Galectin-3 roles in an Alzheimer's model

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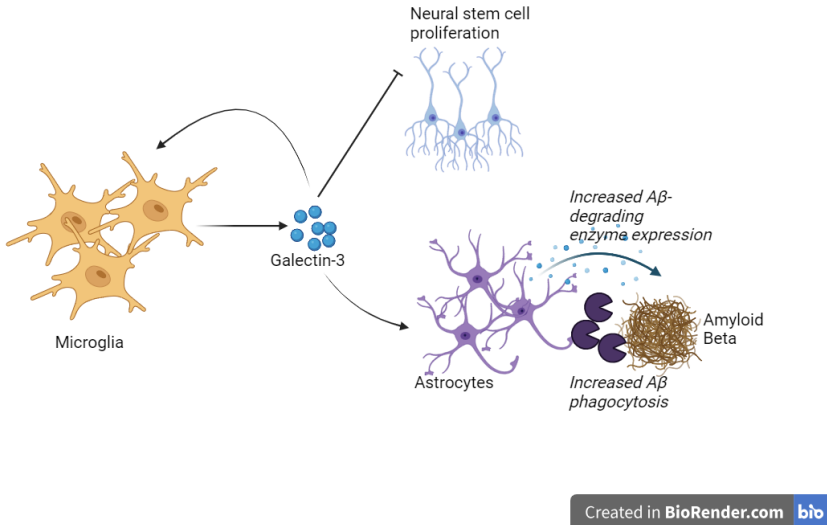

Galectin-3 is upregulated in Alzheimer's Disease (AD) and has been shown to promote amyloid beta (Aβ) oligomerisation and plaque formation. However, little is known about the effect of galectin-3 on neural cells. Our work aims to determine the effect of galectin-3 on neurogenesis and on glial clearance of Aβ. Neurospheres generated from primary murine neural stem cells were treated with galectin-3 or the galectin-3 inhibitor TD139. Proliferation, as determined by neurosphere size after 5 days, was decreased in neurospheres treated with galectin-3. Differentiation, as quantified by proportion of β-III-Tubulin$^+$ neurons and GFAP$^+$ astrocytes, was unchanged in both Galectin-3 and inhibitor treated neurospheres.

To determine the effect of galectin-3 on Aβ phagocytosis by glia, primary murine microglia and astrocytes were treated with 5μM pHrodo-Aβ alone or with galectin-3 or TD139. Fluorescence was plotted over 24 hours. RNA was then harvested from treated cells and gene expression was measured by qPCR. In microglia, no significant difference in phagocytosis was observed when galectin-3 or TD139 was present in the medium. Expression of phagocytosis-related genes was also unaltered. However, in mixed glial cultures, addition of galectin-3 increased microglial clearance of Aβ while TD139 decreased clearance. Additionally, while Aβ-treatment resulted in increase in Mmp2 and Mmp9 expression, addition of galectin-3 further increased the expression of both. In addition, Scarb1 expression was increased in presence of galectin-3 but not Aβ. In conclusion, we show that galectin-3 decreases NSC proliferation without affecting differentiation, and increases astrocytic clearance of Aβ. This is accompanied by an increase in expression of Aβ-degrading enzymes.