Camel Prion Disease

Babelhadj B., A. Adbelkader, Di Bari M.A., Pirisinu L., Chiappini B., Gaouar S.B.S., Riccardi G., Marcon S., I. Kaouadji, K. Meghelli, Agrimi U., Nonno R., Vaccari G.

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Prion diseases or TSEs

Prion diseases are a group of fatal and transmissible neurodegenerative diseases
Prion is devoid of nucleic acid and to consist of a post-translationally modified host protein.

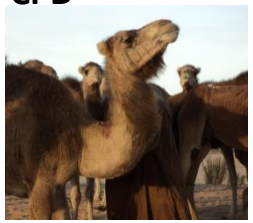
Scrapie


Classical scrapie
Atypical scrapie
C-BSE (2 goats)

CWD

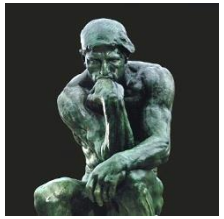
Chronic Wasting Disease

CPD



Camel prion disease

GSS
FFI
Kuru
VPSPr



CJD

- sCJD
- iCJD
- gCJD
- vCJD

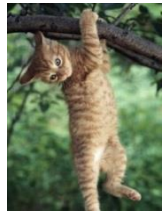
TME

Transmissible mink encephalopathy

BSE

C-BSE
H-BSE
L-BSE (BASE)

FSE

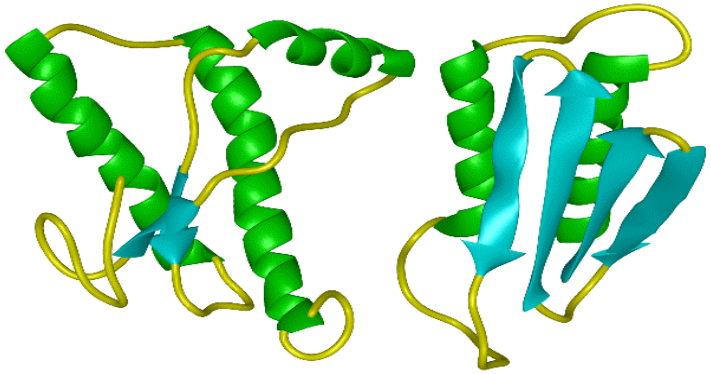



Feline spongiform encephalopathy

Prion Disease Diagnosis

A misfolded and aggregated isoform (PrP^{Sc}) of a cellular protein termed prion protein (PrP^{C}) is the main, if not the sole, component of prions

PrP^{C}



PrP^{Sc}

- **Neurological symptoms at clinical examination, are important for the suspect of prion disease**
- **Neuropathology examination of the brain**
- **Immunohistochemistry for the detection of PrPSc deposition**
- **Western blot analysis for the identification of PrPres**

Where Camel Prion Disease was discovered

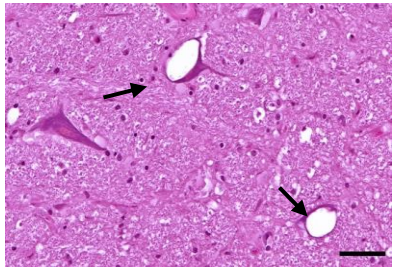
Since 2015 neurologic symptoms have been observed in adult dromedaries at antemortem examination in the abattoir of Ouargla, Algeria.

- ✓weight loss
- ✓behavioral abnormalities
- ✓tremors
- ✓aggressiveness
- ✓hyperactivity
- ✓typical down and upward movements of the head
- ✓hesitant and uncertain gait
- ✓ataxia of the hind limbs
- ✓occasional falls and difficultly getting up

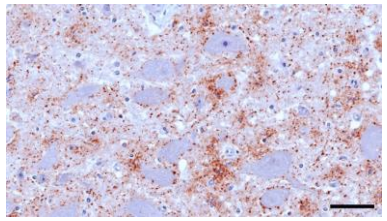
Dr. B. Babelhadj

Babelhadj et al., 2018 EID

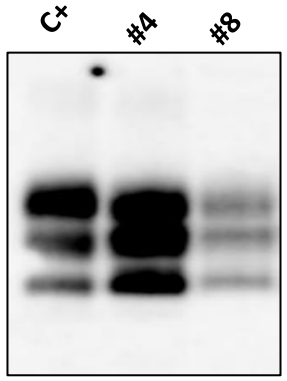
Diagnostic investigations camel prion disease (CPrD)



