The Role of Heparanase in Neural Differentiation

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Heparan sulphate proteoglycans are associated with the cell surface and extracellular matrix. They consist of a core protein to which several heparin sulfate chains are linked. Heparan sulphate proteoglycans have a variety of functions including sequestration of bioactive molecules and increasing of cell adhesion. They also have a central role in embryogenesis, morphogenesis, angiogenesis and cancer metastasis.

Heparanase is a matrix–degrading enzyme which cleaves the sulfate side chains of heparan sulphate proteoglycans. This enzyme plays a role in tissue remodeling, tumor metastasis, inflammation and activation of immune system cells.

It has been shown that embryonic stem cells with heparin sulfate synthesis deficiency are not able to give rise to neural stem/progenitor cells. Additionally, mice with heparin sulfate biosynthesis deficiency die at an early embryonic stage. These observations indicate that heparin sulfate has a crucial role in embryogenesis and development of neural lineages. However, the role of heparanase in neural differentiation is still unclear. The present study focuses on the role of HPSE in neural lineage differentiation including neurons, astrocytes and oligodendrocytes by the usage of wild type (Wt) and HPSE knockout (HPSE-KO) mice.

This project began with dissecting embryonic neural tissues and seeding stem cells on tissue culture dishes with growth factors and medium. The aim was to obtain the primary neurospheres and secondary spheres. After forming a neurosphere, embryonic neural progenitor cells spread out into a monolayer culture with growth factors. One day after preparing neural progenitor cells the withdrawal of growth factors from cells was done. Removal of the growth factors results in neural differentiation. Then at different time points the differentiated cells were stained with neural markers in order to compare the wild type and knock out neural lineage in terms of morphology and quantity.

To monitor the differentiation process we estimated levels of mRNA and protein expression of heparanase as well as different neural lineage markers. The results indicated that there was a delay in neuronal growth and differentiation in heparanase knockout cells and that this enzyme is decreasing during the differentiation process in wild type cells.

Degree project in biology, Master of Science (2 years), 2009-2011
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