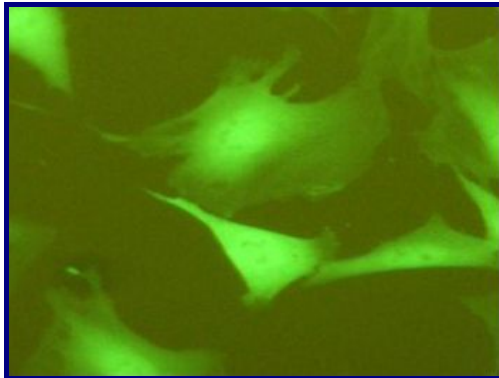




## BBSRC CASE Studentship on The Role of Nucleotides in Vascular Calcification

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)*

According to the World Health Organisation (WHO), an estimated 17 million people die each year of cardiovascular diseases, particularly heart attacks and strokes. 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.

ATP and other nucleotides are now recognised to play important and complex regulatory roles as messenger molecules for cell-to-cell communication. Novel actions of nucleotides on bone cell function have recently been discovered. Numerous P2 nucleotide receptor subtypes are expressed by bone cells, and low concentrations of ATP and ADP selectively block mineralisation of newly formed bone by osteoblasts. Recent results show that skeletal changes can occur when P2 receptors are defective or deficient, suggesting that the ATP – P2 cell signalling system offers some potential for novel bone therapeutics. The role of nucleotides in vascular calcification has yet to be examined.

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.

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### Project Outputs

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The PhD project will aim to deliver:

- Determination of the temporal expression patterns of P2 receptors in calcifying VSMCs derived from wildtype and transgenic mice, which show a vascular calcification phenotype
- Characterisation of the effects of ATP, ADP and UTP exposure on the calcification capability of VSMCs
- Functional data determining if knockdown/overexpression of key P2 receptors alters the calcification capability of VSMCs

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### Commercial Opportunity

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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).

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### Further Information

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

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