The University of Sheffield  
Faculty of Medicine, Dentistry & Health  
Dental School  

RARβ2: differentiation or senescence?

**Supervisor:** Keith Hunter and Dan Lambert

**Project:**
Retinoids (vitamin A analogues) play a vital role in differentiation of squamous epithelia and have been used, with variable success, in the chemoprevention of squamous cell carcinoma (SCC). The loss of certain retinoid receptors occurs early in the development of SCC, and our data suggests that this may be related to escape from replicative senescence (an in-built anticancer mechanism) in addition to changes in differentiation. The aim of the project is to assess the role of one receptor, RARβ2, in the control of replicative senescence and cellular immortalisation in a panel of precancer and SCC cell lines. RARβ2 expression is consistently lost early in the development of SCC, but the functional consequences of this have not been described. From our preliminary data, we hypothesise that RARβ2 directs a novel, p16 independent senescence pathway in these cells. This project will combine monolayer and organotypic culture of SCC cells with phenotypic assays (including senescence, differentiation, apoptosis and proliferation). The phenotypic and gene expression responses to manipulation of RARβ2 expression will be assessed, with investigations into the mechanisms and consequences of loss of RARβ2 expression in the development of cancer.

The ability of RARβ2 to interact with HOX genes, which are also dysregulated in SCC, will also be investigated. The data will allow us to define circumstances in which precancerous lesions are sensitive to retinoid therapy, increasing their use in cancer chemoprevention.


**Enquiries:**
Interested candidates should in the first instance contact Keith Hunter by email (k.hunter@sheffield.ac.uk)

**How to apply:**
Please complete a University Postgraduate Research Application form and provide at least two references. To download the application form please visit: www.shef.ac.uk/postgraduate/research/apply/pgrform.html. Please clearly state the prospective main supervisor in the respective box.

**Scholarship:**
To apply for a University Scholarship you will also need to complete a scholarship application form: www.shef.ac.uk/postgraduate/research/scholarships/faculty.html.

Website: [www.shef.ac.uk/dentalschool](http://www.shef.ac.uk/dentalschool)

**Closing date:** 2 December 2011