double-layer)



○ dsRNA segmented genome



Orbivirus: a vector-borne genus



● 3 economically important diseases for livestock:

- **BTV:** Bluetongue virus
- **EHDV:** Epizootic hemorrhagic disease virus
- **AHSV:** African horse sickness virus

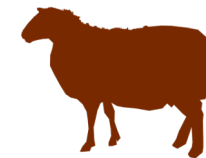


Bluetongue virus

Bluetongue disease



● 1st description: late 19th century, **South Africa.**



Mild to severe disease

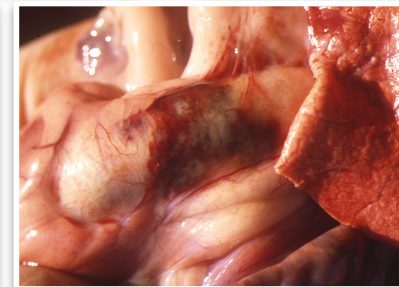
● Most **ruminants** can be infected.

Poorly symptomatic



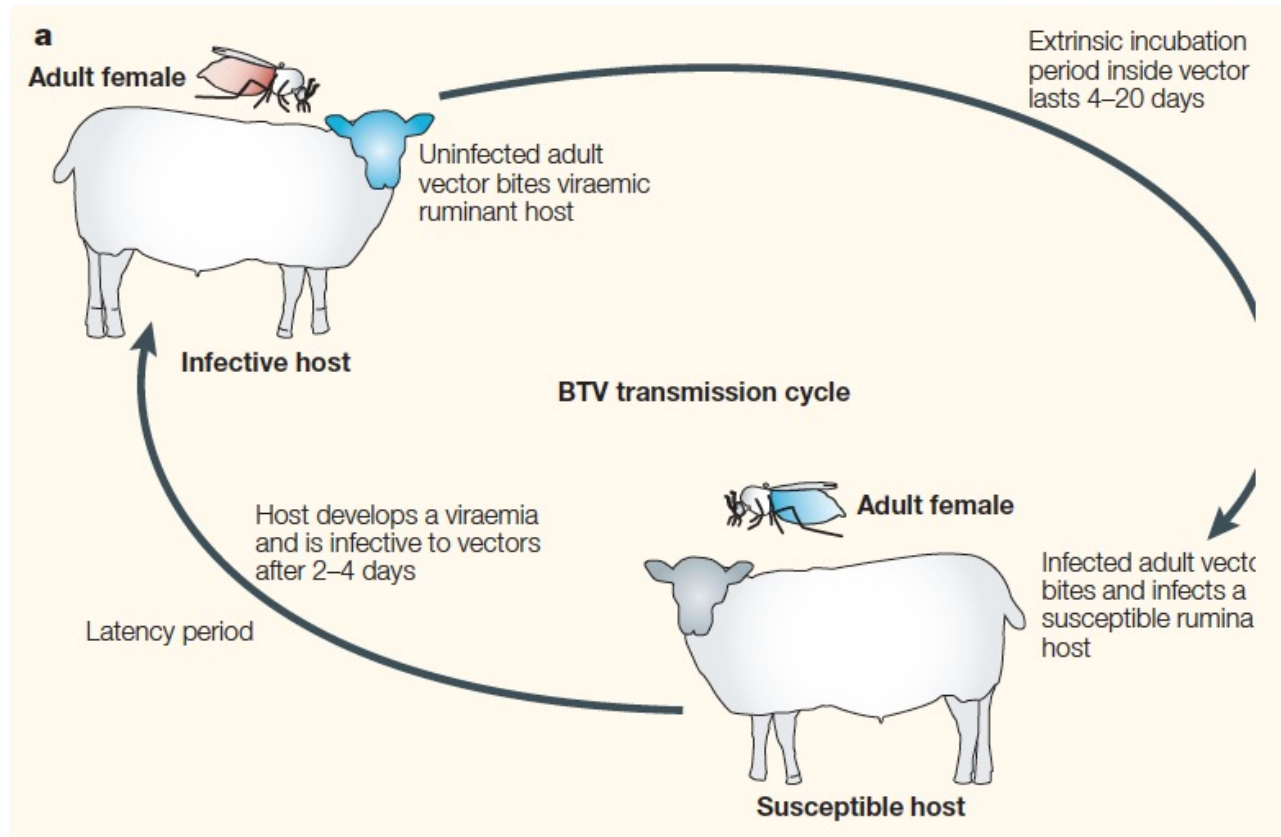
Bluetongue disease

- Fever, oedemas, nasal discharge, lameness, haemorrhages, ulcers, death...

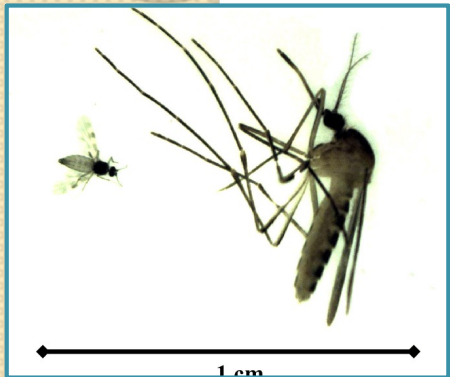


haemorrhage near the base of the pulmonary artery

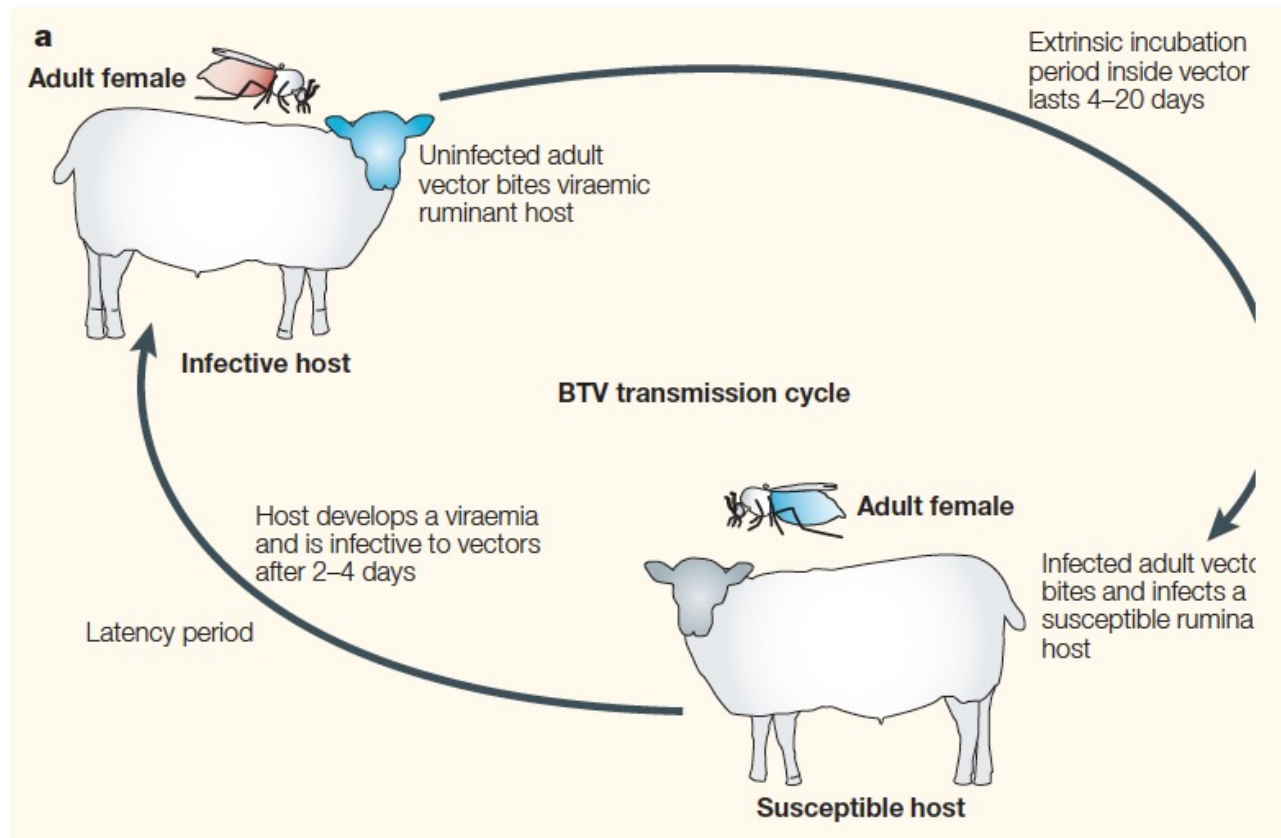
Transmission cycle



Transmission cycle

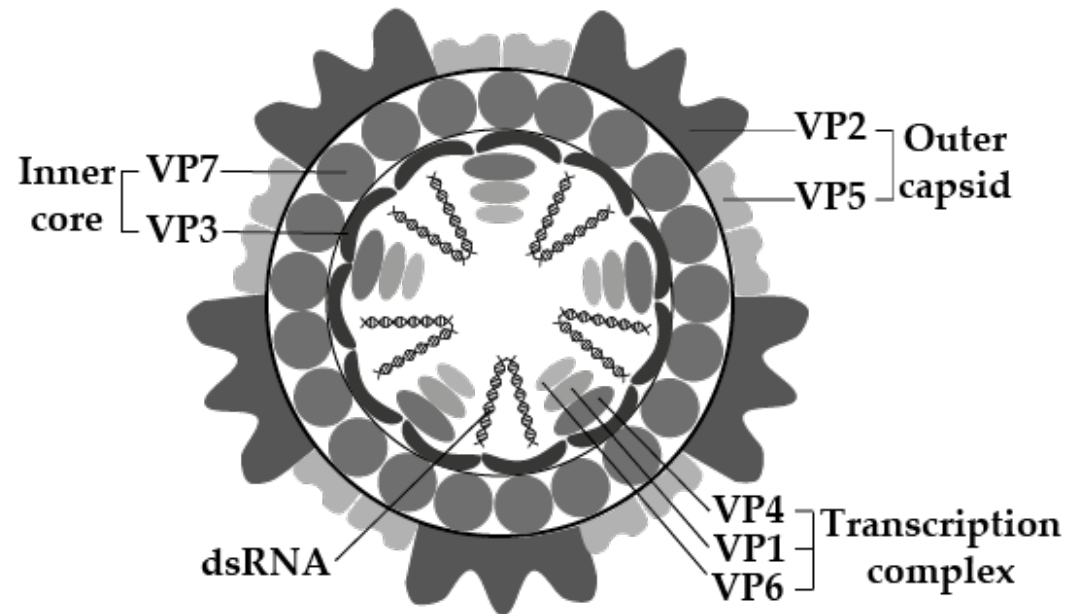


Culicoides midges: 1-3 mm

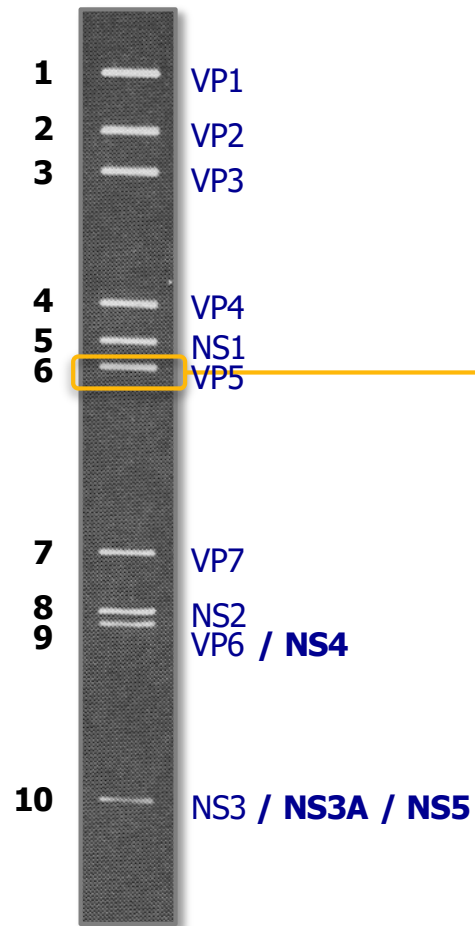


Viral particle

- 24 serotypes before 2008,
- **>35** serotypes today...



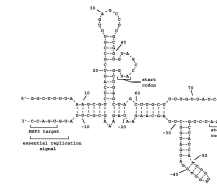
Genome organization



- ✓ 10 dsRNA segments (S1-10)
- ✓ 19.5 kb
- ✓ 3,965 bp (S1) to 765 bp (S10)



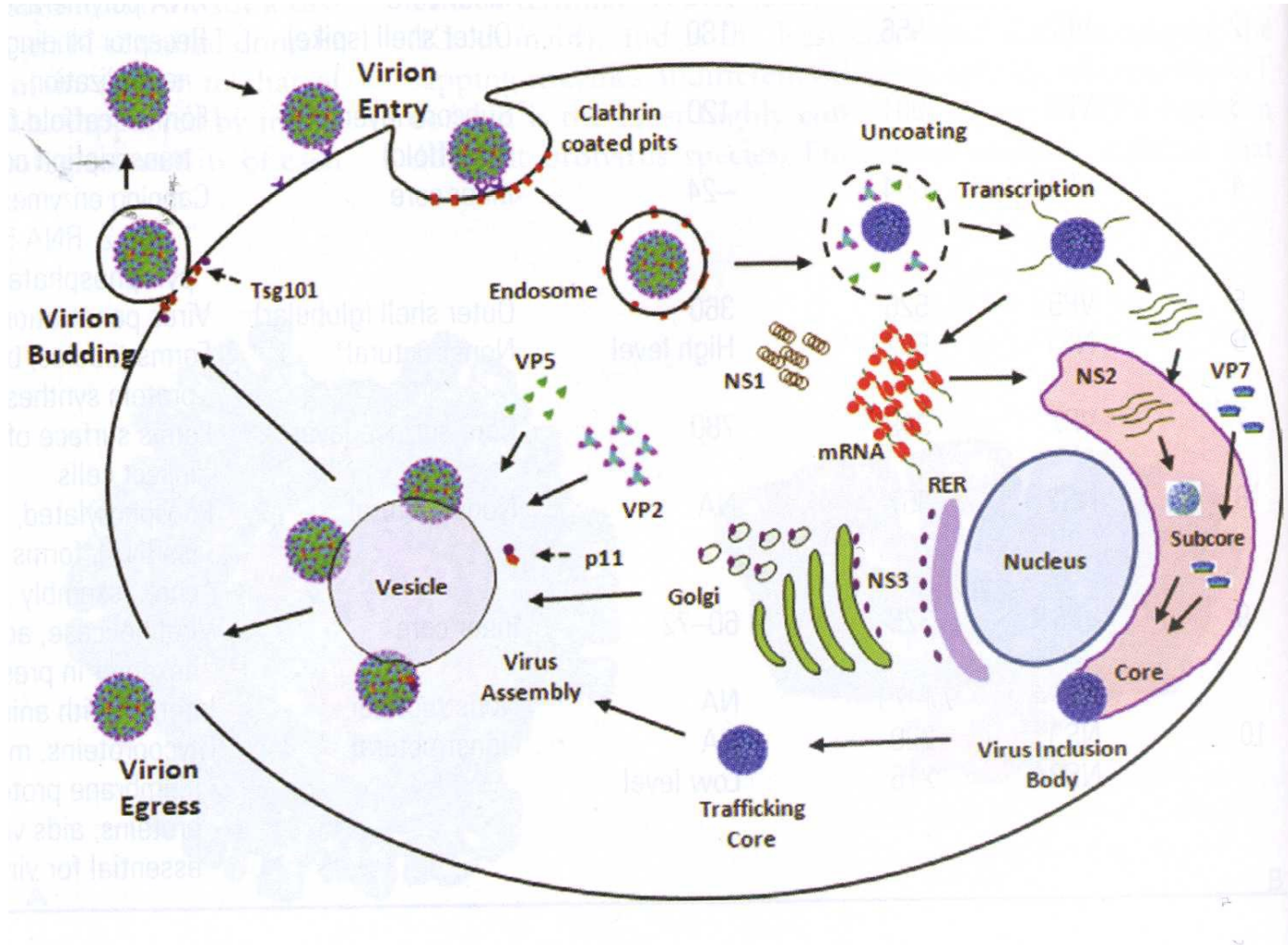
- ✓ 5' and 3' UTR ; **panhandle**
- ✓ Conserved **hexanucleotide** consensus sequence at 5' and 3' end (packaging, translation)
- ✓ The genomic RNA contains **5' cap** structure



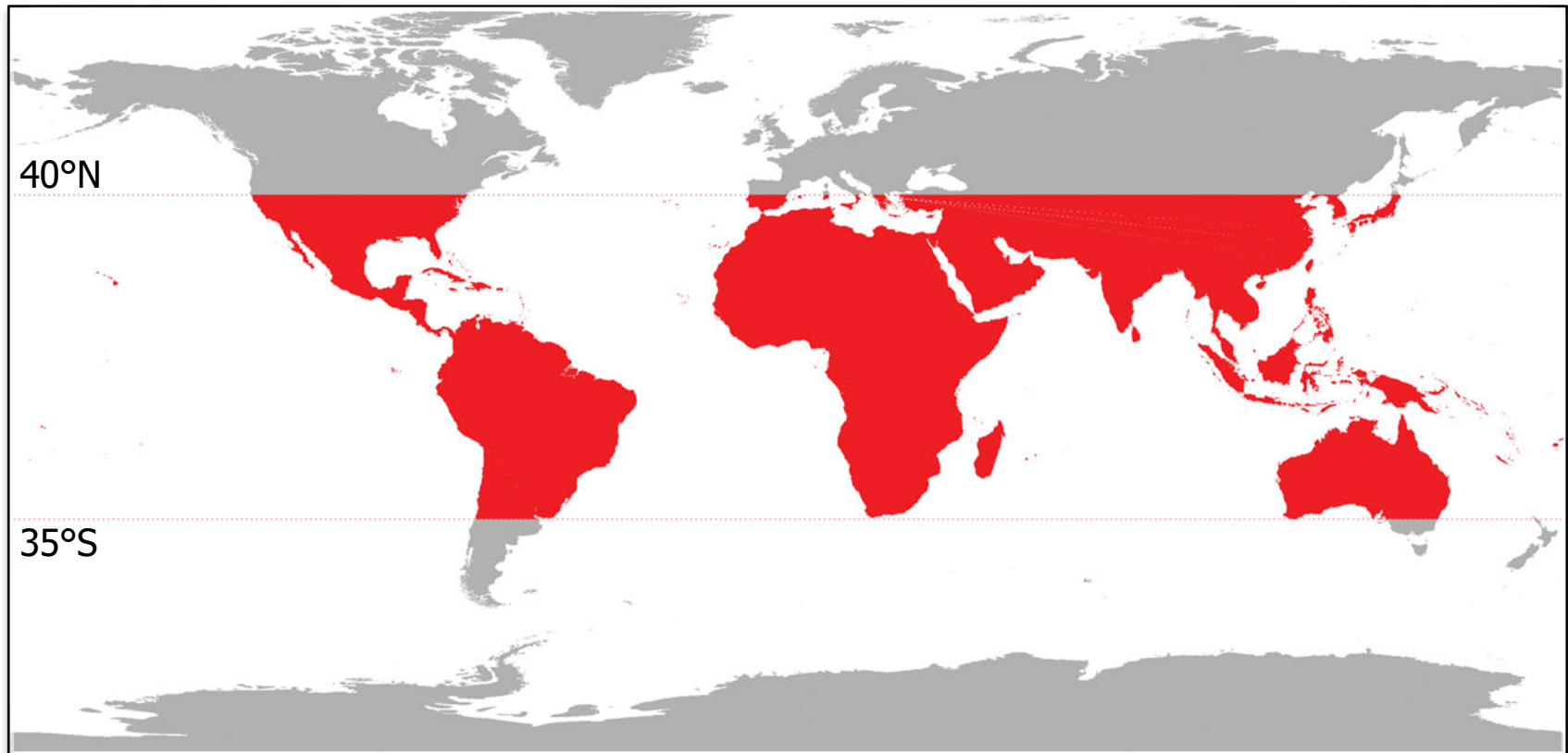
Replication cycle



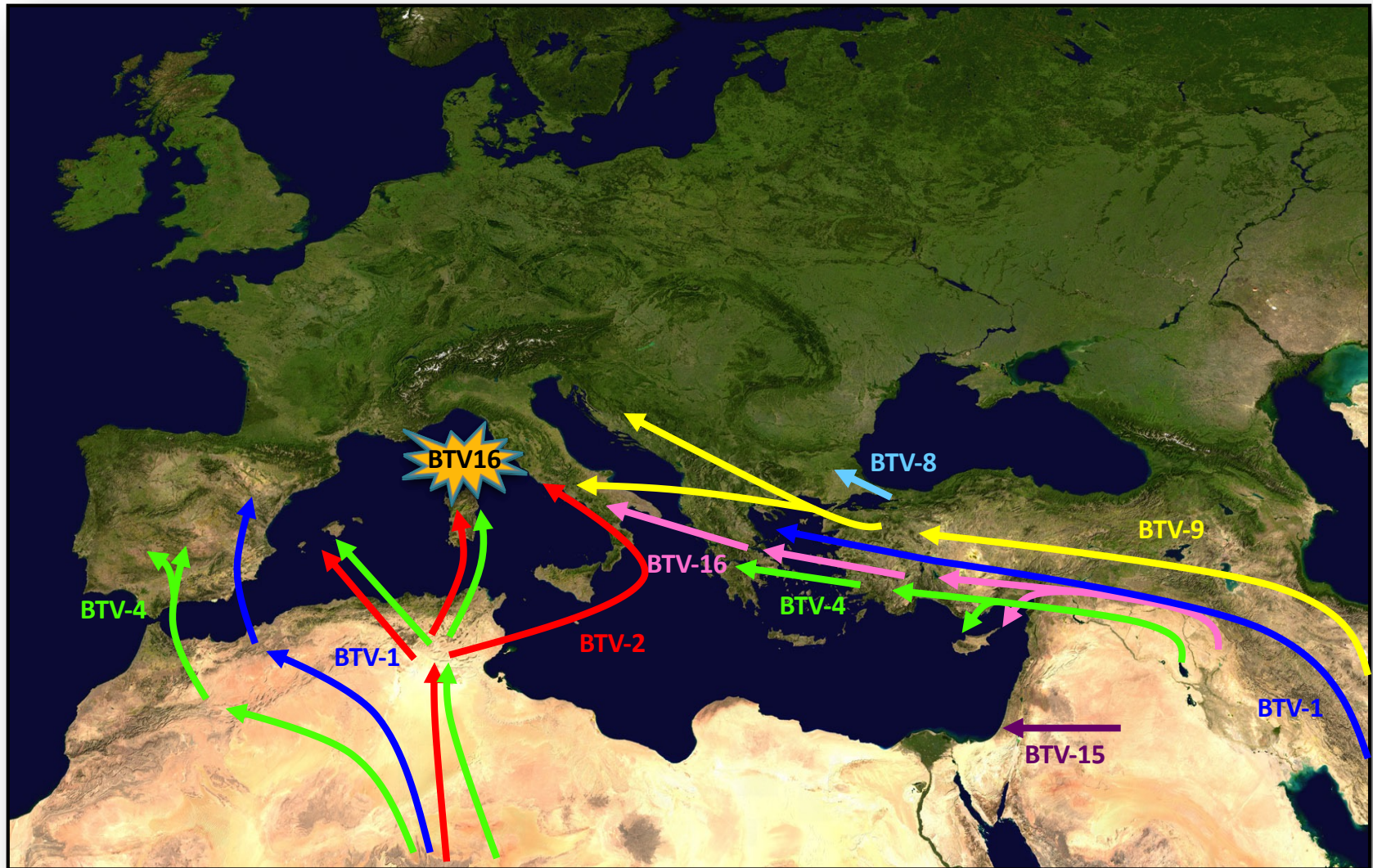
P. Roy (LSHTM, London)



BT global distribution: early to late 20th century



1998-2006: BT circulation in Southern Europe



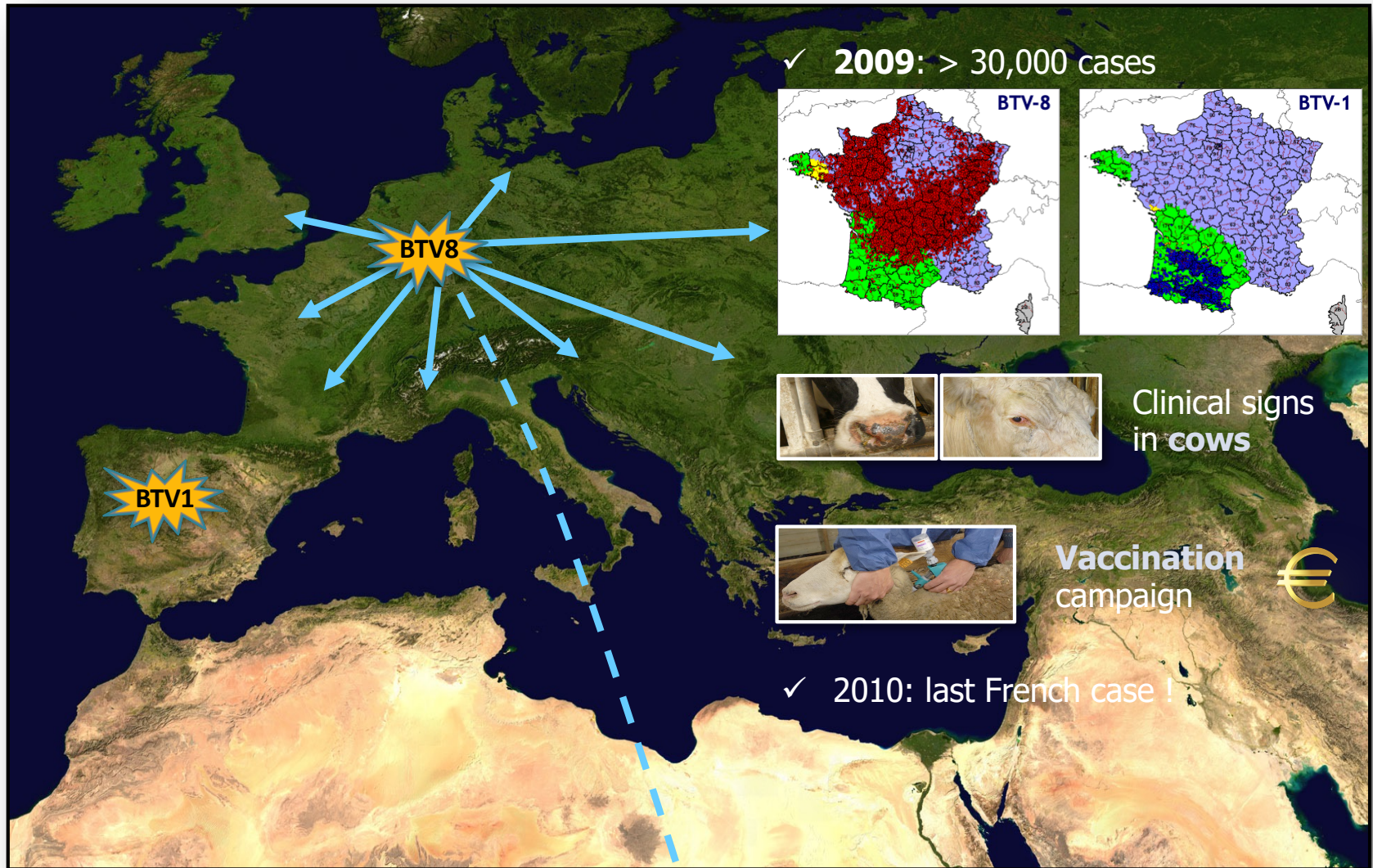
2000-01

2003

2004



2006-2009: BTV8 epizootic in Europe



2000-01 2003 2004 2006-09

BTV2
Corsica

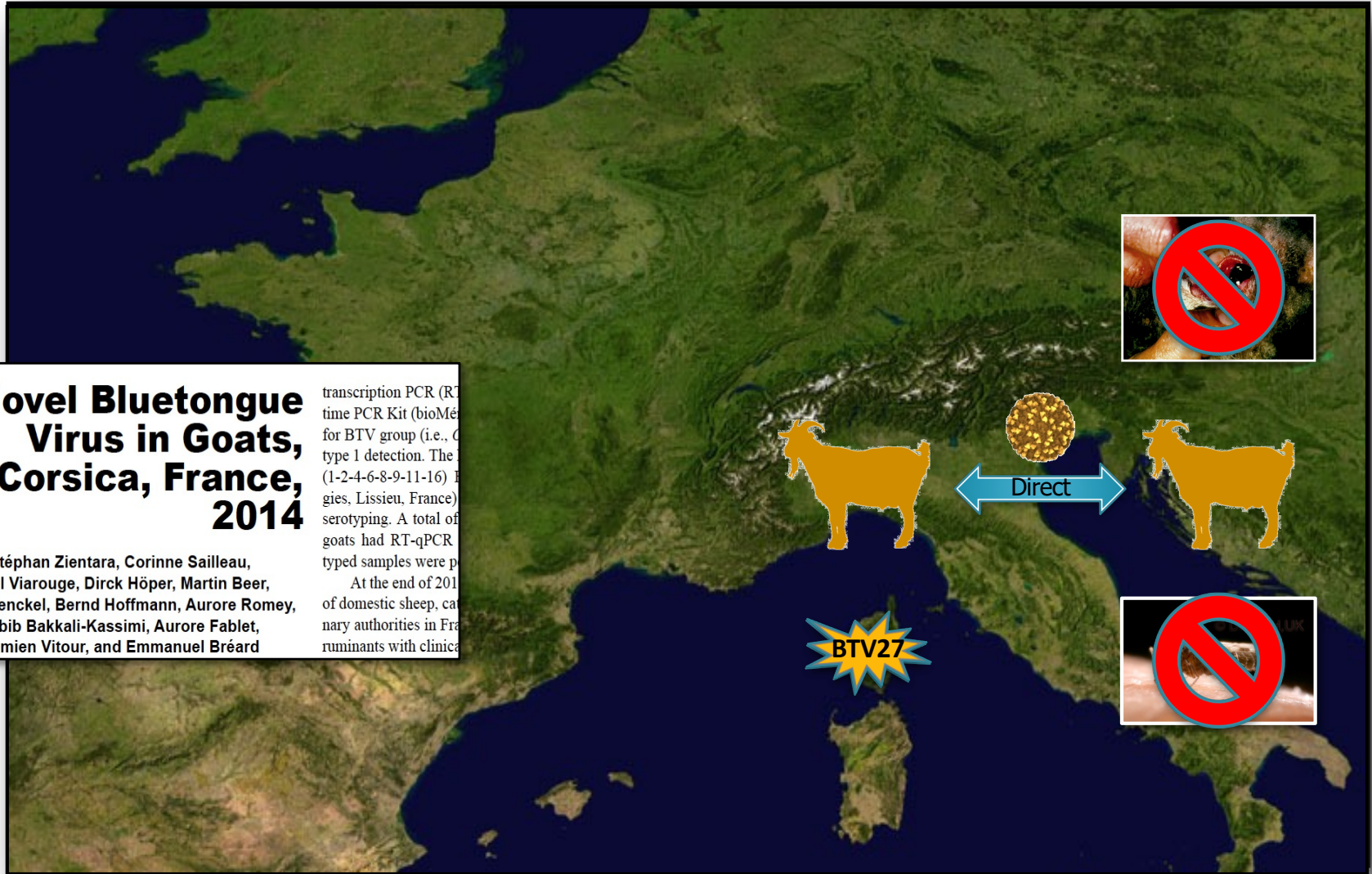
BTV4
Corsica

BTV16
Corsica

BTV8/1
Europe



2013-today: towards endemic BT circulation



Novel Bluetongue Virus in Goats, Corsica, France, 2014

Stéphan Zientara, Corinne Sailleau, Cyril Viarouge, Dirck Höper, Martin Beer, Maria Jenckel, Bernd Hoffmann, Aurore Romey, Labib Bakkali-Kassimi, Aurore Fablet, Damien Vitour, and Emmanuel Bréard

transcription PCR (RT-qPCR) using a real-time PCR Kit (bioMérieux) for BTV group (i.e., Group 1 detection. The BTV group 1 (1-2-4-6-8-9-11-16) BTV serotyping. A total of 10 goats had RT-qPCR confirmed. At the end of 2013, the French authorities in France reported clinical signs in ruminants with clinical

2000-01

2003

2004

2006-09

2013

2014

BTV2
Corsica

BTV4
Corsica

BTV16
Corsica

BTV8/1
Europe

BTV1
Corsica

BTV27
Corsica



2012-today: towards endemic BT circulation

Un foyer de fièvre catarrhale ovine, la « maladie de la langue bleue », découvert dans l'Allier

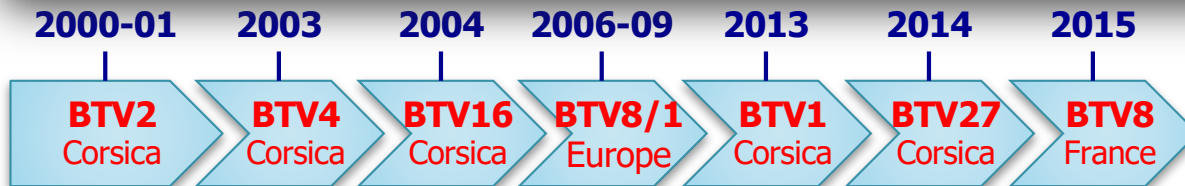
Le Monde.fr par AFP | 11.09.2015 à 17h31 • Mis à jour le 11.09.2015 à 18h24

