sheep scrapie, chronic wasting disease in deer, Creutzfeldt-Jakob Disease (CJD),[1] and Bovine Spongiform Encephalopathy (BSE).[2]

The RT-QuIC assay coupled with the Omega series of plate readers is both faster and more sensitive than past bioassays. This means that prion seeding assays can now be measured with a higher throughput using the RT-QuIC assay and BMG LABTECH's Omega microplate readers.

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P.26: Glycosaminoglycan mimetic and sulfation inhibitor do not prevent the initial uptake of prions but impair the establishment of productive infections

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Transmissible spongiform encephalopathies are caused by prions, unconventional infectious agents predominately composed of misfolded host-encoded prion protein (PrP^{Sc}). PrP^{Sc} is formed by the conformational conversion of the cellular prion protein, PrP^{C}. Alternative heritable conformations of PrP^{Sc} most likely encipher different prion strains. The precise mechanisms and cellular requirements for PrP^{Sc} uptake, the initial PrP^{Sc} formation and the persistent PrP^{Sc} propagation still remain unknown. Glycosaminoglycans (GAGs), highly-sulfated unbranched polysaccharides, present on the cell surface and within endocytic vesicles, might act as co-factors for prion infection and propagation. So far, comparative analysis of the role of GAGs during the individual stages of infection by different prion strains have not been performed. We examined the effect of the GAG mimetic, DS-500, and the sulfation inhibitor, $NaClO_3$, on prion infection by scrapie strains RML and 22L in L929 cells and in prion-infected cerebellar brain slices. Neither the treatment with DS-500 nor $NaClO_3$ inhibited the uptake of RML and 22L PrP^{Sc} by L929 cells, arguing for a sulfated GAG-independent uptake of PrP^{Sc}. Treatment during the early infection stages impaired the establishment of prion infections in cell culture and organotypic cerebellar slice cultures, suggesting that sulfated GAGs are required for the establishment of productive prion infections. Both treatments also reduced PrP^{Sc} levels in persistently infected L929 cells and infected cerebellar brain slices. In conclusion, our findings suggest that different prion strains depend on sulfated GAGs during acute and chronic infections, but sulfated GAGs are not essential for prion uptake.

P.27: Interaction of PrP and nucleic acids: Comparative effects of DNA and RNA molecules

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Keywords: prion, nucleic acid, DNA, RNA, aggregation, misfolding, toxicity

Prion diseases are triggered when the cellular prion protein (PrP^{C}) is enriched in β-sheet-rich secondary structure, generating PrP^{Sc}, the main component of the infectious prion particle. The main hypothesis for prion diseases proposes that conversion of PrP^{C} into PrP^{Sc} occurs without the participation of any other molecule. For decades, it was believed that prion proteins were the only entity necessary to generate misfolding, aggregation and toxicity. However, there are evidences that an adjuvant factor might play a role in PrP^{Sc} formation, lowering the energy barrier between PrP^{C} and PrP^{Sc}. In this context, nucleic acids have aroused as an interesting group of prion protein ligands. Both DNA and RNA interact with PrP and catalyze the misfolding of the cellular PrP (PrP^{C}) into a scrapie-like isoform (PrP^{Sc}). Also, it has been observed that interaction of PrP with nucleic acids can be toxic to cultured cells. Here we investigate whether different aggregation, stability, and toxicity effects are detected when non-related DNA and RNA sequences interact with recombinant PrP constructions, using a spectroscopic approach and cell toxicity studies. Our results show that DNA and RNA bind in different regions of murine PrP, inducing secondary structure changes, aggregation and toxicity at different intensities. Composition and size of these molecules can also interfere in these effects. We believe that nucleic acids can be suitable candidates for prion cofactor, facilitating PrP^{Sc} formation.

P.28: Modeling prion species barriers and the new host effect using RT-QuIC

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The propensity for trans-species prion transmission is related to the structural characteristics of the enciphering and heterologous PrP, but the exact mechanism remains mostly mysterious. Studies of the effects of primary or tertiary prion protein