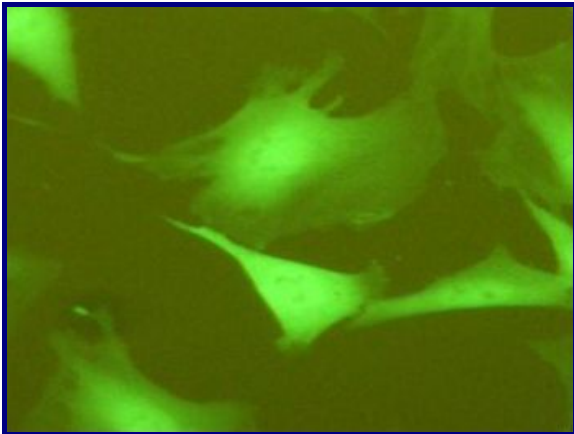




## BBSRC CASE Studentship on The Role of Glucocorticoids in Vascular Calcification

Dr Vicky MacRae is a BBSRC Institute Career Path Fellow at The Roslin Institute. Dr MacRae's research group investigates novel mediators of vascular calcification.



*Vascular Smooth Muscle Cells (showing GFP expression)*

A significant risk factor in the development of cardiovascular disease is vascular calcification. The process of vascular calcification shares many similarities with that of skeletal mineralisation, and involves the deposition of calcium phosphate mineral in arteries, heart valves, and cardiac muscle. Vascular calcification has severe clinical consequences, however, the mediators and mechanisms of vascular calcification have yet to be fully elucidated.

Glucocorticoids have great clinical importance as anti-inflammatory drugs, and can act as potent inducers of osteoblast differentiation in bone. Glucocorticoids have direct effects on the heart and blood vessels, mediated by both glucocorticoid and mineralocorticoid receptors and modified by local metabolism of glucocorticoids by the  $11\beta$ -hydroxysteroid dehydrogenase ( $11\beta$ HSD) enzymes.  $11\beta$ HSD catalyses the interconversion of hormonally active glucocorticoid to their inactive counterparts. In humans,  $11\beta$ HSD1 is predominantly a reductase, regenerating active cortisol from inert cortisone whereas  $11\beta$ HSD2 primarily converts cortisol to cortisone.  $11\beta$ HSD1 is expressed in cardiovascular tissues, and plays a role in vascular function, atherogenesis and vascular remodelling. Furthermore, increased  $11\beta$ HSD1 expression in calcifying vascular smooth muscle cells (VSMCs) has been reported. Therefore, it is likely that glucocorticoid regulation of the  $11\beta$ HSD shuttle is a potential mechanism that may contribute to vascular calcification.

Current studies in the group are examining whether important mediators of skeletal mineralisation also form a regulatory network in vascular calcification.

Current research aims of the research group are to:

- Compare the temporal expression patterns of novel genes during calcification of vascular smooth muscle cells (vascular model) and osteoblasts (bone model) derived from various mouse models
- Study loss and gain-of-function mutations to determine the functional roles of novel genes in the development of vascular calcification
- Study the regulation of key signal transduction pathways in vascular calcification
- Identify potential novel inhibitors of vascular calcification
- Identify novel regulators of vascular calcification using microarray and microRNA analysis

This PhD project will complement these aims.

### Project Outputs

The PhD project will aim to deliver:

- Determination of the effects of glucocorticoids on VSMCs derived from wildtype and transgenic mice, which show a vascular calcification phenotype
- Characterisation of  $11\beta$ HSD1 expression and activity in VSMCs following glucocorticoid exposure
- Functional data determining if inhibition of  $11\beta$ HSD1 alters the calcification capability of VSMCs

### Commercial Opportunity

The University of Edinburgh is looking for an industrial partner to sponsor a BBSRC CASE student to work on this project (contribution of ~£4000 annually). The 4-year project is proposed to start in September 2010.

The partner must be a company registered and trading in the UK with a UK research and/or manufacturing base. (Note: Companies without UK research facilities can be considered on a case-by-case basis by the BBSRC).

### Further Information

For further information on this CASE Studentship with the University of Edinburgh, please contact:

Dr Sonja Vujovic  
Edinburgh Research and Innovation  
The University of Edinburgh  
The Queen's Medical Research Institute  
47 Little France Crescent  
Edinburgh EH16 4TJ  
Scotland, UK

Telephone: +44 (0)131 527 4221  
Email: [Sonja.Vujovic@ed.ac.uk](mailto:Sonja.Vujovic@ed.ac.uk)