Abonnez-vous à la lettre de L'Espresso

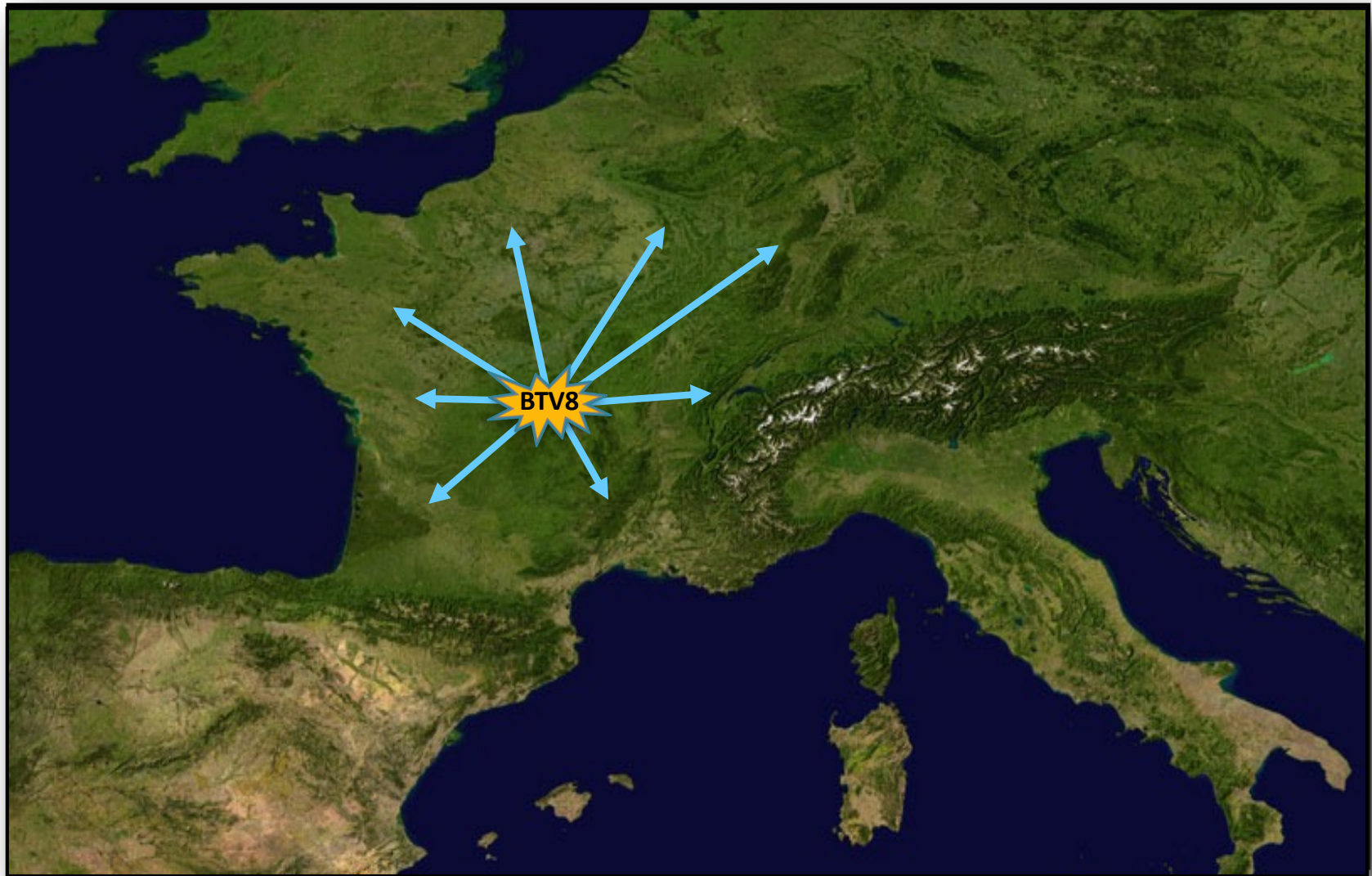
LECTURE Réagir Classer Partager



Julien Buttet, DDCSPP03



2012-today: towards endemic BT circulation



2000-01

2003

2004

2006-09

2013

2014

2015



BTV2
Corsica

BTV4
Corsica

BTV16
Corsica

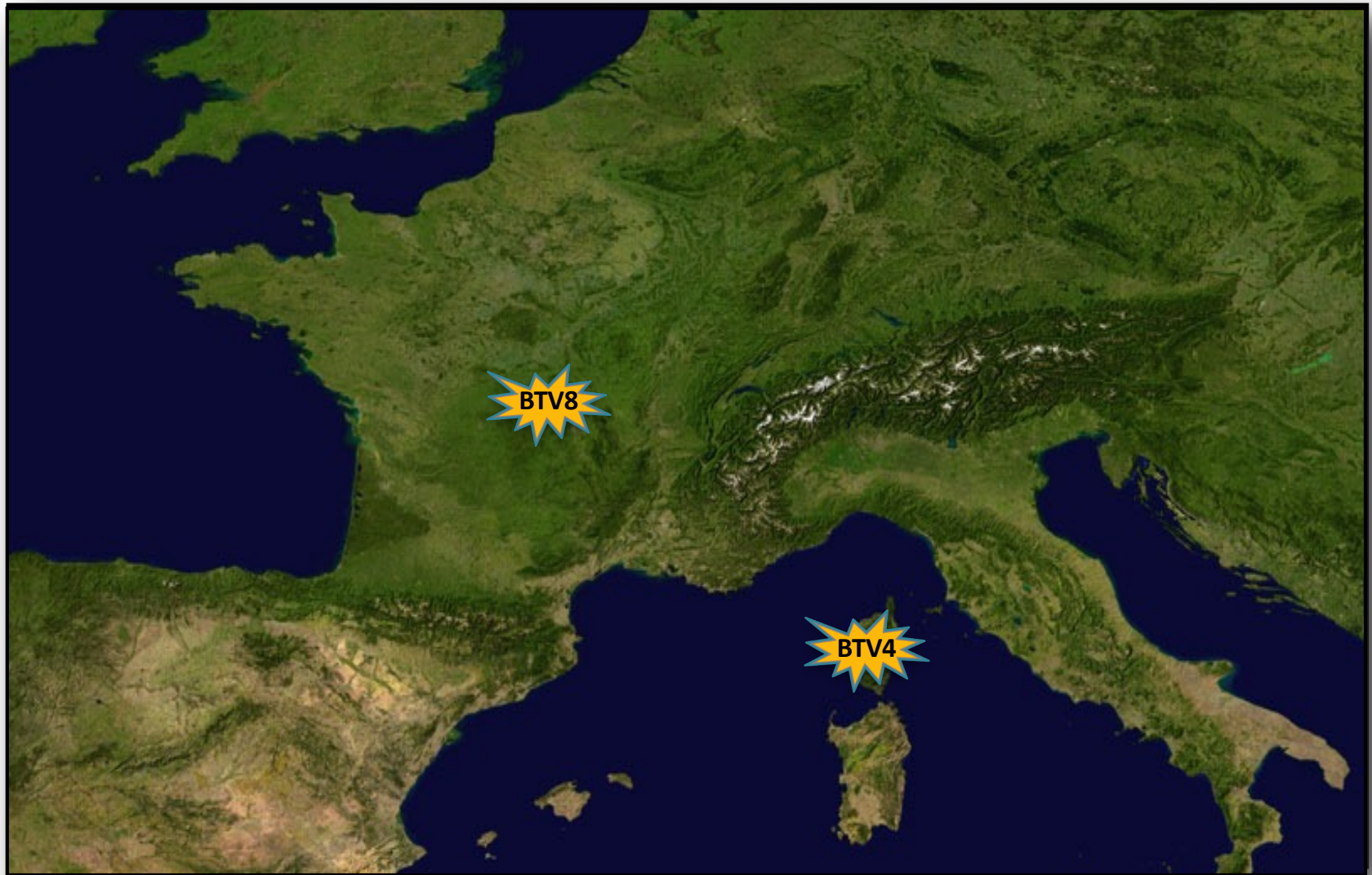
BTV8/1
Europe

BTV1
Corsica

BTV27
Corsica

BTV8
France

2012-today: towards endemic BT circulation



2000-01 2003 2004 2006-09 2013 2014 2015 2016

BTV2
Corsica

BTV4
Corsica

BTV16
Corsica

BTV8/1
Europe

BTV1
Corsica

BTV27
Corsica

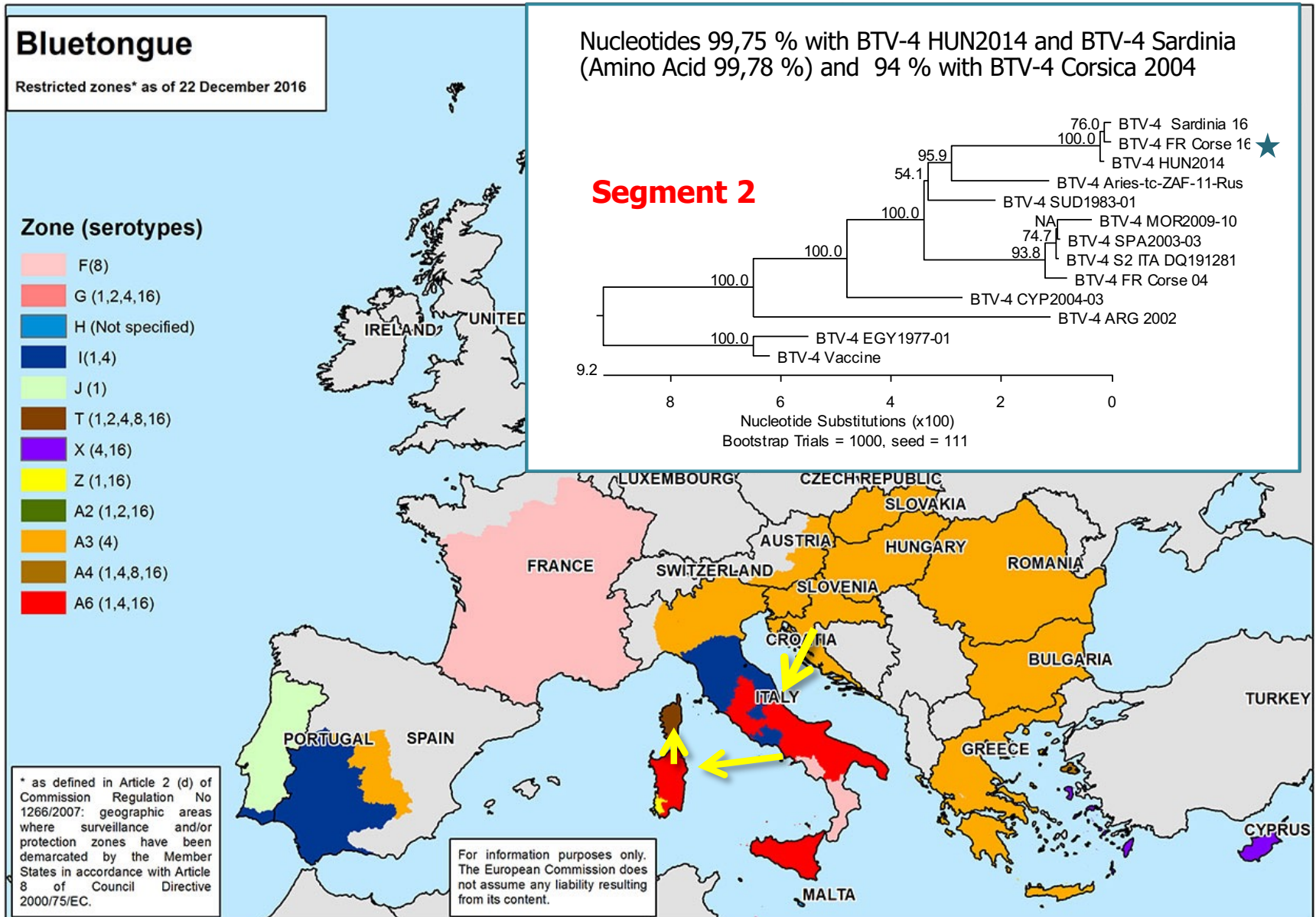
BTV8
France

BTV4
Corsica

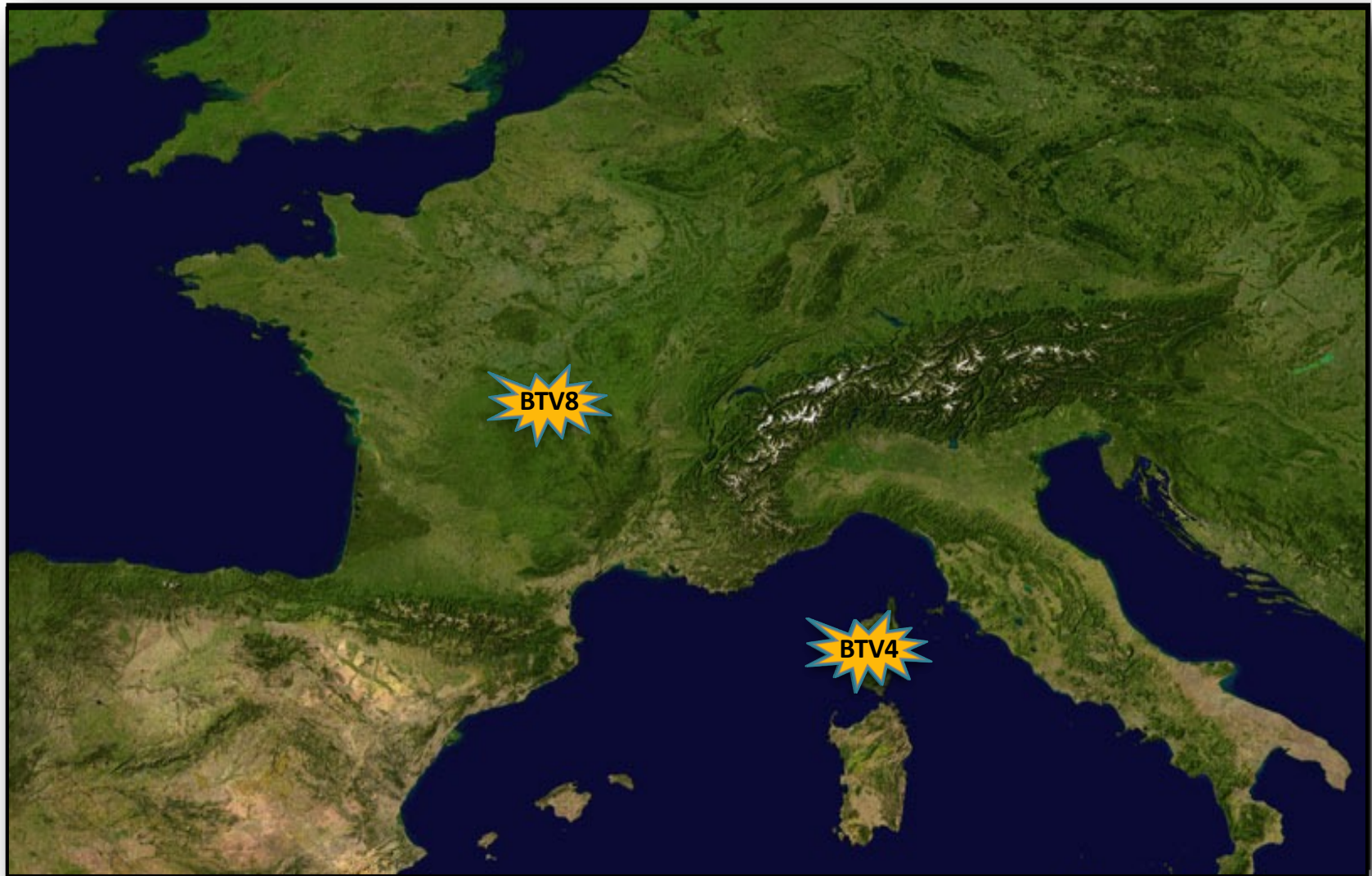


2012-today: towards endemic BT circulation

2016 – BTV-4 Corsica



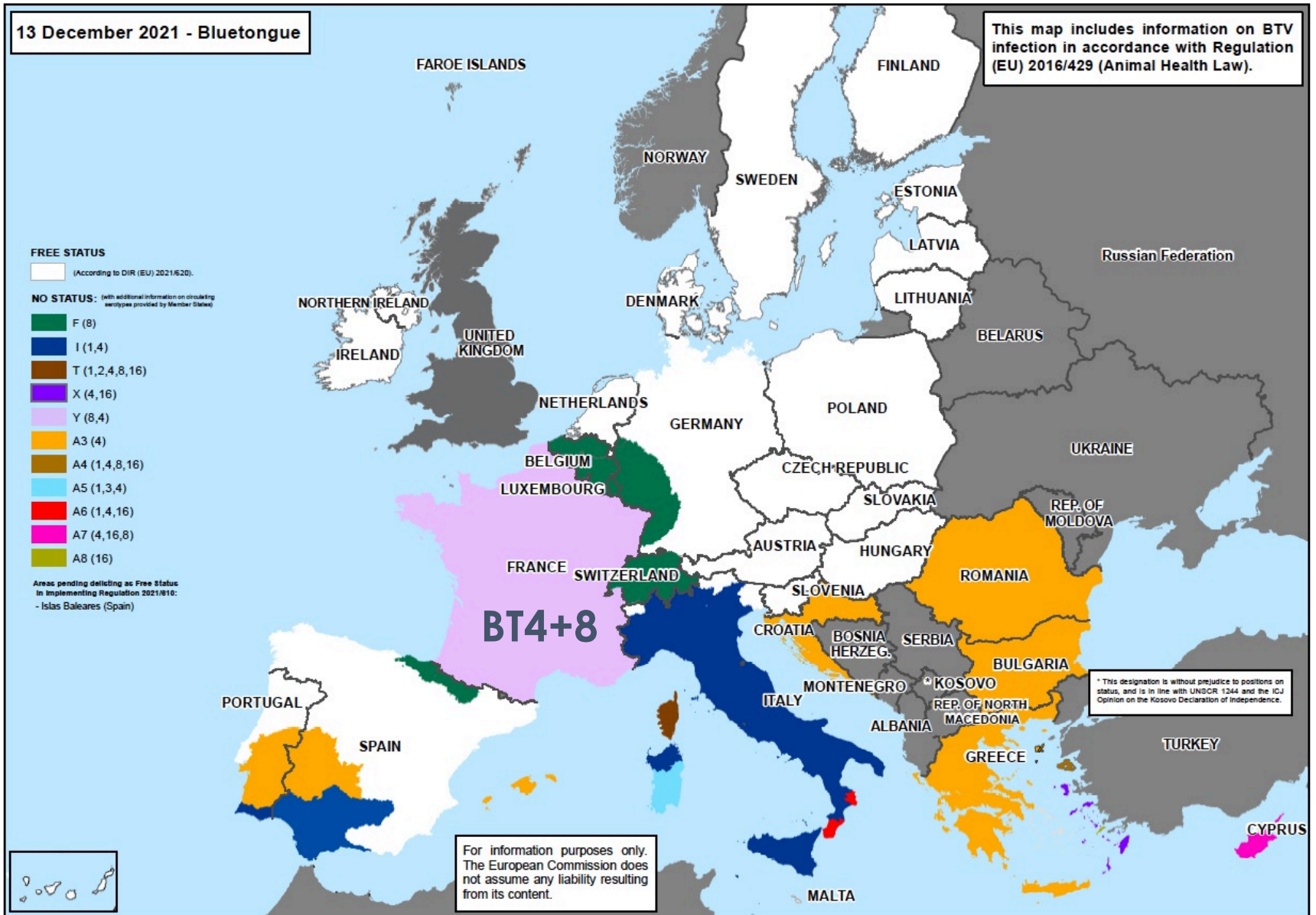
2012-today: towards endemic BT circulation



2000-01 2003 2004 2006-09 2013 2014 2015 2016 2017



2012-today: towards endemic BT circulation



2023: new BT emergences in France and Europe

LADEPECHE.fr

17°/24° Toulouse Rechercher

mercredi 17 octobre 2023, Saint-Baudouin

Aveyron : une recrudescence de cas de fièvre catarrhale ovine



Le virus de la FCO provoque l'inflammation des muqueuses, ce qui entraîne de l'hyperthermie, des difficultés de locomotion, des ulcérations dans la bouche, de l'hypersalivation, voire une langue bleue.

← Aller à la page régionale

Epidémie de "langue bleue" : des foyers détectés dans l'Aveyron et le Tarn font trembler les éleveurs

Publié le 14/09/2023 à 13h12
Texte par [Fabrice Duchange](#)



Le fievre catarrhale ovine (FCO), également appelée fièvre catarrhale de la langue bleue, affecte de nombreuses espèces de ruminants et notamment le ovins, les caprins.

BOISE

Aveyron

Occitanie

ASN

Depuis août 2023, une recrudescence inquiétante de la fièvre catarrhale ovine (FCO), communément appelée "langue bleue", sévit dans le sud du Massif Central, en particulier en Aveyron. Les rapports font état de treize foyers détectés dans le département voisin du Tarn.

04/08/2023: **BTV-8** outbreak in Aveyron.

2023: new BT emergences in France and Europe

LA DEPECHE.fr 17°/24° Toulouse Rechercher

Le mardi 17 octobre 2023, Saint-Baudouin

Aveyron : une recrudescence de cas de fièvre catarrhale ovine



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Publié le 14/09/2023 à 13h12
Texte par [Sébastien Duchange](#)



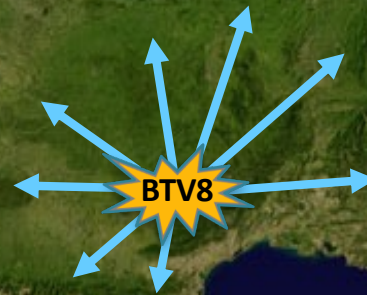
Le FCO, communément appelé "langue bleue", sévit dans le sud du Massif Central, en particulier en Aveyron. Les rapports font état de treize foyers détectés dans le département voisin du Tarn.

RISQUE
Aveyron
Occitanie
Ain

Highly lethal in sheep ;
clinical signs in cattle.

A new strain of BTV-8... !!

genome segment	viral proteins	closest homology in GenBank		
		% homology	BTV strain	n° accession
S1	VP1	97,60%	BTV-8 GER 2006	MN837926
S2	VP2	96,73	BTV-8 FR 2006	KJ872780
S3	VP3	97,94	BTV-5 Af. Sud 2011	MG255451
S4	VP4	98,57	BTV-2 Tun 2000	KP821279
S5	NS1	98,09	BTV-3 Isr 2018	MN213159
S6	VP5	98,96	BTV-8 Fr 2016	OQ860839
S7	VP7	98,53	BTV-24 Af. Sud 2017	MG255595
S8	NS2	98,58	BTV-5 Af. Sud 2011	MG255457
S9	VP6	95,81	BTV-5 Af. Sud 2011	MG255454
S10	NS3	97,8	BTV-13 Af. Sud 2017	MT043227

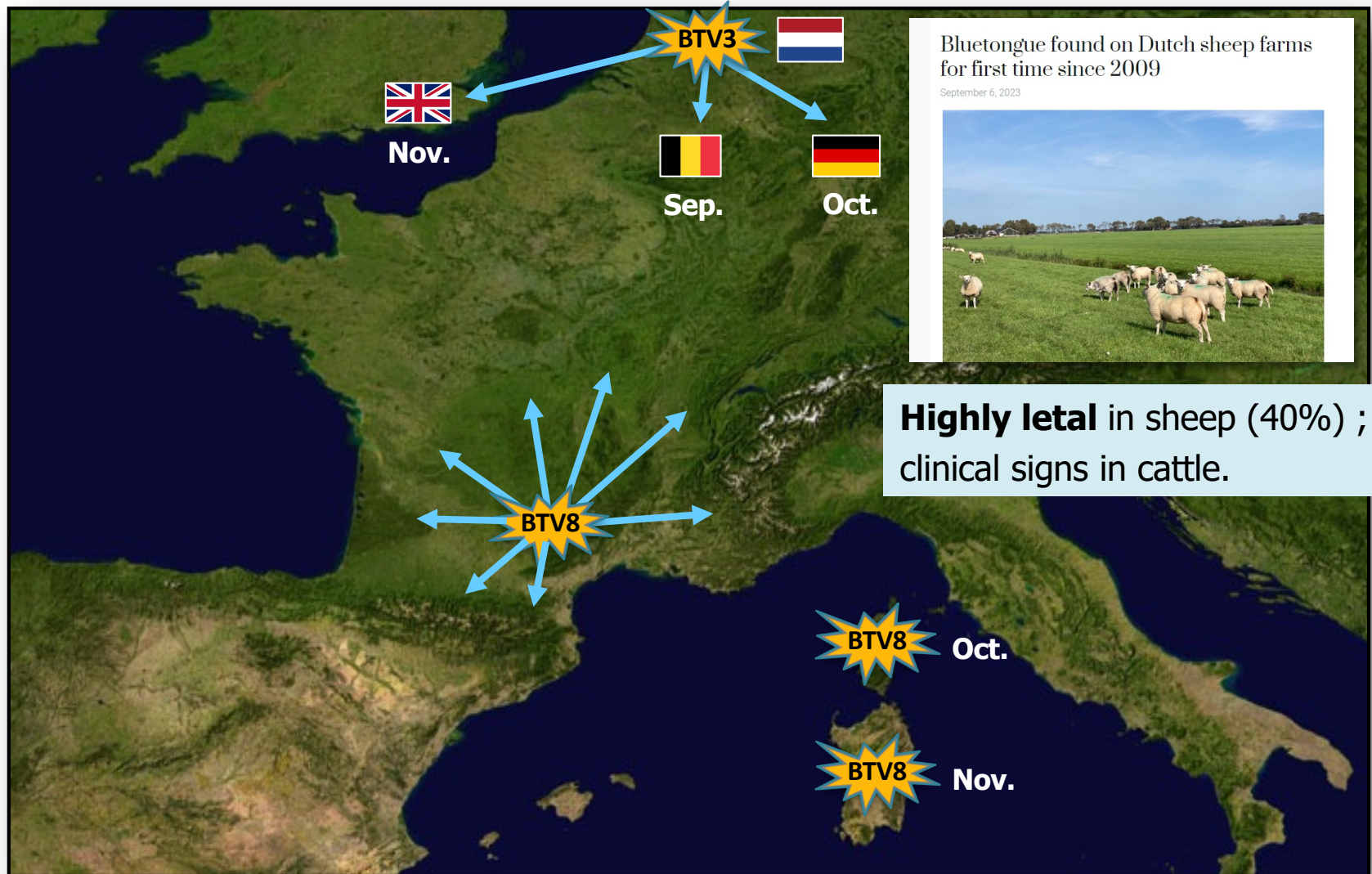


BTV8 Oct.

BTV8 Nov.

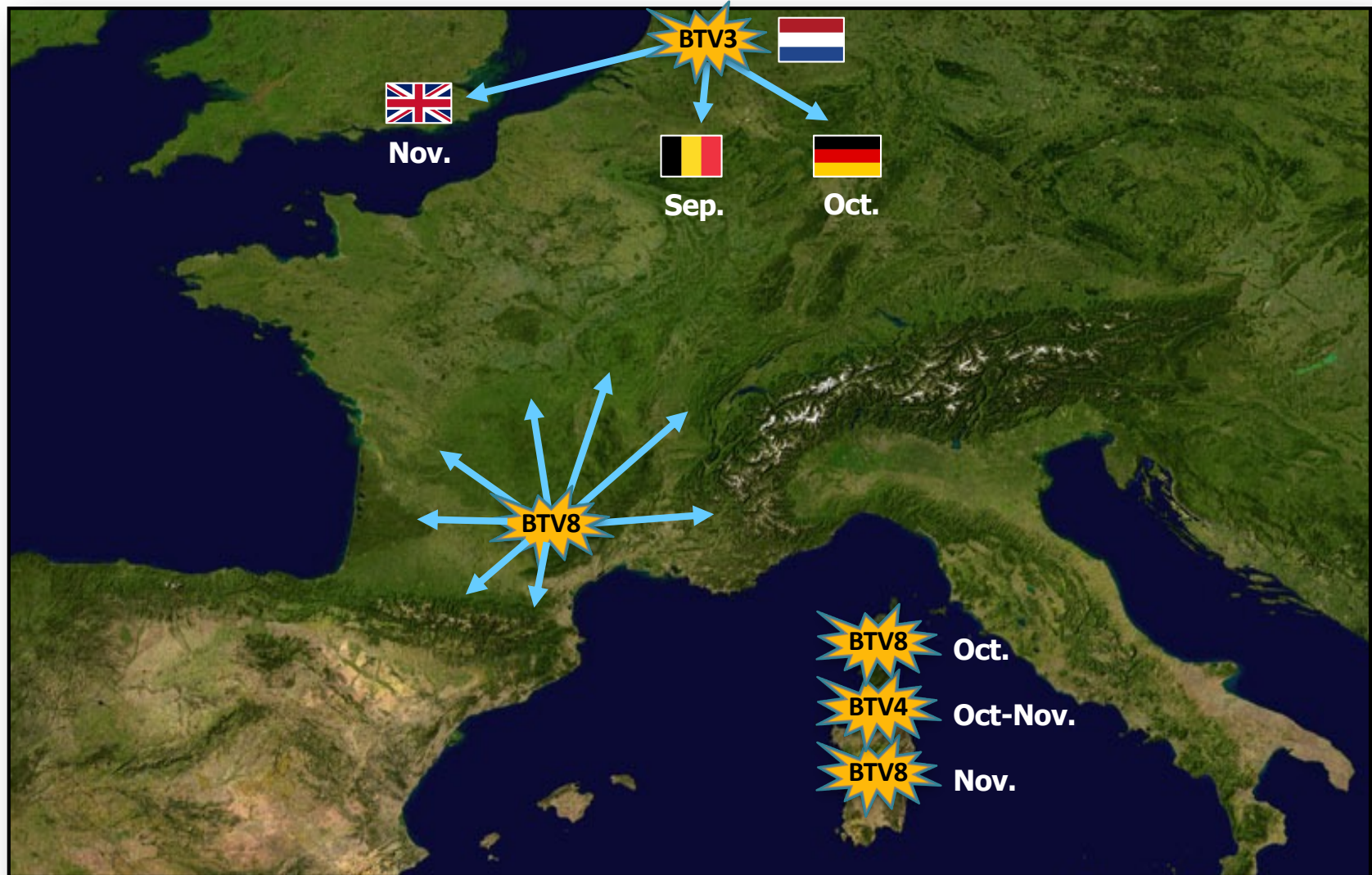
- 04/08/2023: **BTV-8** outbreak in Aveyron.
- 30/10/2023: **>600 outbreaks** in 17 departments.

2023: new BT emergences in France and Europe



- 04/09/2023: **BTV-3** outbreak in The Netherlands.
- 17/11/2023: **>4,000** outbreaks in NL.

2023: new BT emergences in France and Europe



● 04/09/2023: **BTV-3** outbreak in The Netherlands.

● 17/11/2023: **>4,000** outbreaks in NL.



Epizootic hemorrhagic disease virus

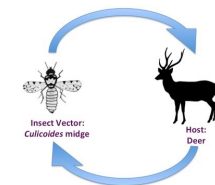
Epizootic hemorrhagic disease virus (EHDV)



- 1st described after a severe outbreak in **white-tailed deer** (*Odocoileus virginianus*) in New Jersey in 1955.
- 90% lethal in WTD.



Disease Transmission Cycle of Epizootic Hemorrhagic Disease (EHD)



- **Fulminant EHD** characterised by excessive **bleeding** (haemorrhagic disease), dehydration, diarrhoea, and death.

Epizootic hemorrhagic disease virus (EHDV)



- Emerging disease in **cattle** ; added to the **WOAH** list of notifiable diseases in May 2008.

- Bluetongue-like disease:** fever, loss of appetite, haemorrhages, weakness, excessive salivation, respiratory distress, ulceration (buccal mucosa, tongue...), diarrhoea, lameness...

1. Conjonctivite surinfectée.
© Laboratoire de santé animale



2. Érosions des muqueuses dans la cavité buccale d'un bovin après une infection expérimentale par le virus de la maladie épizootique hémorragique.
© Laboratoire de santé animale



Viremia with no clinical signs



Resistant

Epizootic hemorrhagic disease virus (EHDV)

7 recognized serotypes...

...and new putative serotypes

Serological and genetic characterisation of putative new serotypes of bluetongue virus and epizootic haemorrhagic disease virus isolated from an Alpaca

IM Wright
22054146

Dissertation submitted in partial fulfillment of the requirements for the degree of *Magister Scientiarum* at the *Potchefstroom Campus of the North-West University*

Supervisor: Prof AA van Dijk
Co-supervisor: Dr AC Potgieter

May 2014

S. Africa



Microbes, Genomes and Evolution 11 (2017), 66–68
Contents lists available at ScienceDirect
Infection, Genetics and Evolution
journal homepage: www.elsevier.com/locate/iegesj

Research paper

Characterization of genome segments 2, 3 and 6 of epizootic hemorrhagic disease virus strains isolated in Japan in 1985–2013: Identification of their serotypes and geographical genetic types

Hiroaki Shirafuji^{1*}, Tomoko Kato¹, Makoto Yamakawa², Toru Tanaka³, Yutaka Minemori⁴, Tohru Yanase⁵

¹ Osaka Research Station, National Institute of Animal Health (NIHA), National Epizootic and Prof Research Organization (NEPRO), Japan

² Osaka Research Station, National Institute of Animal Health (NIHA), Japan

³ Osaka University, Japan

⁴ Osaka University, Japan

⁵ National Institute of Animal Health (NIHA), Japan

* Author for correspondence: hshirafuji@niha.affrc.affrc.go.jp

Japan



Novel Serotype of Epizootic Hemorrhagic Disease Virus, China

Heng Yang¹, Zhuoran Li¹, Jinping Wang, Zhanhong Li, Zhenxing Yang, Defang Liao, Jianbo Zhu, Huachun Li

Author affiliation: Yunnan Animal Science and Veterinary Institute, Kunming, China

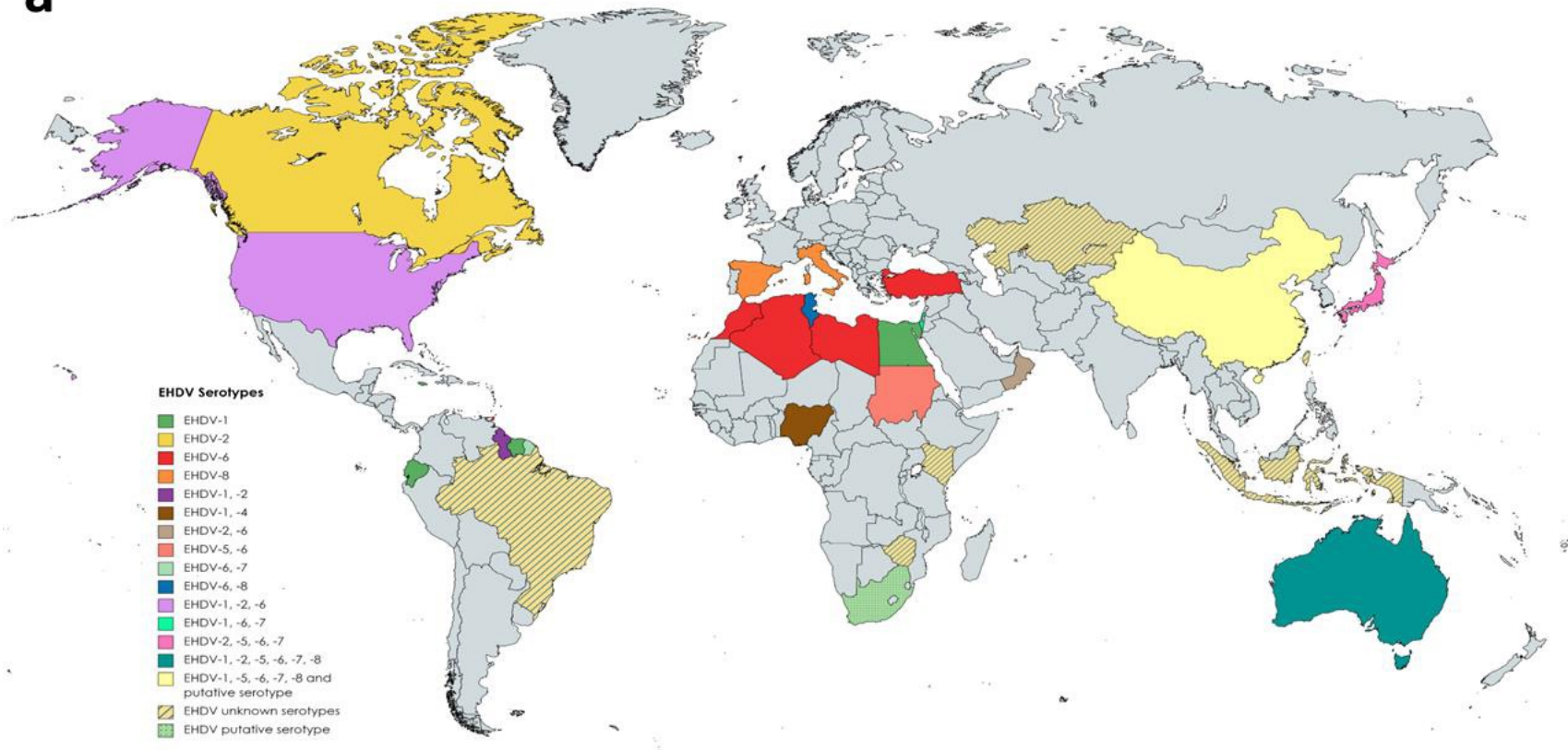
DOI: <https://doi.org/10.3201/eid2612.191301>

In 2018, a strain of epizootic hemorrhagic disease virus (EHDV), named YNDH1/0793, was isolated from a sentinel calf in Mangshi County, Yunnan, China. Nucleotide sequencing and phylogenetic analysis revealed that the virus belongs to a novel serotype that had not been reported previously.

China



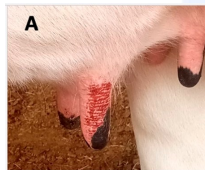
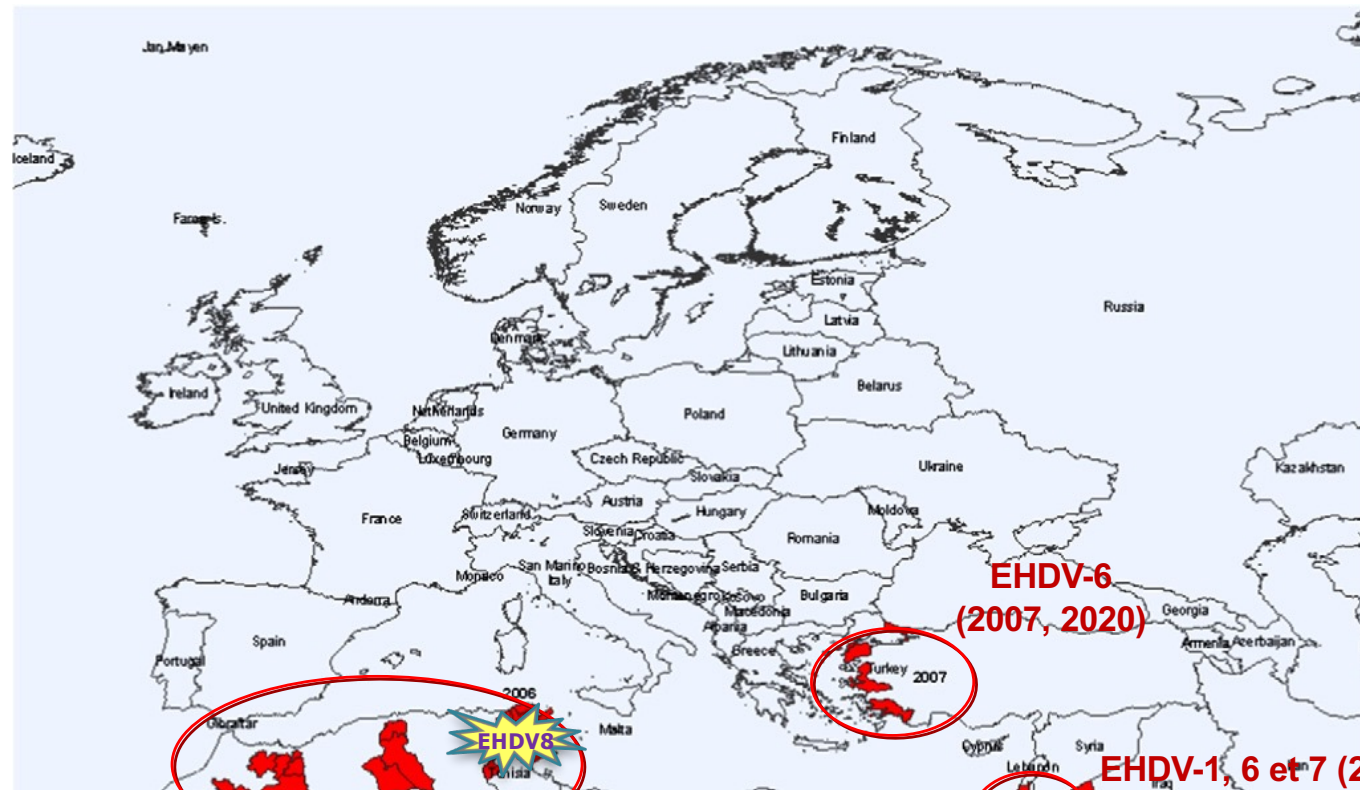
a



French Antilles
Guyane
La Réunion
Mayotte

Emergence of EHDV-8

- **2021**: emergence of a new **EHDV-8** strain in **Tunisia** (200 outbreaks).



viruses MDPI

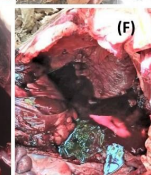
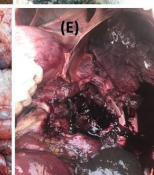
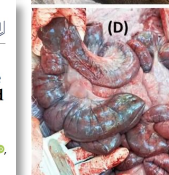
Article
Epizootic Haemorrhagic Disease Virus Serotype 8 in Tunisia, 2021

Soufien Sghaier ¹, Corinne Sailleau ², Maurilia Maracci ³, Sarah Thabet ¹, Valentina Curini ³, Thameur Ben Hassine ⁴, Liana Teodor ¹, Ottavio Portanti ³, Salah Hammami ⁵, Lucija Jurisic ^{3,4}, Massimo Spedicato ³, Lydie Postic ³, Ines Gazani ⁷, Raja Ben Osman ⁵, Stephan Zientara ², Emmanuel Bréard ³, Paolo Calistri ³, Jürgen A. Richt ³, Edward C. Holmes ³, Giovanni Savini ³, Franca Di Giallonardo ³ and Alessio Lorusso ^{3,*}

viruses MDPI

Article
Characterization of Epizootic Hemorrhagic Disease Virus Serotype 8 in Naturally Infected Barbary Deer (*Cervus elaphus barbarus*) and *Culicoides* (Diptera: Ceratopogonidae) in Tunisia

Sarah Thabet ¹, Soufien Sghaier ², Thameur Ben Hassine ¹, Darine Slama ⁴, Raja Ben Osmane ⁵, Ridha Ben Omrane ⁶, Wiem Muelhi ⁷, Massimo Spedicato ³, Alessandra Leone ⁶, Liana Teodor ¹, Valentina Curini ³, Moncef Othmani ⁸, Shadia Berjaoui ⁹, Paola Ripà ⁵, Makram Orabi ⁷, Bassem Belhaj Mohamed ¹⁰, Ayda Sayadi ⁵, Sonia Ben Slama ⁷, Maurilia Maracci ³, Giovanni Savini ³, Alessio Lorusso ^{3,*} and Salah Hammami ¹



Emergence of EHDV-8

- **2021:** emergence of a new **EHDV-8** strain in **Tunisia** (200 outbreaks).
- **Oct-Nov 2022:** **EHDV-8** reached Sardinia, Sicilia and Andalusia.

