

Identification of Novel Binding Proteins for Cellular Prion Protein in the Olfactory Epithelium

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Introduction: Prion diseases involve the conversion of the endogenous cellular prion protein, PrP^C, into a misfolded infectious isoform, PrP^{Sc} (prion scrapie). Several functions have been attributed to PrP^C, but a consensus about its role remains uncertain. Its physiological function has also been investigated in the olfactory system. It has been reported that PrP^C is expressed in the olfactory bulb (OB) and olfactory epithelium (OE). The OE has previously been demonstrated to be a site of prion infection. Moreover, *Prnp*^{-/-} mice show retarded behavior in olfactory tests. **Objective:** Our aim is the identification of PrP^C ligands in the olfactory epithelium, in an effort to address the physiological role of PrP^C in olfaction. **Materials and methods:** A yeast two-hybrid screen was performed in a mouse OE cDNA library, using PrP^C as bait. Pull down assay was conducted to confirm the interactions. **Results and Discussion:** From yeast two-hybrid screening, 53 isolated clones were obtained. Eighteen out of the clones had their library's insert sequence in correct frame. Ten interactions were validated by cross mating assay and interactions with β -catenin and Stub1 were also confirmed by pull-down assay. The PrP^C ligands we obtained are involved in many functions, such as cellular proliferation and apoptosis, cytoskeleton and vesicles transport, ubiquitination of proteins, stress response and other

physiological processes. Interestingly, all putative PrP^C binding proteins are not exclusive to the OE, suggesting that these interactions may occur in other tissues and play general biological functions. **Conclusion:** Our results provided the identification of 10 novel PrP^C molecular patterns, which may help in the elucidation of the PrP^C physiological role. The PrP^C interactions with β -catenin and Stub1 were described here for the first time. Physiological and pathological implications of both ligations are under investigation.

Keywords: PrP^C, Yeast two-hybrid, olfactory epithelium