Histopatological examination revealed the typical spongiform changes



Immunohistochemical examination revealed evident PrP^{Sc} deposition



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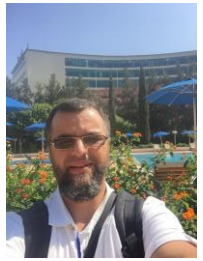
Western blot analysis revealed PrP^{Sc} with a PrP^{res} classical electrophoretic profile

M.A. Di Bari

L. Pirisinu



S.B.S. Gaouar

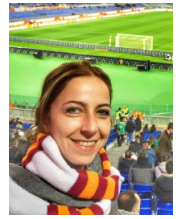
B. Babelhadj

ID	Clinical symptoms	Spongiform changes	PrPSc Deposition	PrP^{res}
# 3	Yes	Yes	Yes	
# 4	Yes	Yes	Yes	Yes
# 8	Yes	Yes	Yes	Yes
# 5	No	No	No	

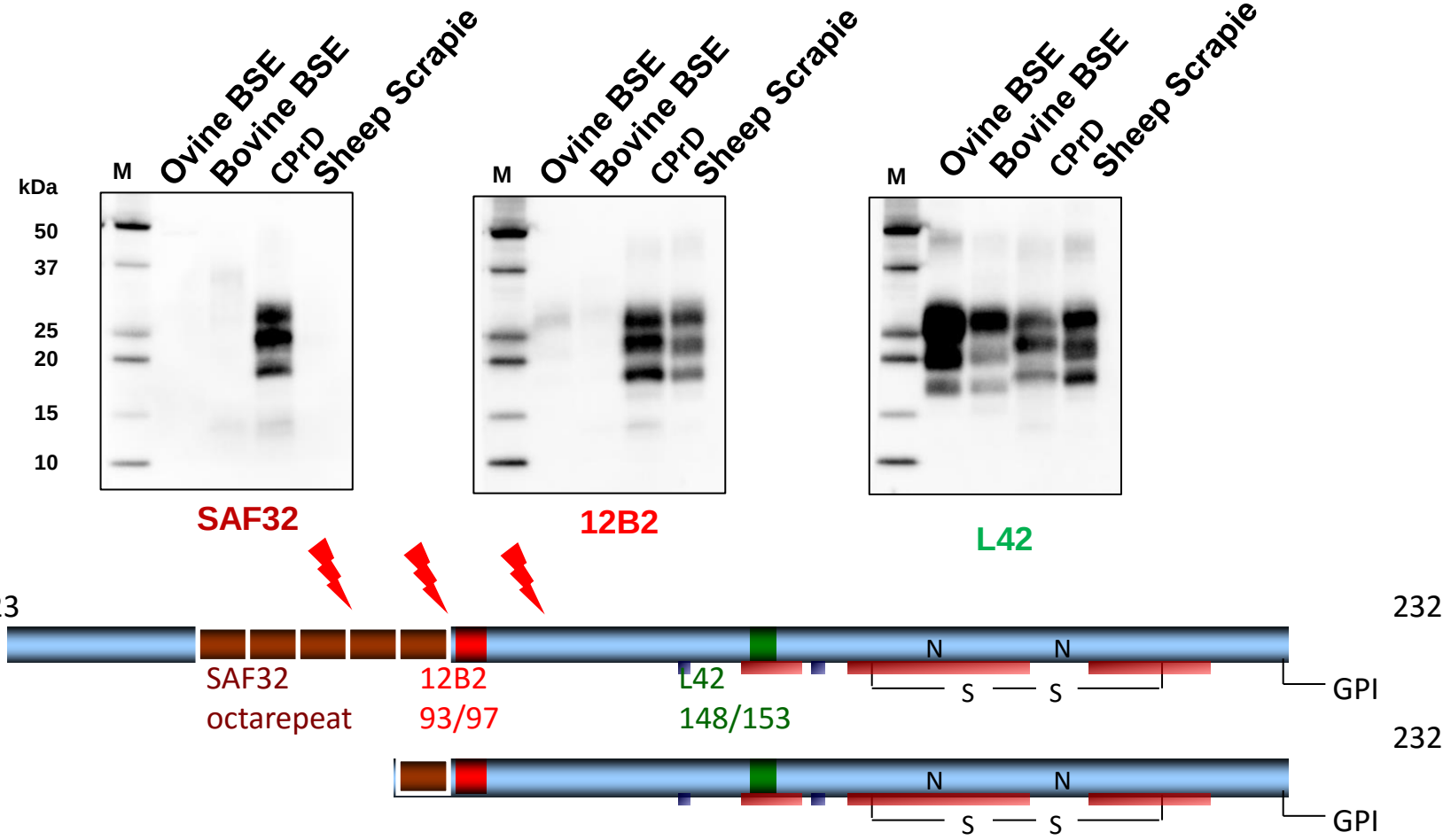
We confirmed diagnosis by detecting pathognomonic neurodegeneration and disease-specific PrP^{Sc} in brain tissues from dromedary camels and designate it as camel prion disease (CPrD)

