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working at the Istituto Superiore di Sanità in Rome (Italy), where he focussed his research activities on prion diseases of animals and humans, mainly working on the characterization and discrimination of prion strains and on their interspecies transmissibility. Romolo Nonno is the head of the Italian Reference Laboratory for genetics and strain typing of animal TSEs (as a part of the Italian NRL on TSEs) and is responsible for strain typing activities within the European Reference Laboratory for TSEs.

Recent cryo-EM studies of infectious, *ex vivo,* prion fibrils from hamster 263K and mouse RML prion strains revealed a broadly similar, parallel in-register intermolecular β-sheet (PIRIBS) amyloid architecture in both strains. Rungs of the fibrils are composed of single prion protein (PrP) monomers that fold to create distinct N- and C-terminal lobes. However, observed structural variations between these fibrils are conflated by differences in hamster/mouse PrP sequence, which precludes resolving how divergent prion strains can emerge from an identical PrP substrate. It is, therefore, now important to obtain more prion fibril structures from the same species and/or of strains that can cross the mouse/hamster species barrier to gain further insight into the mechanism of prion strain diversity. Another puzzle pertains to the presence of paired fibril assemblies in *ex vivo* prion preparations. Are they biologically relevant? It remains to be seen if the future collection of near-atomic resolution structures of both single and double-protofilament assemblies can uncover the structural basis for unique glycoform ratios characterising various prion strains.

Chronic wasting disease risk assessment in Portugal: results and future work

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Principal Investigator (PI) of the project "Chronic wasting disease risk assessment in Portugal" funded by the Portuguese Foundation for Science and Technology.

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The project intitles "Chronic Wasting Disease Risk Assessment in Portugal" reference PTDC/CVT-CVT/29947/2017, was financed by FCT with 239.897,23€, started in October 2018, and it was extended until September 2022 in consequence of the COVID pandemic situation.

Three institutions are associated with the best success of the proposed aims: UTAD, the lead institution, INIAV with the skills for the TSE diagnosis, and the IPCB, the major institution for samples harvester.

This project has 7 tasks, developed during these years.

Task 1, Training and sample collection is complete. Five hundred samples from 3 different species of cervids that live in Portugal (*Cervus elaphus, Dama dama* and *Capreolus capreolus*) were harvested in hunting in Castelo Branco and the north of Portugal, at UTAD.

In task 2, the lymph nodes and brainstem of these animals were screened for PrPres at INIAV, which became all negative. The central nervous system histopathology is ongoing, and no severe pathologies have been diagnosed yet. Most cases of *Capreolus capreolus* were from necropsies and other lesions were diagnosed as parasites and traumatic lesions, and one case of renal carcinoma.

Task 3 is the determination of *prnp* genotypes in the Portuguese cervid population and will be exposed in oral communication: "*Chronic wasting disease (CWD) risk assessment in Portugal: - The genetic approach to study prion protein gene (PRNP) variability in Portuguese populations of three cervid species: Red deer, Fallow deer and Roe deer*".

In task 4 we intend to determine the identification of other risk factors as related to the positive cases of BSE and scrapie near the wild hunted cervid population, imports of cervids and hunting tourism.

We also proposed to make a transmission assay of atypical scrapie to cervid Tg-mice. In this 5th task, the transmission ability of atypical scrapie to cervids is being studied by bioassay in transgenic mouse models expressing either Deer PrP (226Q-DePrPTg146) or Elk PrP (226E-ElkPrPTg152). To do this, these two newly generated mouse lines have been inoculated with a collection of Portuguese Atypical Scrapie isolates. Currently, these experiments are underway but we will have to wait to have conclusive results.

The last 2 tasks are in progress, statistical analysis and modelling, defining the risk of occurrence of prion diseases in cervids in Portugal, and the dissemination of the results in international meetings, international papers, and book chapters contributions. This Iberian Congress is one example of this project dissemination.

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Oral Communications:
Prion diseases and prion-like diseases in humans

O1 | Regional differences in neuroinflammation-associated gene expression in the brain of sporadic Creutzfeldt-Jakob disease patients

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Neuroinflammation is an essential part of neurodegeneration. Yet, current understanding of neuroinflammation associated molecular events in distinct brain regions of prion disease patients is insufficient to lay the ground for effective treatment strategies targeting this complex neuropathological process. To address this problem, we analyzed expression of 800 neuroinflammation associated genes to create a profile of biological processes taking place in frontal cortex and cerebellum of patients, who suffered from sporadic Creutzfeldt-Jakob disease. The analysis was performed using NanoString nCounter technology, human neuroinflammation panel+. The observed gene expression patterns were regionally and sub-regionally distinct, suggesting variable neuroinflammatory response. Interestingly, the observed differences could not be explained by the molecular subtypes of sporadic Creutzfeldt-Jakob disease. Furthermore, analyses of canonical pathways and upstream regulators based on differently expressed genes indicated an overlap between biological processes taking place in different brain regions. This suggests that even smaller scale spatial data reflecting subtle changes in brain cells' functional heterogeneity and their immediate pathologic microenvironments are needed to explain the observed differential gene expression in a greater detail.