

Peste des Petits Ruminants: state of affairs and the road towards eradication

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Peste des Petits Ruminants (PPR)

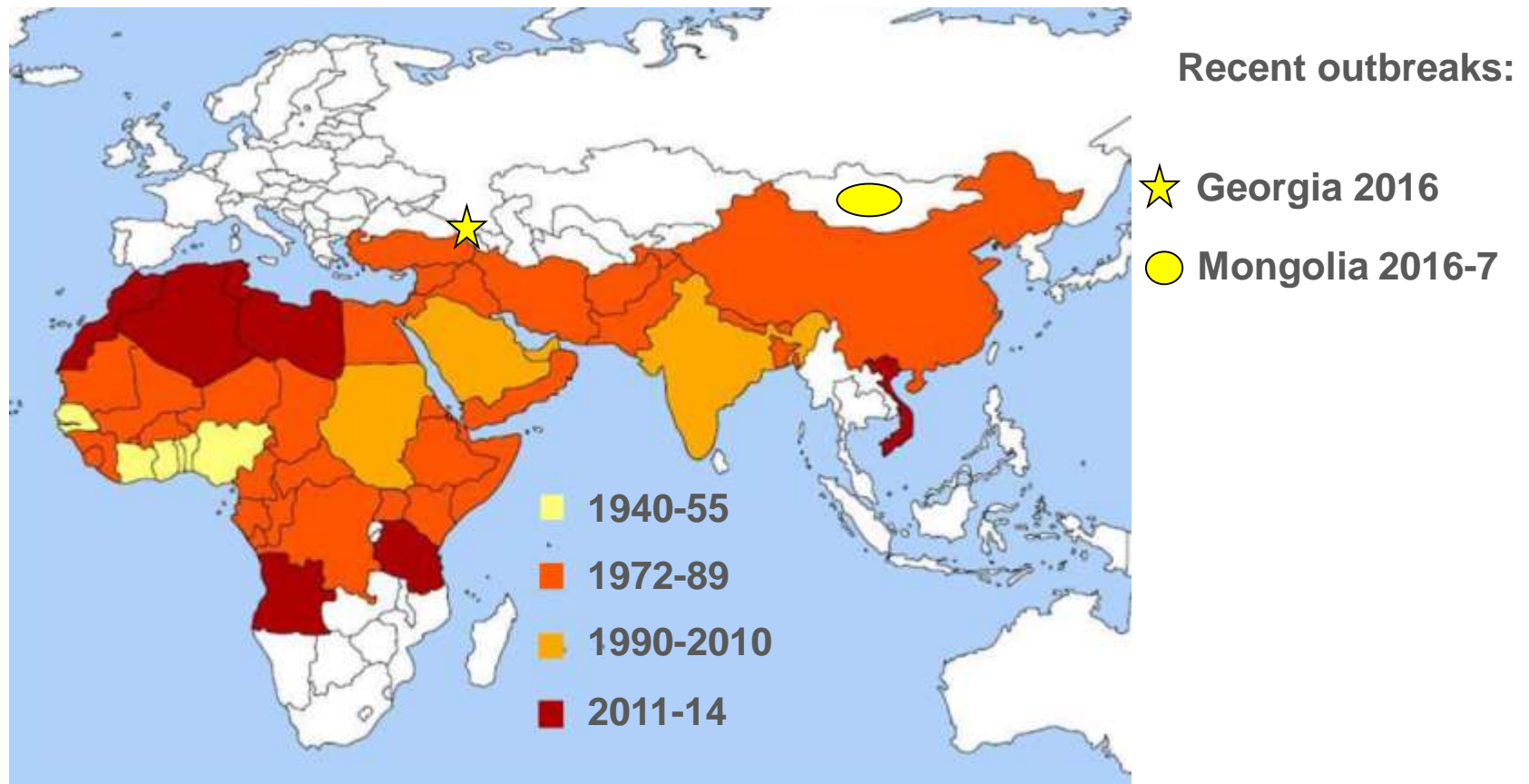
- Most widespread and devastating infectious disease of domestic small ruminants (goats, sheep)
- Mucopurulent ocular and nasal discharges, erosion of the mucosa, acute diarrhoea (mortality up to 100%)
- Camels and some wild ruminants also susceptible



Pictures 1-3: H. Salami

Peste des Petits Ruminants (PPR)

- Widespread in Africa, Middle East and Asia
- A disease still progressing, becoming a threat to Europe



