1. Record Nr. UNINA9910137089803321

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Titolo	Promiscuous functions of the prion protein gene family
Pubbl/distr/stampa	Frontiers Media SA, 2015
Descrizione fisica	1 electronic resource (113 p.)
Collana	Frontiers Research Topics
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Sommario/riassunto	The cellular prion protein PrPC is a ubiquitous GPI-anchored protein. While PrPC has been the focus of intense research for its involvement in a group of neurodegenerative disorders known as transmissible spongiform encephalopathies (TSE), much less attention has been devoted to its physiological function. This notably relates to the lack of obvious abnormalities of mice, goat or cattle lacking PrPC. This apparently normal phenotype in these PrPC-deficient animals however contrasts with the very high degree of conservation of the prion protein gene (Prnp) in mammalian species (over 80%), and the presence of genes with similarities to Prnp in birds, reptiles, amphibians and fish. This high conservation together with its ubiquitous expression, - albeit at highest levels in the brain-, suggest that PrPC has major physiological functions. Dissecting PrPC function is further complicated by the occurrence, in mammals, of two potentially partially redundant homologues, Doppel, and Shadoo. The biological overlaps between members of the prion protein family are still under investigation and much debated. Similarly, although in vitro analyses have suggested various functions for PrPC, notably in cell death and survival processes, some have yielded conflicting results and/or discrepancies with in vivo studies. This Research Topic brings together the accumulated knowledge regarding the biological roles of the prion protein family, from the animal to the molecular scale.