Clinical signs

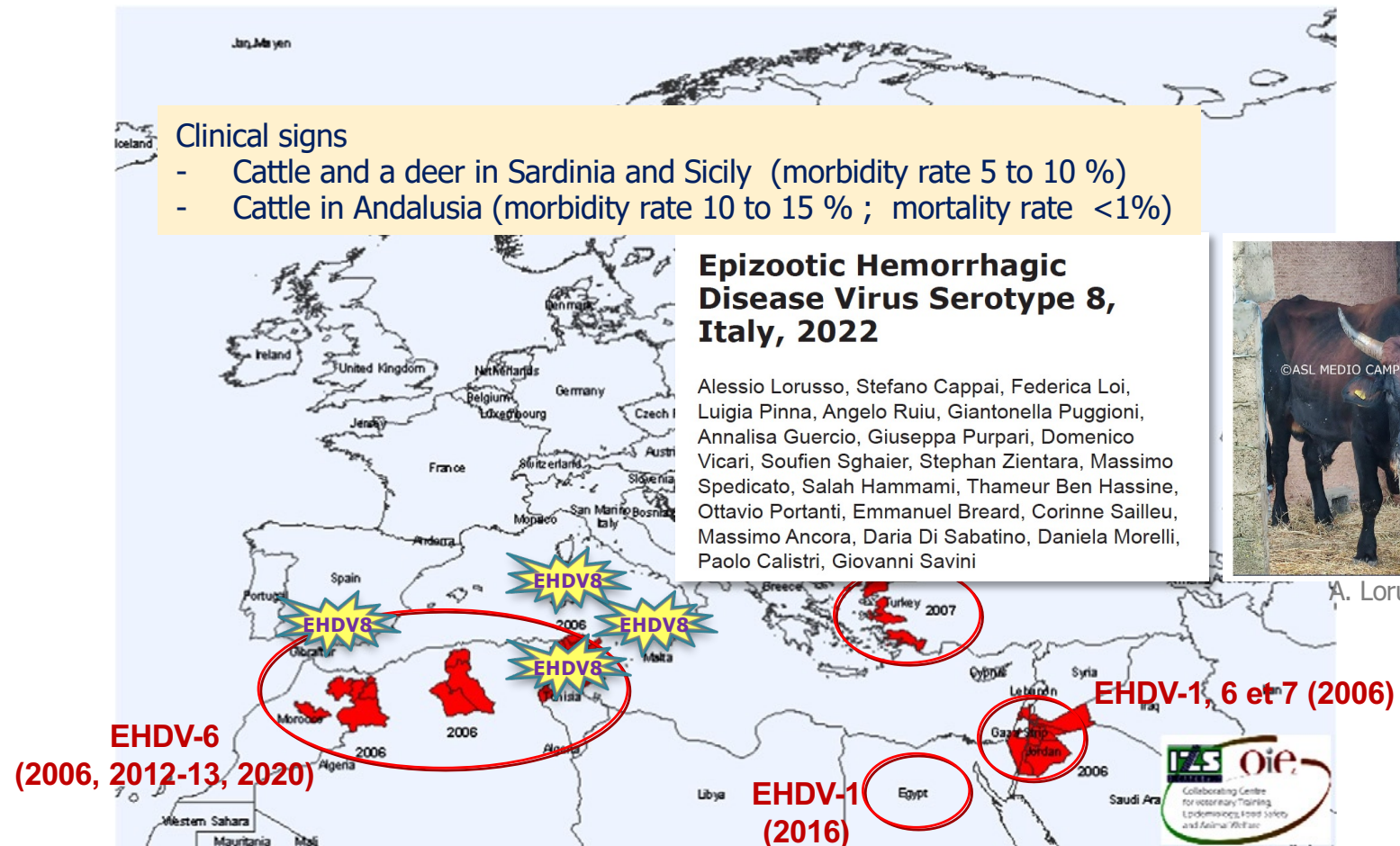
- Cattle and a deer in Sardinia and Sicily (morbidity rate 5 to 10 %)
- Cattle in Andalusia (morbidity rate 10 to 15 % ; mortality rate <1%)

Epizootic Hemorrhagic Disease Virus Serotype 8, Italy, 2022

Alessio Lorusso, Stefano Cappai, Federica Loi, Luigia Pinna, Angelo Ruiu, Giantonella Puggioni, Annalisa Guercio, Giuseppa Purpari, Domenico Vicari, Soufien Sghaier, Stephan Zientara, Massimo Spedicato, Salah Hammami, Thameur Ben Hassine, Ottavio Portanti, Emmanuel Breard, Corinne Sailleu, Massimo Ancora, Daria Di Sabatino, Daniela Morelli, Paolo Calistri, Giovanni Savini



A. Lorusso, IZST



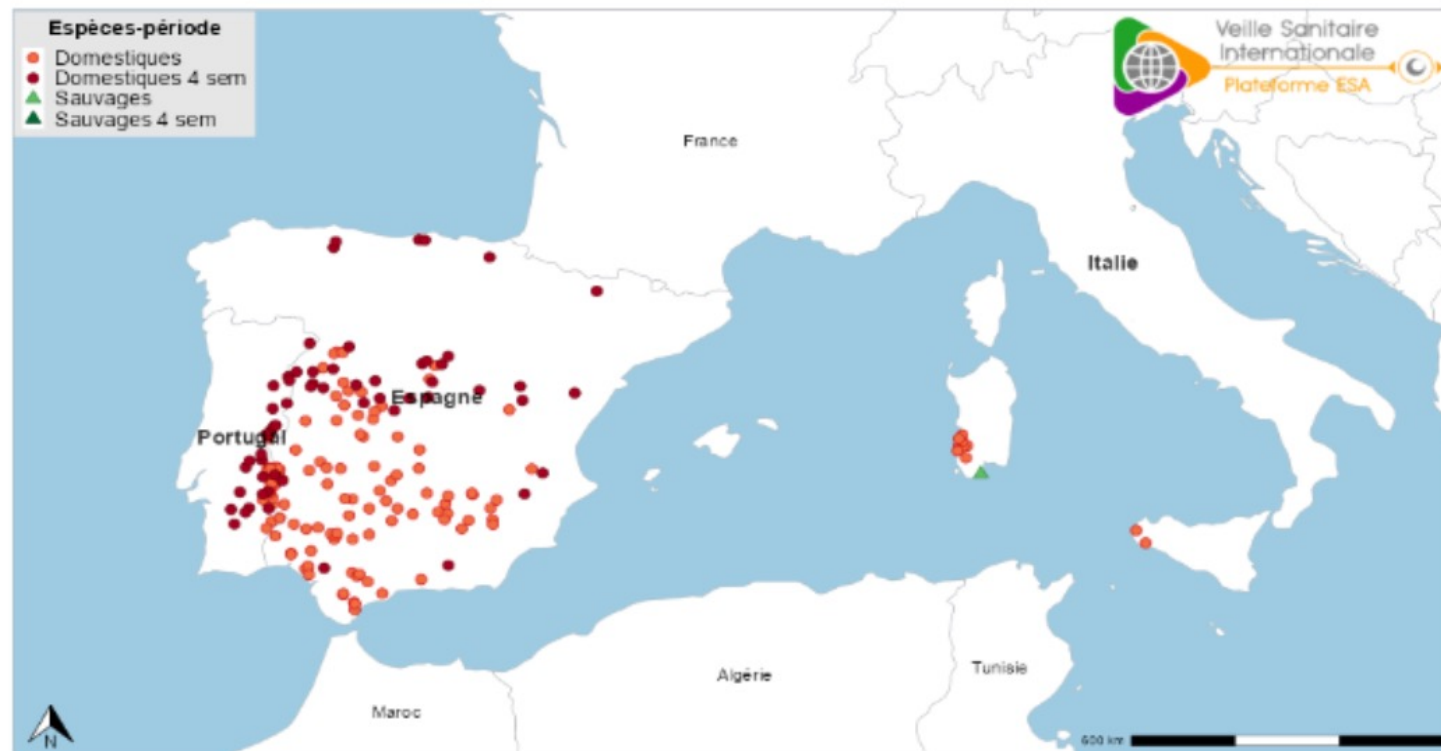
Emergence of EHDV-8

18 July 2023



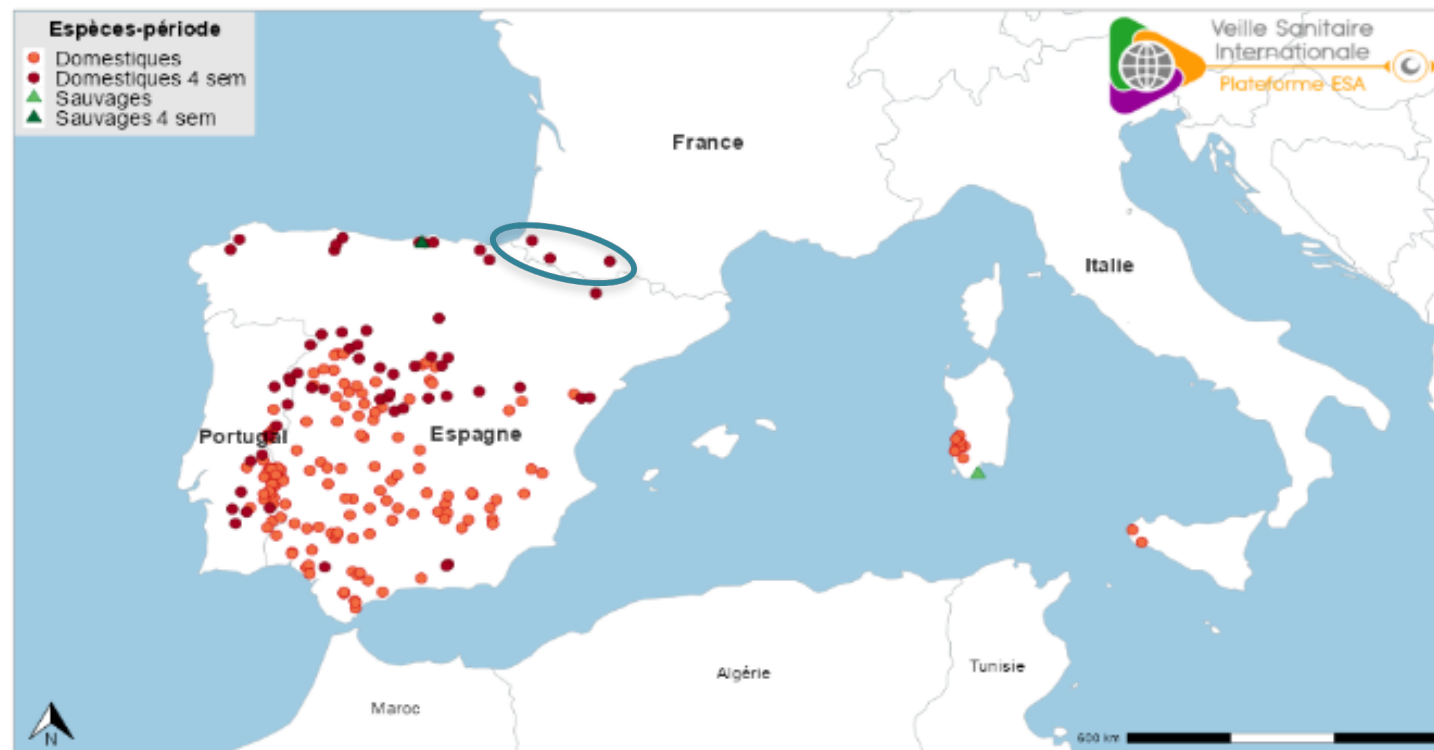
Emergence of EHDV-8

Sept 2023



Emergence of EHDV-8

18 Sept 2023



Emergence of EHDV-8

18 Sept 2023

franceinfo

vidéos radio jt émissions

21/09/2023 1 min

Maladie hémorragique épizootique : trois cas dans Pyrénées-Atlantiques et dans les Hautes-Pyrénées une première en France

Pour la première fois, la maladie hémorragique épizootique (MHE) a été détectée sur des bovins, dans les Pyrénées-Atlantiques et les Hautes-Pyrénées. Si les animaux touchés peuvent tomber gravement malades voire mourir, ils ne sont revanche pas contagieux.

France Info - avec France Bleu Pays basque

Publié le 18/09/2023 10:06



Premiers cas de maladie hémorragique épizootique en France

Trois bovins ont été diagnostiqués avec la maladie hémorragique épizootique (MHE) en France. Il s'agit des premiers cas survenus sur le territoire. Ils ont été confirmés le 18 septembre 2023 par le laboratoire de santé animale de l'An Celui-ci est laboratoire de référence sur cette maladie pour la France et pour l'Organisation mondiale de la santé animale (OMSA). Les cas ont été déclarés dans les départements des Pyrénées-Atlantiques et des Hautes-Pyrénées.

LA NOUVELLE REPUBLIQUE des Pyrénées

Rechercher sur le site.

JE COMMANDE

Accueil > Economie > Agriculture

Hautes-Pyrénées : détection d'un cas de maladie hémorragique épizootique (MHE) dans un élevage bovin

ABONNÉS



Bovins et ovins sont atteints d'une nouvelle maladie transmise par les cerfs et les chevreuils, via les pucierons.

DDM - CEDRIC MERAVILLES

Le Monde

Consulter le journal

Planète Comprendre le réchauffement climatique 9 Indicateurs de l'urgence climatique

PLANÈTE - AGRICULTURE & ALIMENTATION

En France, les premiers cas de maladie hémorragique épizootique dans des élevages détectés

Cette maladie n'est pas transmissible à l'homme. Trois élevages sont concernés dans ces deux départements du Sud-Ouest.

Le Monde avec AFP

Publié aujourd'hui à 10h45, modifié à 15h46

Lecture 1 min.

Ajouter à vos sélections



La Slovénie : Petit pays, grandes aventures

Maladie Hémorragique Epizootique au Pays basque : quelles conséquences pour les éleveurs de la région ?

Accueil - Sud Ouest Eco - Agriculture

Lecture 1 min



La MHE est une maladie réglementée au niveau européen et à déclaration obligatoire, poursuit le communiqué. Les pays impactés ont l'obligation d'instaurer des mesures de surveillance afin de suivre l'évolution de la maladie dans l'espace et dans le temps.

© Credit photo : ARCHIVES SUD-OUEST



Le Parisien

Maladie hémorragique épizootique : de premiers cas détectés en France dans des élevages de bovins

Trois élevages sont concernés par cette maladie dans les Hautes-Pyrénées et les Pyrénées-Atlantiques. L'exportation de bovins vivants a été interdite dans la zone.



AGRICULTURE - PÊCHE

Trois cas d'une nouvelle maladie bovine au Pays basque et dans les Hautes-Pyrénées, une première en France

Le virus qui provoque la maladie hémorragique épizootique chez les cervidés, les bovins et les caprins, est arrivé en France, après s'être propagé en Sardaigne, Sicile et en Espagne. Deux cas ont été formellement identifiés mardi au Pays basque, un troisième a été identifié dans les Hautes-Pyrénées.

Hasparren

Ethebar

De Simon Cardona, Marlon Aquilino

Mardi 20 septembre 2023 à 10:54 - Mis à jour le jeudi 21 septembre 2023 à 11:14

Par France Bleu Pays Basque, France Bleu Béarn Bigorre, France Bleu, France Bleu Occitanie



Après l'Italie et l'Espagne, le virus arrive dans des élevages du Pays basque. © AFP - GALOZIA POZE

21 septembre 2023 Communiqué de presse

Ministère de l'Agriculture et de la Souveraineté alimentaire

COMMUNIQUÉ DE PRESSE

Santé animale : détection de premiers foyers de MHE en élevages bovins

santé animale filière bovine

Partager la page



Le laboratoire national de référence de santé animale de Maisons-Alfort (ANSES) vient de confirmer la présence du virus de la Maladie Hémorragique Epizootique (MHE) sur des bovins dans 3 élevages situés dans les Pyrénées-Atlantiques et les Hautes-Pyrénées. Les mesures de gestion de cette maladie sont mises en place par

Qu'est-ce que la MHE, maladie virale repérée dans des élevages français ?

Des cas de Maladie Hémorragique Epizootique (MHE) ont été détectés dans trois élevages du Sud-Ouest. Une maladie transmise aux bovins, ovins et caprins par un moucheron.

Julien VERCHÈRE le jeudi 21 septembre 2023



NOUVEAU RENAULT ESPACE E-TECH FULL HYBRID 200 CH

comparez les

le journal de montréal

HEURE - SERVICES

Premiers cas en France de maladie hémorragique épizootique dans des élevages

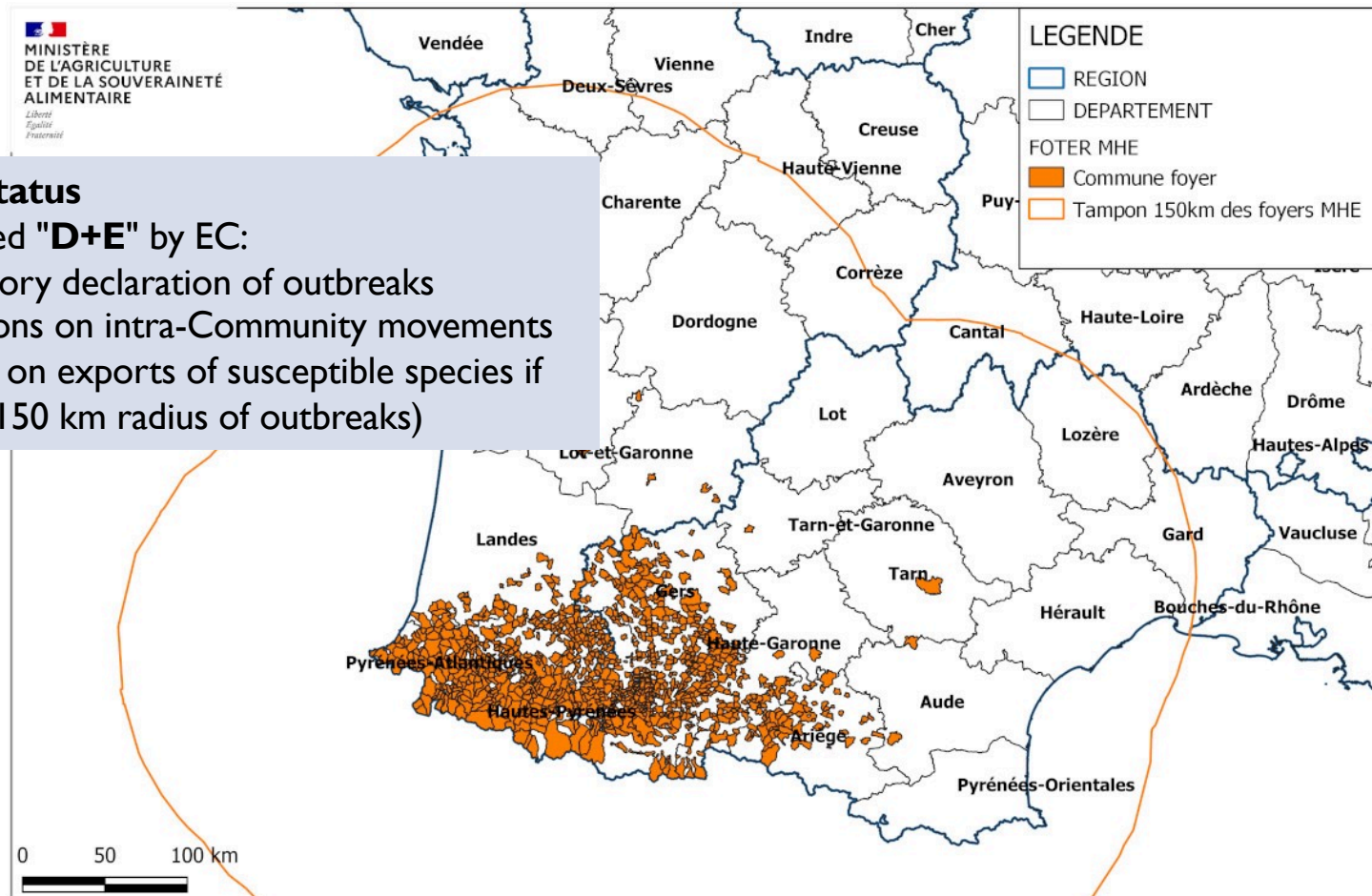


Emergence of EHDV-8

28 Sept 2023

● Lack of efficient control measures (no vaccine).

- **Loss of free status**
- EHD categorized "**D+E**" by EC:
 - ✓ Compulsory declaration of outbreaks
 - ✓ Restrictions on intra-Community movements (E.g.: Ban on exports of susceptible species if within a 150 km radius of outbreaks)

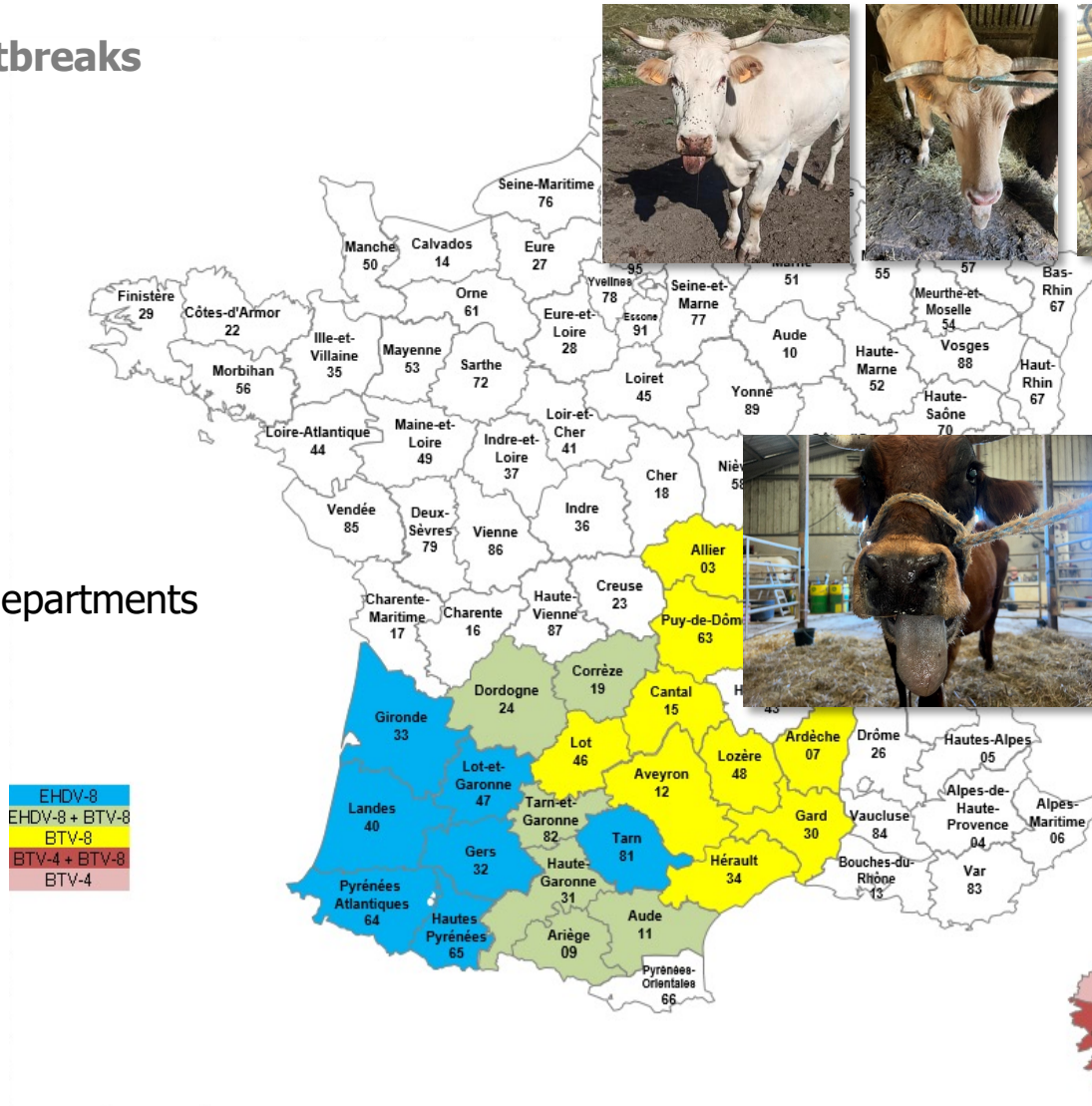


Emergence of EHDV-8

6 Nov 2023

> 2,000 outbreaks

13 infected departments



Dr Vivien Philis, Lannemezan
Dr Mylène Lemaire-Meyer (LVD09)



Dr Alberto Jorda Blanco (Aude)
Dr Mylène Lemaire-Meyer (LVD09)

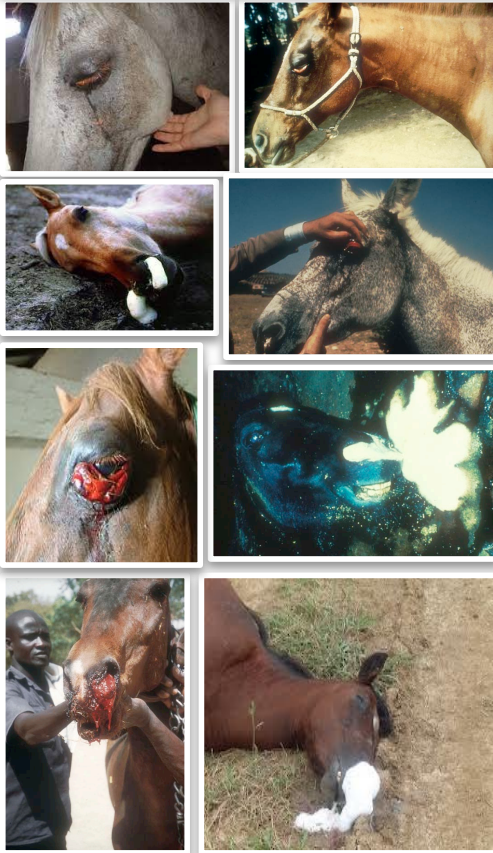


African horse sickness virus

African horse sickness virus (AHSV)



S. Zientara

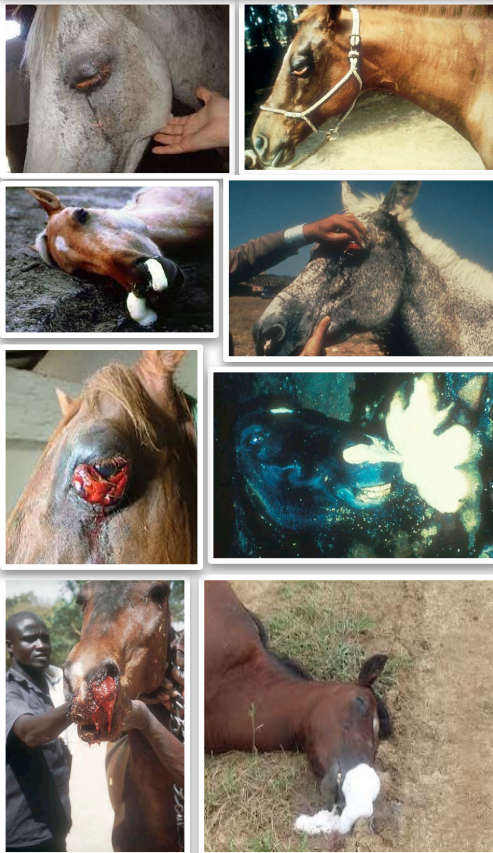


- **1327**: 1st description in Yemen.
- Haemorrhagic disease ("Equine Ebola") ; **highly lethal in horses.**
- **9 serotypes.**

African horse sickness virus (AHSV)



S. Zientara



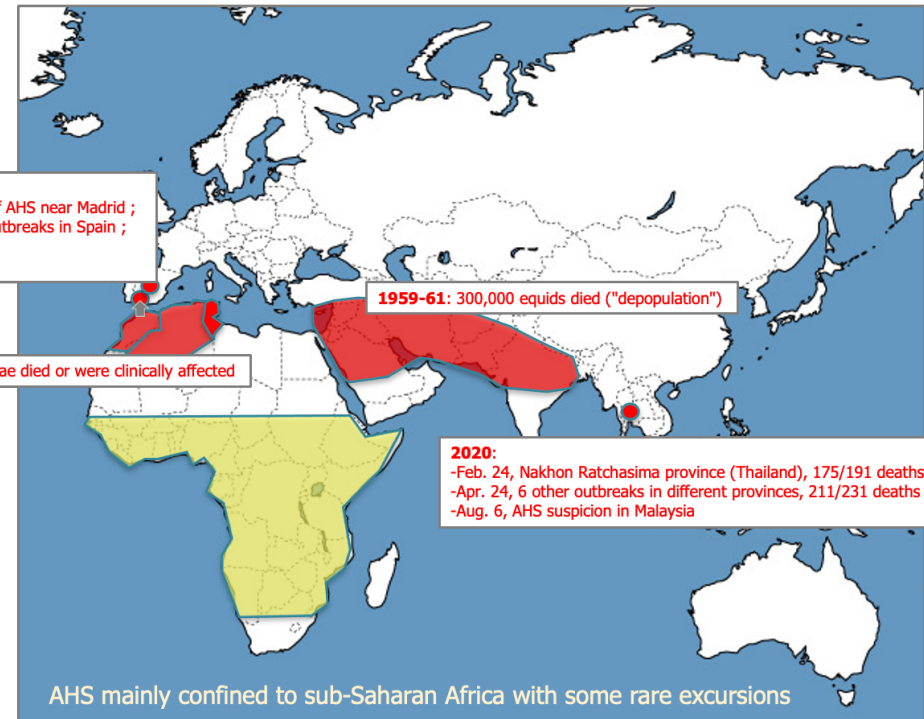
- **1327:** 1st description in Yemen.
- Haemorrhagic disease ("Equine Ebola") ; **highly lethal in horses.**
- **9 serotypes.**

1987-91:
-Jul. 87, 27 cases of AHS near Madrid ;
-1988-90, severe outbreaks in Spain ;
-1989, Portugal ;
-1989-91: Morocco.

1959-61: 300,000 equids died ("depopulation")

1965-66: 77 equidae died or were clinically affected

2020:
-Feb. 24, Nakhon Ratchasima province (Thailand), 175/191 deaths ;
-Apr. 24, 6 other outbreaks in different provinces, 211/231 deaths ;
-Aug. 6, AHS suspicion in Malaysia

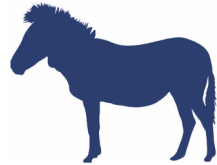


AHS mainly confined to sub-Saharan Africa with some rare excursions

Vertebrate hosts

EQUIDS

RESERVOIR



Zebbras
rarely display clinical signs

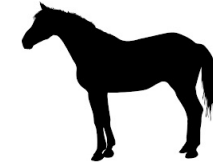
ACCIDENTAL/INDICATOR HOSTS



Donkeys
(10% death)



Mules
(50% death)



Horses
(50-95% death)



susceptibility

OTHERS



Dogs
dead-end hosts
highly susceptible
oral ingestion +++



Camels

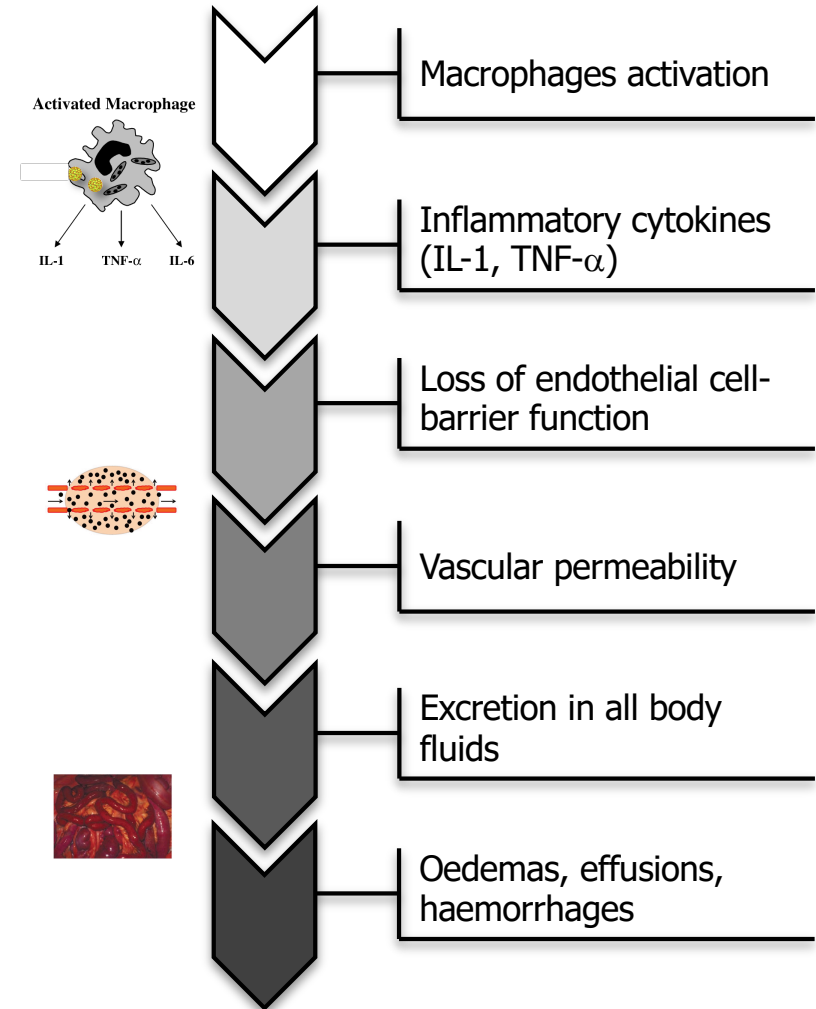
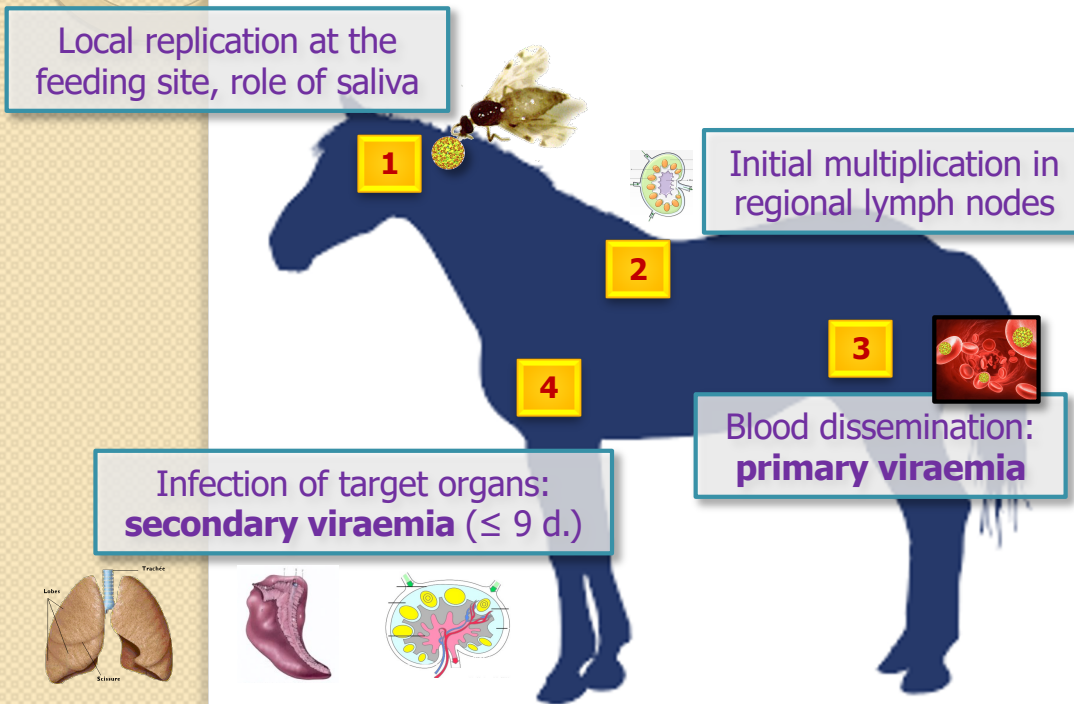
Antibodies detected with inconsistencies in other species ; limited epidemiological role.