Peste des Petits Ruminants virus (PPRV)

- Envelopped, single-stranded negative-sense RNA virus (genus *Morbillivirus*)
- ~16kb genome coding for 6 structural and 2 non-structural proteins

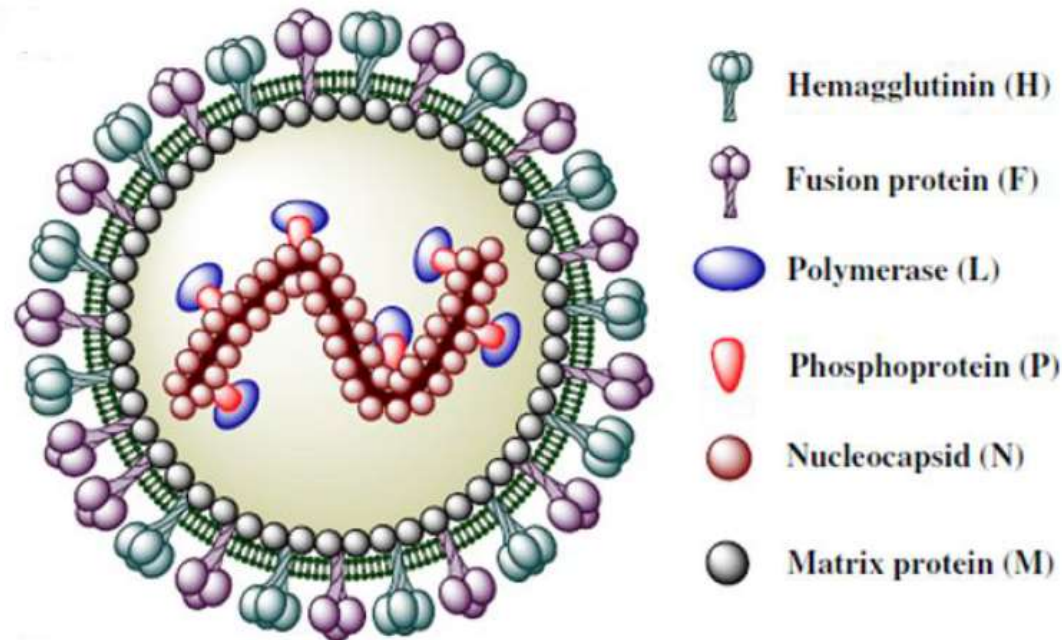


figure: Liu *et al.* (2016)

Peste des Petits Ruminants virus (PPRVV)

- Four distinct phylogenetic lineages (but one serotype)
- Lineage IV spreading from Asia to Africa, L-II replacing L-I

