

Dr S Cowley – Transcriptional Control of Stem Cell Differentiation

The ability to regulate the transcriptional activity of protein coding genes is one of the most fundamental processes of life. The transcriptional potential of a gene is directly related to its chromatin context, which in turn, is influenced by the covalent modification of its core histone components. Transcription factors are able to inhibit gene expression by recruiting histone deacetylase (HDAC) enzymes to specific genes, where they deacetylate histone tails and produce a more restrictive chromatin conformation. This epigenetic control of gene expression by HDACs has been implicated in many processes including, cell cycle progression, DNA repair, differentiation, genomic stability and cancer.

Our laboratory studies the function of HDACs using embryonic stem (ES) cell lines in which we can conditionally inactivate HDAC1, HDAC2 or HDAC8. ES cells are an excellent model system because they can be made to differentiate into almost any cell type. The requirement for these individual HDACs during the differentiation process, which requires the simultaneous activation and repression of thousands of genes, can be assessed by comparing the transcriptional profile of normal and HDAC deleted cells. Erroneous transcriptional changes are identified by whole transcriptome microarray analysis, followed by RT-PCR and Western blotting.

Prospective PhD students will have the opportunity to learn a wide-variety of skills and techniques including, stem cell culture, protein and RNA isolation, flow cytometry and microarray analysis. Applications for PhD studentships are welcome from candidates who hold or expect to hold a first or upper second class degree. Informal enquiries, including a CV, should be sent to Dr. Shaun Cowley by email at smc57@le.ac.uk.

Further information is available at <http://www2.le.ac.uk/departments/biochemistry/staff/cowley>

References

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