Not zoonotic

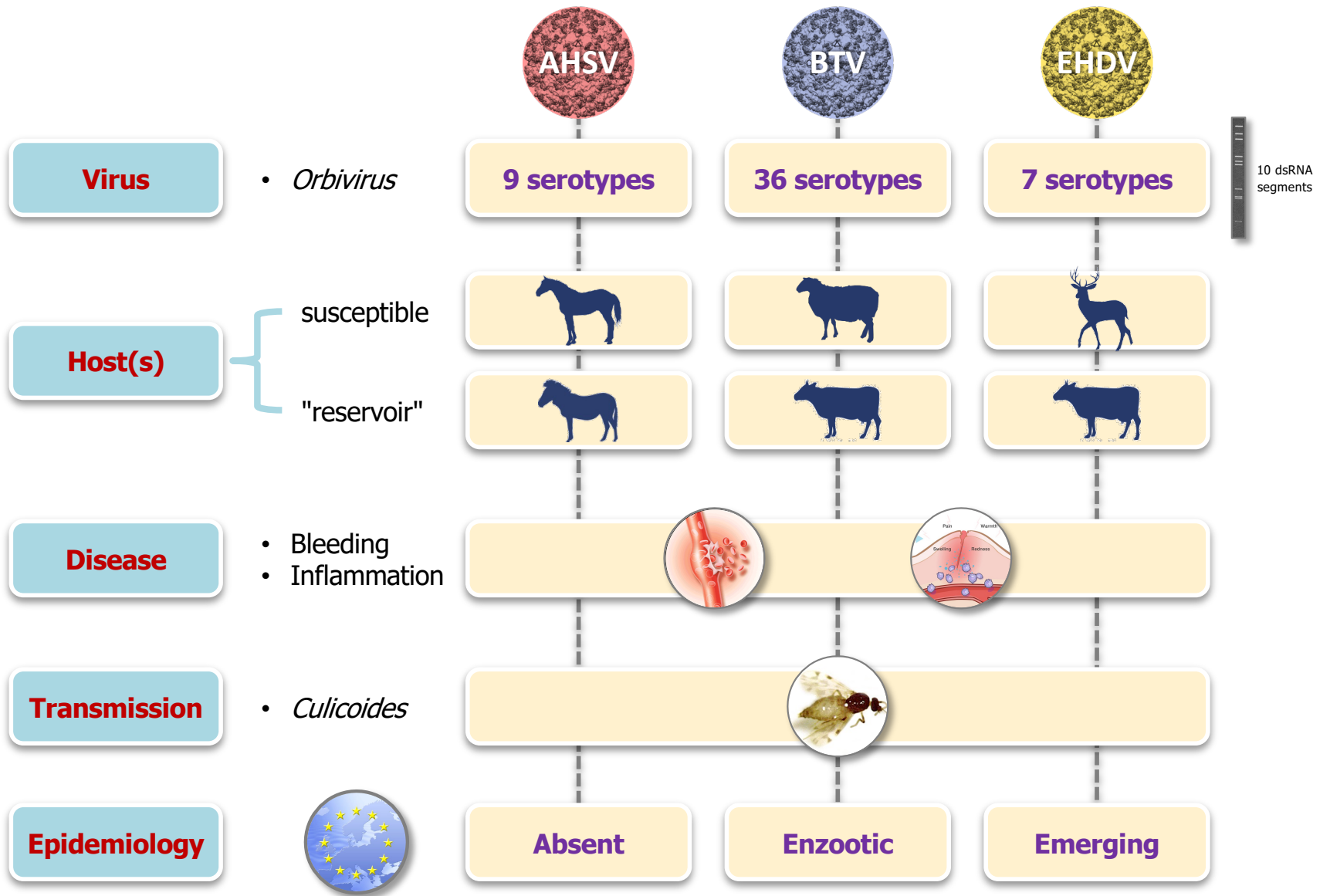


AHS pathogenesis



● 4 clinical forms ; **pulmonary form** = most severe form (**>95% lethality**)

AHSV-BTV-EHDV: common and distinct features



Prevention and control measures



Biology of Orbiviruses (BIOR): research activities

- Understanding disease features
- Diagnostics and tools
- Epidemiology
- Vaccination
- Innate AV response
- Interactomics
- Others



Biology of Orbiviruses (BIOR): research activities

Understanding disease features

Diagnostics and tools

Epidemiology

Vaccination

Innate AV response

Interactomics

Others



Understanding disease features

Received: 7 July 2017
DOI: 10.1111/tbed.12746

ORIGINAL ARTICLE

WILEY *Journal of Transboundary and Emerging Diseases*

Experimental infection of sheep, goats and cattle with a bluetongue virus serotype 4 field strain from Bulgaria, 2014

C. Schulz¹ | C. Sailleau² | E. Bréard² | J. Flannery³ | C. Viarouge² | S. Zientara² | M. Beer¹ | C. Batten³ | B. Hoffmann¹

Received: 20 July 2018 | Revised: 1 October 2018 | Accepted: 13 January 2019
DOI: 10.1111/tbed.13131

ORIGINAL ARTICLE

WILEY *Journal of Transboundary and Emerging Diseases*

Evidence of reduced viremia, pathogenicity and vector competence in a re-emerging European strain of bluetongue virus serotype 8 in sheep

John Flannery¹ | Beatriz Sanz-Bernardo¹ | Martin Ashby¹ | Hannah Brown¹ | Simon Carpenter¹ | Lyndsay Cooke¹ | Amanda Corla¹ | Lorraine Frost¹ | Simon Gubbins¹ | Hayley Hicks¹ | Mehnaz Qureshi¹ | Paulina Rajko-Nenow¹ | Christopher Sanders¹ | Matthew Tully¹ | Emmanuel Bréard² | Corinne Sailleau² | Stephan Zientara² | Karin Darpel^{1,*} | Carrie Batten^{1,*}

Experimental infection of calves with seven serotypes of Epizootic Hemorrhagic Disease virus: production and characterization of reference sera

Corinne Sailleau¹, Emmanuel Bréard¹, Cyril Viarouge¹, Guillaume Belbis², Thomas Lilin², Damien Vitour¹ and Stephan Zientara¹

¹UMR Virologie, INRA, Ecole Nationale Vétérinaire d'Alfort, laboratoire de santé animale d'Alfort, ANSES, Université Paris-Est, 94700 Maisons-Alfort, France.

²Ecole Nationale Vétérinaire de Maisons Alfort, France.

*Corresponding author at: ANSES - Laboratoire Santé Animale - UMR 1161, 14 Rue Pierre et Marie Curie, ACI-BAC-002, 94700 Maisons-Alfort, France. Tel.: + 01.49.77.27.07 / 13.39, e-mail: corinne.sailleau@anses.fr.

Veterinaria Italiana 2019, **55** (4), 339-346. doi: 10.12834/Vettl.2104.11179.1
Accepted: 16.12.2019 | Available on line: 31.12.2019

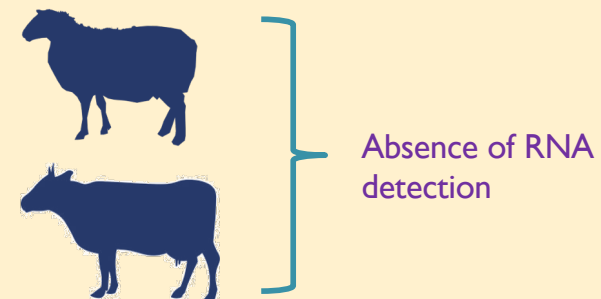
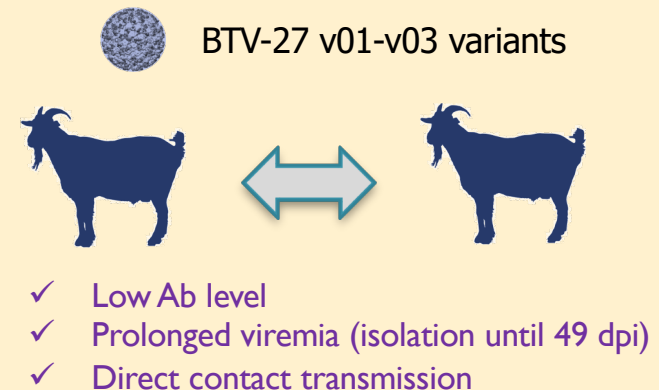
Received: 7 July 2017
DOI: 10.1111/tbed.12780

ORIGINAL ARTICLE

WILEY *Journal of Transboundary and Emerging Diseases*

Bluetongue virus serotype 27: Experimental infection of goats, sheep and cattle with three BTV-27 variants reveal atypical characteristics and likely direct contact transmission BTV-27 between goats

E. Bréard¹ | C. Schulz² | C. Sailleau¹ | C. Bernelin-Cottet³ | C. Viarouge¹ | D. Vitour¹ | B. Guillaume⁴ | G. Caignard¹ | A. Gorlier¹ | H. Attoui¹ | M. Gallois⁵ | B. Hoffmann² | S. Zientara¹ | M. Beer²



Understanding disease features

IFNAR^{-/-}



OPEN ACCESS Freely available online

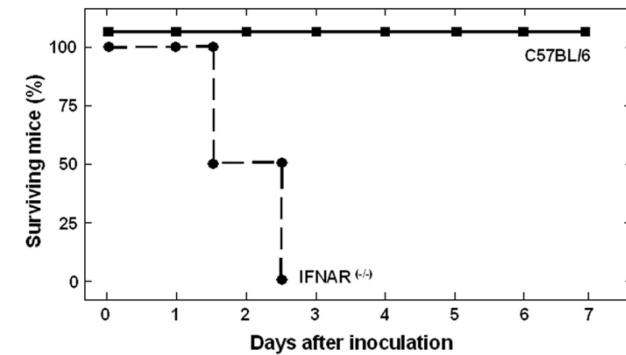
PLOS one

Establishment of a Bluetongue Virus Infection Model in Mice that Are Deficient in the Alpha/Beta Interferon Receptor

Eva Calvo-Pinilla¹, Teresa Rodríguez-Calvo¹, Juan Anguita², Noemí Sevilla¹, Javier Ortego^{1*}

¹ Centro de Investigación en Sanidad Animal, CISA-INIA, Madrid, Spain, ² Department of Veterinary and Animal Sciences, University of Massachusetts Amherst, Amherst, Massachusetts, United States of America

A



Understanding disease features

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Veterinary Microbiology 155 (2012) 417–419

Contents lists available at SciVerse ScienceDirect



ELSEVIER

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic



Short communication

Epizootic hemorrhagic disease virus infection of type I interferon receptor deficient mice

Michael Eschbaumer^{a,*}, Markus Keller^b, Martin Beer^a, Bernd Hoffmann^a

^a Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Südufer 10, 17493 Greifswald - Insel Riems, Germany

^b Institute of Novel and Emerging Infectious Diseases, Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

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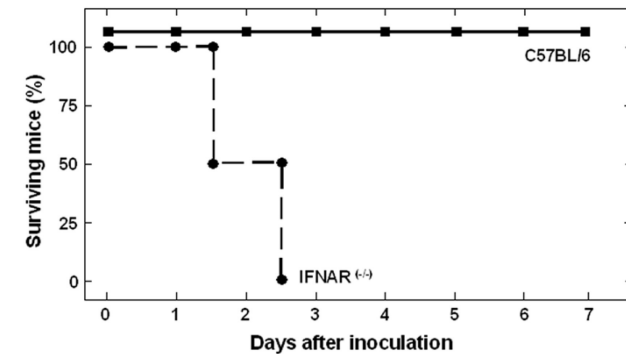
PLoS one

A Modified Vaccinia Ankara Virus (MVA) Vaccine Expressing African Horse Sickness Virus (AHSV) VP2 Protects Against AHSV Challenge in an IFNAR^{-/-} Mouse Model

Javier Castillo-Olivares^{1*}, Eva Calvo-Pinilla², Isabel Casanova², Katarzyna Bachanek-Bankowska¹, Rachael Chiam³, Sushila Maan¹, Jose Maria Nieto², Javier Ortego², Peter Paul Clement Mertens¹

¹ Institute for Animal Health, Pirbright, Woking, Surrey, United Kingdom, ² Centro en Investigación y Sanidad Animal (CISA), Valdeolmos, Madrid, Spain, ³ Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, United Kingdom

A



Understanding disease features

IFNAR^{-/-}



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PLoS one

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Eva Calvo-Pinilla¹, Teresa Rodríguez-Calvo¹, Juan Anguita², Noemí Sevilla¹, Javier Ortego^{1*}

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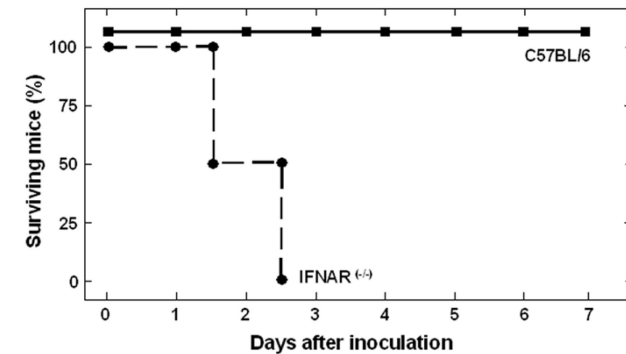
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¹ Institute for Animal Health, Pirbright, Woking, Surrey, United Kingdom, ² Centro en Investigación y Sanidad Animal (CISA), Valdeolmos, Madrid, Spain, ³ Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, United Kingdom

A



Virulence testing in isolator

- ✓ AHSV strains
- ✓ BTV-8 Aveyron-2023

Biology of Orbiviruses (BIOR): research activities

Understanding disease features

Diagnostics and tools

Epidemiology

Vaccination

Innate AV response

Interactomics

Others



- Expertise for the ministry of agriculture
- Kits evaluation
- EILA
- Management of a network of 52 LVDs

Diagnostics and tools

Clinical diagnosis

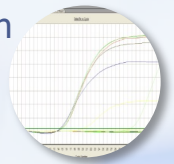
- ✓ Clinical signs and lesions not always obvious.
- ✓ Post-mortem examination, epidemiological factors (seasonal occurrence).
- ✓ Complicated differential diagnosis in the early stages of the infection or mild symptoms.

Virological/lab. tests

- ✓ **Direct:** detection of the virus and its constituents



- Virus isolation and amplification
- Antigenic detection
- Genome detection



- ✓ **Indirect:** antibodies detection



- Seroneutralisation
- ELISA
- Miscellaneous (WB, IF, agglutination...)

Diagnostics and tools

Received: 24 April 2018 | Revised: 22 June 2018 | Accepted: 2 July 2018
DOI: 10.1111/tbed.12968

ORIGINAL ARTICLE

WILEY *Transboundary and Emerging Diseases*

Assessment of reproducibility of a VP7 Blocking ELISA diagnostic test for African horse sickness

Manuel Durán-Ferrer¹ | Montserrat Agüero¹ | Stephan Zientara² | Cécile Beck² | Sylvie Lecollinet² | Corinne Sailleau² | Shirley Smith³ | Christiaan Potgieter^{3,4} | Paloma Rueda⁵ | Patricia Sastre⁵ | Federica Monaco⁶ | Ruben Villalba⁴ | Cristina Tena-Tomás¹ | Carrie Batten⁷ | Lorraine Frost⁷ | John Flannery⁷ | Simon Gubbins⁷ | Baratang A. Lubisi⁸ | José Manuel Sánchez-Vizcaíno⁹ | Michelle Emery¹⁰ | Tracy Sturgill¹⁰ | Eileen Ostlund¹⁰ | Javier Castillo-Olivares⁷

Received: 18 December 2019 | Revised: 4 March 2020 | Accepted: 31 March 2020
DOI: 10.1111/tbed.13586

ORIGINAL ARTICLE

WILEY *Transboundary and Emerging Diseases*

Evaluation of a commercial ELISA for detection of epizootic haemorrhagic disease antibodies in domestic and wild ruminant sera

Emmanuel Bréard¹ | Cyril Viarouge¹ | Fabien Donnet² | Corinne Sailleau¹ | Sophie Rossi³ | Philippe Pourquier² | Damien Vitour¹ | Loïc Comtet² | Stéphan Zientara¹

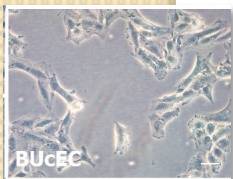
International Journal of
Molecular Sciences

MDPI

Article

Bovine Organospecific Microvascular Endothelial Cell Lines as New and Relevant In Vitro Models to Study Viral Infections

Anne-Claire Lagrée¹, Fabienne Fasan², Clotilde Rouxel¹, Marine Pivet², Marie Pourcelot³, Aurore Fablet³, Aurore Romey³, Grégory Caignard³, Damien Vitour³, Sandra Blaise-Boisseau³, Claudine Kieda^{2,4}, Henri-Jean Boulouis¹, Nadia Haddad¹ and Catherine Grillon^{2,4}



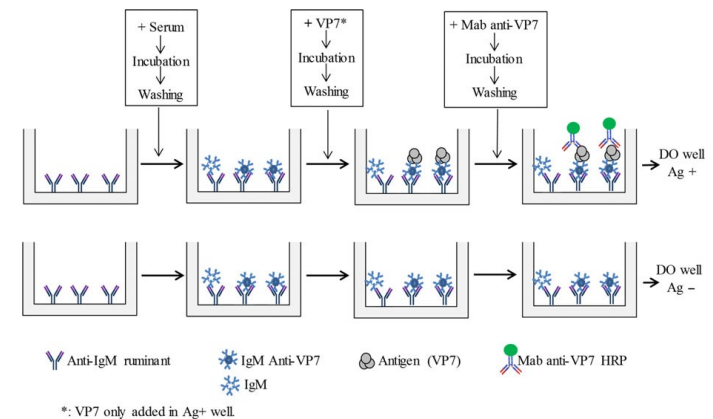
Received: 11 June 2018 | Revised: 10 September 2018 | Accepted: 15 October 2018
DOI: 10.1111/tbed.13060

ORIGINAL ARTICLE

WILEY *Transboundary and Emerging Diseases*

Evaluation of an IGM-specific ELISA for early detection of bluetongue virus infections in domestic ruminants sera

Emmanuel Bréard¹ | Axel Gorlier¹ | Cyril Viarouge¹ | Fabien Donnet² | Corinne Sailleau¹ | Claudia Schulz³ | Bernd Hoffmann³ | Loïc Comtet² | Martin Beer³ | Stéphan Zientara¹ | Damien Vitour¹



viruses

MDPI

Article

Development and Validation of an ELISA for the Detection of Bluetongue Virus Serotype 4-Specific Antibodies

Emmanuel Bréard^{1,*}, Mathilde Turpaud¹, Georges Beaud¹, Lydie Postic¹, Aurore Fablet¹, Martin Beer², Corinne Sailleau¹, Grégory Caignard¹, Cyril Viarouge¹, Bernd Hoffmann², Damien Vitour¹ and Stéphan Zientara¹

Diagnostics and tools



Mathilde Gondard

Funding ANR PrepMedVet
Platform IdentityPath
Adapted from Teramo colleagues

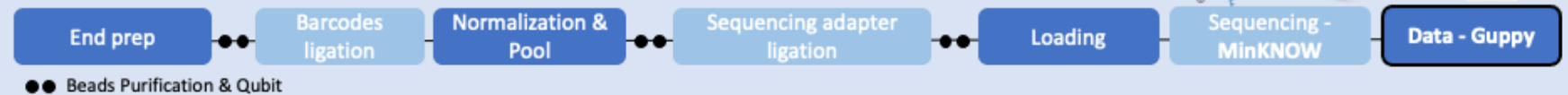
Whole genome sequencing – *Orbivirus* (BTV, EHDV)

✓ Sequencing workflow development

- Sample preparation using SISPA approach (Sequence-Independent, Single-Primer Amplification)
 - Combination of random and specific primers targeting orbivirus segment the conserved extremities



- Library preparation & MinION sequencing (Oxford nanopore)
 - Kit NBD114.24, FLOMIN114 flowcells



- Sequencing data analysis
 - Mapping on reference sequences

geneious prime



✓ Applications

- Characterization of 17 BTV genomes and 2 EHDV genomes from Cuba 2023 (Submitted in viruses)
- Characterization of the BTV and EHDV strains responsible of BT and EHD in France 2023 (BTV-8, BTV-4, EHDV-8)

Biology of Orbiviruses (BIOR): research activities

- ▣ Understanding disease features
- ▣ Diagnostics and tools
- ▣ **Epidemiology**
- ▣ Vaccination
- ▣ Innate AV response
- ▣ Interactomics
- ▣ Others



Epidemiology: worldwide



Epidemiology: Europe and Mediterranean basin

Received 20 May 2021
DOI: 10.1111/1365-3113.12198

ORIGINAL ARTICLE WILEY

Serological status for BTV-8 in French cattle prior to the 2015 re-emergence

N. Courtejoie¹ | B. Durand¹ | E. Breard¹ | C. Salliau¹ | D. Vitou¹ | S. Zientara¹ | A. Gorfer¹ | F. Baurier¹ | C. Goumelen¹ | F. Benoit¹ | H. Achou¹ | C. Millet¹ | S. Pollak¹ | C. Pagnou¹ | C. Vairoux² | G. Zanella³

viruses MDPJ

Red deer (*Cervus elaphus*) Did Not Play the Role of Maintenance Host for Bluetongue Virus in France: The Burden of Proof by Long-Term Wildlife Monitoring and *Culicoides* Snapshots

Sophie Rossi^{1,2}, Thomas Balenghien^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}

Received 4 June 2021
DOI: 10.1111/1365-3113.12198

RESEARCH ARTICLE Open Access

Estimation of French cattle herd immunity against bluetongue serotype 8 at the time of its re-emergence in 2015

L. Bourne¹ | S. Casades¹ | C. Salliau¹ | E. Breard¹ | G. Zanella² | S. Zientara¹ | A. Pedraza¹ | E. Cori¹ | L. Tournier¹ | J. Dor¹ | F. Hendrikx¹ and D. Cabaret¹

Received 21 June 2021
DOI: 10.1111/1365-3113.12198

SHORT COMMUNICATION WILEY

Circulation of bluetongue virus 8 in French cattle, before and after the re-emergence in 2015

N. Courtejoie¹ | B. Durand¹ | L. Bourne¹ | A. Gorfer¹ | E. Breard¹ | C. Salliau¹ | D. Vitou¹ | S. Zientara¹ | F. Baurier¹ | C. Goumelen¹ | F. Benoit¹ | H. Achou¹ | C. Millet¹ | S. Pollak¹ | C. Pagnou¹ | C. Vairoux² | G. Zanella³

Received 4 June 2021
DOI: 10.1111/1365-3113.12198

SHORT COMMUNICATION WILEY

Complete genome sequence of bluetongue virus serotype 4 that emerged on the French island of Corsica in December 2016

C. Salliau¹ | E. Breard¹ | C. Vairoux² | A. Gorfer¹ | H. Quémener¹ | E. Hirschaut¹ | F. Touzin¹ | Y. Blanchard¹ | D. Vitou¹ | S. Zientara¹

SHORT COMMUNICATION

Epizootic haemorrhagic disease virus circulation in Tunisia

Sahar Ahmed¹, Mohamed Abd El-Fatah Mahmoud¹, Cyrille Vairoux², Corinne Salliau³, Alessio Lorusso⁴, Stefania Babay, Giovanna Savini, Stephan Zientara⁵ and Salah Hamman⁶

viruses MDPJ

Epizootic Haemorrhagic Disease Virus Serotype 8 in Tunisia, 2021

Sahar Ahmed¹, Corinne Salliau², Alessio Lorusso³, Stefania Babay⁴, Mohamed Abd El-Fatah Mahmoud⁵, Cyrille Vairoux⁶, Giovanna Savini⁷, Stephan Zientara⁸, Salah Hamman⁹

Received 2 March 2021 | Revised 17 July 2021 | Accepted 17 July 2021
DOI: 10.1111/1365-3113.12198

RAPID COMMUNICATION WILEY

Emergence of bluetongue virus serotype 4 in mainland France in November 2017

Corinne Salliau¹ | Emmanuel Breard¹ | Cyril Vairoux² | Axel Gofier¹ | Aurélie Leroux¹ | Edouard Hirschaut¹ | Pierrick Lucas¹ | Yannick Blanchard¹ | Damien Vitou¹ | Marie Grandjean-Chabot¹ | Stephan Zientara³



Epizootic Hemorrhagic Disease Virus Serotype 8, Italy, 2022

Alessio Lorusso, Stefano Cappai, Federica Loi, Luigia Pinna, Angelo Ruiu, Giontonella Puggioni, Annalisa Guercio, Giuseppe Purpani, Domenico Vicari, Soufien Sghaier, Stephan Zientara, Massimo Spedicato, Salah Hammami, Thameur Ben Hassine, Ottavio Portanti, Emmanuel Breard, Corinne Salliau, Massimo Ancora, Diana Di Sabatino, Daniela Morelli, Paolo Calistri, Giovanni Savini

Journal homepage: www.blackwell-synergy.com/doi/full/10.1111/1365-3113.12198

Infection, Genetics and Evolution

Journal homepage: www.blackwell-synergy.com/doi/full/10.1111/1365-3113.12198

Research paper

Presence of bluetongue and epizootic hemorrhagic disease viruses in Egypt in 2016 and 2017

Sahar Ahmed¹, Mohamed Abd El-Fatah Mahmoud¹, Cyrille Vairoux², Corinne Salliau³, Stephan Zientara⁴, Emmanuel Breard⁵

2015: understanding BTV-8 re-emergence



Julien Buttet, DDCSPP03

2015: understanding BTV-8 re-emergence

- **Global aim:** To investigate the origin and transmission history of BTV-8 in Europe using a genomic sequence comparison approach.

PLOS BIOLOGY

M. Palmarini (CVR, Glasgow)

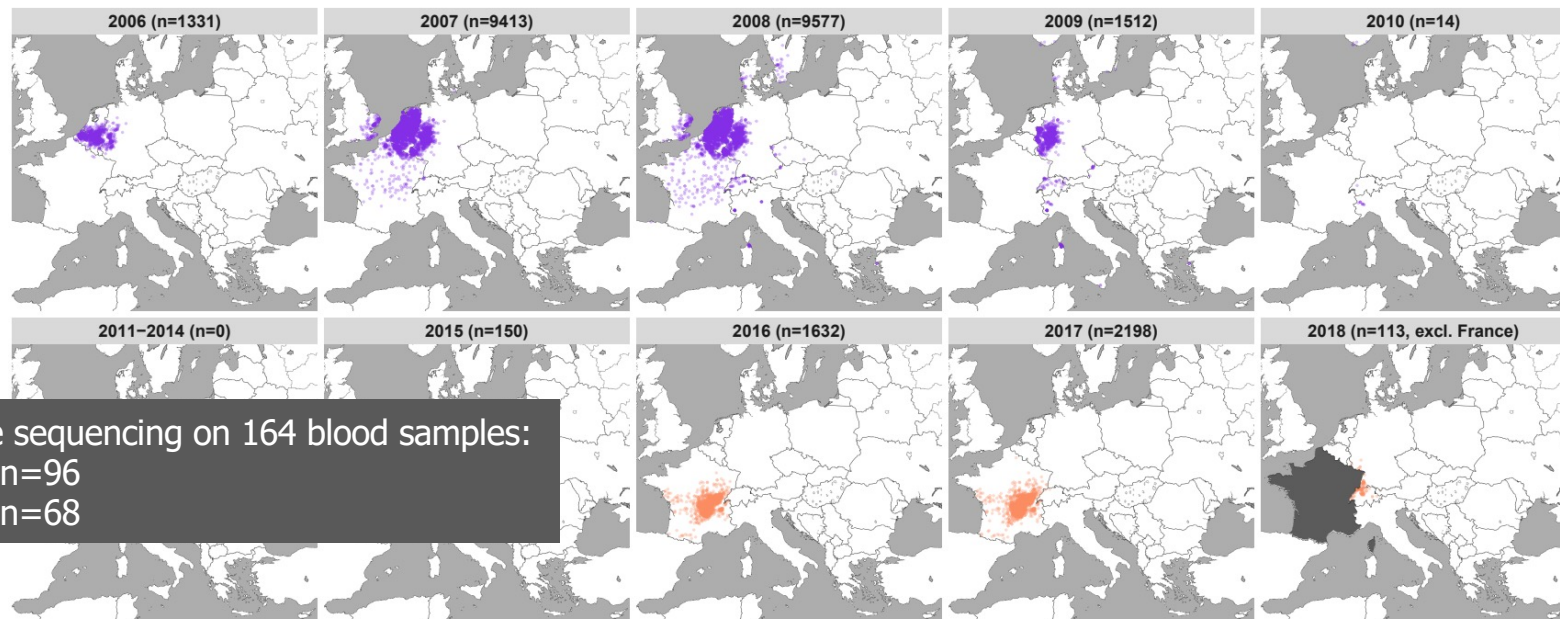


SHORT REPORTS

“Frozen evolution” of an RNA virus suggests accidental release as a potential cause of arbovirus re-emergence

David J. Pascall^{1*}, Kyriaki Nomikou^{2,3*}, Emmanuel Bréard⁴, Stephan Zientara⁵, Ana da Silva Filipe⁶, Bernd Hoffmann⁷, Maude Jacquot^{6,7}, Joshua B. Singer⁸, Kris De Clercq⁹, Anette Botner^{9,10}, Corinne Sailleau⁴, Cyril Viarouge⁴, Carrie Batten¹¹, Giantonella Puggioni¹², Ciriaco Ligios¹², Giovanni Savini¹³, Piet A. van Rijn^{14,15}, Peter P. C. Mertens^{3,11}, Roman Biek^{11*}, Massimo Palmarini^{2,16*}

BTV-8 in Europe 2006-2018



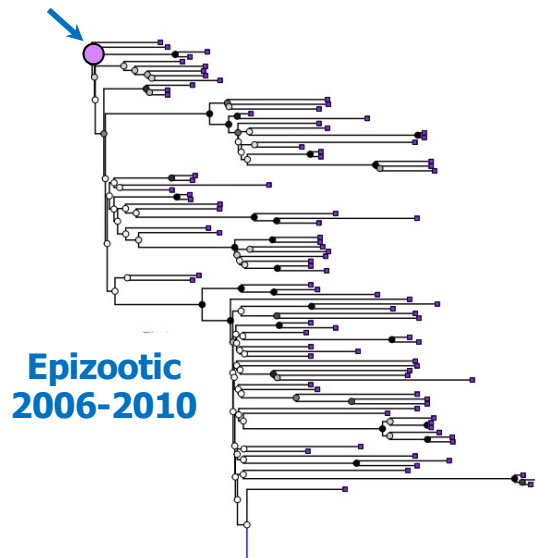
- Full-genome sequencing on 164 blood samples:
- 2006-2009: n=96
- 2015-2018: n=68

- **Specific objective:** explore the origin and transmission of BTV-8 in France in 2015.

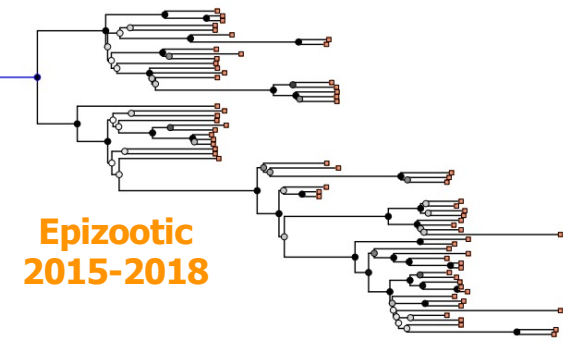
2015: understanding BTV-8 re-emergence

● Chronological phylogenetic tree.

2006 ancestor



Period with no apparent infection

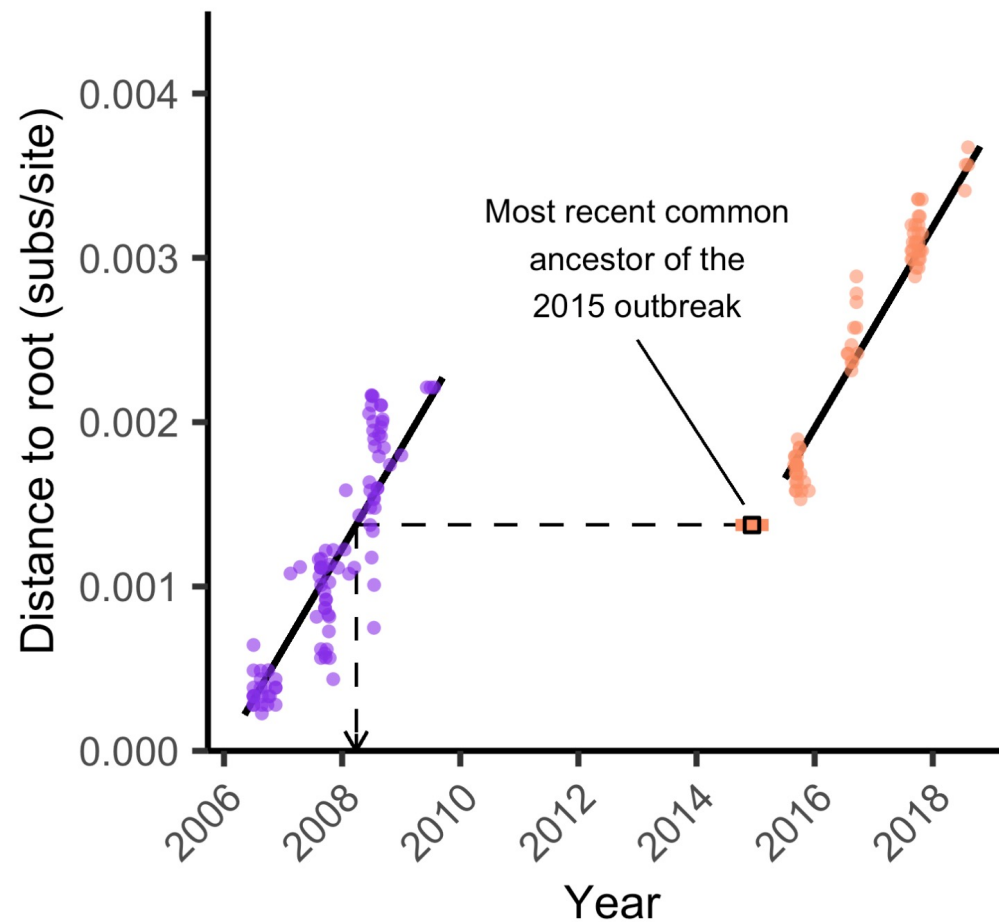


Posterior Probability
1.00
0.75
0.50
0.25
0.00

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019

2015: understanding BTV-8 re-emergence

- Genetic and temporal evolution between the two epizootics.

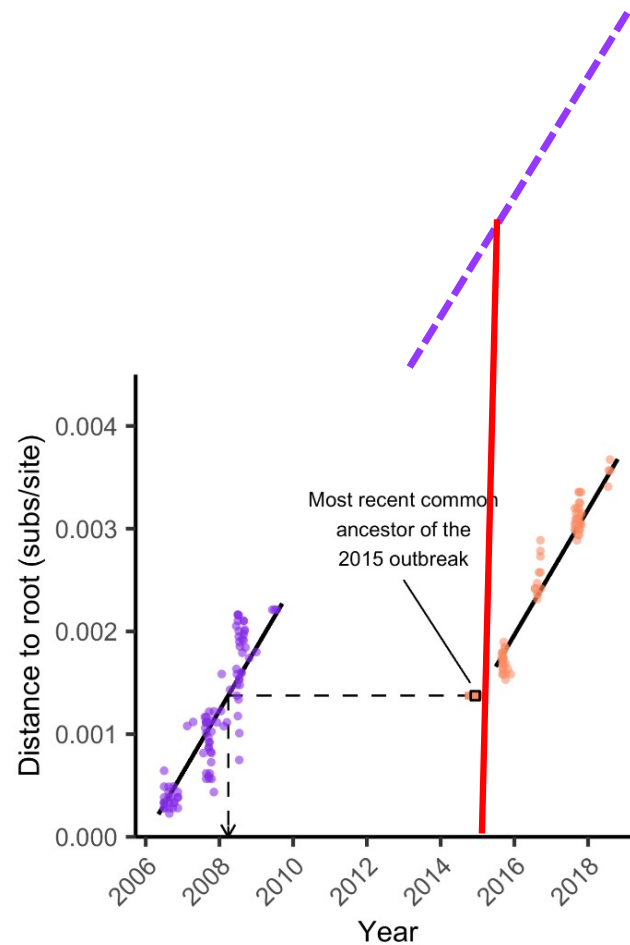


Based on its distance from the root, the **2015 re-emerging virus** is a direct **descendant** of the **2006-2010 circulating strain**.

2015: understanding BTV-8 re-emergence

Circulation silencieuse ?

Silent circulation?

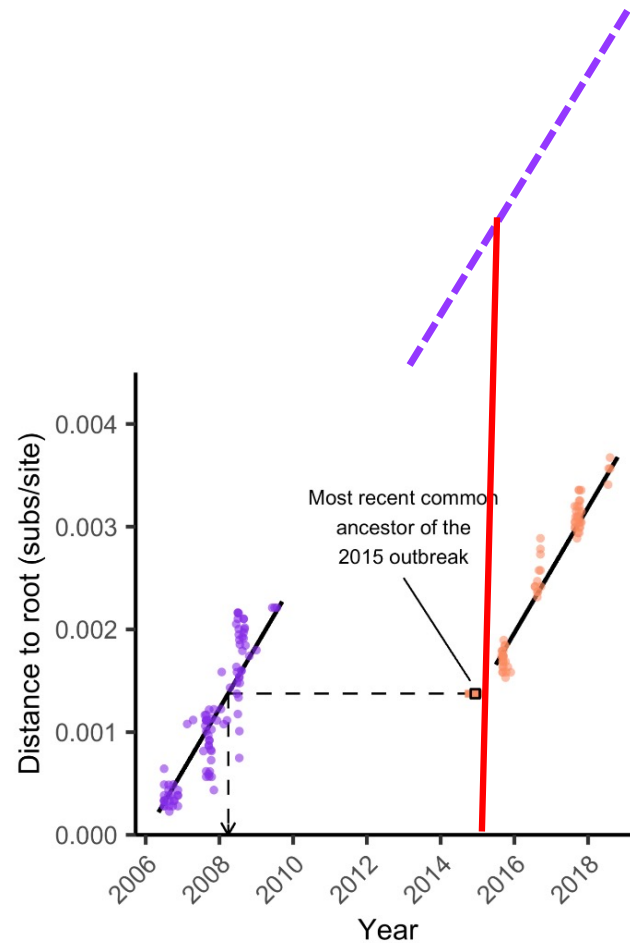


2015: understanding BTV-8 re-emergence

Circulation silencieuse ?

