

P056 The cellular prion protein PrP^c is involved in the proliferation of epithelial cells and in the distribution of junction-associated proteins

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The physiological function of the ubiquitous cellular prion protein, PrP^c, is still under debate. We already reported that PrP^c is targeted to cell-cell junctions of polarized epithelial cells, where it interacts with c-Src. We show that, in cultured human enterocytes and in intestine *in vivo*, the mature PrP^c is differentially targeted to the nucleus in dividing cells and to cell-cell contacts in polarized/differentiated cells. We demonstrate that the junctional PrP^c interacts with the desmosome-associated proteins and we evidence a complexe associating PrP^c, desmoglein and c-Src. Through siRNA strategy, we show that PrP^c is necessary to complete the process of cell proliferation and for the sub-cellular distribution of proteins involved in cell-cell junctions. Moreover, a net decrease in the intestinal villi length was observed in PrP^c knock-out mice. From these results, PrP^c must be considered as a potential new partner involved in the balance between proliferation and polarization/differentiation in epithelial cells.