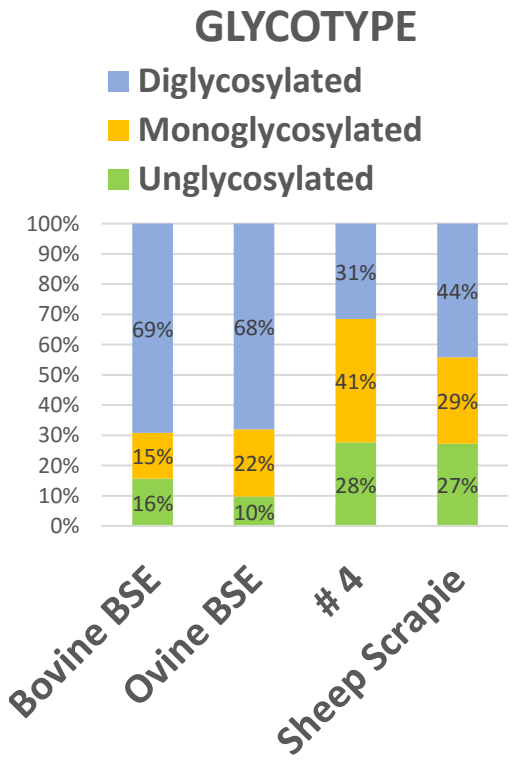
Babelhadj et al., 2018 EID

Is CPrD similar to other animal prion?


L. Pirisinu


S. Marcon





Molecular investigations show differences between CPrD and BSE or scrapie however is not possible to exclude any potential link

Bioassays in a panel of rodent models are ongoing for a thorough prion strain characterization of CPrD

