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): Dr Anna Pilbrow, Prof Vicky Cameron	
Department: Medicine	Institution: UOC
Phone: 364 0451	E-mail: anna.pilbrow@otago.ac.nz
Mailing Address: Christchurch Heart Institute, UOC, PO Box 4345, Christchurch 8140	

Research Category (Choose one category only – to be used for judging the students' presentations):		
Clinical	**Laboratory** ☐	**Community**

Project Title (20 words MAXIMUM):

Improving Cardiovascular Risk Prediction in the General Population

Project Description:

Aim

This summer studentship aims to identify circulating protein biomarkers that predict the risk of future cardiovascular events in asymptomatic individuals.

Susceptibility to heart disease results from interactions between lifestyle and genetic factors and some families are particularly affected [1]. This project forms part of a larger study that investigates how family history contributes to susceptibility to heart disease with the aim of identifying new biomarkers that will allow screening and early detection of those at risk. We have already shown that certain biochemical pathways within cells in the heart and vessels are altered in individuals who are genetically predisposed to heart disease [2]. We now propose to use this information to discover new circulating protein biomarkers that signal the very early stages of heart disease in susceptible individuals who do not yet have symptoms.

Background

Coronary artery disease is a leading cause of morbidity and mortality in Aoteoroa/New Zealand and is especially prevalent among Maori and Pacific peoples [3]. In the general population, screening for risk of cardiovascular events is performed in primary care using the New Zealand 5-year Cardiovascular Disease Risk Score [4], which incorporates traditional risk factors such as age, sex, lipid levels, smoking and blood pressure. However, traditional risk factor profiling fails to identify many high-risk individuals, with more than 50% of heart disease deaths occurring in people with no previous symptoms or warning signs who, using current screening, would be considered to be at only moderate cardiovascular risk [5]. This highlights the need for new strategies for large-scale screening of the general population to identify people who are at impending risk of an acute cardiovascular event. To address this challenge, we will use our existing genomics data to identify candidate biomarkers associated with genetic susceptibility to heart disease. Measuring circulating levels of these proteins may help us identify individuals who may be predisposed to heart disease, prior to the onset of symptoms.

Methods

This project is centered on a rare and valuable resource of blood samples from a cohort of more than 3,000 healthy volunteers of middle- to older-age. Although none of the volunteers had heart disease at the time of recruitment, nearly 200 have subsequently experienced an acute cardiac event, such as a heart attack, within 3 years of recruitment. We therefore have a large number of samples prospectively collected prior to an unexpected cardiovascular event, making us ideally placed to examine new circulating markers for risk of future cardiovascular events.

Candidate protein biomarkers will be selected from our previous genomics research, which has identified genes/proteins in heart and vessel tissues that are in cell pathways altered in

association with genetic risk factors for coronary artery disease [2]. A previous summer studentship project confirmed the feasibility of this strategy by confirming that changes in myocardial gene expression lead to altered protein levels in plasma (for example, vascular cell adhesion molecule-1). The student conducting this study will use ELISA assays to measure up to 3 candidate proteins in a group of healthy volunteers, to determine whether circulating levels discriminate between healthy volunteers who have had a cardiovascular event within 1 year of recruitment (n=40) from those who remain event-free for at least 5 years (n=40, matched for age and gender). This study is part of an ongoing project approved by the Canterbury Ethics Committee to discover new circulating biomarkers to support better assessment of cardiovascular risk in communities (Ethics reference CTY/01/05/062).

Significance

Cardiovascular diseases are common complex traits with a strong inherited component. In Aoteoroa/New Zealand, cardiovascular disease is the leading cause of death, accounting for 40% of all deaths per year [6], with rates doubling over the past 20 years [7]. This project has the potential to identify new biomarkers that may improve assessment of cardiovascular risk in the general population, leading to better monitoring and use of preventative strategies in those at risk.

References

[1] Mayer B, Erdmann J, Schunkert H. Genetics and heritability of coronary artery disease and myocardial infarction. Clin Res Cardiol. 2007;96:1-7.
[2] Pilbrow AP, Folkersen L, Pearson JF, et al. The chromosome 9p21.3 coronary heart disease risk allele is associated with altered gene expression in normal heart and vascular tissues. PloS one. 2012;7:e39574.
[3] Robson B, Harris R. Hauora: Maori Standards of Health IV: A study of the years 2000-2005.: Wellington: Te Ropu Rangahau Hauora a Eru Pomare; 2007.
[4] Group N. New Zealand cardiovascular guidelines handbook: A summary resource for primary care practitioners. 2nd Edition ed2009.
[5] Perrone-Filardi P, Musella F, Savarese G, et al. Coronary computed tomography: current role and future perspectives for cardiovascular risk stratification. Eur Heart J-Card Img. 2012;13:453-8.
[6] Hay D. Cardiovascular Disease in New Zealand, 2004. A Summary of Recent Statistical Information. 2004.
[7] Elliott J, Richards AM. Heart attacks and unstable angina (acute coronary syndromes) have doubled in New Zealand since 1989; how do we best manage the epidemic? New Zealand Medical Journal. 2005;118:1223.