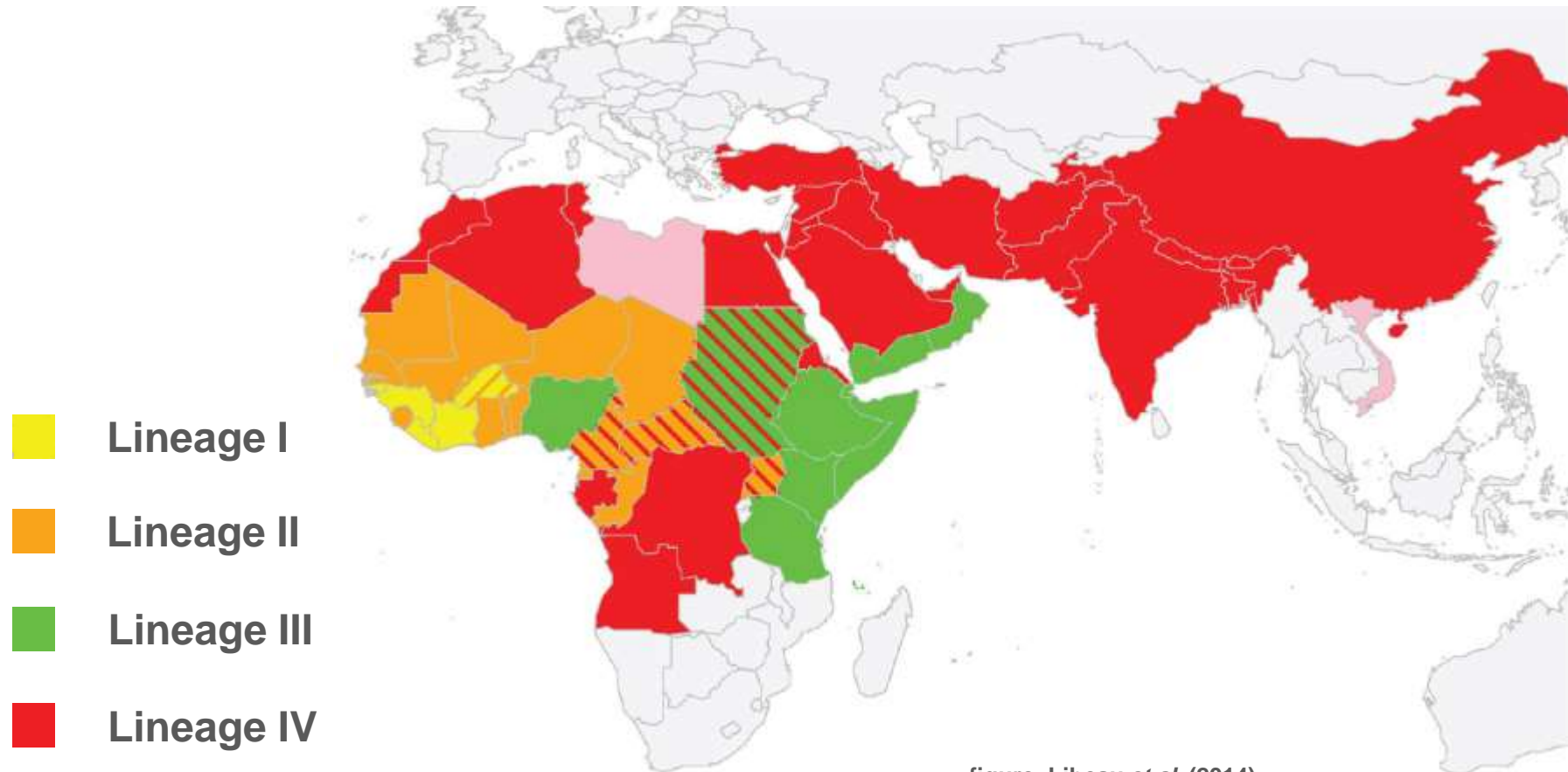


figure: Libeau *et al.* (2014)

Peste des Petits Ruminants (PPR)

- High economic impact and food security threat
- New target for global eradication (FAO/OIE, 2015)
- Based on massive vaccination campaigns
- 70% immunity needed to stop virus circulation
- Good conditions for success but gaps in knowledge



Progressive step-wise approach for the prevention and control of PPR (FAO/OIE, 2015)

Vaccines: what is available?

Live, attenuated homologous vaccines available

- Efficacy, innocuity, long-term, no residual side effects
- Cheap to produce, scalable for mass production
- Lyophilization for stability, but to be used within few hours when resuspended



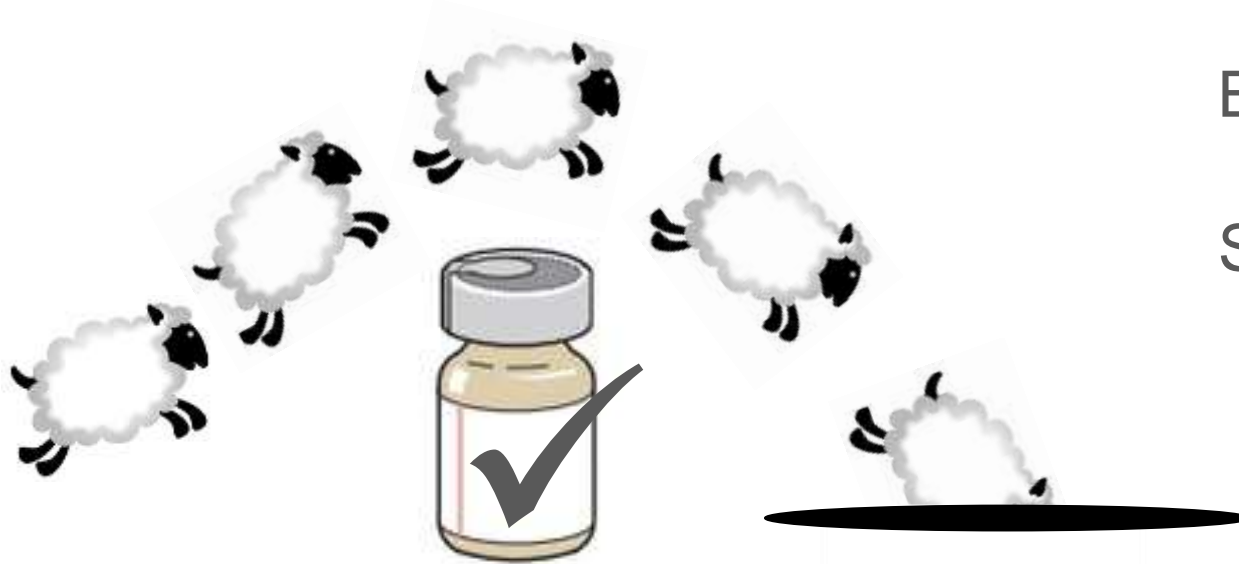
Different strains:

- Nigeria 75-1
(oldest, best studied)
- Sungri 96
- Arasur 87
- Coimbatore 97
- Maroc 2008
- ...

Vaccines: what is available?

Live, attenuated homologous vaccines available

- Efficacy, innocuity, long-term, no residual side effects
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But

Some pitfalls...

Vaccines: what is needed?

Quality control

- **Tests for identity, purity, safety, potency, stability**
 - Provided by independent body (AU-PANVAC)
 - But not compulsory except for African producers
 - Some vaccines with no external quality control

AFRICAN UNION

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CENTRE**



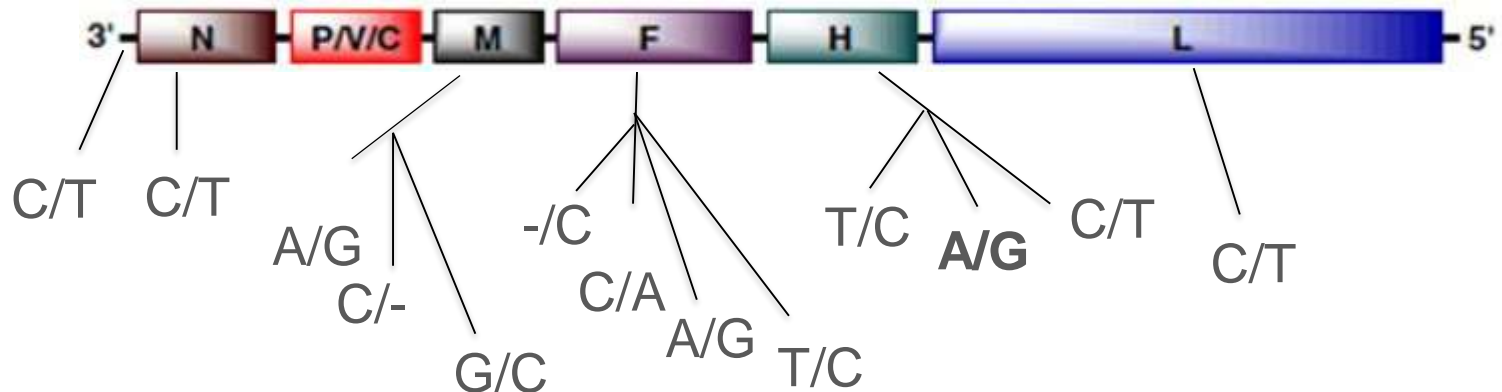
UNION AFRICAINE

**CENTRE PANAFRICAIN DES VACCINS
VETERINAIRES**

Vaccines: what is needed?

Quality control

- Tests for identity, purity, safety, potency, stability
- **Only few passages from master seed recommended**
 - Not controlled up to now
 - Way possible: comparing genome master seed/vaccine
 - Master seed of PPR strain Nigeria 75-1 sequenced
 - 13 differences from GenBank reference X74443
 - New reference (KY628761) basis for vaccine drift control



Vaccines: what is needed?

Quality control

- Tests for identity, purity, safety, potency, stability
- Only few passages from master seed recommended
- **Efficacy and innocuity not always tested**
 - When done, not always with same model systems (hard to do comparative studies)
- New studies coming out

Vaccination of goats with PPR-VAC confers a full protection against a PPR virulent challenge

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(Epizone poster)

Vaccines: what is needed?

Quality control

- Tests for identity, purity, safety, potency, stability
 - Only few passages from master seed recommended
 - Efficacy and innocuity not always tested
-
- Not always sure what is inside vaccine sold
 - Buyers may go for price not quality
 - Impact vaccination campaigns and risks of emergence
 - Standard quality control needed for all vaccines sold internationally



Vaccines: what is needed?