Silent circulation?

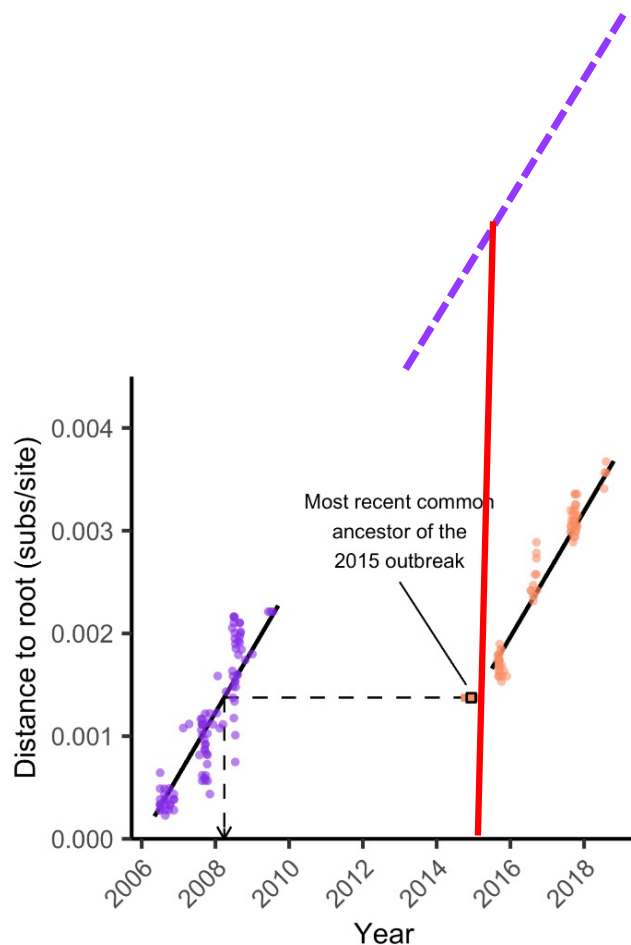
Lab escape?



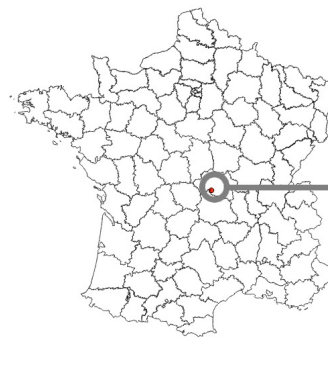
2015: understanding BTV-8 re-emergence

Circulation silencieuse ?

Silent circulation?



Lab escape?



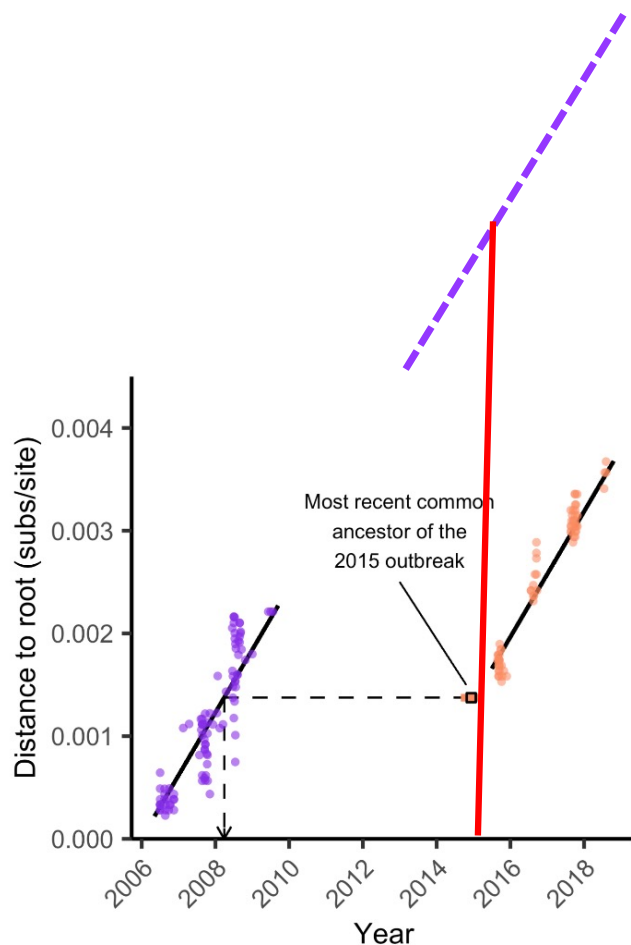
Cycle in unknown host(s)...



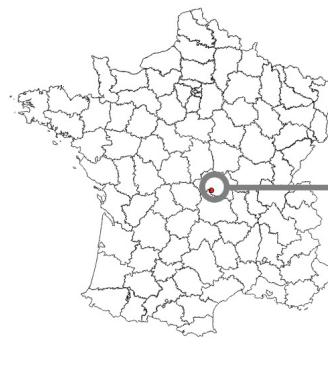
2015: understanding BTV-8 re-emergence

Circulation silencieuse ?

Silent circulation?



Lab escape?



Cycle in unknown host(s)...



So what ?

2015: understanding BTV-8 re-emergence

Récolte de semence

Assurance production

La récolte est faite en présence d'une vache en chaleur, avec un vagin artificiel. C'est la méthode qui se rapproche le plus des conditions naturelles et qui est la plus fiable.

- > Toutes races de taureaux



Contrôle fertilité



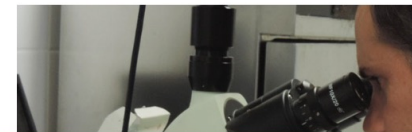
Analyse du sperme au microscope :

- Motilité
- % de vivant

Analyse au spectro-photomètre :

- Concentration (nb spz/mm³)

- > Contrôle qualité de semence en frais



Production de semence monte privée

Hypothesis: accidental infection by insemination with frozen semen containing BTV-8.

2015: understanding BTV-8 re-emergence

Récolte de semence

Assurance production

La récolte est faite en présence d'une vache en chaleur, avec un vagin artificiel. C'est la méthode qui se rapproche le plus des conditions naturelles et qui est la plus fiable.

> Toutes races de taureaux



Contrôle fertilité



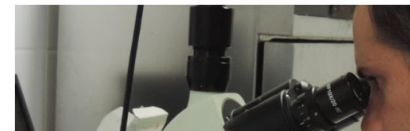
Analyse du sperme au microscope :

- Motilité
- % de vivant

Analyse au spectro-photomètre :

- Concentration (nb spz/mm³)

> Contrôle qualité de semence en frais



Production de semence monte privée

Hypothesis: accidental infection by insemination with frozen semen containing BTV-8.



2021



Article

Transmission of Bluetongue Virus Serotype 8 by Artificial Insemination with Frozen–Thawed Semen from Naturally Infected Bulls

Kris De Clercq ^{1,*,†}, Leen Vandaele ^{2,†}, Tine Vanbinst ¹, Mickaël Riou ³, Isra Deblauwe ⁴, Wendy Wesselingh ², Anne Pinard ³, Mieke Van Eetvelde ², Olivier Boulesteix ³, Bart Leemans ², Robert Gélineau ³, Griet Vercauteren ⁵, Sara Van der Heyden ⁵, Jean-François Beckers ⁶, Claude Saegerman ⁷, Donal Sammin ⁸, Aart de Kruif ² and Ilse De Leeuw ¹

Biology of Orbiviruses (BIOR) activities

- Understanding disease features
- Diagnostic tools
- Epidemiology
- Vaccination**
- Innate AV response
- Interactomics
- Others



Vaccination



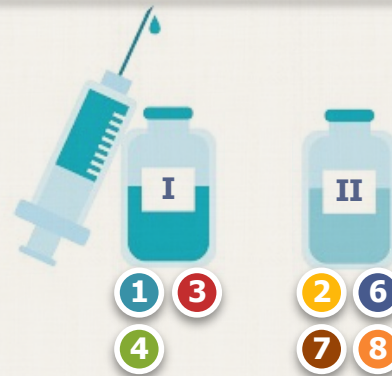
L.A.V. – Live-attenuated vaccines (or modified-live vaccines, MLV)

Live-attenuated vaccines

Polyvalent LAVs



Thailand (2020)



But...



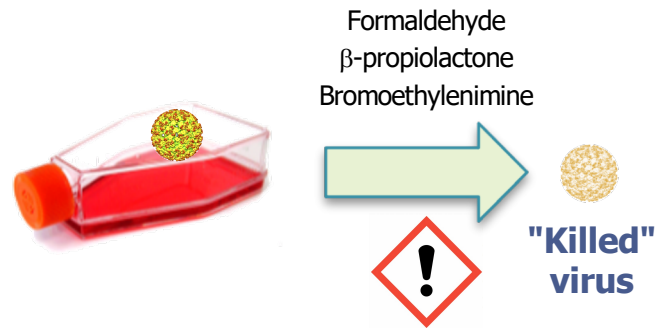
- Possible reversion to virulence
- Few standard formulations
- Variable protection
- Viraemia
- Not DIVA
- No license in Europe
- Transmission by vectors
- Reassortments with field strains

Vaccination



L.A.V. – Live attenuated vaccines

Inactivated vaccines



- Biocontainment risk.
- Adjuvant required.
- Several inoculations.
- Expensive.
- Risk of uncomplete inactivation.
- Not DIVA.



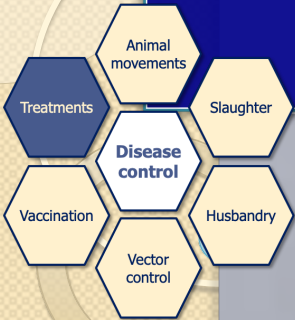
Article






Serological Responses in Cattle following Booster Vaccination against Serotypes 4 and 8 Bluetongue Virus with Two Bivalent Commercial Inactivated Vaccines

Corinne Sailleau ^{1,*}, Lydie Postic ¹, Xavier Chatenet ², Olivier Salat ³, Mathilde Turpaud ¹, Benoit Durand ⁴, Damien Vitour ¹, Stéphan Zientara ¹ and Emmanuel Bréard ¹

Need for
alternatives
vaccines

Vaccination



-  Subunit
-  Virus-like particles
-  DNA
-  Virus-vectored
-  Reverse genetics

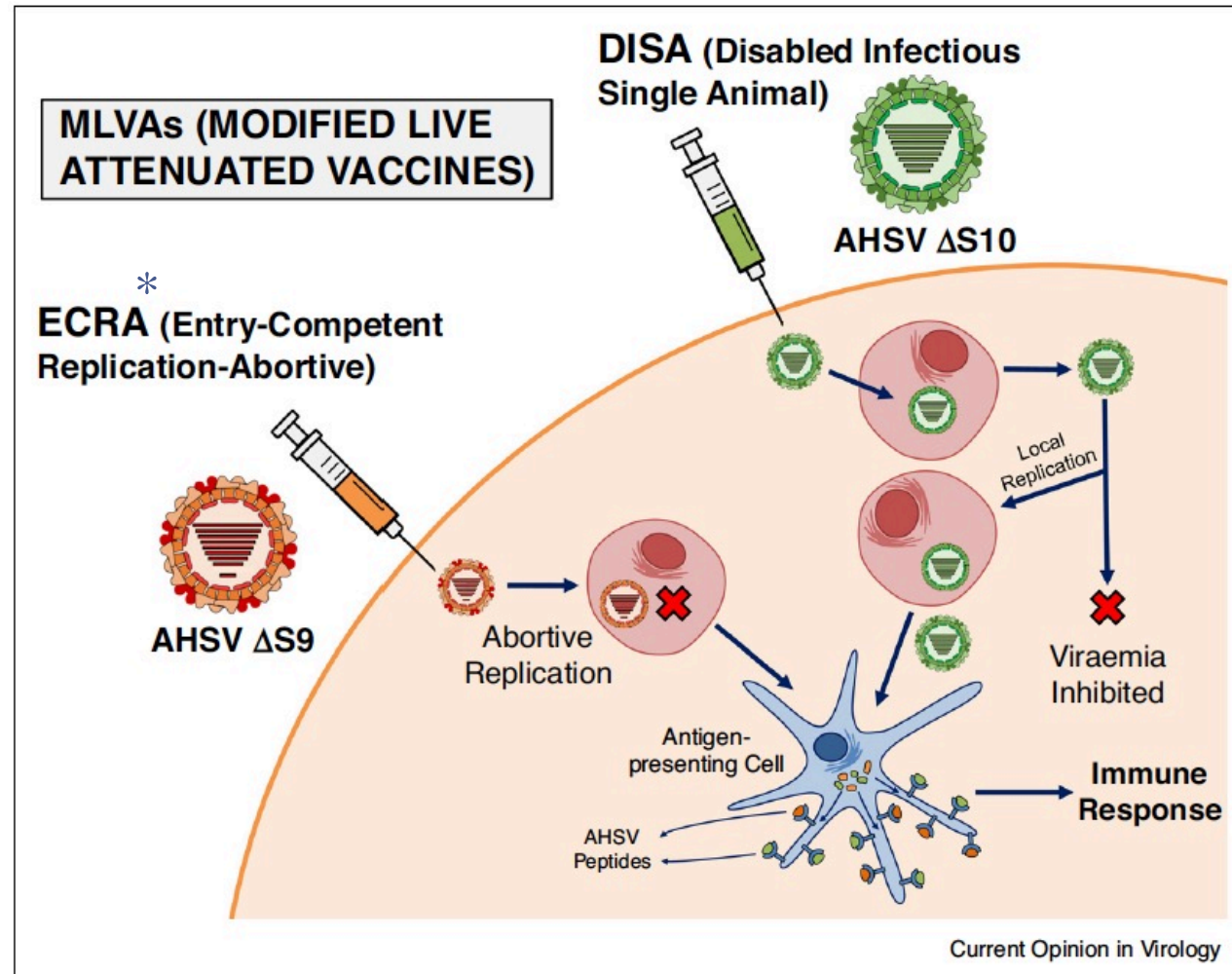


L.A.V. – Live attenuated vaccines

AHSV vaccines based on reverse genetics

ECRA: Lulla (2016, 2017)

DISA: Van de Water (2015), Feenstra (2015), Van Rijn (2018-1/2)



*previously called Disabled Infectious Single Cycle (DISC) vaccines

Dennis (2019), Roy (2020), Calvo-Pinilla (2020)

Vaccination

Vaccine 39 (2021) 3161–3168

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Vaccine

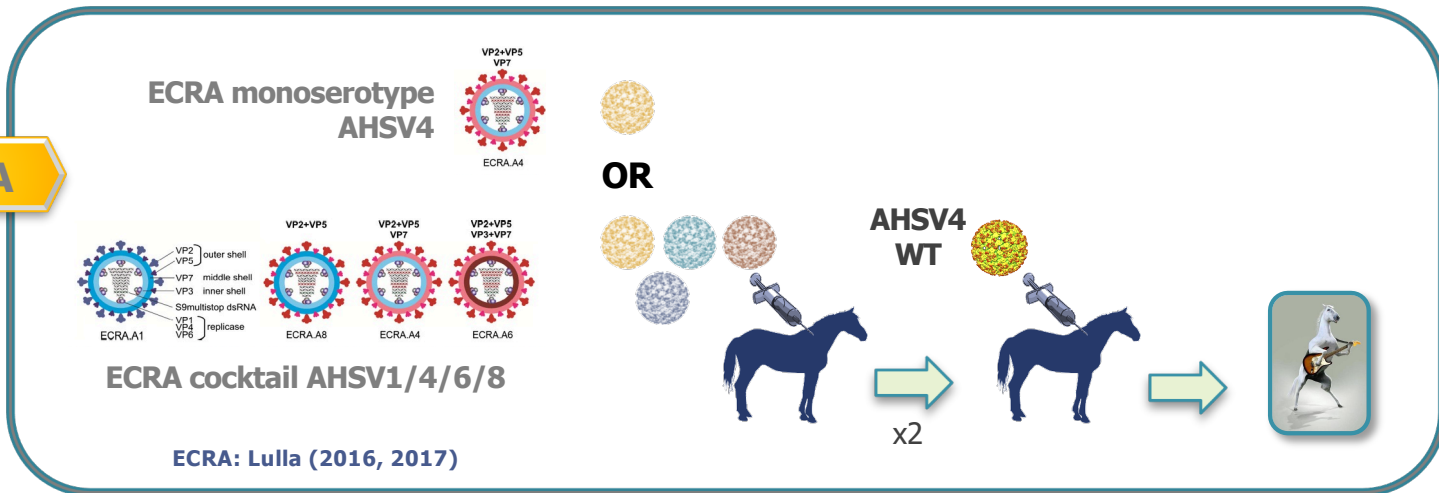
journal homepage: www.elsevier.com/locate/vaccine

Entry-competent-replication-abortive African horse sickness virus strains elicit robust immunity in ponies against all serotypes

Edward Sullivan^a, Sylvie Lecollinet^b, Adeline Kerviel^a, Erika Hue^{c,d}, Stéphane Pronost^{c,d}, Cécile Beck^b, Marine Dumarest^b, Stephan Zientara^b, Polly Roy^{a,*}

^a Department of Infection Biology, Faculty of Infectious and Tropical Disease, London School of Hygiene and Tropical Medicine, United Kingdom
^b Université Paris-Est ANSES Alfort, UMR 1161 Virologie ANSES, INRA, ENVA, Maisons-Alfort, France
^c LABEO Frank Duncombe, 14280 Saint-Contest, France
^d BIOTARGEN, Normandie Univ, UNICAEN, 14000 Caen, France

ECRA



But,
 complicated
 and
 expensive
 ...

SPIDVAC project: new AHSV vaccine



SPIDVAC

Safe Priority Infectious Diseases VACCines



End 2025

Budget: **5.6 millions €**

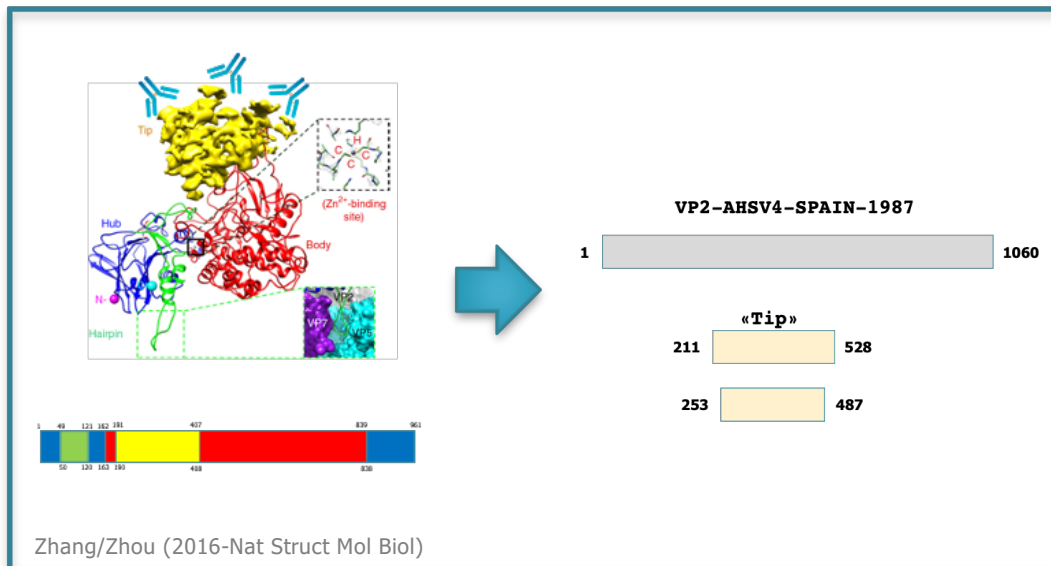
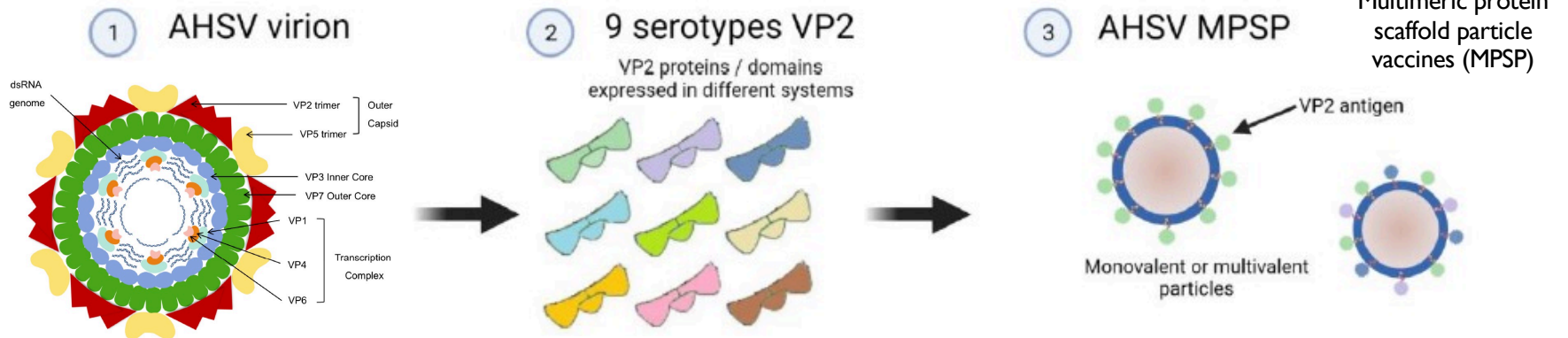
SPIDVAC project: new AHSV vaccine



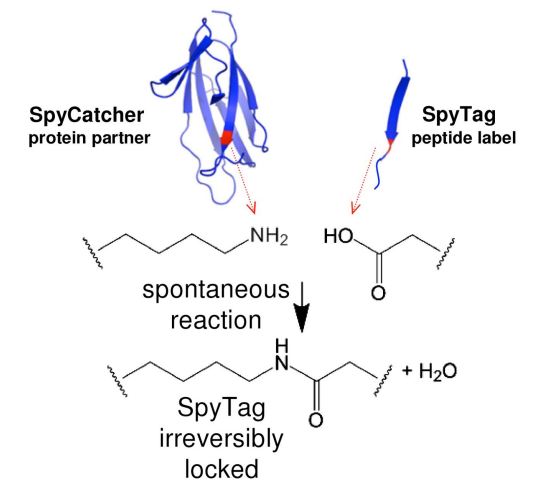
Safe Priority Infectious Diseases VACCines

→ End 2025

Budget: 5.6 millions €



« protein superglue »



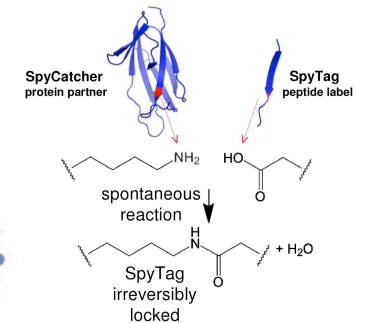
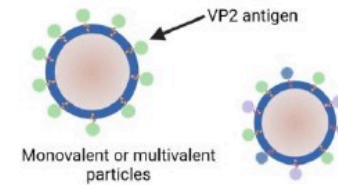
SPIDVAC project: new AHSV vaccine

Andrea Aebischer

conjugation

- Domain 1 : VP2 aa 250-530-SpyTag
 - Domain 2 : VP2 aa 219-530-SpyTag
- SpyCatcher-mi3

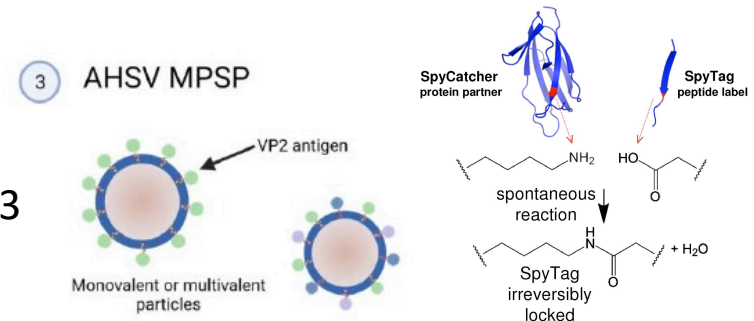
3 AHSV MPSP



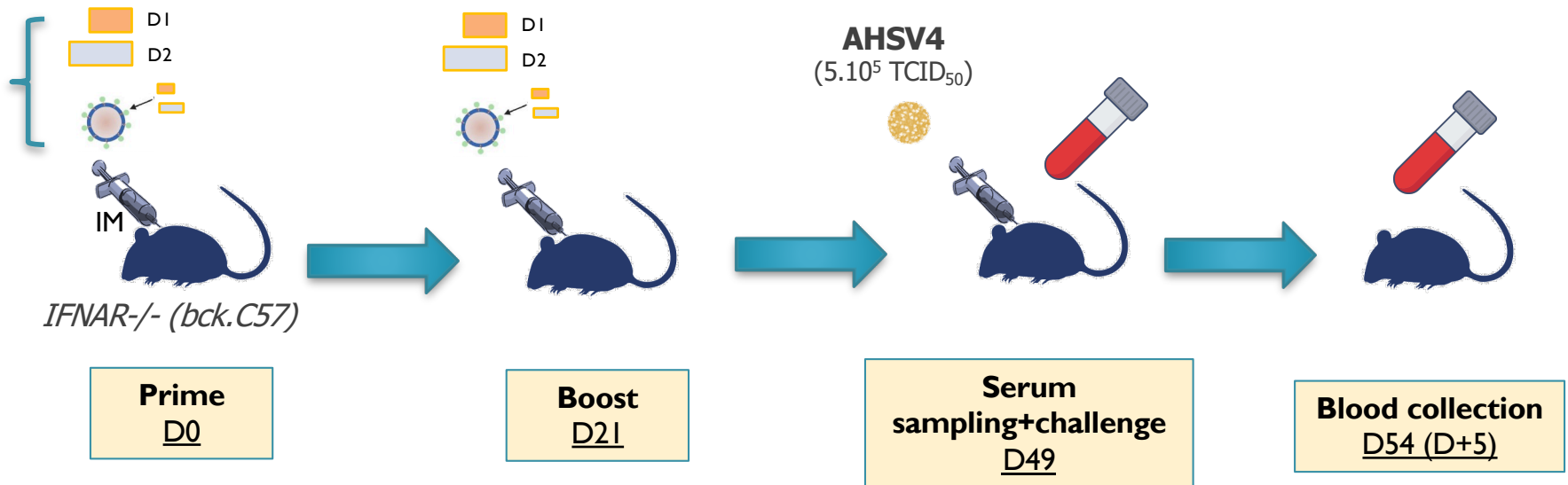
SPIDVAC project: new AHSV vaccine

Andrea Aebischer

- conjugation
- Domain 1 : VP2 aa 250-530-SpyTag
 - Domain 2 : VP2 aa 219-530-SpyTag
- SpyCatcher-mi3



20µg* conjugated or unconjugated D1 or D2



*adjuvanted with Montanide ISA71 (Seppic)

SPIDVAC project: new AHSV vaccine

Antigen	Animal ID	RT-qPCR	SNT
		Cq value	Titer
Domain 1	2337	26,38	<1/10
	2003	no Cq	1/640
	2137	36,66	1/320
	2317	32,62	<1/10
	1938	37,17	1/10
	2333	34,21	1/10
Domain 2	2186	31,61	<1/10
	2341	37,32	1/40
	2185	35,8	<1/10
	2406	no Cq	1/320
	2079	no Cq	1/320
	2095	no Cq	1/20
Domain 1 + mi3	2133	no Cq	1/1280
	2063	no Cq	1/640
	1934	38,19	1/240
	2190	no Cq	1/640
	2182	no Cq	>1/1280
	2393	no Cq	1/960
Domain 2 + mi3	2254	37,61	1/60
	2323	no Cq	1/480
	4162	no Cq	1/640
	3823	no Cq	1/1280
	2181	no Cq	1/480
	1935	37,05	1/120
Control	2189	24,64	<1/10
	1943	26,14	<1/10
	2014	26,55	<1/10

- All vaccinated animals protected from clinical disease
- Unconjugated antigens were not able to prevent replication of the challenge virus as it was shown by RT-qPCR analysis
- The majority of the vaccinated animals had developed neutralizing antibodies
- However, mice receiving the antigens conjugated to mi3 showed a markedly improved immune response

Biology of Orbiviruses (BIOR) activities

- Understanding disease features
- Diagnostic tools
- Epidemiology
- Vaccination
- Innate AV response**
- Interactomics
- Others

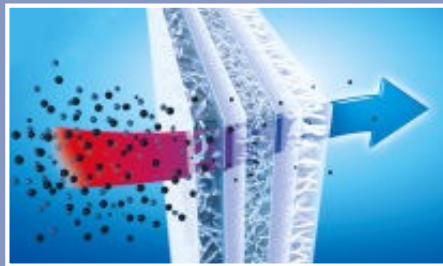
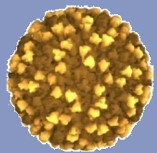


Biology of Orbiviruses (BIOR) activities

- Understanding disease features
- Diagnostic tools
- Epidemiology
- Vaccination



Innate antiviral response



- ✓ Sentinel
- ✓ Early detection
- ✓ Disease control
- ✓ Prepare the adaptive response
- ✓ **Type-I interferons** (and other pro-inflammatory cytokines)

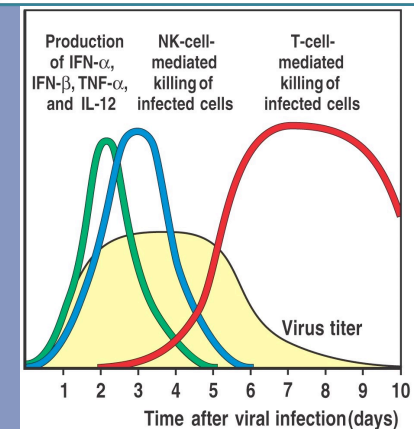
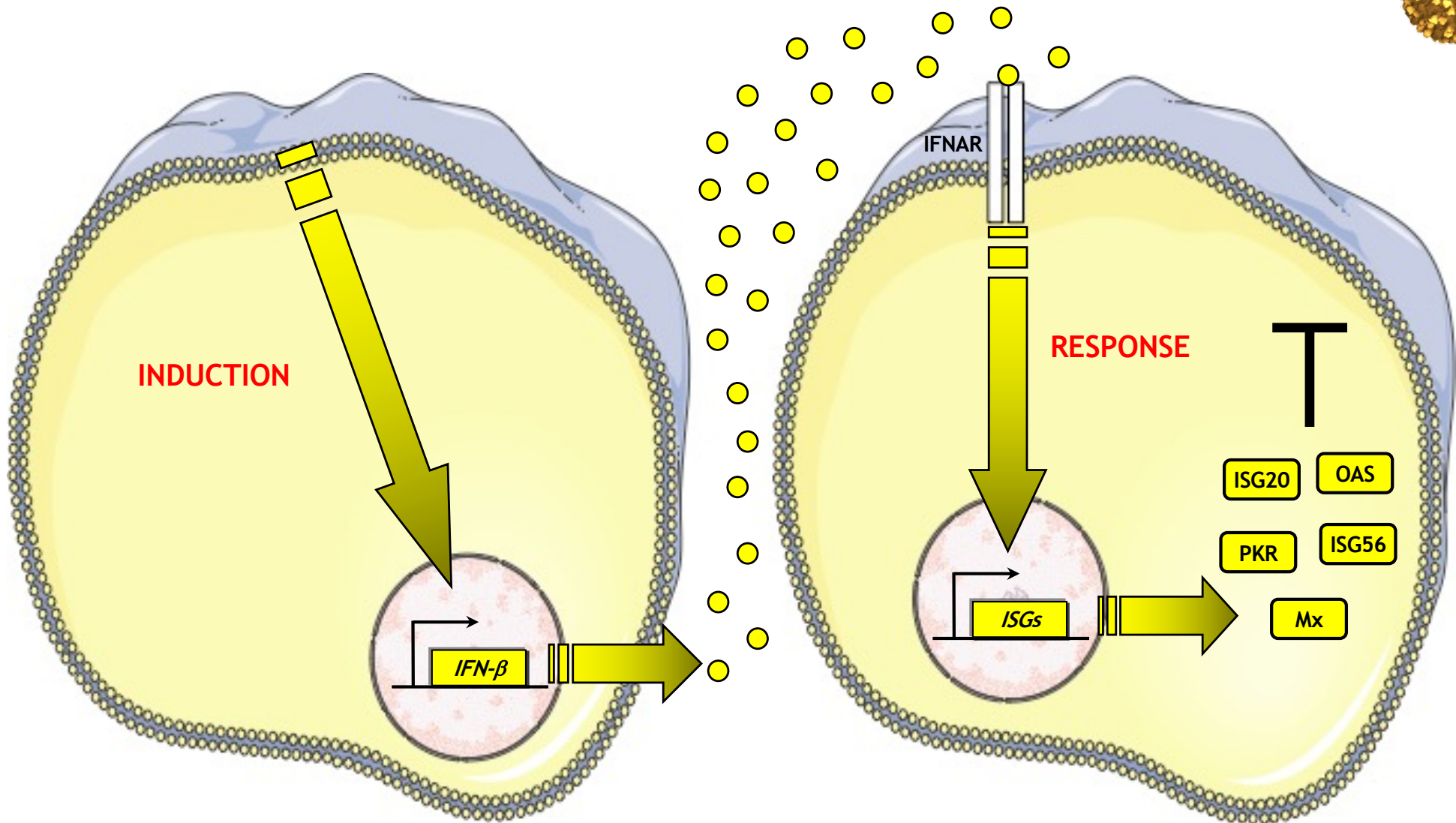
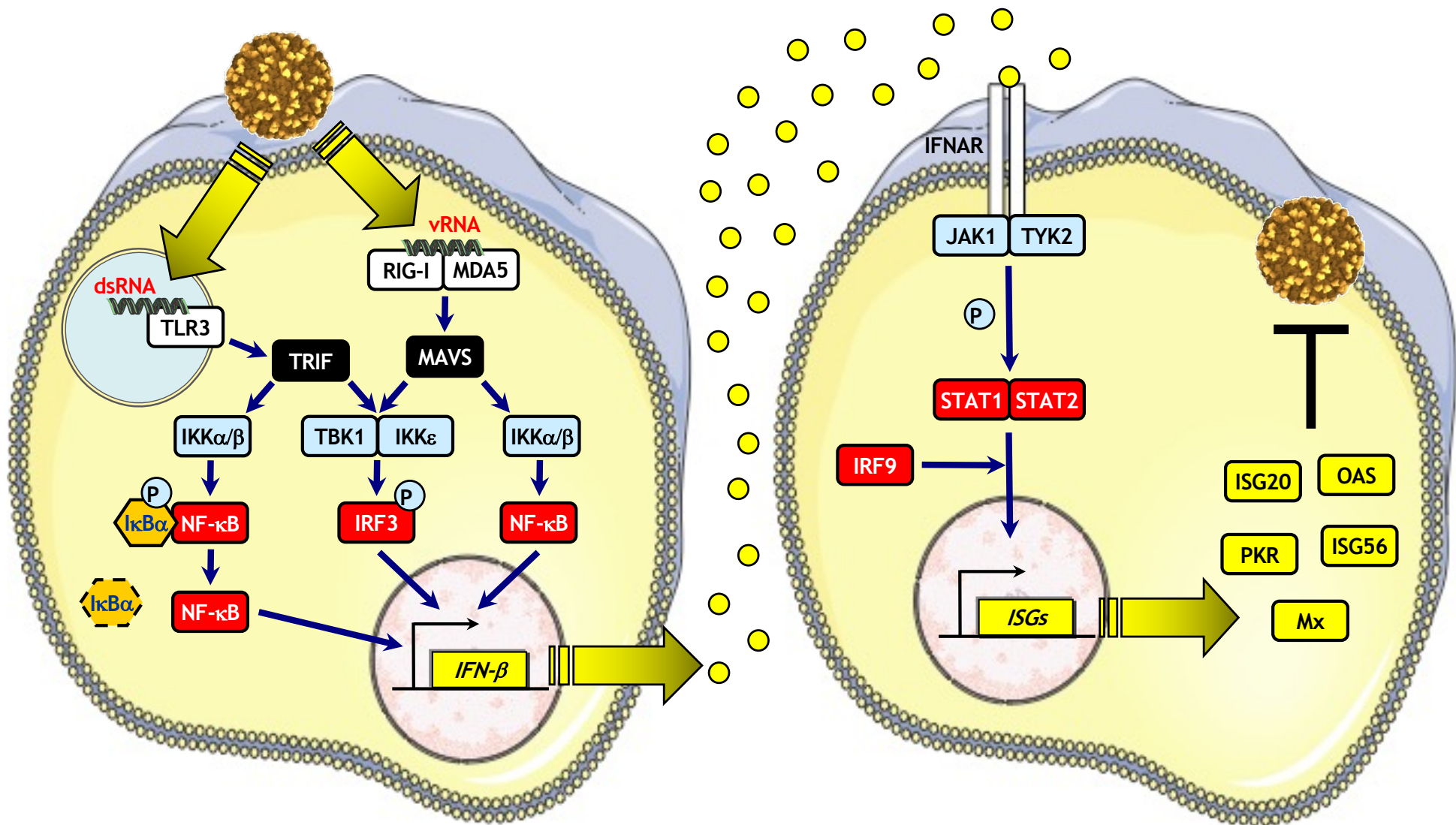


Figure 2-49 Immunobiology, 6/e, © Garland Science 2005

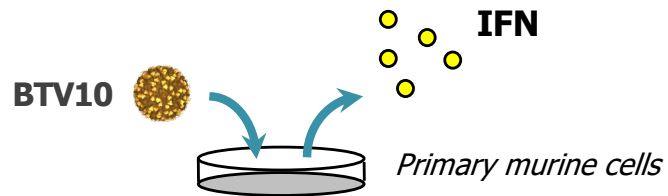
Type-I interferon (IFN- α/β) signaling pathway



