2014/2015 Summer Studentship Project Application Form

Send to: Research Office, University of Otago Christchurch, PO Box 4345, Christchurch, by 5pm on **4 July** 2014

Supervisor Information (First named supervisor will be the contact):	
Supervisor's Name(s): Prof Margreet Vissers, Dr Tim Woodfield, Prof Gary Hooper	
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Research Category (Choose one category only – to be used for judging the students' presentations):		
Clinical	**Laboratory X**	**Community**

Project Title (20 words MAXIMUM):

Investigating the pathology of cobalt-induced pseudo-tumour formation.

Project Description:

We are looking for a keen and energetic student to investigate the pathology of pseudo-tumour formation in people with failing hip prostheses. The project is hosted by the Department of Pathology and the Department of Orthopaedic Surgery and offers the student an opportunity to work on an exciting and novel project in a supportive environment, together other researchers working on related projects.

BACKGROUND:

Metal ions are known to be toxic in high concentrations, and metals such as Co^{2+} are known to activate cell stress pathways. In particular, Co^{2+} acts as a hypoxia mimetic in stimulating the activity of the transcription factor hypoxia-inducible factor (HIF)-1. Among other things, HIF-1 enhances tumour growth.

Up-regulation of HIF-1 results in gene transcription of proteins associated with glycolysis, angiogenesis, vascular function, and cell survival pathways. In human cancer, HIF-1 is up-regulated by the hypoxic stress induced by the rapidly growing tumour, but it can respond to a number of other conditions.

Pseudotumours are growths that form in patients with failing hip prostheses. The degenerating joint releases heavy metals, including Co^{2+}, and this could activate HIF-1 in the surrounding tissues, generating the growth factors conducive to tumour formation.

AIMS:

The aim of this project is to analyse pseudotumour tissue to determine determine whether HIF-1 is activated in the tissue and whether pro-angiogenic and tumour-forming proteins are expressed.

METHODS:

The student will analyse pseudo-tumour tissue and samples from patients, looking for evidence of HIF-1 activation and expression of downstream gene markers. Immuno-detection techniques will be used to measure HIF-1α protein, vascular endothelial cell growth factor (VEGF), carbonic anhydrase and BNIP3 (a pro-survival protein). Specific techniques to be employed are:

1. Tissue extraction procedures and quantification of protein and DNA content.
2. Protein analysis by western blotting (HIF-1α, downstream gene proteins BNIP3, GLUT1, CAIX)
3. Protein analysis by ELISA (VEGF)
4. Immunohistochemistry of tissue sections for morphology investigations including the presence of blood vessels and necrotic tissue.
5. Immunohistochemistry for localization of HIF-1α and downstream gene expression.

All general laboratory methods are established in our group, and the student will be trained to carry out all procedures. The project should be completed within 10 weeks.

SIGNIFICANCE:

This project will provide important and interesting information on the formation of pseudotumours, and will also be relevant to furthering our understanding of the importance of HIF-1 in tumour formation.