Vaccine delivery

- Cold chain or storage infrastructure limited in some countries/regions.
- Animals dispersed, difficulty to reach
- Vials of 100 doses – not used within time of certified efficacy
- Some work on thermotolerant vaccine but nothing out
- Regional adapted logistics needed

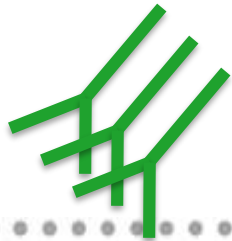


Vaccines: what is needed?

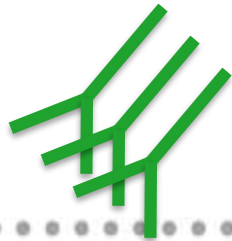
Vaccine differentiating infected from vaccinated animals (DIVA)

- Better monitoring post-vaccination
- Could be used in PPR-free countries/regions
- Prototypes in development/validation

Vaccination



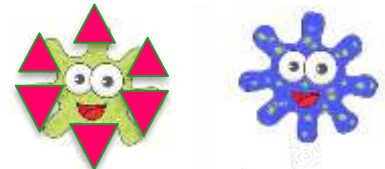
PPRVV-infected



DIVA vaccine



DIVA/co-infected



Diagnostic tools

Fit for purpose, in OIE manual

Method	Purpose					
	Target	<u>Confirmation of clinical cases</u>	<u>Population freedom from infection</u>	<u>Individual freedom from infection</u>	Prevalence of infection - <u>Surveillance</u>	Immune status in individual animals - <u>Vaccination</u>
ICE- ELISA	Protein	+++				
RT-PCR	Gene	+++				
QRT-PCR	Gene	+++				
Virus isolation	Virus	++				
VNT	Antibody		+++	+++	+++	+++
C-ELISA	Antibody		++	++	+++	+++

- Tools can be adapted to non-invasive sampling (e.g. feces)
- Rapid field tests available (or soon)



Some new kits commercialized without proper validation

Diagnostic tools



Some new kits commercialized without proper validation

Qualitative **Human** Peste Des Petits Ruminants (PPR) ELISA Kit

Store All Reagents At 2°C-8°C !

Package Size: 48T/Kit or 96 T/Kit

Valid Period: Six Months (2°C-8°C)

IN VITRO RESEARCH USE ONLY! NOT FOR THERAPEUTIC OR DIAGNOSTIC APPLICATIONS!



Transboundary transmission dynamics

- PPR transmission and spread linked to livestock trade
- Need for better understanding of regional virus transmission dynamics for efficient control and eradication
- Need phylogenetic data

Transboundary transmission dynamics

- PPR transmission and spread linked to livestock trade
- Need for better understanding of regional virus transmission dynamics for efficient control and eradication
- Need phylogenetic data **to study PPR emergence**

Even short reads (255bp N gene) are informative

Link of Georgia outbreak with NE Africa



Identification of Peste des Petits Ruminants, Georgia

Marina Donduashvili¹, Ketevan Goginashvili¹, Natela Toklikishvili¹, Tamar Tigilauri¹, Lamara Gelashvili¹, Lasha Avaliani², Natia Khartskhia², Angelika Loitsch³, Amaud Bataille⁴, Olivier Kwiatak⁴, Geneviève Libeau⁴, Adama Diallo⁴, William G. Dundon⁵.