Type-I interferon (IFN- α/β) signaling pathway



IFN- α/β synthesis upon BTV infection



H. Huismans (VRI, Onderstepoort)

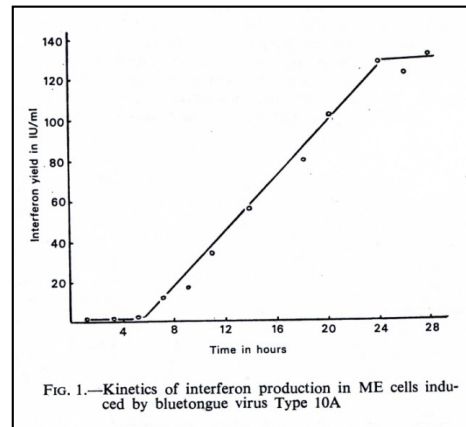
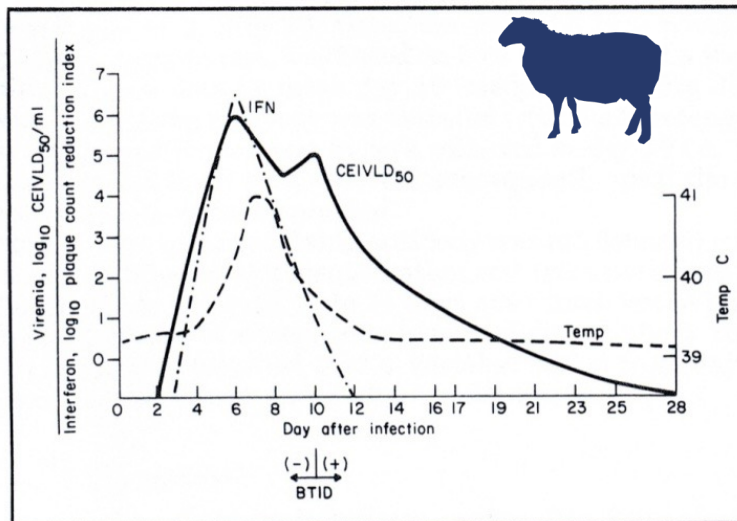
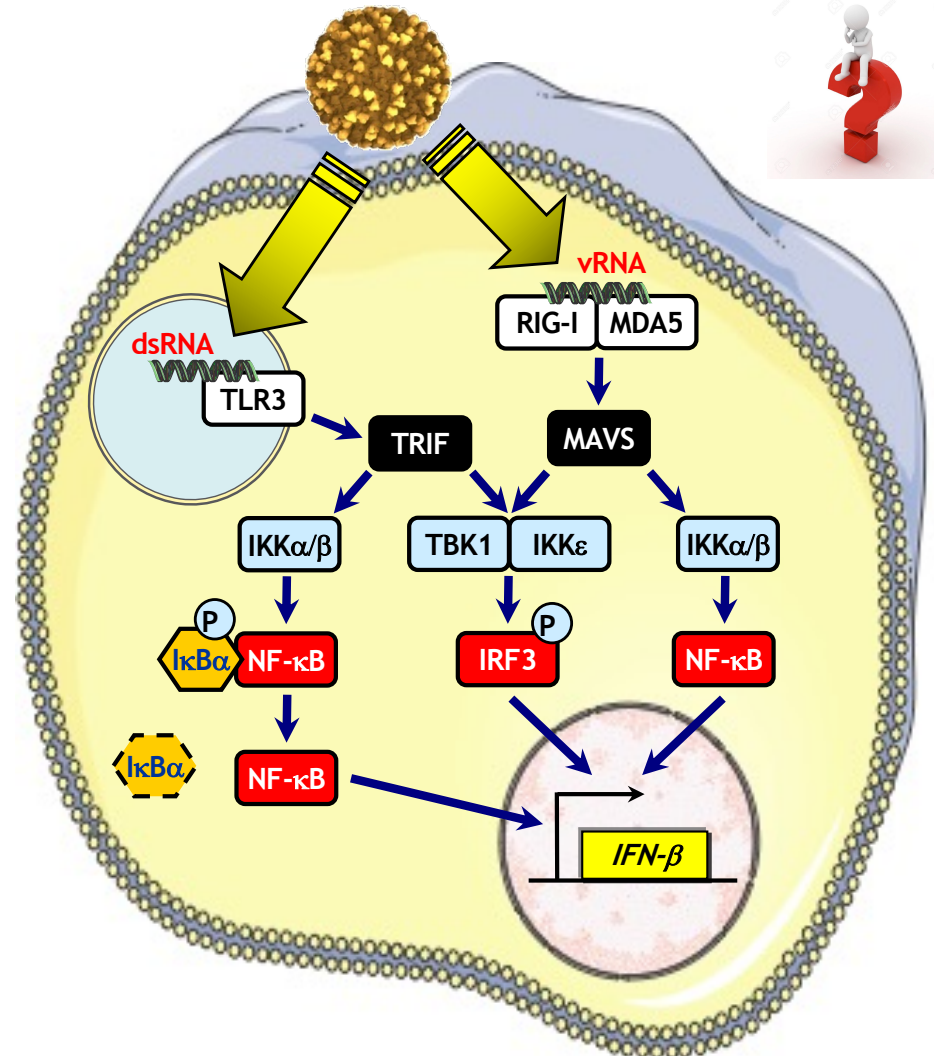


FIG. 1.—Kinetics of interferon production in ME cells induced by bluetongue virus Type 10A

Huismans (OJVR, 1969)



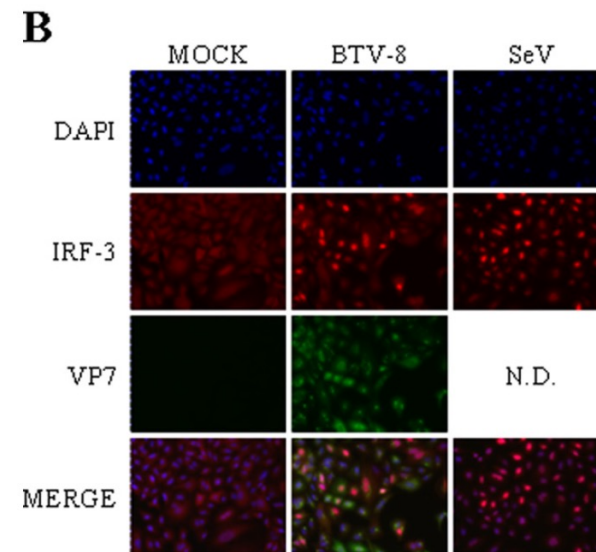
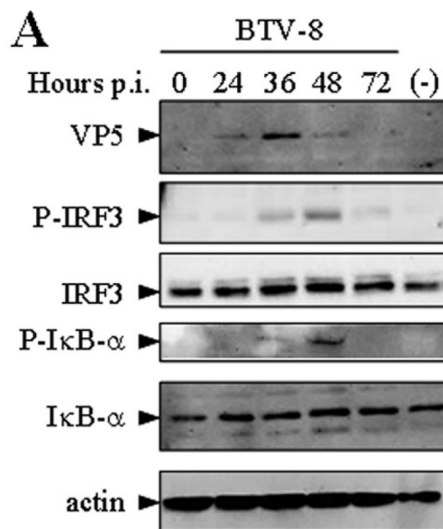
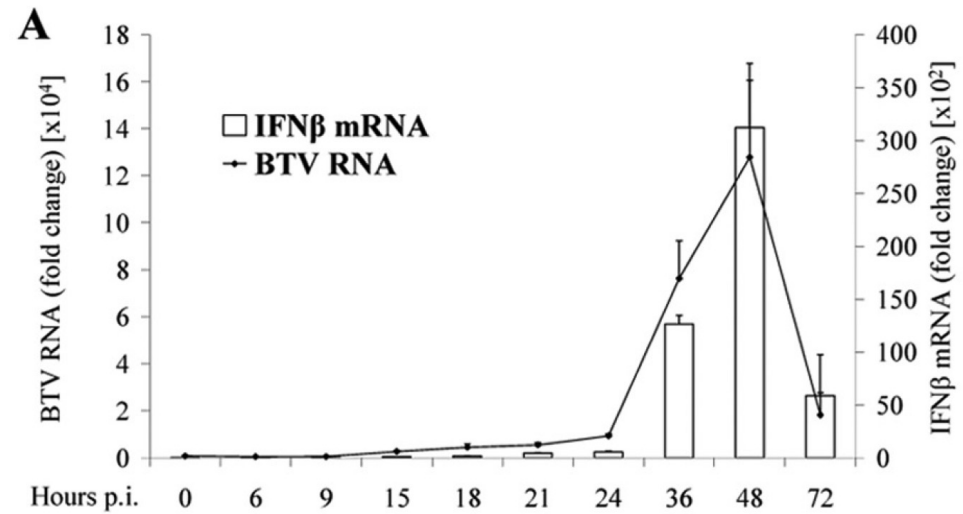
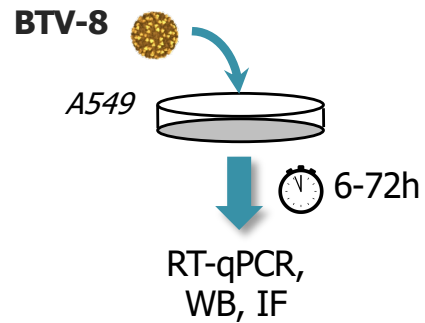
Foster (Am J Vet Res, 1991)



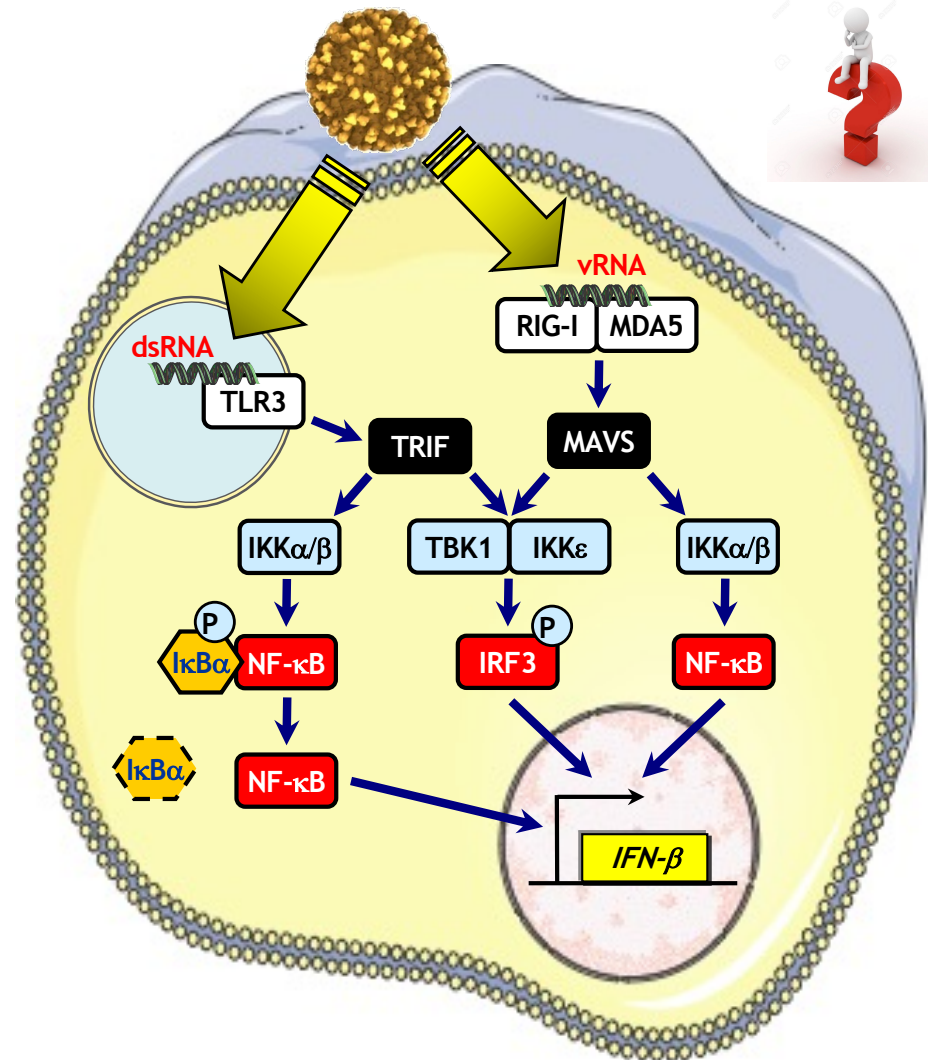
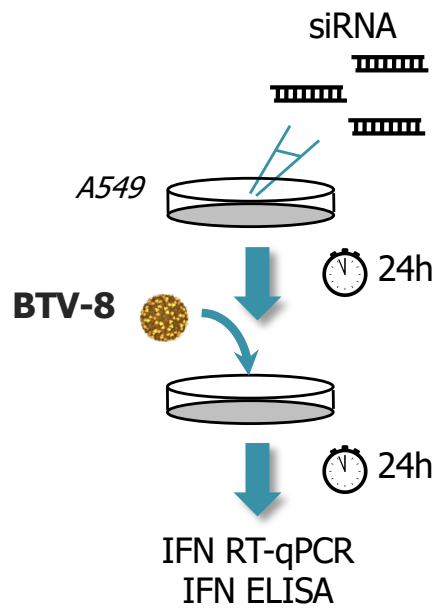
IFN- α/β synthesis upon BTV infection



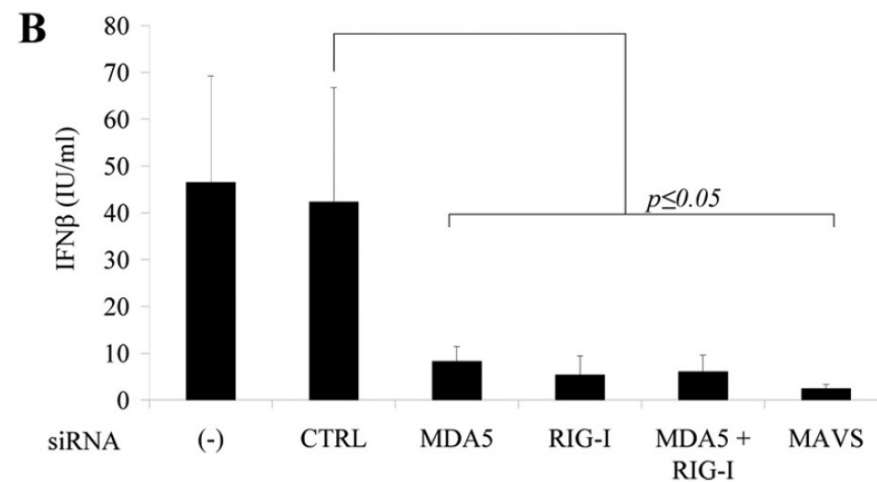
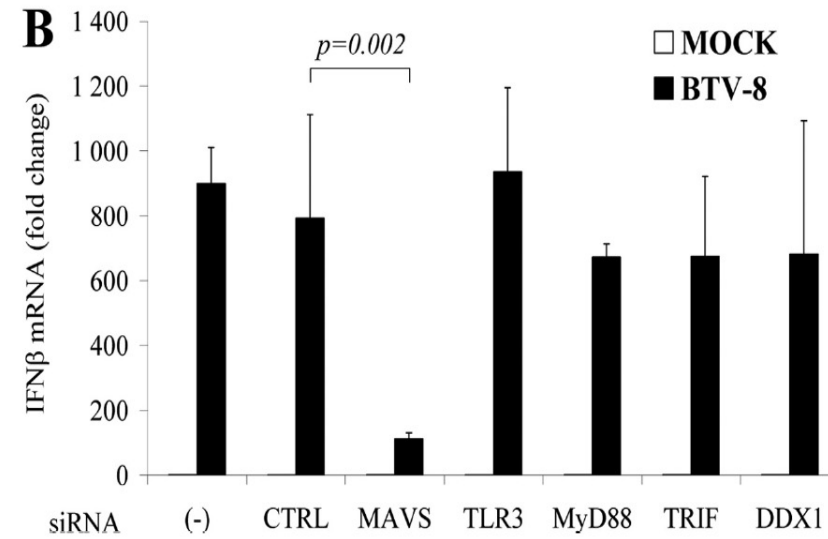
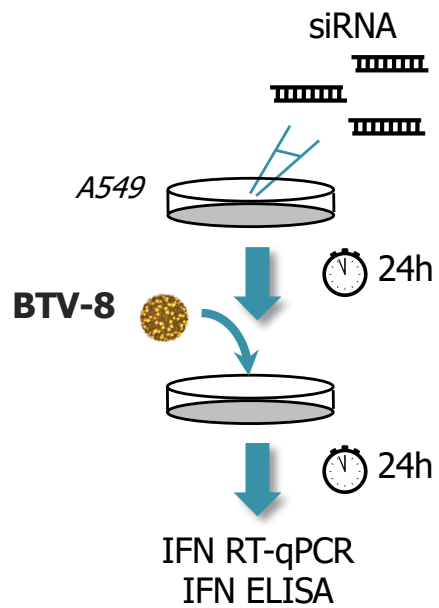
E. Chauveau



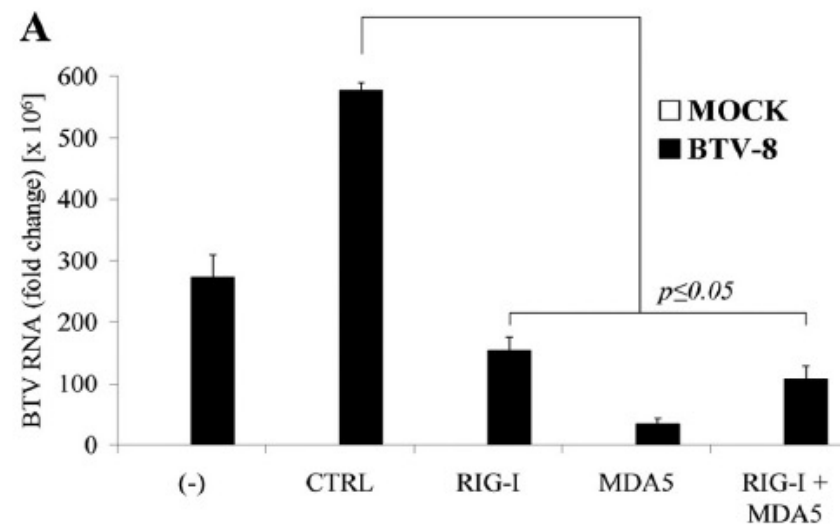
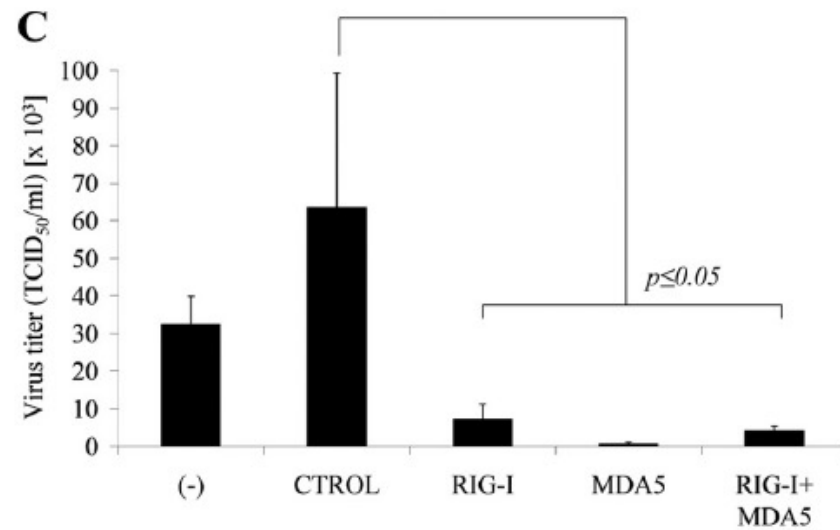
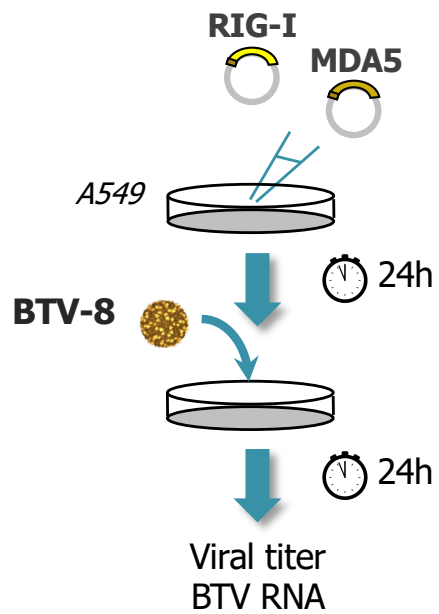
IFN- α/β synthesis upon BTV infection



IFN- α/β synthesis upon BTV infection



IFN- α/β synthesis upon BTV infection



Most of viruses can inhibit the IFN pathway

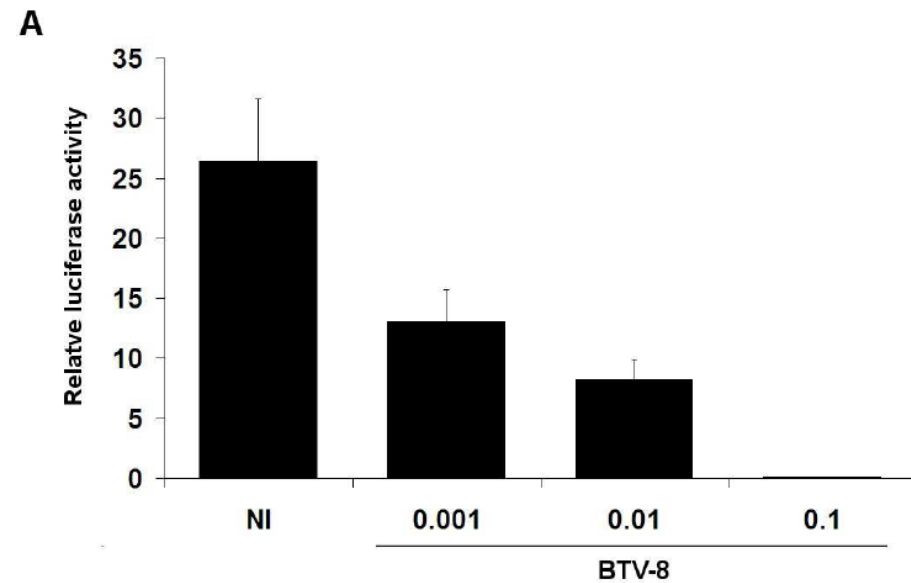
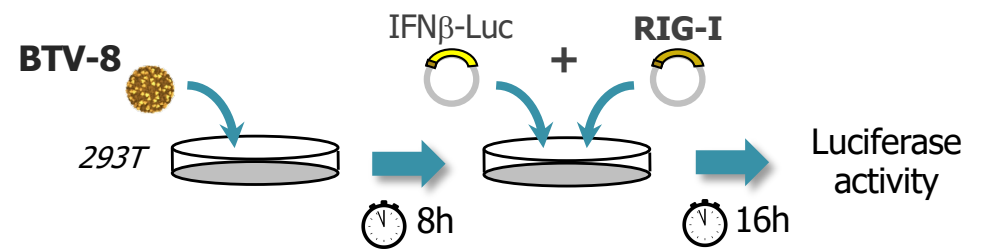
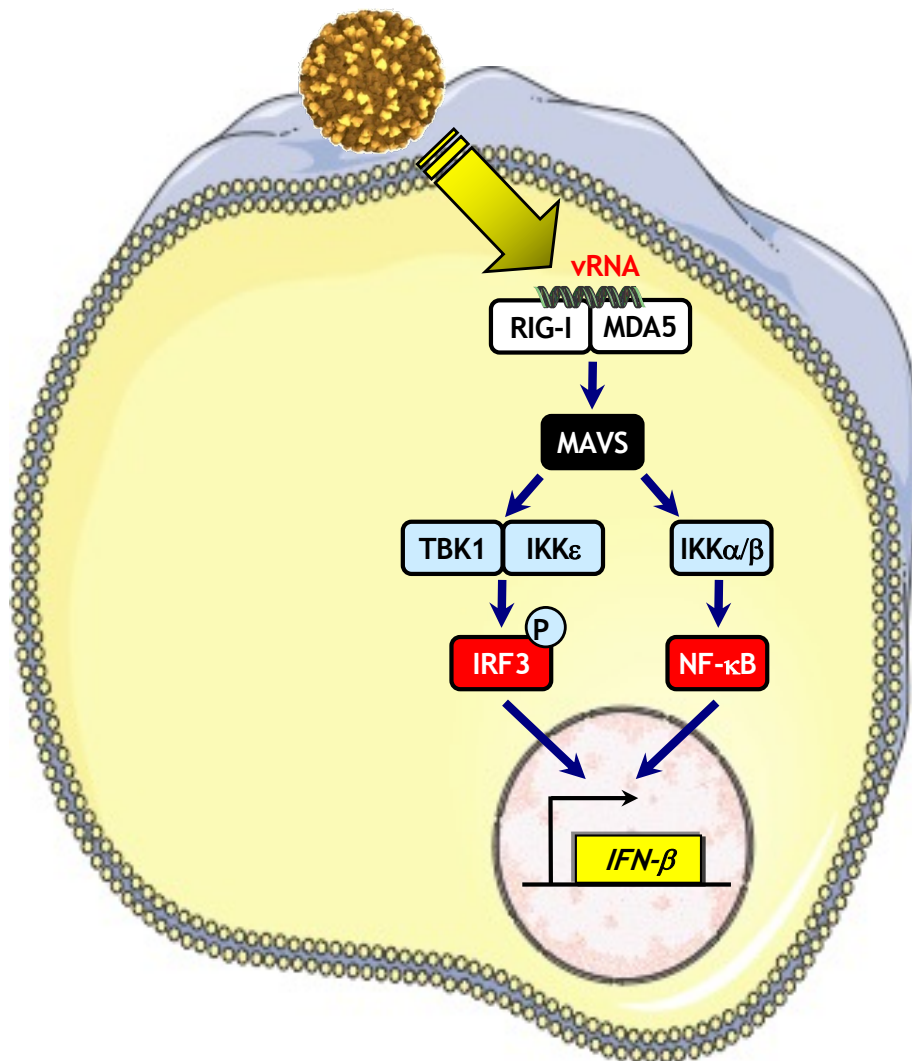


**ANTIVIRAL
RESPONSE**

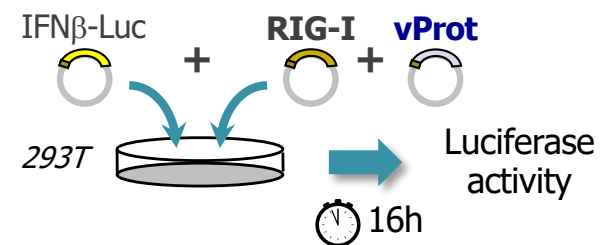
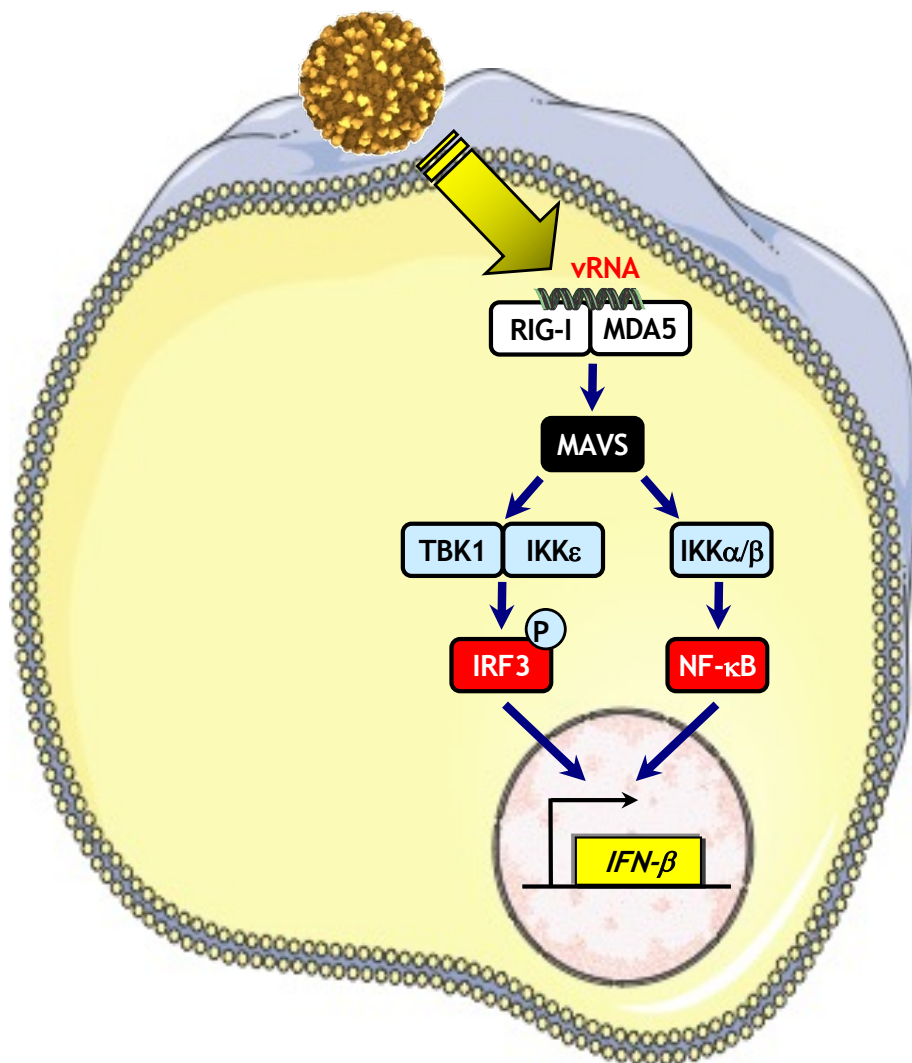
**ESCAPE
STRATEGIES**

Antagonist function of BTV on IFN- α/β signaling

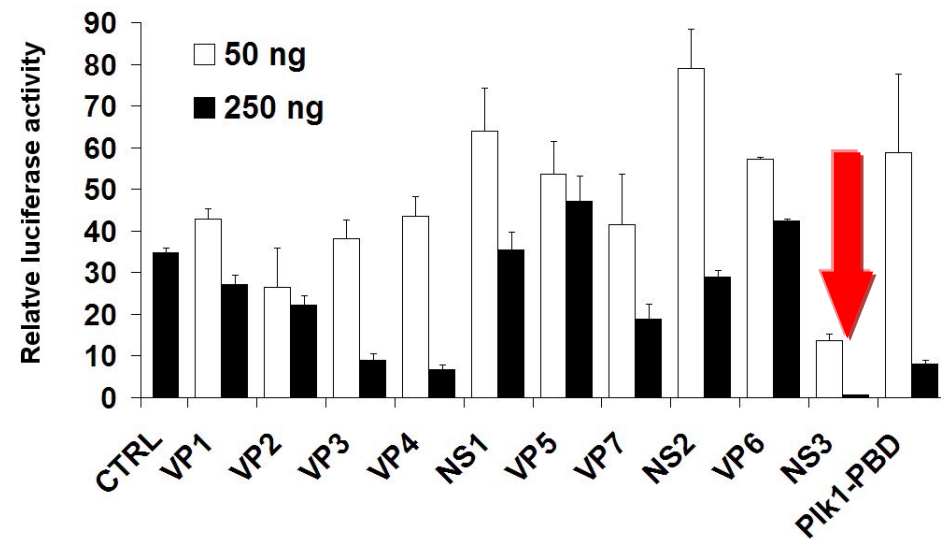
E. Chauveau, V. Doceul



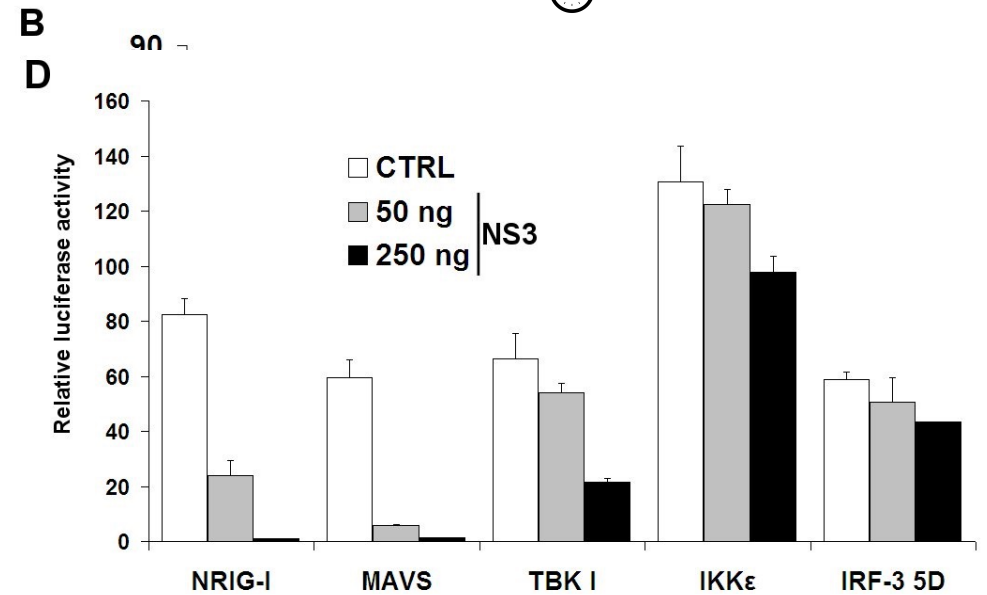
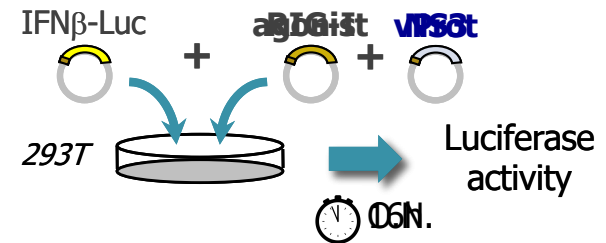
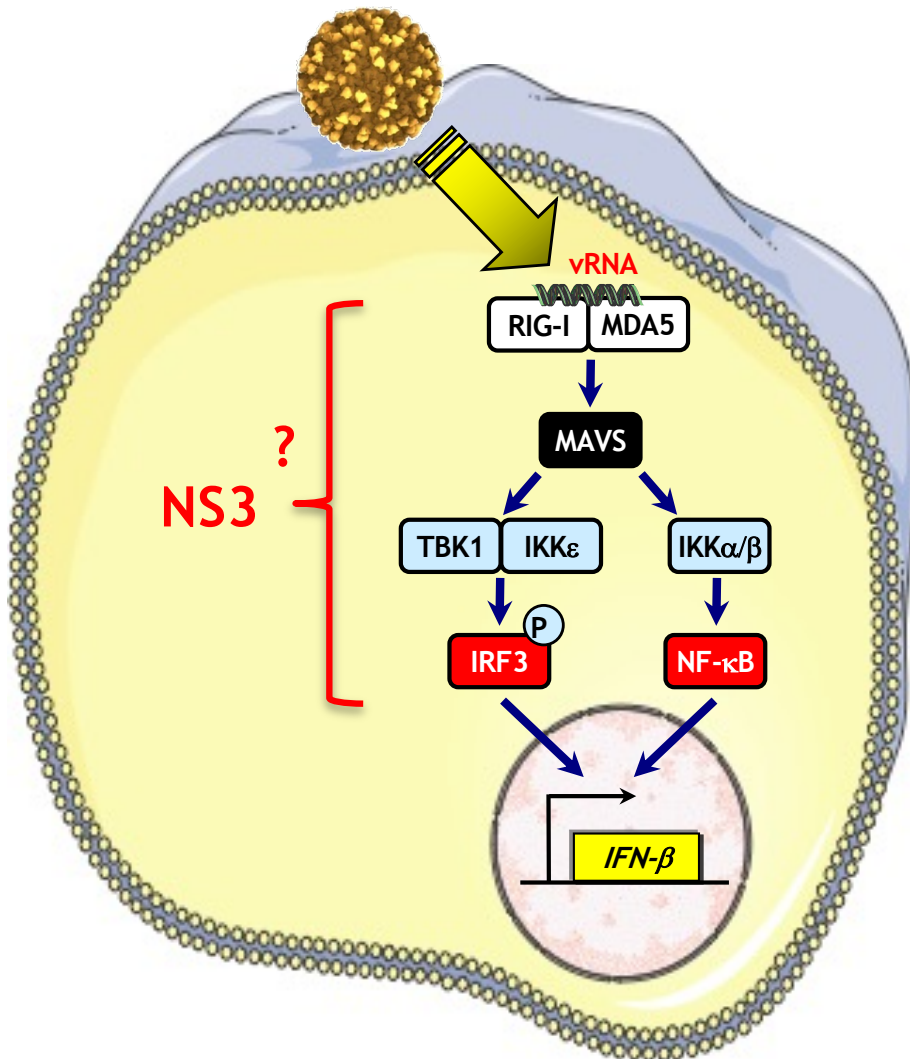
Antagonist function of BTV on IFN- α/β signaling



