F3/contactin subfamily and the differentiation of neural stem cells

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Both Notch and the amyloid precursor protein (APP) are type I transmembrane proteins mediating cell fate selection. Their core signaling mechanisms involve Regulated Intramembrane Proteolysis (RIP) through g-secretase-dependent cleavage. We have identified F3/NB-3 as trans-acting extracellular ligands of Notch, a Deltex1-dependent signaling that may promote oligodendrocyte differentiation from neural stem cells. Recently, we have further demonstrated that human bone marrow stromal cells (hBMSCs) can be induced to differentiate into cells with oligodendrocytic characteristics in mouse retina in vivo through predifferentiation by triggering F3/Notch signaling in vitro. Moreover, we have identified TAG-1 as a ligand of APP, an interaction to trigger g-secretase-dependent APP intracellular domain (AICD) activity. APP and TAG-1 co-localize in the neural stem cell niche of the fetal ventricular zone. Neurogenesis is enhanced in neural precursor cells isolated from TAG-1-null, APP-null and TAG-1/APP double knock-out mice. TAG-Fc or AICD reversed the enhancement in TAG-1-null mice. These results describe a TAG-1/APP signaling pathway that triggers AICD activation and negatively modulates neurogenesis.

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The aim of his research is to understand the molecular events that mediate communication among cells, including brain tumour cells, in the nervous system during development, regeneration, degeneration, myelination, neurostem cells differentiation, learning and memory, using different approaches, such as methods of cell biology, morphology, molecular biology, and electrophysiology.