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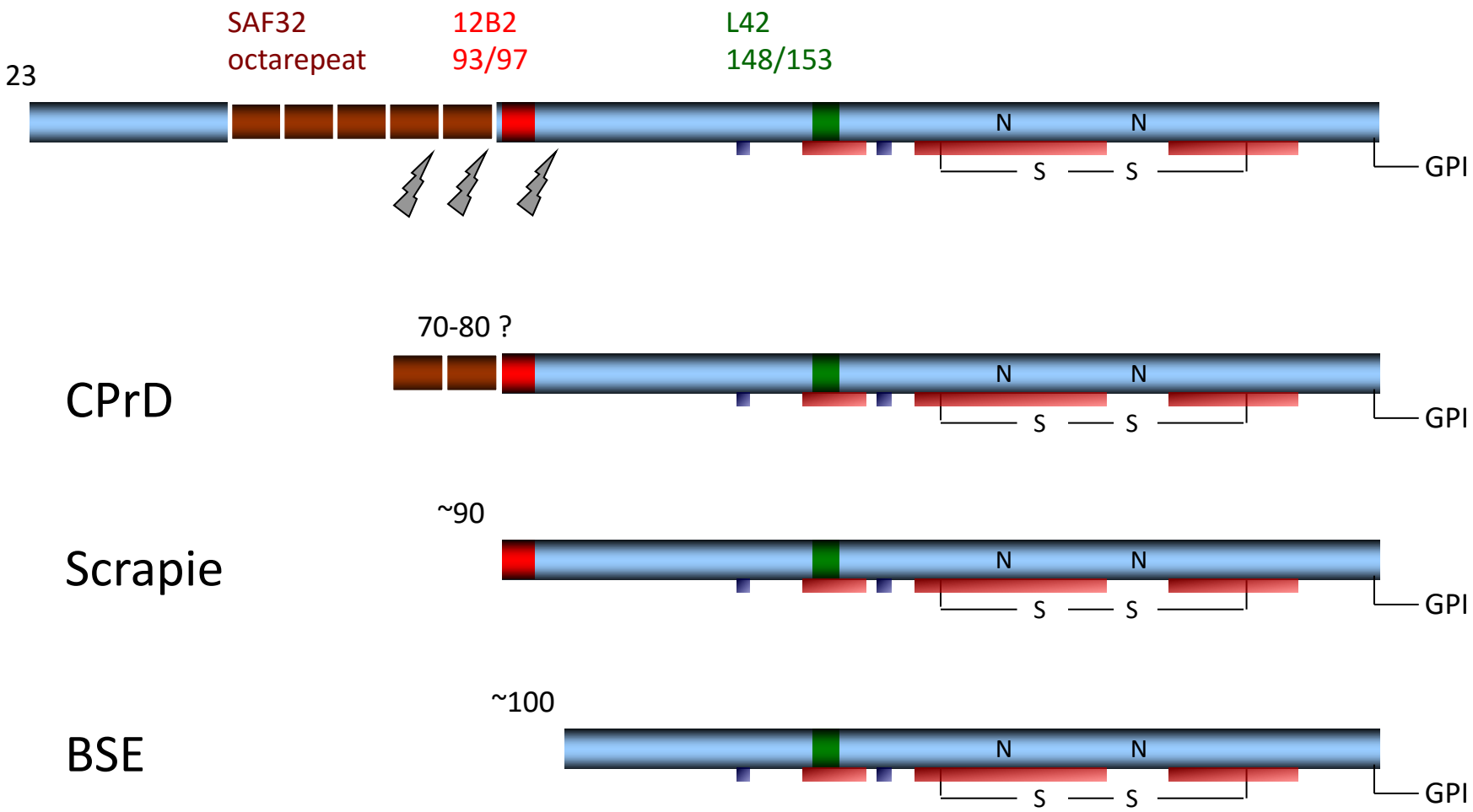
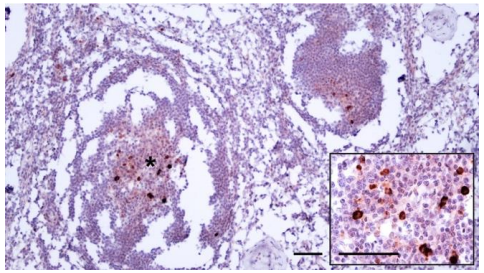
Molecular typing of PrP^{Sc}

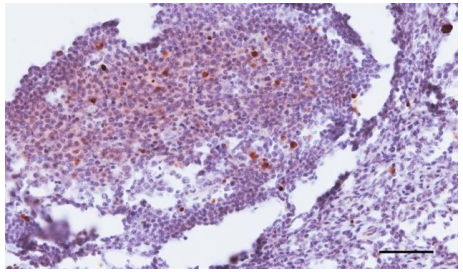


Immunohistochemical examination of lymphoid tissues

M.A. Di Bari

G. Riccardi





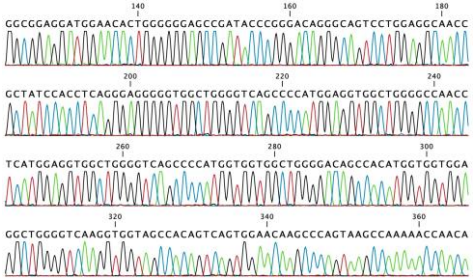
Cervical, prescapular, and lumbar aortic lymph nodes were collected from one from one symptomatic animal

Immunoystochemistry revealed that all lymph nodes were PrP^{Sc}-positive

PrP^{Sc} deposits involved >80% of primary and secondary follicles suggesting an abundant involvement.