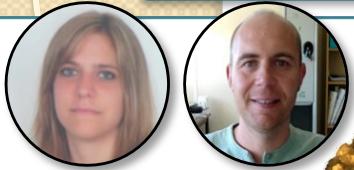
B



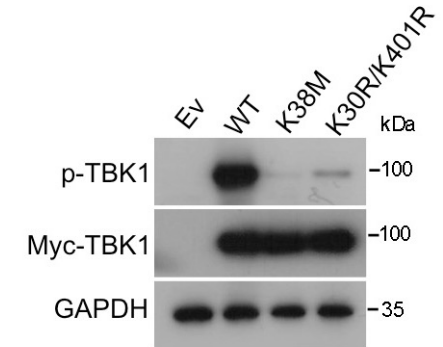
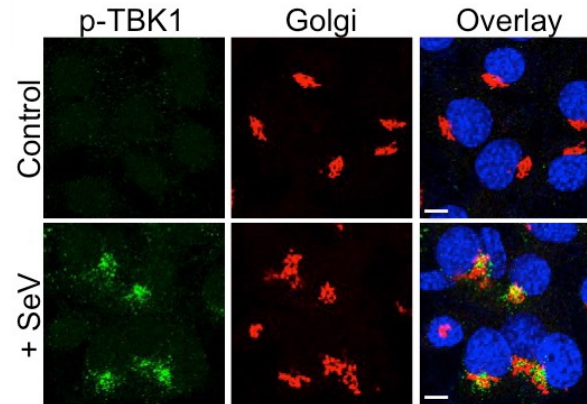
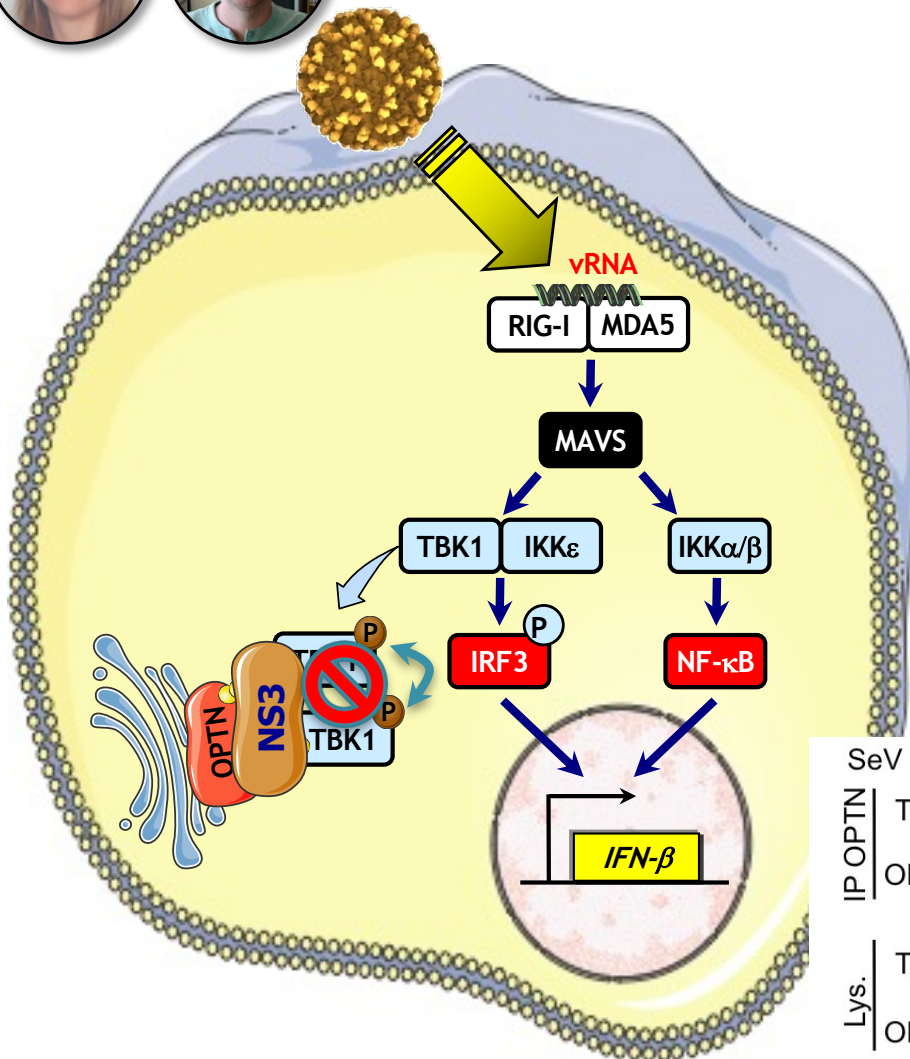
Antagonist function of BTV on IFN- α/β signaling



Antagonist function of BTV on IFN- α/β signaling

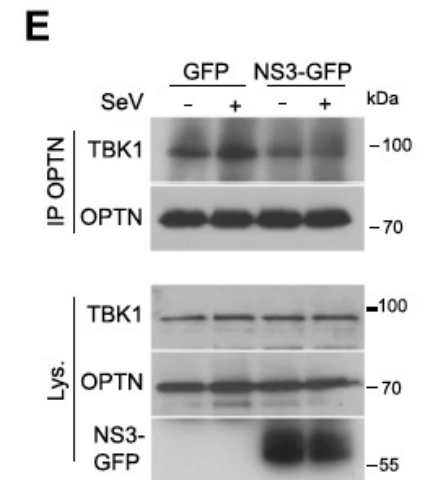
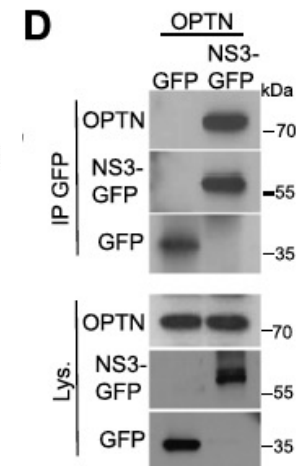
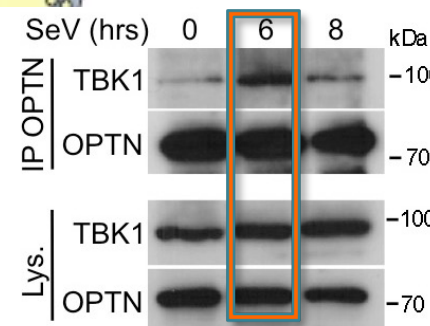
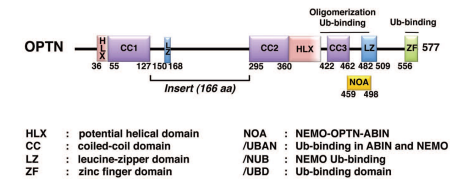


M. Pourcelot, D. Arnoult
(Inserm U1197, Villejuif)



Optineurin (OPTN):

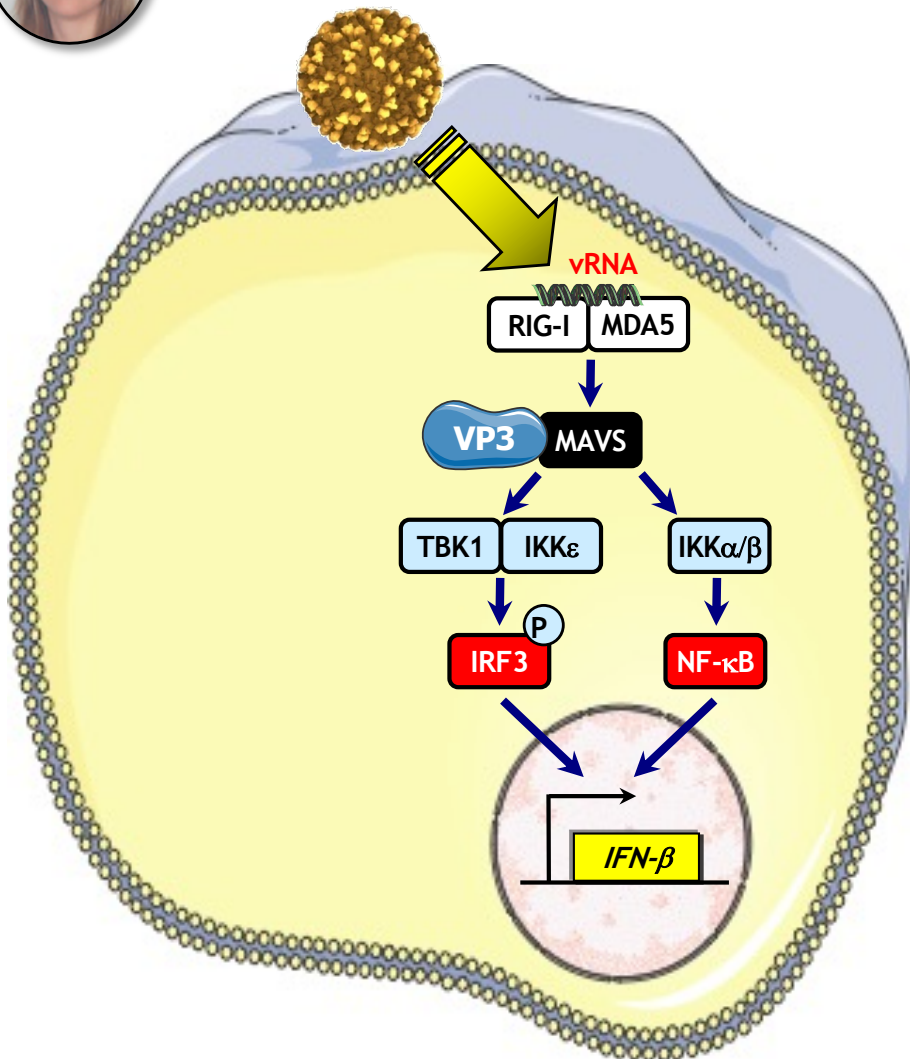
- Golgi
- Ubiquitin-binding domain
- Required for optimal TBK1 activation



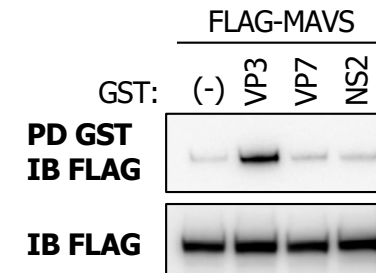
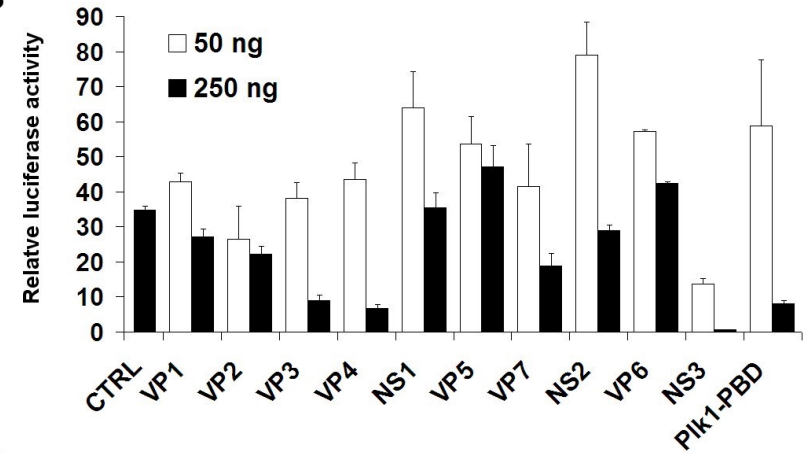
Antagonist function of BTV on IFN- α/β signaling



M. Pourcelot



B



Biology of Orbiviruses (BIOR) activities

- Understanding disease features
- Diagnostic tools
- Epidemiology
- Vaccination
- Innate AV response
- Interactomics**
- Others



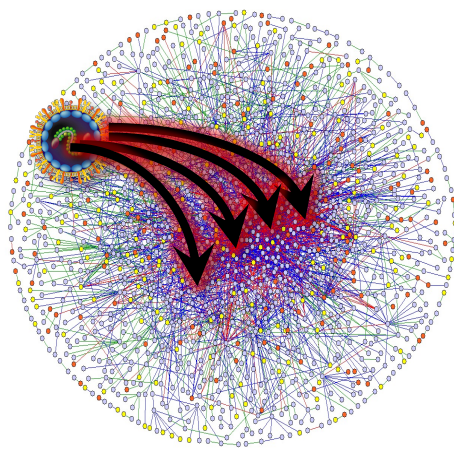
Context - Objectives



Despite recent breakthroughs in our understanding of BTV replication and virulence, many issues remain unresolved, regarding:

- ✓ Pathogenesis
- ✓ Host response
- ✓ Transmission

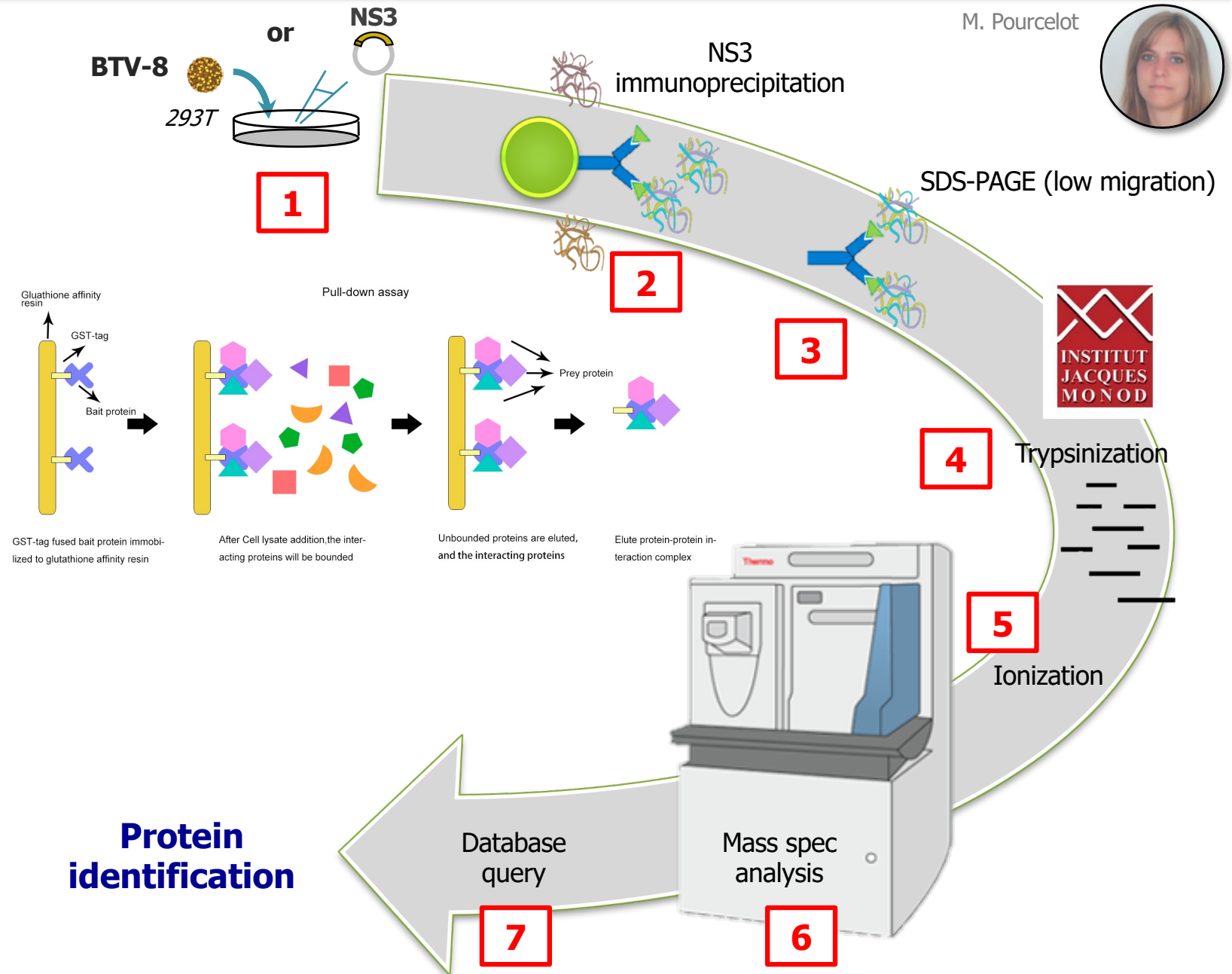
Study dialogue between BTV and its mammalian and arthropod hosts at the molecular level



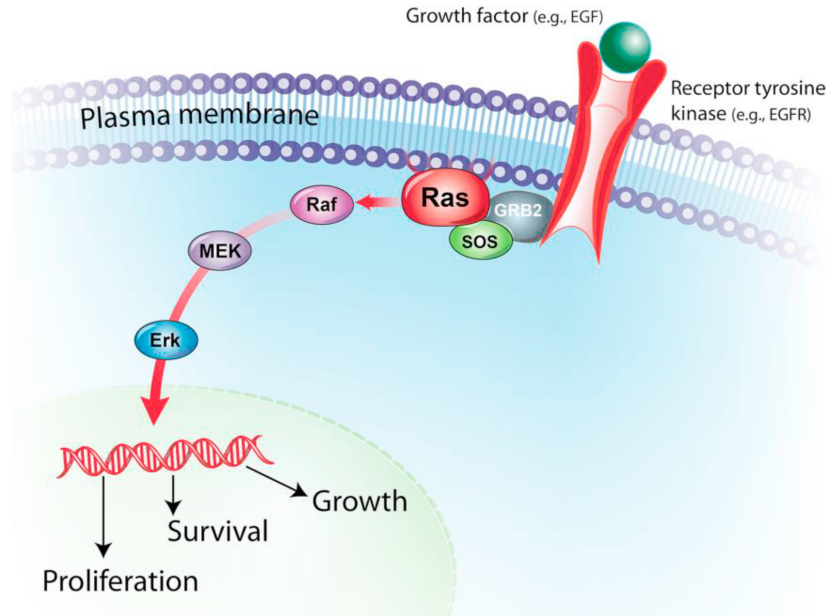
Identify protein-protein interactions (PPI) between BTV and cellular proteins

BTV8 NS3 interactome by co-AP / mass. spec.

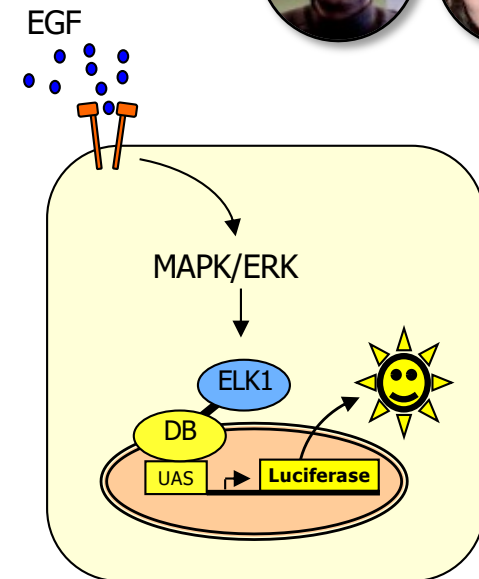
M. Pourcelot



BTV NS3 activates the MAPK/ERK pathway



G. Caignard, C. Kundlacz



Research in Veterinary Science 89 (2010) 460–464

Contents lists available at ScienceDirect

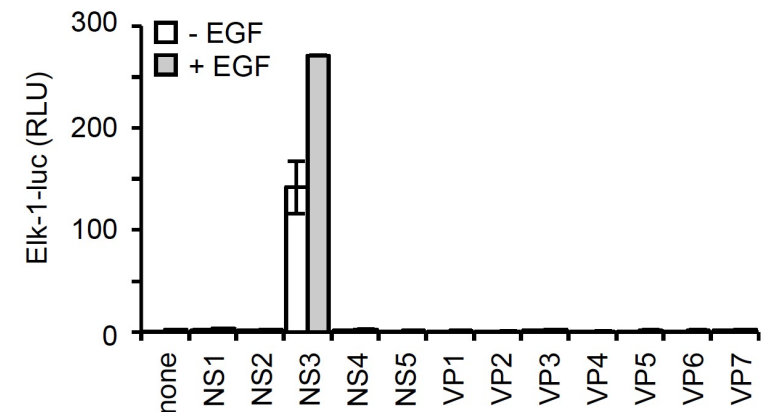
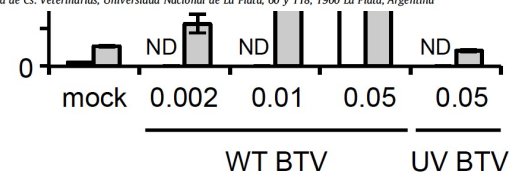
Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

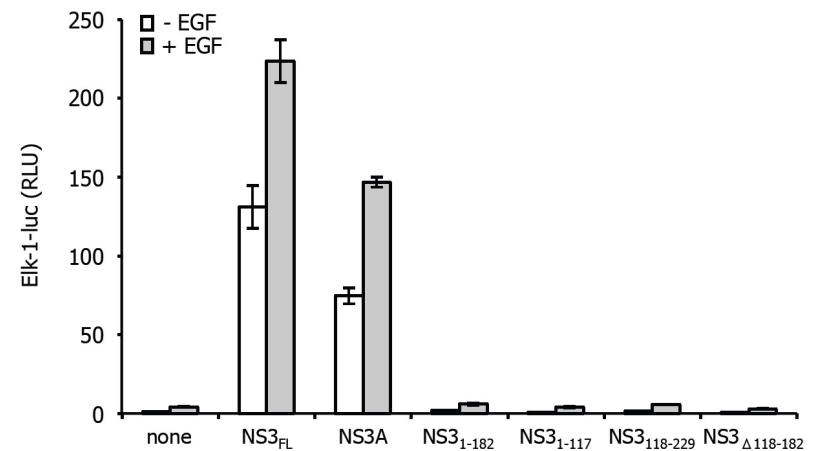
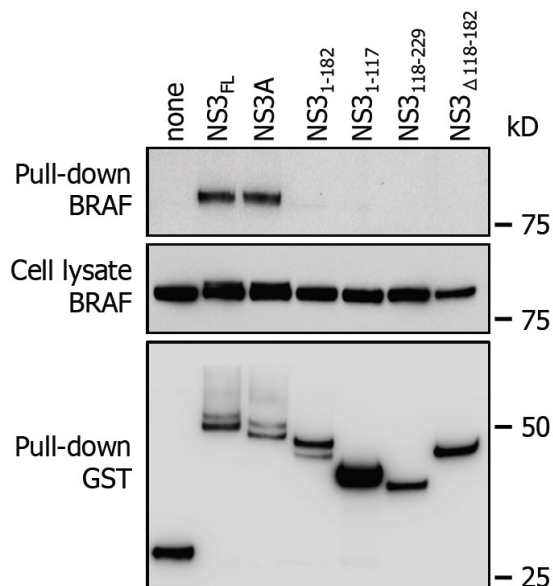
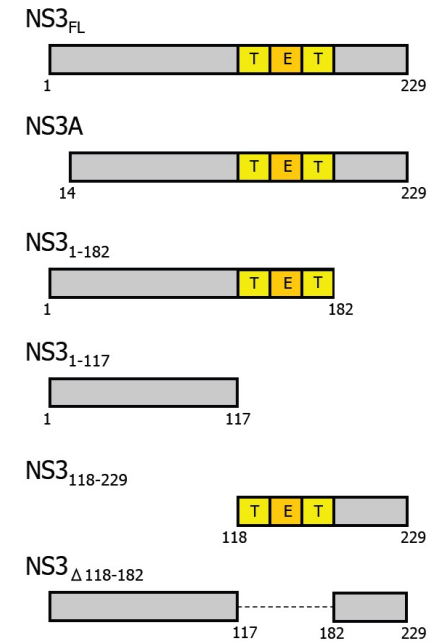
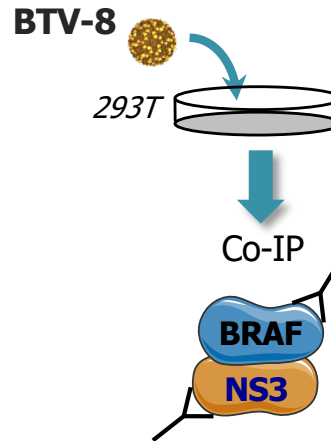
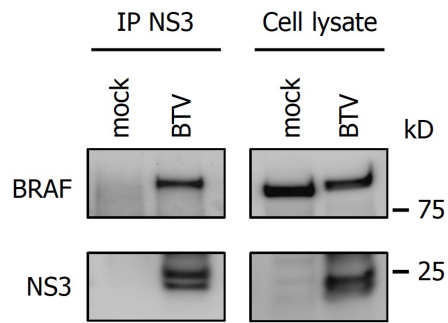
Bluetongue virus infection: Activation of the MAP kinase-dependent pathway is required for apoptosis

Eduardo Mortola*, Alejandra Larsen

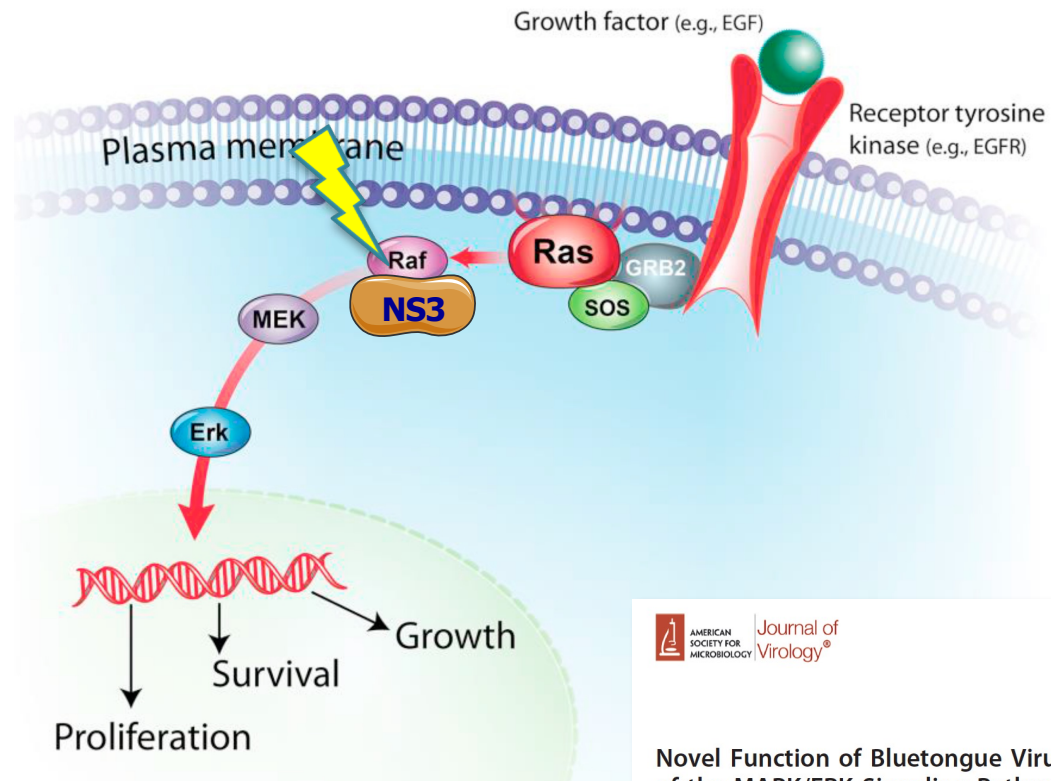
Immunología Veterinaria, Facultad de Cs. Veterinarias, Universidad Nacional de La Plata, 60 y 118, 1900 La Plata, Argentina



BTV NS3 activates the MAPK/ERK pathway



BTV NS3 activates the MAPK/ERK pathway



Novel Function of Bluetongue Virus NS3 Protein in Regulation of the MAPK/ERK Signaling Pathway

Cindy Kundlacz,^a Marie Pourcelot,^a Aurore Fablet,^a Rayane Amaral Da Silva Moraes,^a Thibaut Léger,^b Bastien Morlet,^b Cyril Viarouge,^a Corinne Sailleau,^a Mathilde Turpaud,^a Axel Gorlier,^a Emmanuel Beard,^a Sylvie Lecollinet,^a Piet A. van Rijn,^{c,d} Stephan Zientara,^a Damien Vitour,^a Grégory Caignard^a

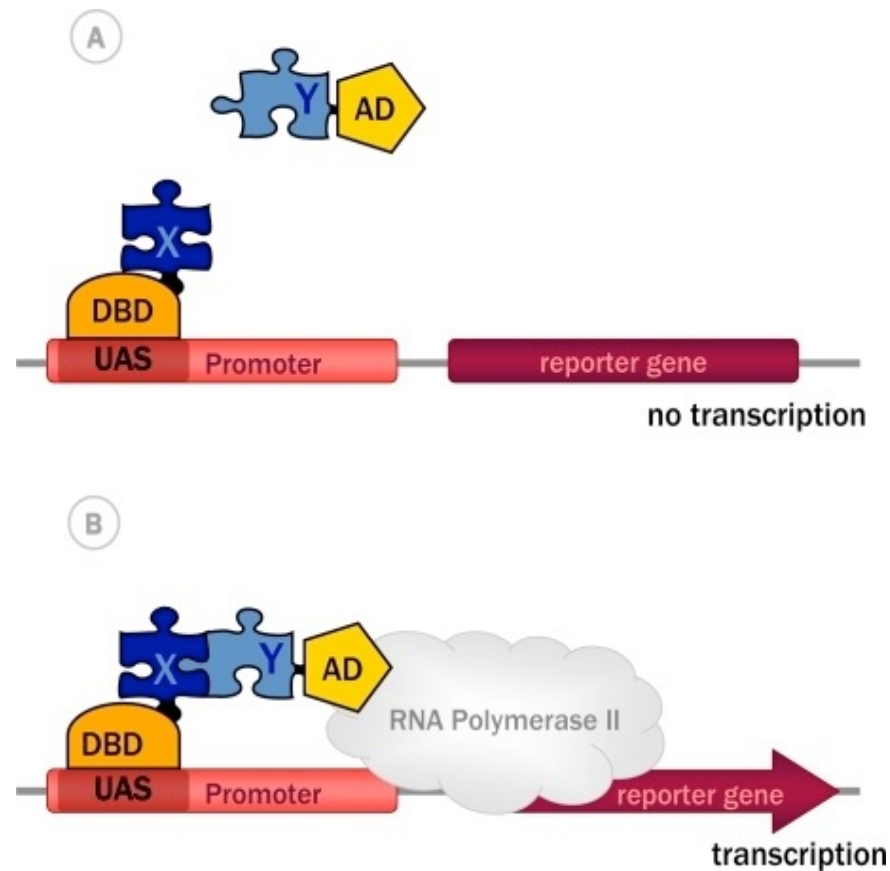
^aUMR Virologie, INRA, École Nationale Vétérinaire d'Alfort, ANSES, Université Paris-Est, Maisons-Alfort, France

^bMass Spectrometry and Proteomics Facility, Jacques Monod Institute, UMR 7592, Paris Diderot University, CNRS, Paris Cedex 13, France

^cDepartment of Virology, Wageningen Bioveterinary Research, Lelystad, The Netherlands

^dDepartment of Biochemistry, Centre for Human Metabolomics, North-West University, Potchefstroom, South Africa

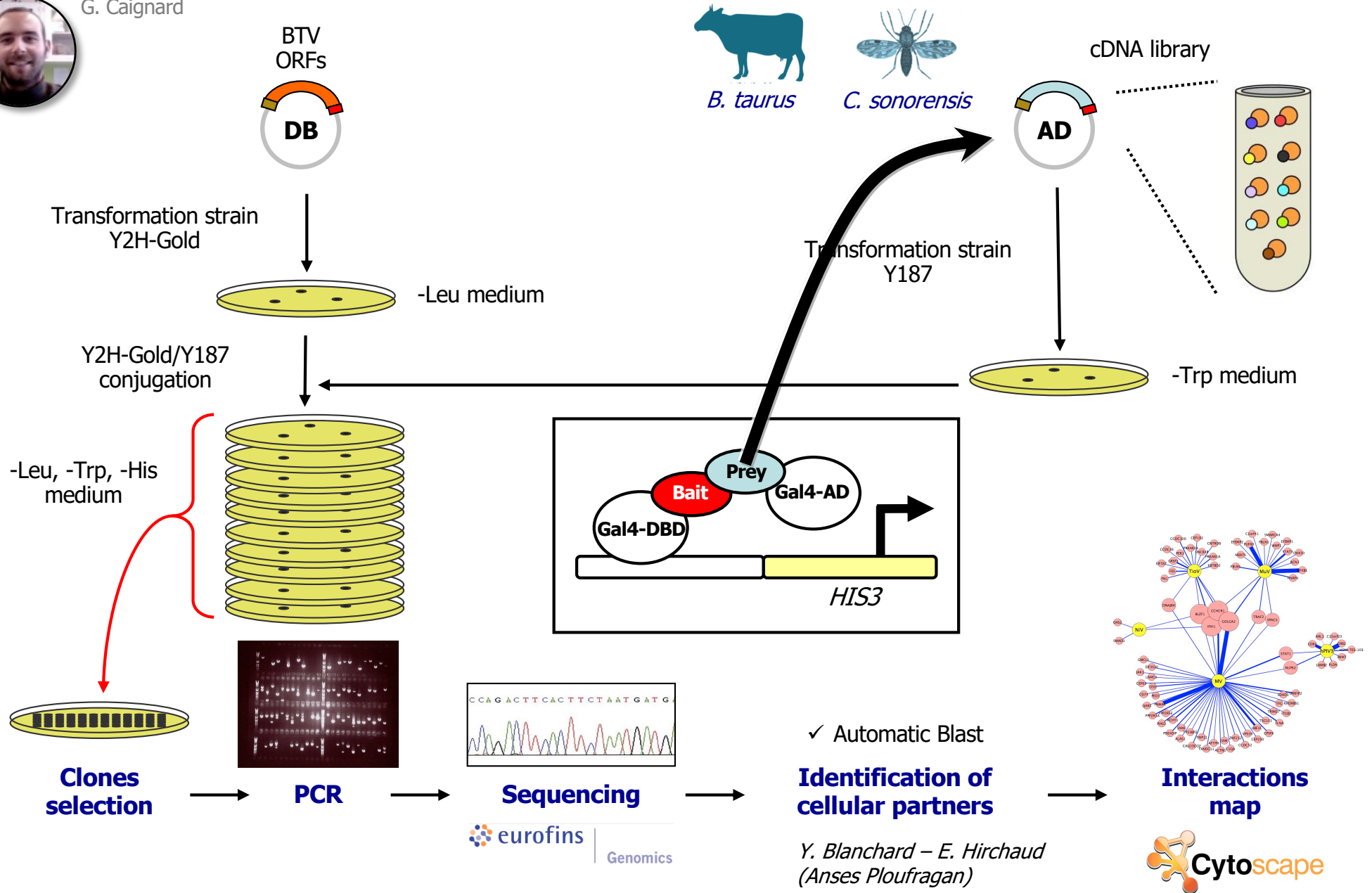
High throughput study of PPI using yeast two-hybrid (Y2H) approach



Identification of BTV8/27 – hosts PPI by Y2H

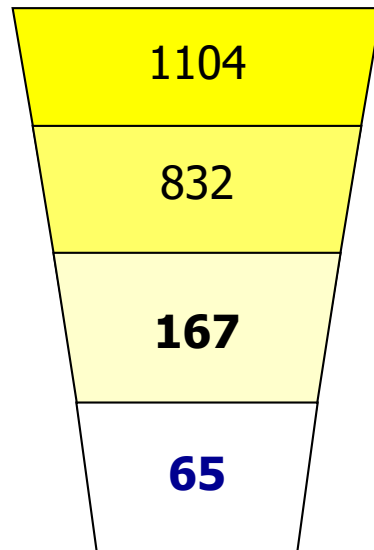


G. Caignard



BTV8/27: quantitative analysis

BTV8

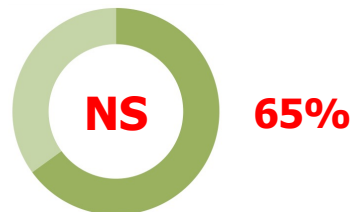
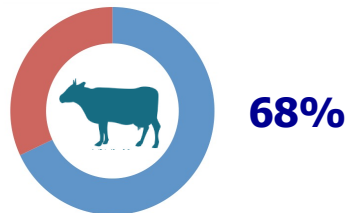


Picked colonies

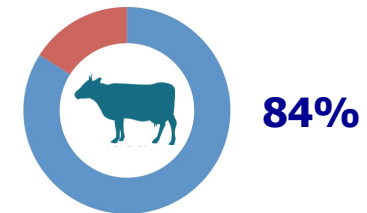
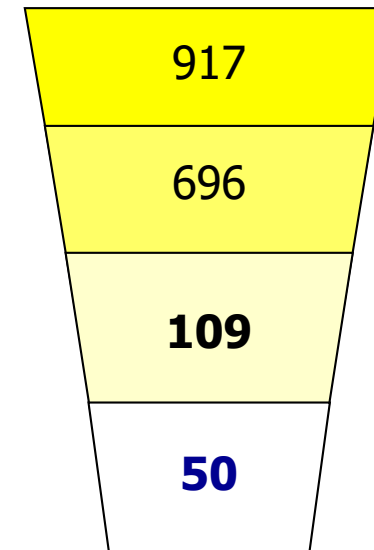
Interactions