Article in revision

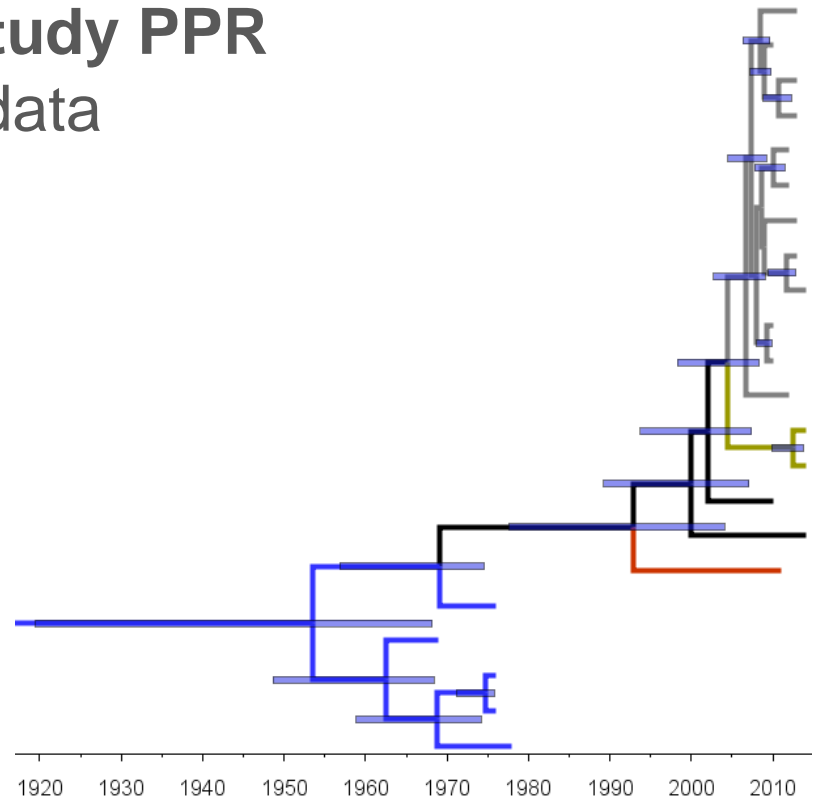
Transboundary transmission dynamics

- PPR transmission and spread linked to livestock trade
- Need for better understanding of regional virus transmission dynamics for efficient control and eradication
- Need phylogenetic data **to study PPR evolutionary history**: genomic data from historical samples needed

Mutation rate:
0.0014 sub/site/year
(95%HPD: 0.0008/0.0023)

TMRCA LII
1960 (1945-1969)

TMRCA LII in Senegal
2008 (2006-2009)



Transboundary transmission dynamics

- PPR transmission and spread linked to livestock trade
- Need for better understanding of regional virus transmission dynamics for efficient control and eradication
- Need phylogenetic data **to study PPR lineage diversity and distribution**

Lineage IV spreading in West Africa

Lineage I still circulating in Mali and Niger

(Epizone poster)



Distribution and genetic diversity
of Peste des Petits Ruminants virus in Mali



KADIDIA TOUNKARA¹, MAMADOU NIANG², ARNAUD BATAILLE¹, GENEVIEVE LIBEAU¹

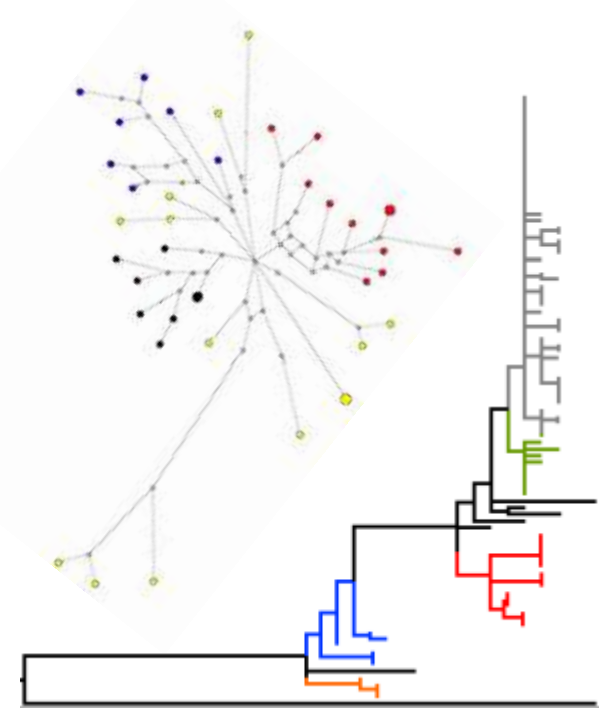
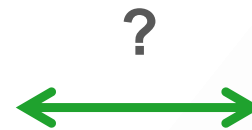
¹ CIRAD, UMR ASTRE, F-34398 Montpellier, France, INRA, UMR1309 ASTRE, F-34398 Montpellier, France, ² LCV, Laboratoire Central Vétérinaire du Mali

Transboundary transmission dynamics

- PPR transmission and spread linked to livestock trade
- Need for better understanding of regional virus transmission dynamics for efficient control and eradication
- Need phylogenetic data **to link transboundary transmission with trade**