Such results concur to suggest the infectious nature of CPrD

PRNP sequencing analysis



PRNP sequencing analysis showed that two animals were homozygous for the wild type allele described in dromedary

B. Chiappini

Babelhadj et al., 2018 EID

Epidemiological investigations

	2015		2016		2017		2018	
Month	N. of animals presented at the abattoir	N. of clinical suspects	N. of animals presented at the abattoir	N. of clinical suspects	N. of animals presented at the abattoir	N. of clinical suspects	N. of animals presented at the abattoir	N. of clinical suspects
January	63	/	67	3	178	7	276	10
February	70	2	83	4	187	9	304	5
March	86	1	73	3	228	11	340	6
April	79	2	85	3	213	7	242	10
May	97	3	93	4	319	12	120	9
June	81	1	117	5	299	13	355	6
July	92	2	135	6	182	10	231	7
August	121	4	145	7	183	5	142	5
September	31	1	44	5	80	5	97	4
October	42	1	110	4	191	4	220	6
November	89	2	164	4	242	8	264	8
December	86	1	206	3	314	7	301	7
Total	937	20	1322	51	2616	98	2892	83

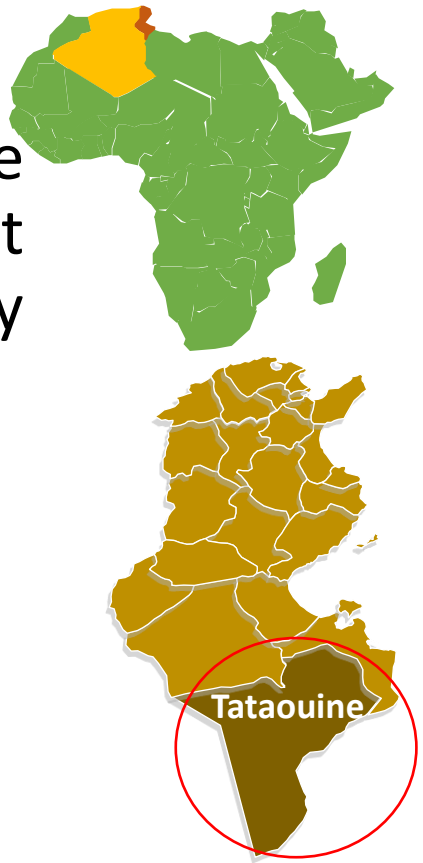
B. Babelhadj

- Retrospective analysis at abattoir, indicated a 3.1% prevalence of animals with neurologic signs suggestive of the disease.
- That figure appears to be reliable given that clinical suspicion was confirmed in all animals sampled
- The prevalence calculated on aged animals would be conceivably higher

CPD surveillance in Tunisia

Prof. A. Adbelkader

- After the identification of CPrD in Algeria, an epidemiological surveillance network was set up in Tunisia to monitor neurological diseases in dromedaries with a syndromic approach



- Brain and one lymph node were sampled in 2018 from a female dromedary with neurological symptoms that was presented at the abattoir of Tataouine in the south of Tunisia, at the veterinary services for authorization to slaughter

- Rabies was excluded
- In 2019 we received the samples from Prof. Amara Abdelkader

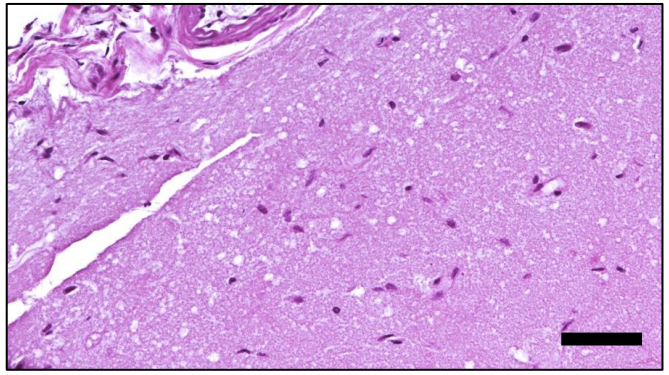
Diagnostic investigations camel prion disease (CPrD)

