Prion function and pathophysiology in non-mammalian models

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 More than thirty years have passed since the discovery of the prion protein (PrP) and its causative role in transmissible spongiform encephalopathy. Since a combination of both gain- and loss-of-function mechanisms may underlay prion pathogenesis, understanding the physiological role of PrP may give important clues about disease mechanisms. Historically, the primary strategy for prion research has involved the use of human tissue, cell cultures and mammalian animal models. Nevertheless, experimental difficulties of in vivo studies and controversial observations obtained in these systems have stimulated the search for alternative animal models. PrPC is highly conserved in mammals, and PrPC-related orthologs are expressed in zebrafish, a vertebrate model organism suitable to study the mechanisms associated with human diseases. Invertebrate models, as they do not express PrPC have served to investigate the neurotoxic mechanisms of mammalian PrP. Here we