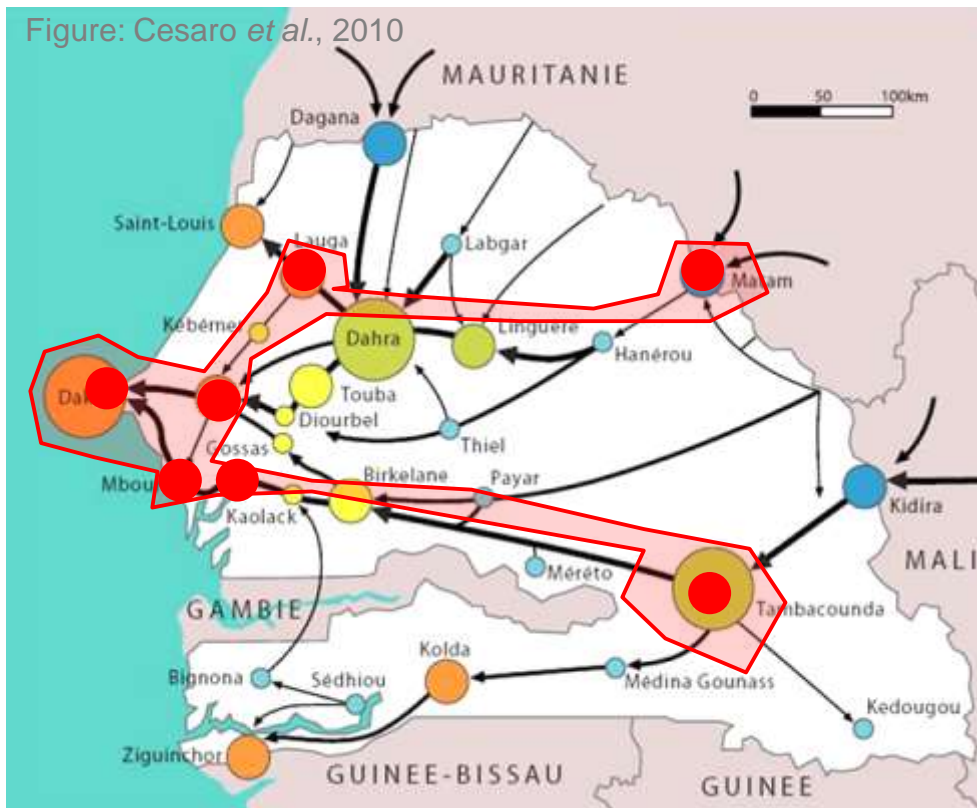


Small ruminant market trade network in Mauritania and Senegal



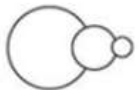
Transboundary transmission dynamics

Figure: Cesaro *et al.*, 2010



Association with animal trade

Market importance



Flow importance



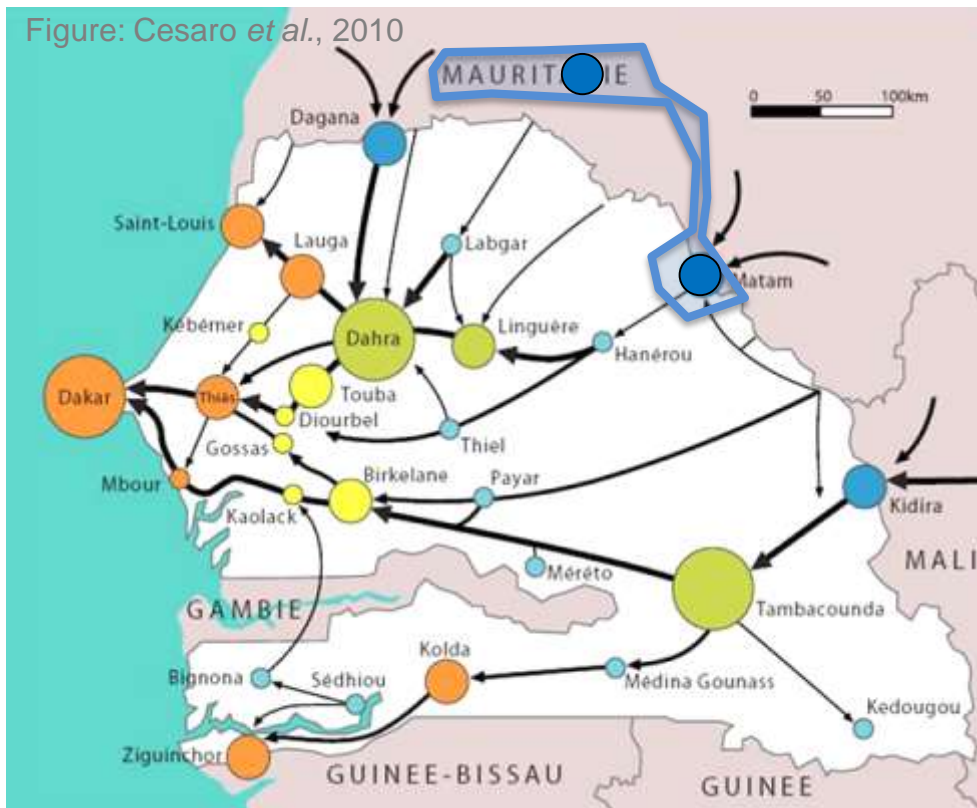
Type

- Transboundary
- Intermediary
- Local
- Consumption
- Regional hub

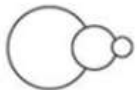


Transboundary transmission dynamics

Figure: Cesaro *et al.*, 2010



Market importance



Flow importance



Type

- Transboundary
- Local
- Intermediary
- Consumption
- Regional hub

Association with animal trade



Epidemiology of PPR

Large gaps in knowledge:

Factors determining virulence, host susceptibility

- Highly variable even in controlled settings

Breed	Strain	Dose/animal	Adm Route	Mortality
Ovine Djallonké	CI 89	5,0E+02	IN	2 (40%)
Ovine Sahel	CI 89	5,0E+02	IN	4 (100%)
Goat Sahel	CI 89	5,0E+02	IN	3 (60%)
Dwarf goat	CI 89	5,0E+02	IN	4 (80%)
Ovine Djallonké	Ethiopie 94	5,0E+02	IN	1 (20%)
Ovine Sahel	Ethiopie 94	5,0E+02	IN	0
Goat Sahel	Ethiopie 94	5,0E+02	IN	1 (25%)
Dwarf goat	Ethiopie 94	5,0E+02	IN	2 (40%)
Ovine Djallonké	India 94	5,0E+02	IN	1 (20%)
Ovine Sahel	India 94	5,0E+02	IN	0
Goat Sahel	India 94	5,0E+02	IN	4 (80%)
Dwarf goat	India 94	5,0E+02	IN	7 (100%)

From Couacy-Hymann et al

Epidemiology of PPR

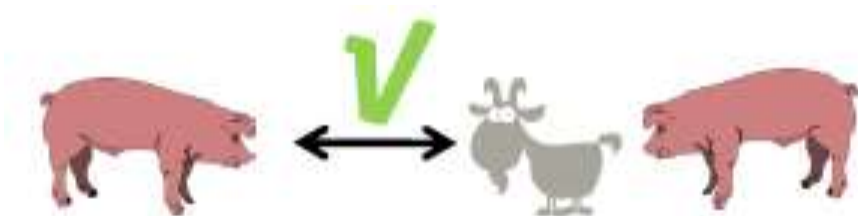
Large gaps in knowledge:

Role of other hosts in epidemiology (pigs, camels, wildlife)

Are they dead-end hosts or reservoirs?

- Pigs excrete and transmit PPR (but not wild boars)
- No evidence of PPR excretion in camels during experiment