Histopathological, immunohistochemical examinations and PET-blot analysis

M.A. Di Bari

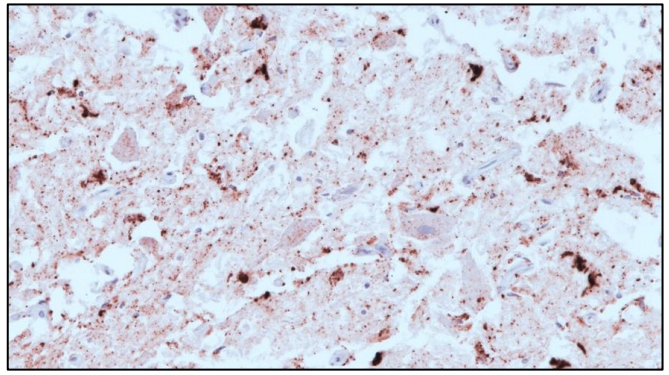
G. Riccardi

Spongiform change

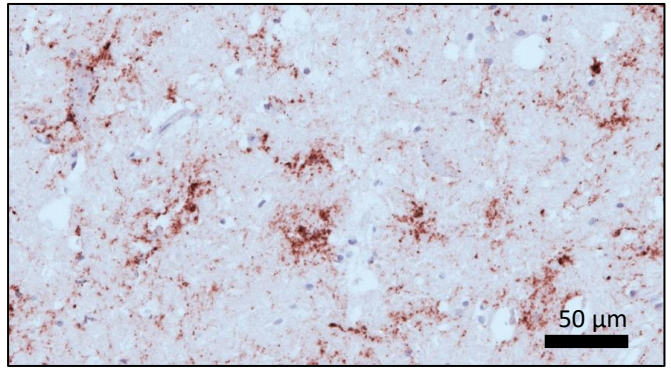


Temporal cortex

PrP^{Sc} distribution

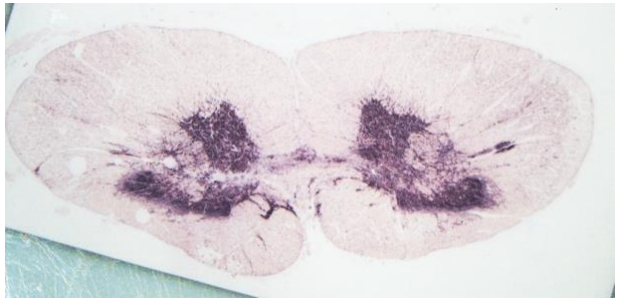


Dorsal nucleus of vagus nerve

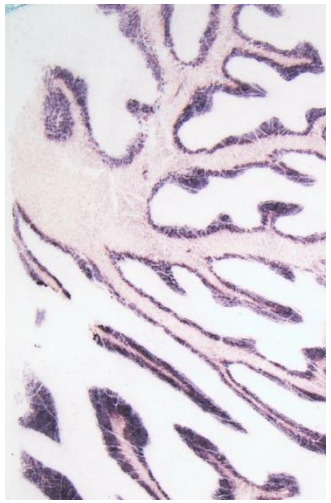


Thalamus

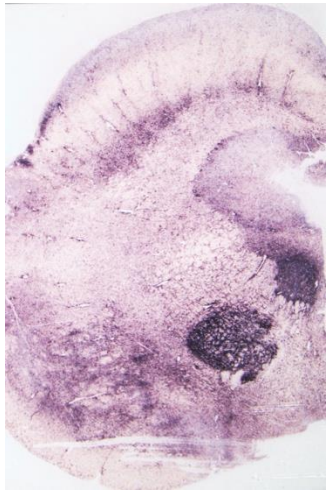
Paraffin-embedded blot



Medulla



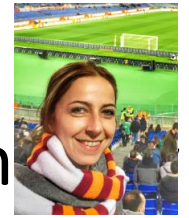
Cerebellum



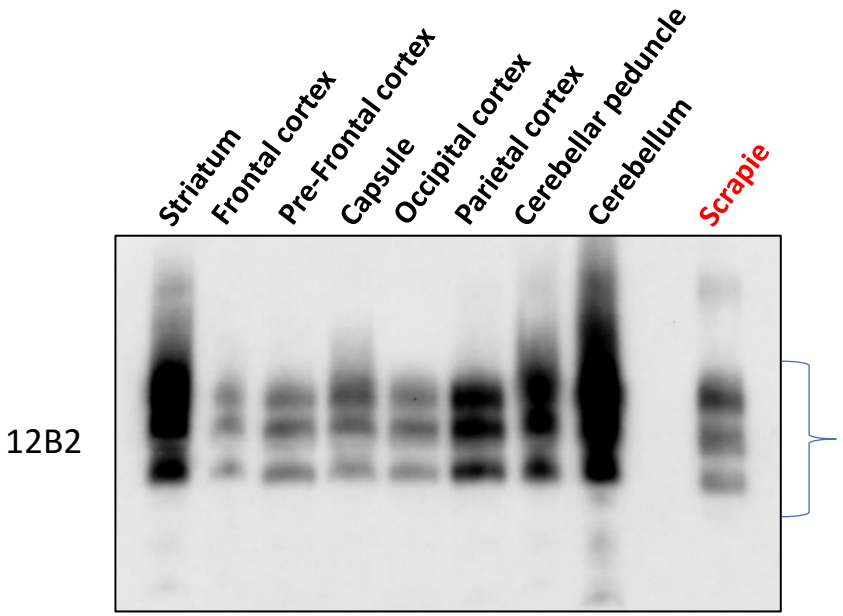
Pons

Diagnostic investigations camel prion disease (CPrD)

Western Blot for PrPSc on several brain areas of the drom brain sample


L. Pirisinu


S. Marcon



