Prion protein: orchestrating neurotrophic activities

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PrP^C is highly expressed in both the central and peripheral nervous systems from early stages of development and in adulthood. Its major conformational change and conversion into an abnormal form (PrP^{Sc}) has been associated with the generation of prions, the infectious agent of transmissible spongiform encephalopathies (TSEs). The massive neurodegeneration presented by individuals suffering from these diseases has been associated with the gain of neurotoxic activity of PrP^{Sc}. On the other hand, major neurodegeneration is also observed in transgenic mice expressing PrP^C molecules deleted of specific domains, which points to important functional domains within this molecule, and supports the hypothesis that loss-of PrP^C function may contribute to the pathogenesis of TSEs. Furthermore, a large body of data demonstrates direct or indirect interaction of PrP^C with extracellular matrix proteins, soluble factors, transmembrane proteins, G-protein coupled receptors and ions channels. The ability of PrP^C to drive the assembly of multi-component complexes at the cell surface is likely the basis for its neurotrophic functions. These properties indicate that PrP^C may be relevant for not only the spongiform encephalophaties, but also as an ancillary component of the pathogenesis of other neurodegenerative diseases, and therefore amenable to therapeutic targeting.