Chemistry / Biochemistry
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Chemistry of Neuro-Disorders: Their Mechanism, Diagnostics and Drug Development

Speaker:

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Polysaccharides in prion formation

Prions are the infective agents of fatal neurodegenerative diseases like bovine spongiform encephalopathy (BSE), Creutzfeldt-Jakob disease (CJD) in human or scrapie in sheep. They are composed primarily of a host protein, the so-called *prion protein* (PrP). In comparison to its cellular isoform (PrP^{C}) the infectivity-associated isoform of PrP (PrP^{Sc}) shows changes in secondary structure and builds up insoluble and infective aggregates which are highly stable against degradation. In 1982 Stanley B. Prusiner introduced a model of the infective agent, stating that prions are *proteinaceous infective particles lacking nucleic acids*. The *prion model* – for which Prusiner was awarded with the Nobel prize in 1997 – was verified by *in vitro* generation of synthetic prions from recombinant PrP only (1, 2). The molecular details of prion formation are, however, not yet fully understood, especially since synthetic prions led only to small titers of infectivity. Therefore it is essential to understand misfolding and aggregation of PrP in the context of other known non-PrP components of naturally occuring prions.

We did show that such a common non-PrP component of natural prions is a glucose-polysaccharide amounting up to 15 % (w/w) of the infective agent. By chemical, enzymatical and mass spectrometrical analyses we demonstrated its close relationship to glycogen (3, 4). The structural conversion, aggregation and fibrillization of recombinant PrP in the presence of glycogen was examined by different spectroscopical and microscopical methods, utilizing an *in vitro* conversion system, in which we can induce PrP^{C}-like structures as well as the structural conversion to PrP^{Sc}-like aggregates (5, 6).

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