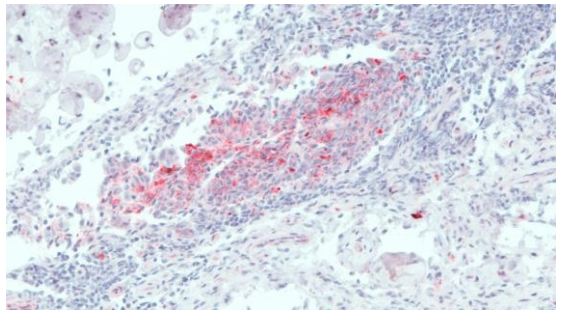
Western Blot analysis demonstrate the presence of the pathognomonic protease resistant PrP^{Sc} In different brain areas of the dromedary sample

We confirmed diagnosis of CPrD by detecting pathognomonic neurodegeneration and disease-specific PrP^{Sc} in brain tissues from the dromedary camel

Immunohistochemical examination of lymphoid tissue

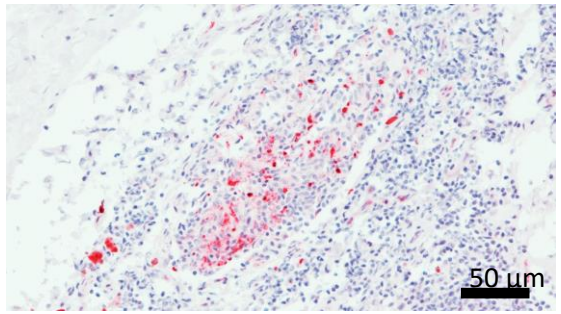
M.A. Di Bari

G. Riccardi



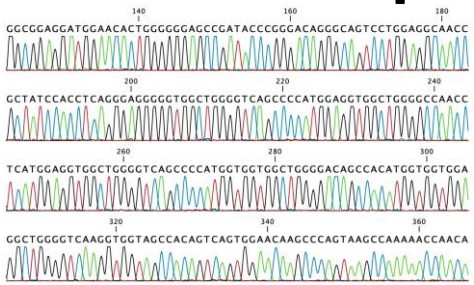
Retrosplenial lymph node was collected from the symptomatic animal and

Immunohistochemistry revealed PrP^{Sc}-positivity



PrP^{Sc} deposits involved >80% of primary and secondary follicles suggesting an abundant involvement.

