The Role of Glycogen Synthase Kinase-3 in Early Embryonic Stem Cell Differentiation

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Summary

Embryonic stem cells, and the biochemical mechanisms underling their pluripotency has been the focus of intense research in recent years. Glycogen Synthase Kinase 3 (GSK3) has recently been implicated in a diverse array of cellular functions including embryonic stem cell pluipotency, and the aim of this thesis was to detail and investigate the regulation and role of GSK3 activity in controlling pluripotency and differentiation.

This thesis has demonstrated that GSK3 kinase activity, normally considered constitutive, is suppressed in ES cells and is rapidly activated upon the commencement of differentiation. Activation of GSK3 enables phosphorylation and degradation of c-myc, which has been previously shown to be required for ES cell differentiation.

Furthermore, this thesis presents evidence that GSK3 activity in ES cells may be regulated by subcellular translocation and phosphatases in response to signalling mediated by cellular attachment and other differentiation inducing events.

A clearer understanding of the biology of pluripotent cells is necessary in order to better understand embryogenesis and the mechanisms of development, and to move towards the therapeutic potential of stem cells for use in cell based therapies. This study has added to our knowledge of GSK3 regulation with respect to its influence on the differentiation of embryonic stem cells.