(Schulz et al, FLI, Epizone 2016)



Outbreak in Sudan, 2004

Epidemiology of PPR

Large gaps in knowledge:

Role of other hosts in epidemiology (pigs, camels, wildlife)

Are they dead-end hosts or reservoirs?

- High seroprevalence in east african wildlife, but no virus isolated, or disease reported

Species	Prevalence (%)
Buffalo	50
Grant's gazelle	66
Thomson's gazelle	0
Wildbeest	50
Impala	100

(Tanzania, Mahapatra et al 2015)

Epidemiology of PPR

Large gaps in knowledge:

Role of other hosts in epidemiology (pigs, camels, wildlife)

Are they dead-end hosts or reservoirs?

- PPR cases in wild and captive artiodactyls
- PPR outbreak in endangered saïga populations (Mongolia 2016-2017)
- Spill-over from livestock

PPR a threat to biodiversity



Conclusions

PPR eradication can be reached but efficiency of campaign could be increased with:

- Strict vaccine quality control
- New generation of vaccines (DIVA)
- Regionally adapted vaccination strategies
- Basic scientific research on PPR
 - Transmission dynamics
 - Epidemiology
 - Evolutionary history

Any delay represents a threat to economy, food security, and nature conservation

PPR Team



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PPR expertise
Co-head PPR ref lab

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PPR expertise
Co-head PPR ref lab



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head microbiology group

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Kadidia Tounkara
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Lab techniques



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