CELLULAR PRION PROTEIN AND ITS LIGANDS STIMULATE NEURITOGENESIS IN DORSAL ROOT GANGLIA NEURONS THROUGH PKC AND PI-3K ACTIVATION

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Prions are infectious pathogens associated to neurodegenerative diseases generated by structural conversion from its cellular prion protein isoform (PrPc), a glycoprotein, abundantly expressed in the nervous system. We have previously characterized PrPc partners and their associated cellular functions. We showed that laminin and vitronectin, extracellular matrix glycoproteins, interact specifically with PrPc mediating neuritogenesis. We also observed that PrPc binds to Stress Inducible Protein 1 (STI1) inducing neuroprotection and neuritogenesis. In this study, we investigated the signaling pathways triggered by PrPc-ligands interaction which are responsible for axonal growth. Wild-type (*Prnp*$^{+/+}$) and PrPc-null (*Prnp*$^{0/0}$) dorsal root ganglia cells were cultured in the presence of laminin, vitronectin and STI1. The signaling pathways required to mediate axonal growth were addressed by cell treatment with inhibitors of PKA, MAPK, PI3K and PKC. Laminin, vitronectin and STI1 were able to increase the percentage of cells with axons while the axonal length was positively modulated only by laminin. Peptide γ-1 (PrPc binding domain at laminin molecule) and vitronectin peptide 309-322 (PrPc binding region on vitronectin) mimicked the effect of full-length proteins only in *Prnp*$^{+/+}$ neurons, confirming the specific effect of PrPc interaction on neuritogenesis. PI3K and PKC inhibitors decreased the percentage of cells with axon, supporting a specific role of these pathways in PrPc mediated neuritogenesis.
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