PRNP sequencing analysis



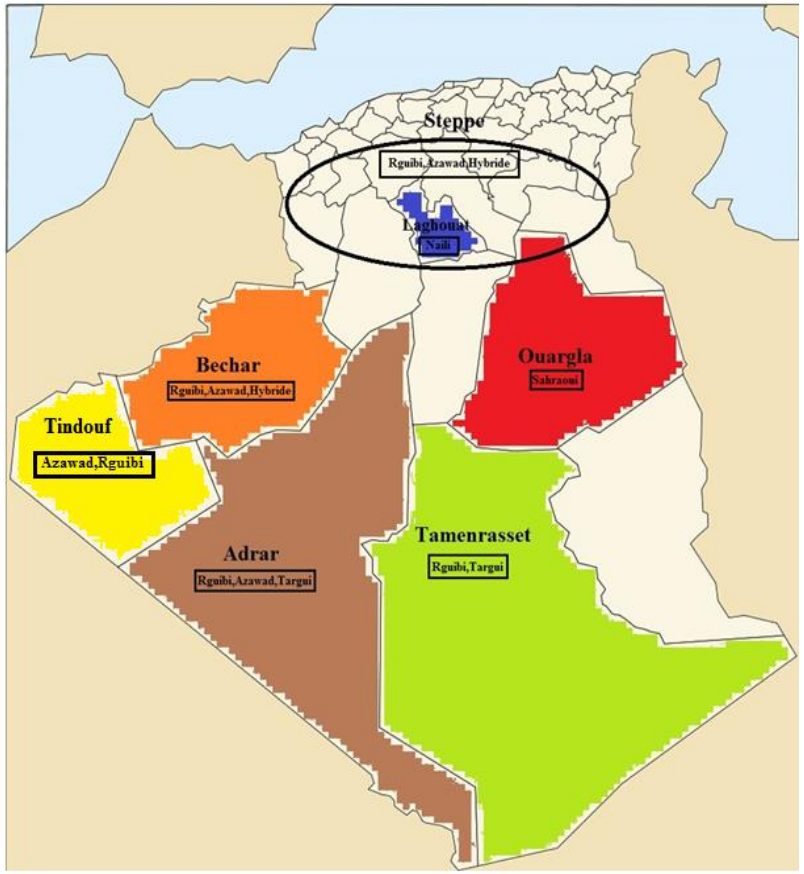
PRNP sequencing analysis showed that the animal was homozygous for the wild type allele described for dromedary

B. Chiappini

PRNP variability of the in Algerian dromedaries populations

I. Kaouadji

K. Meghelli



Breed	69 G/G	69 G/S	134 G/G	134 G/E
Azawad (n=38)	100%	0%	97,4%	2,6%
Hybride (n=13)	100%	0%	92,3%	7,7%
Naili (n=23)	100%	0%	100%	0%
Rguibi (n=56)	100%	0%	92,9%	7,1%
Sahraoui (n=16)	100%	0%	100%	0%
Targui (n=86)	98,8%	1,2%	100%	0%

Kaouadji et all., 2020 Animal Gene

Where Camel Prion Disease has been identified

	Animal N°	Neurological symptoms	CNS	Lymphoreticular
Algeria	3	+	+	+
	6	+	+	NA
	1	-	+	NA
	1	-	-	+
	41	-	-	NA
Total	52			
Tunisia	1	+	+	+
	4	+	+	NA
	1	+	-	NA
Total	6			NA tissue not available

Where Camel Prion Disease can be expected

Dromeadaries in northen Africa are bred extensively, without the use of feeds and the grazing

For dromedaries extensively breed, the borders between Tunisa, at the East with Libya and West with Algeria are permeable

Conclusion

- **CPrD is present in two bordering North African countries**
- **Evidences suggest that CPrD has an high prevalence in the Ouargla region**
- **It would be important to understand the spread of the disease in Algeria, Tunisia and other Countries were camels are raised**
- **Molecular characterization of CPrD suggest that it differs from main other animal TSE although *in vivo* experiments are ongoing**
- **The risk for Human is unknown and is under investigation**
- **Results obtained up to know suggest that CPrD is a new, emerging and infectious prion disease of dromedary camels**

B. Babelhadj

M.A. Di Bari

L. Pirisinu

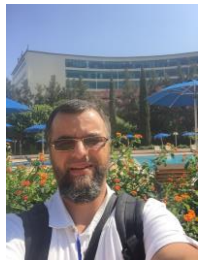
B. Chiappini

I. Kaouadji K. Meghelli

G. Riccardi

S. Marcon

U. Agrimi



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