

P051 Transcriptomic Analysis of Embryonic Stem Cell Self-Renewal: Identifying Downstream Effects of PI3K-Dependent Signalling

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Embryonic stem cells (ESC) and their progeny hold enormous potential for cell-based regenerative therapies. ESC pluripotency relies on the ability of ES cells to self-renew and in murine ESC we have previously described a requirement for PI3K signalling in maintaining self-renewal.

Using pharmacological and molecular genetic approaches, combined with microarrays and qPCR, we have identified 425 transcriptional changes (>1.5-fold change in expression, $p < 0.05$) associated with PI3K-dependent regulation of ESC self-renewal. Gene ontology analyses show no statistical over-representation associated with cell cycle regulators, supporting earlier data that suggests the effects of PI3Ks on self-renewal are separate from effects on the cell cycle. Interestingly, we demonstrate a functional role for PI3Ks in the regulation of the pluripotency transcription factor Nanog. Further evidence suggests this involves the inhibitory action of PI3Ks on GSK3. To identify potentially novel regulators of self-renewal ongoing analysis of transcriptional changes downstream of PI3K signalling is concentrating on transcription factors and genes with unknown function. Loss of function analysis using RNAi, along with the microarray data is providing the first functional insights into the regulation of ESC self-renewal by PI3Ks.