Total interactors

Interactors ≥ 2 times



BTV27



G. Caignard






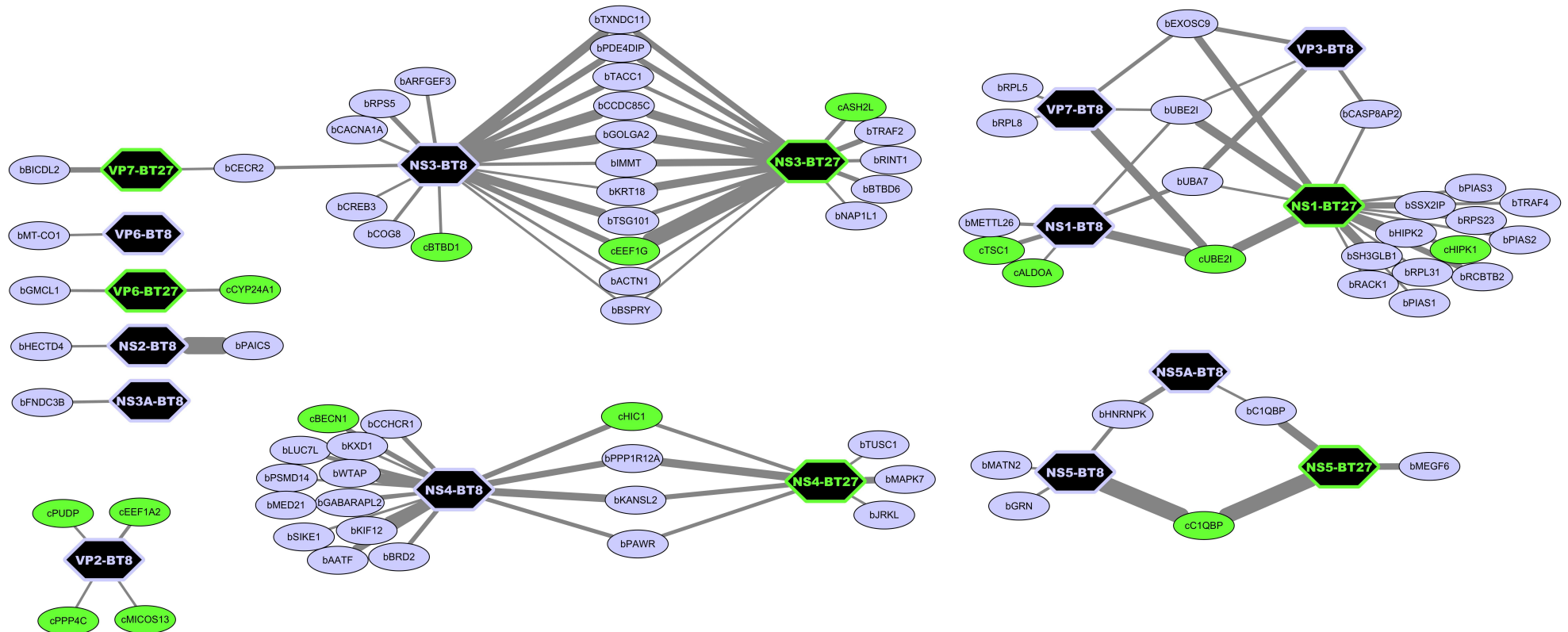
C. Kundlacz



A. Fablet

BTV8/27: interactions map

-  Viral protein
-  Bovine interactor
-  Culicoides interactor



Identified interactors ≥ 2 times

NS4 BTV-8 interacts with WTAP



Aurore Fablet



viruses

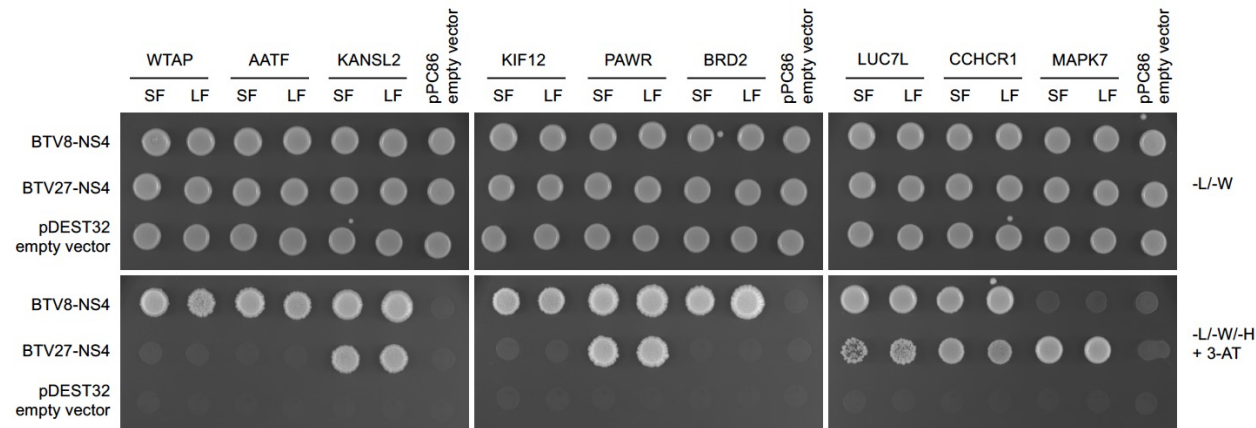


Article

Comparative virus-host protein interactions of the Bluetongue virus NS4 virulence factor

Aurore Fablet^{1,†}, Cindy Kundlacz^{1,2,†}, Juliette Dupré¹, Edouard Hirchaud³, Lydie Postic¹, Corinne Sailleau¹, Emmanuel Bréard¹, Stéphan Zientara¹, Damien Vitour^{1,†,*} and Grégory Caignard^{1,†,*}

A

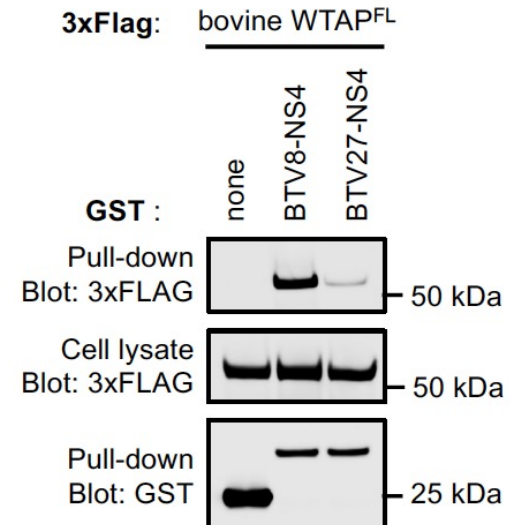
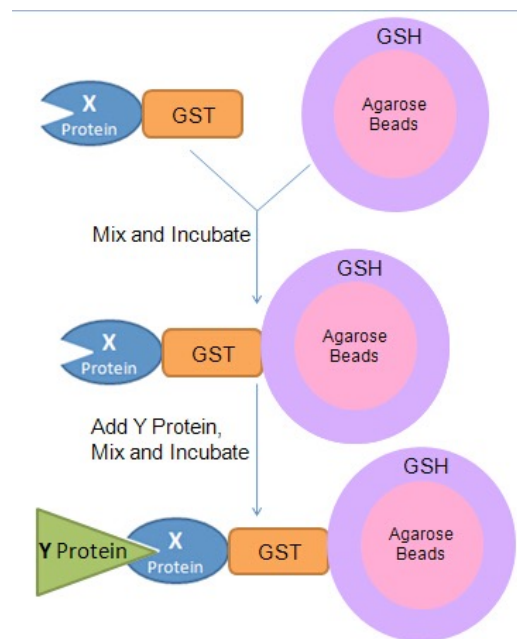


B

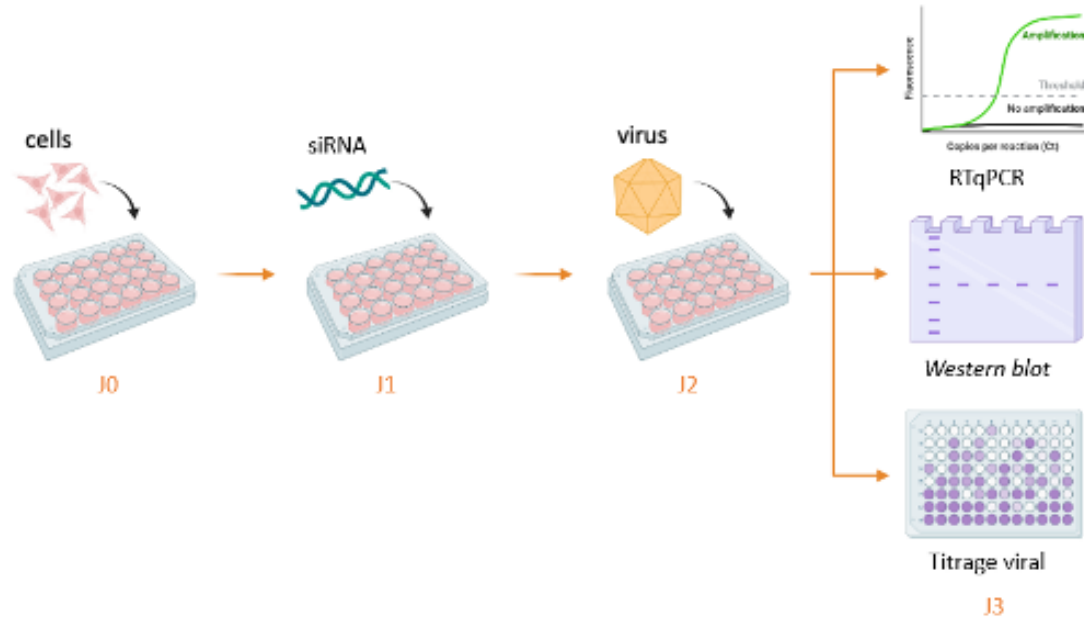


NS4 BTV-8 interacts with WTAP

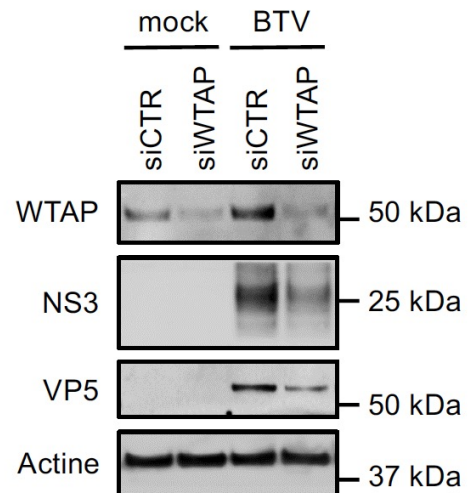
GST pulldown



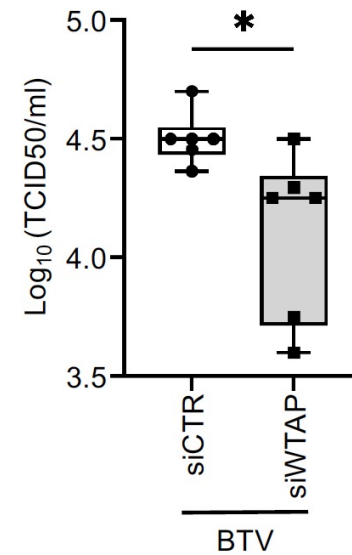
WTAP is a proviral factor



B



C



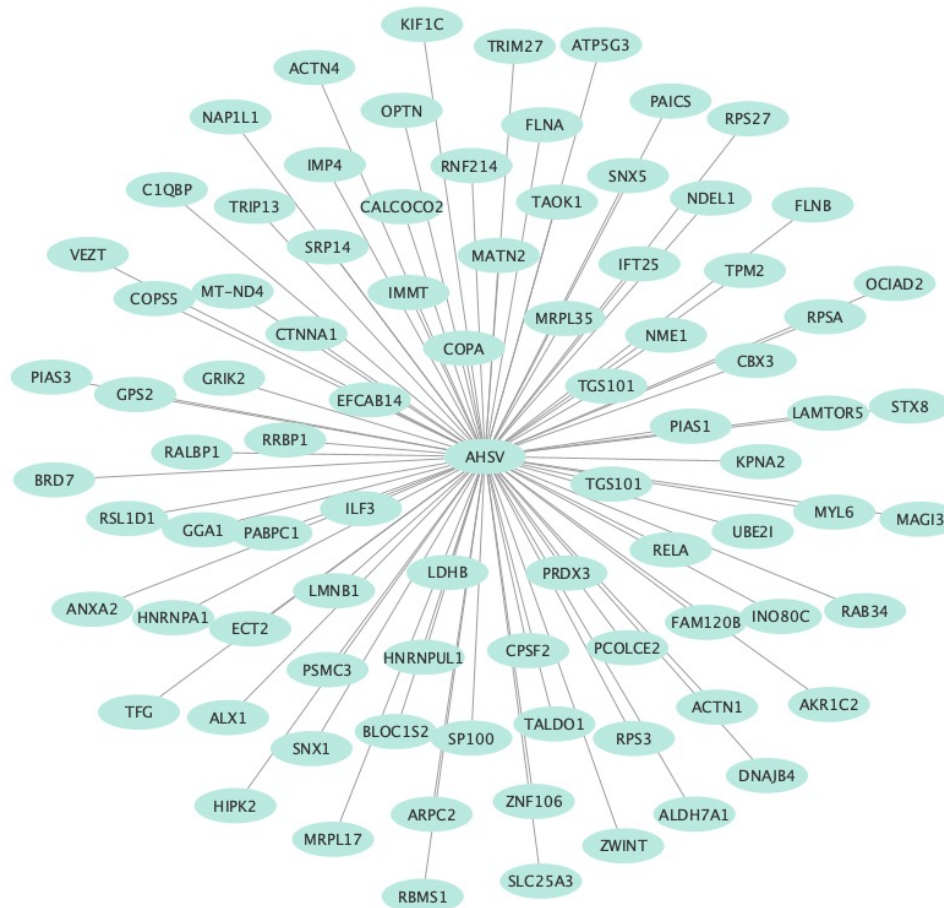
Towards comparative interactomics



Marine Lemesle

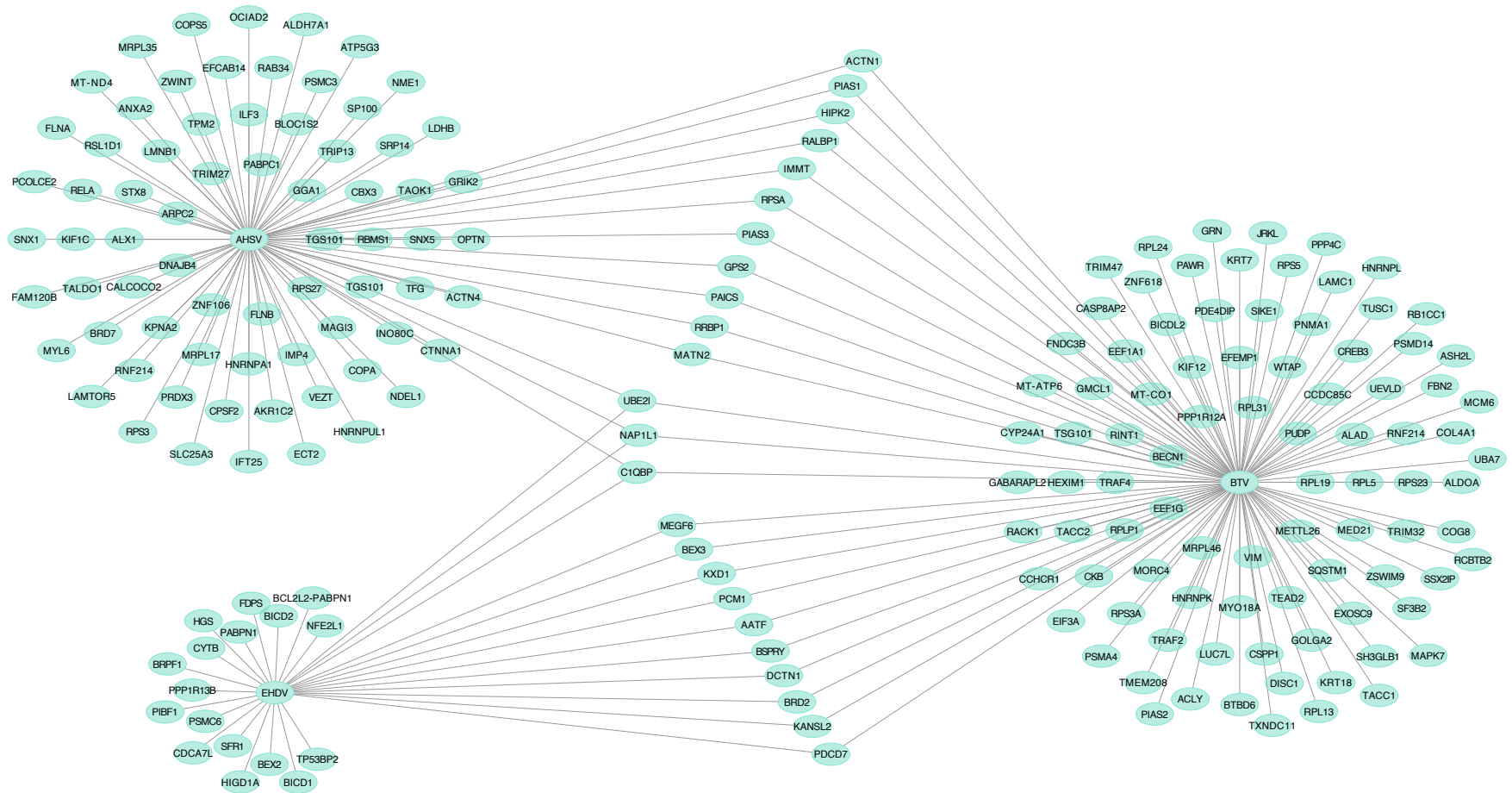


AHSV interactome map

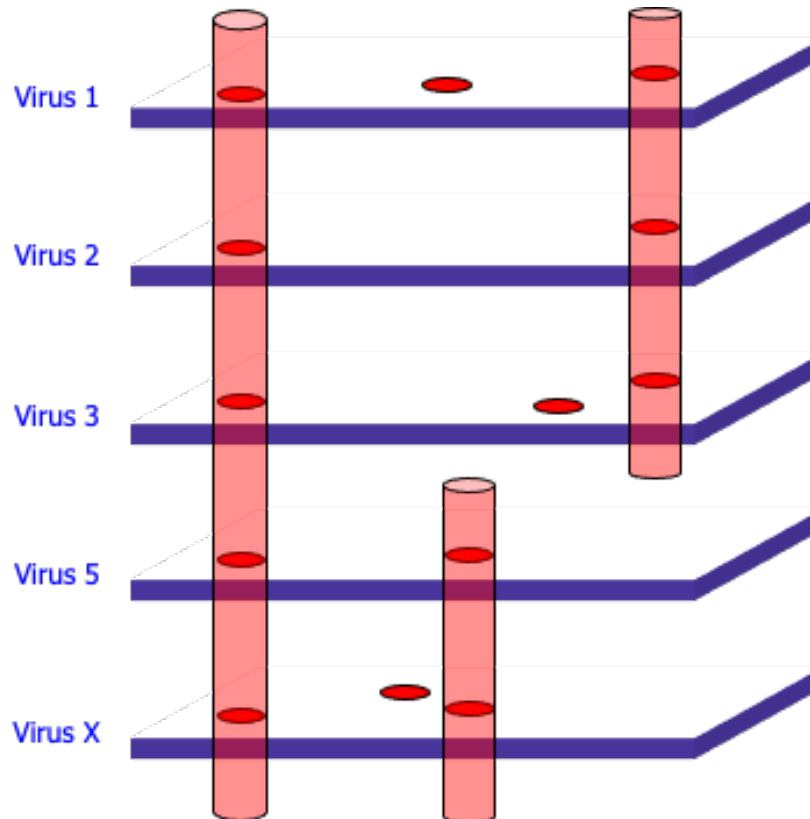


Towards comparative interactomics

Orbiviruses interactome maps



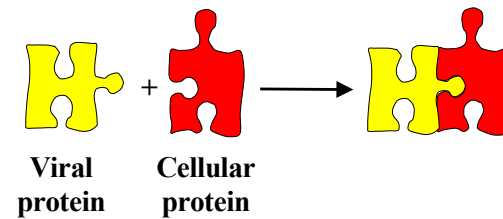
Towards comparative interactomics



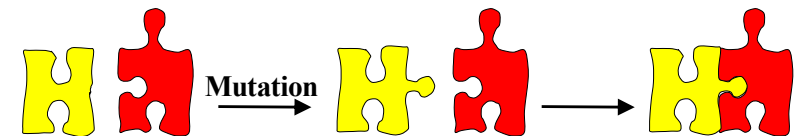
- pathogen / non pathogen

- virulent / attenuated

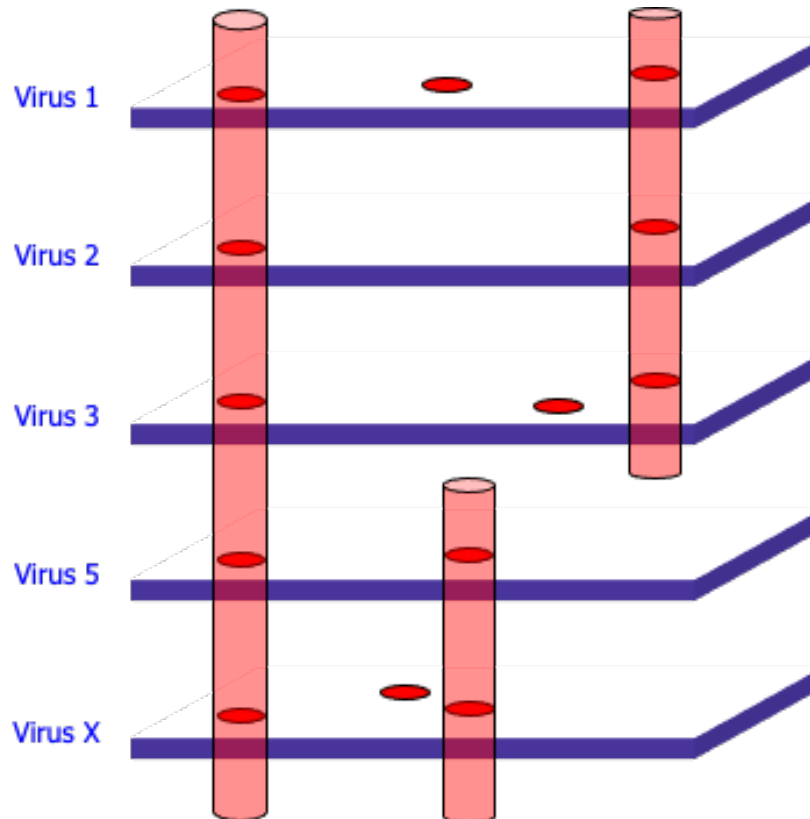
New factors of pathogenicity/virulence



New factors of interspecies transmission



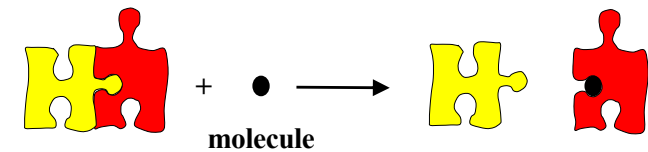
Towards comparative interactomics



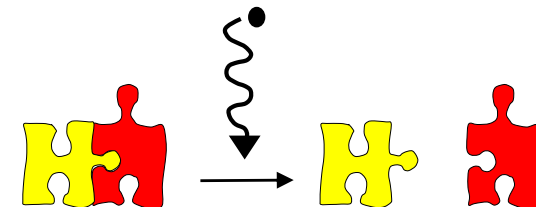
- pathogen / non pathogen

- virulent / attenuated

Direct inhibitors of virus-host interactions



Indirect inhibitors of virus-host interactions



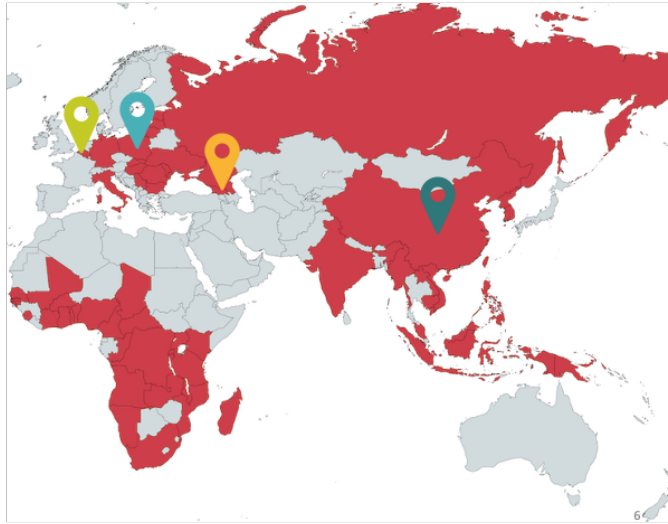
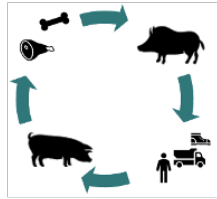
Biology of Orbiviruses (BIOR) activities

- Understanding disease features
- Diagnostic tools
- Epidemiology
- Vaccination
- Innate AV response
- Interactomics
- Others**



African swine fever virus (ASFV)

Epidémiologie de la PPA : aujourd'hui



-  2007 - Géorgie
-  2014 - Pologne
-  2018 - Belgique
-  2018 - Chine



G. Caignard



J. Dupre

ELEVAGE
LA PESTE NE DOIT PAS ARRIVER

Résumé: La peste porcine africaine peut apparaître du jour au lendemain. La prévention s'organise.

LES FAITS: La peste porcine africaine est une maladie virale qui affecte les porcins. Elle est présente dans plus de 50 pays d'Afrique, d'Asie et d'Océanie. Elle est considérée comme l'une des maladies animales les plus dangereuses.

LA PESTE PORCINE AFRICAINE (PPA): Cette maladie est causée par le virus de la peste porcine africaine (VPPA). Elle se transmet principalement par contact direct entre animaux, mais aussi par des insectes vecteurs comme les mouches et les tiques.

LES SYMPTÔMES: Les animaux atteints de PPA présentent des symptômes tels que la fièvre, l'écoulement nasal et oculaire, des plaques cutanées, et des hémorragies internes et externes.

LA PRÉVENTION: La prévention de la PPA repose sur des mesures strictes de biosécurité, notamment l'interdiction de l'importation de produits porcins d'origine suspecte, le contrôle des insectes vecteurs, et la mise en place de zones de quarantaine.

LES DÉFIS: La PPA est une maladie complexe à diagnostiquer et à contrôler. Elle nécessite une coopération internationale et des ressources humaines et matérielles importantes.

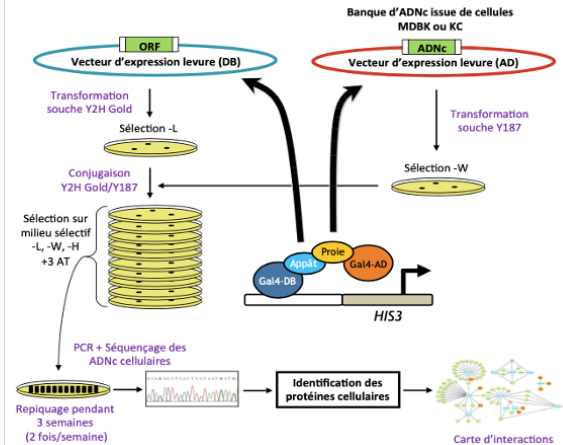
LES PERSPECTIVES: La recherche continue de travailler sur la compréhension de la biologie du virus et de ses interactions avec l'hôte, afin de développer de nouvelles stratégies de prévention et de traitement.

Plus d'infos: [www.oie.int/fr/medias/2018/08/20180821-PPA](#)



1. Recherche des interacteurs cellulaires

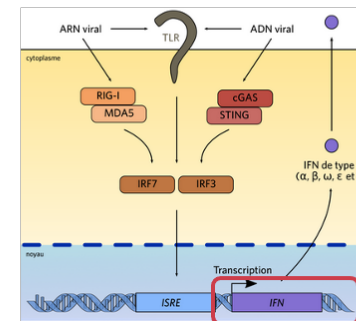
Le double-hybride en levure



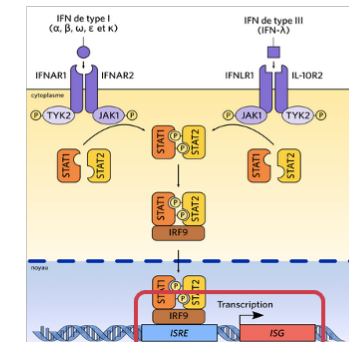
2. Antagonistes de la voie IFN

Tests rapporteurs luciférase

IFNβ-luciférase

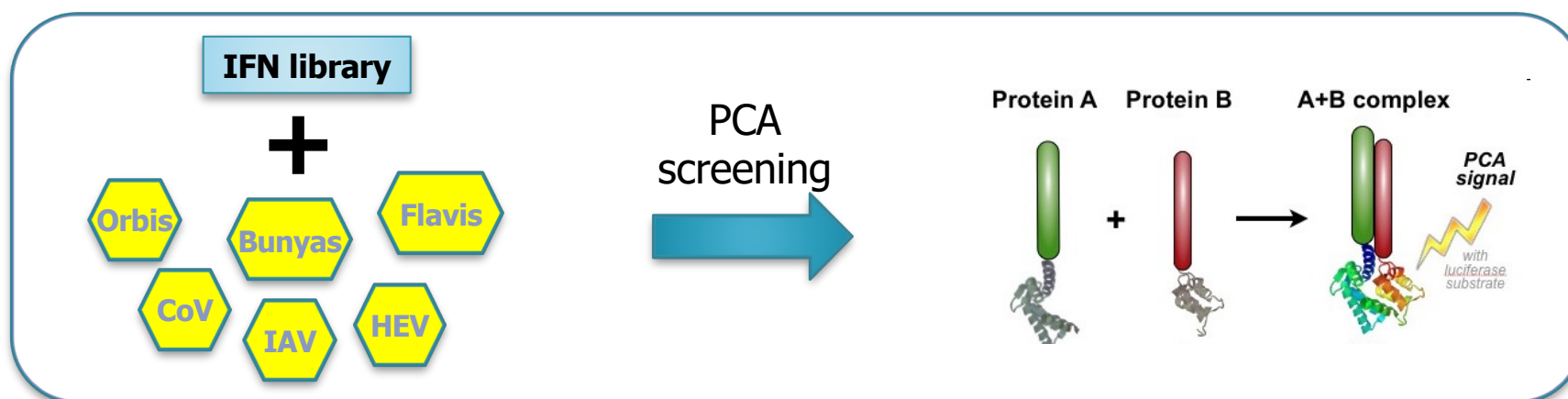
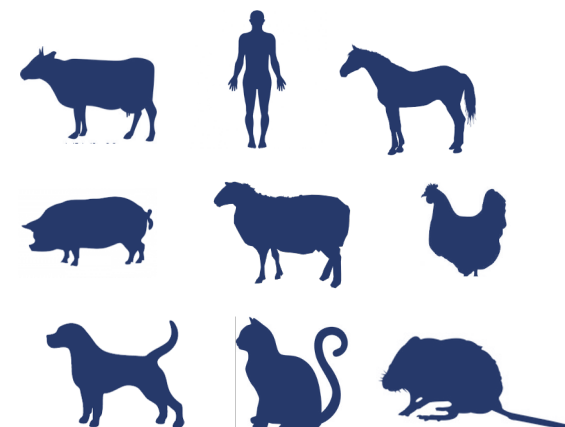
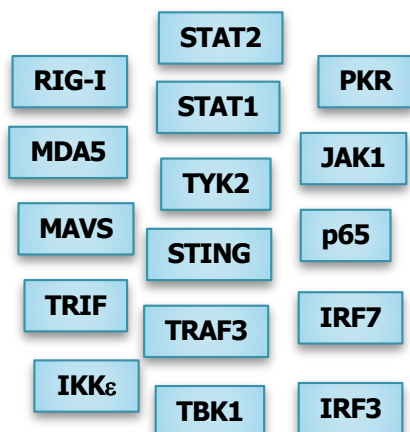
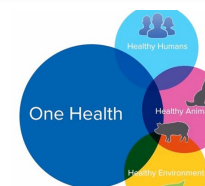


ISRE-luciférase



Interspecies "interferactomics"

PPI for preferentially targeted proteins of the **IFN pathway** in **multiple species**: **"Interferactomics"**.



« Conciliate interactomics and interferon response to investigate pathogenesis and host restriction mechanisms. »

Interplay between FMDV/IFN/persistence



Article

Host-Specific Interplay between Foot-and-Mouth Disease Virus 3D Polymerase and the Type-I Interferon Pathway

Morgan Sarry ^{1,2,*}, Grégory Caignard ¹, Juliette Dupré ¹, Stephan Zientara ¹, Damien Vitour ¹, Labib Bakkali Kassimi ¹ and Sandra Blaise-Boisseau ^{1,*}

¹ UMR VIROLOGIE, INRAE, École Nationale Vétérinaire d'Alfort, ANSES Laboratoire de Santé Animale, Université Paris-Est, 94700 Maisons-Alfort, France

² AgroParisTech, 16 Rue Claude Bernard, 75005 Paris, France

* Correspondence: morgan.sarry@anses.fr (M.S.); sandra.blaise-boisseau@anses.fr (S.B.-B.)

Foot-and-mouth disease



- highly contagious disease
- Can persist for >4 weeks (not in pigs)

Interplay between FMDV/IFN/persistence



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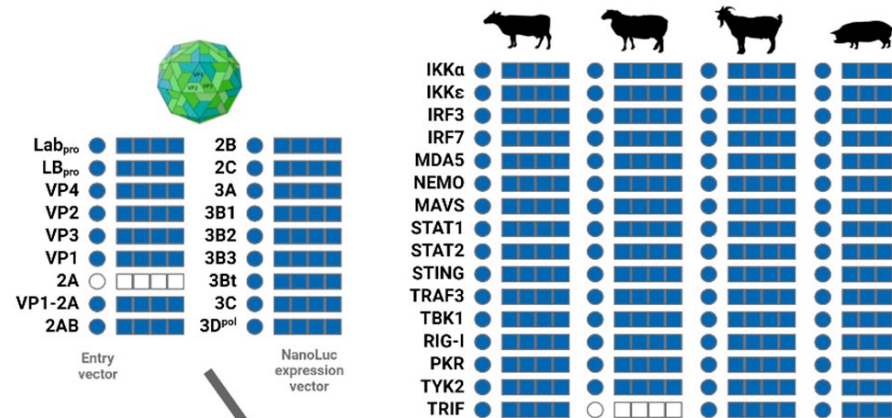
¹ UMR VIROLOGIE, INRAE, École Nationale Vétérinaire d'Alfort, ANSES Laboratoire de Santé Animale, Université Paris-Est, 94700 Maisons-Alfort, France
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Foot-and-mouth disease

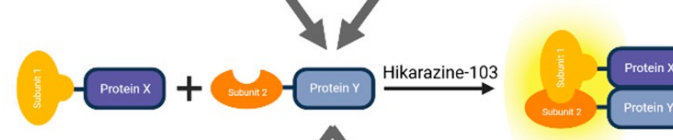


- highly contagious disease
- Can persist for >4 weeks (not in pigs)

Generation of NanoLuc expression vector libraries



Screening of FMDV/Host protein-protein interactions by NanoLuc-2-Hybrid assays



Interplay between FMDV/IFN/persistence

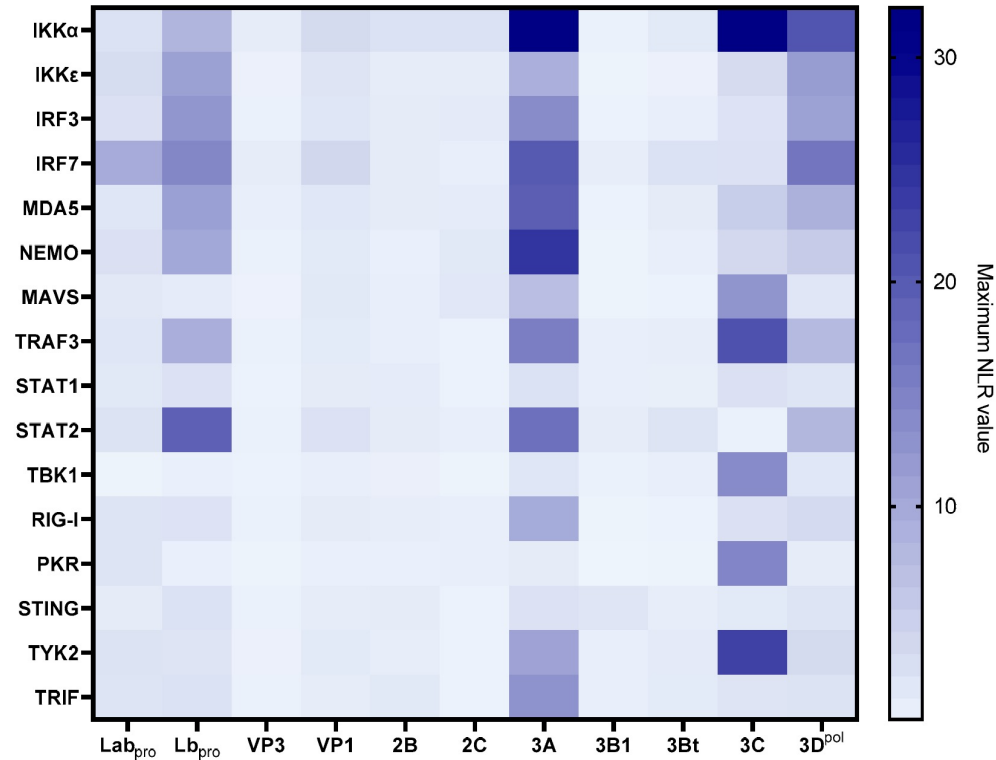
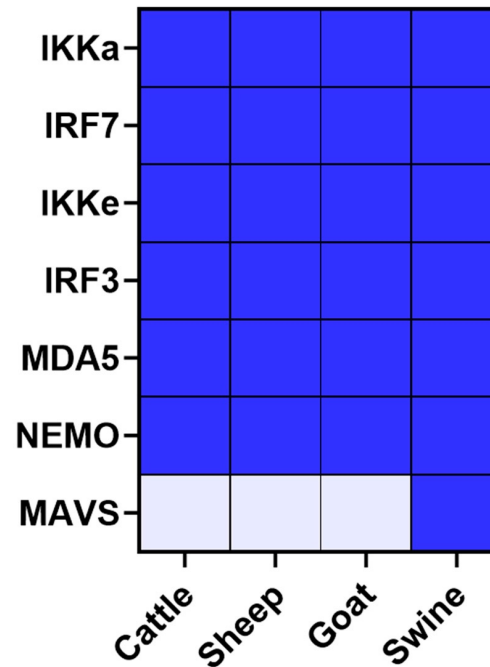


Figure 2. Screening for protein-protein interactions between eleven FMDV proteins and the sixteen selected IFN pathway proteins from the cattle library. HEK293T cells were co-transfected with a vector encoding a luminescent protein used for normalisation, as well as one of the four vectors corresponding to each protein, enabling the expression of proteins carrying one of the two nanoluciferase subunits at their N-ter or C-ter extremity. For each pair of interactors, eight combinations were assessed. The high luminescence values associated with each interactor pair were

Interplay between FMDV/IFN/persistence



- The **3D^{pol}** protein of FMDV only interacts with **porcine MAVS**, and not with its bovine, ovine or caprine orthologs.
- Role in **persistence** ?



Thank you for your attention