

2017/2018 Summer Studentship Project Application Form

Send to: Research Office, University of Otago Christchurch, PO Box 4345, Christchurch, by 5pm on 3 July 2017

Supervisor Information (First named supervisor will be the contact):

First **Supervisor's** Name and Title: Paul Bridgman, Clinical Senior Lecturer and CDHB Cardiologist

Department - UOC &/or CDHB (if applicable): Dept. of Medicine, CSM and CDHB Cardiology

First Supervisors Phone: 0274 314 783

Email: paul.bridgman@cdhb.health.nz

First Supervisors Mailing Address: Dept of Cardiology, Christchurch Hospital, Private Bag 4710, Chch

Co-Supervisors Name and Title(s): Prof Martin Kennedy, Dept of Pathology, U of O. Dr Kit Doudney, Molecular Pathology, CDHB.

Research Category (Choose one category only – to be used for judging the students' presentations):

Clinical

Laboratory X

Community

Project Title (20 words MAXIMUM):

Who should die of a broken heart? A genetic and electrocardiographic study in earthquake stress cardiomyopathy.

Project Description:

Introduction:

"Alas, my liege, my wife is dead to-night;
Grief of my son's exile hath stopp'd her breath."
Lord Montague, Romeo and Juliet.

Astute observers of humanity have long known that you can die of a broken heart. Following the major Christchurch and Kaikoura earthquakes, Christchurch Hospital has seen unprecedented case clusters of broken heart syndrome, also known as stress cardiomyopathy or takotsubo cardiomyopathy. This has been of widespread public and scientific interest. Many news media reports have drawn attention to the case clusters and there have been numerous scientific publications from our collaborative group of cardiologists, psychological medicine experts and genetics researchers. We obtained a \$100 000 HRC/CMRF grant to examine the genetics of the condition and have recently submitted a major manuscript detailing our genetic research. Our results point towards Ca and K channels possibly being involved in the mechanism and that might help explain why sudden cardiac death can occur in the condition.

Dr Doudney's laboratory has found an unusually high number of copy number variant abnormalities in the cases studied thus far. In this studentship the student would be working with Dr Doudney to perform array CGH to extend our previous study. They would work with Dr Bridgman in a descriptive study of the QT prolongation in the Christchurch earthquake cohort, and they would also gain exposure to clinical cardiology at Christchurch Hospital. There will also be some exposure to psychological medicine for the student. Dr Cameron Lacey from the Department of Psychological Medicine led some of our earlier work. He is in the process of applying to reactivate our ethics committee approval for this study. As in our previous work, psychological questionnaires will be completed by the patients.

Primary Aims:

One: To perform array CGH in an additional 5 patients from the Kaikoura earthquake cohort.

Two: To measure QT interval in ECGs from patients in the case cluster and from sporadic cases. We would document the frequency and severity with which prolongation occurs as part of the syndrome and look for correlation with age, echocardiographic pattern and genetic abnormalities.

Three: For the student to be imbedded in a Cardiology Department and learn some clinical medicine.

Possible impact (in lay terms):

Doctors and the public recognise that psychological factors influence physical illness. In all of medicine, broken heart syndrome provides the most pure example of the mind-body interaction. In this condition an acute psychological stress provokes an illness that can be fatal. Researchers agree that the mechanism for this is unknown. Our research and that of others suggests a multi-factor model including environmental and genetic factors. This project will look at the chain of events that break a heart. It will specifically explore genes related to cardiac ion channels and may help explain why some people die from a broken heart.

Method:

aCGH Study

Following arrayCGH analysis of 28 earthquake triggered Stress Cardiomyopathy cases, 12 were found to harbour rare copy number variants, often containing cardiac function or development genes. In this extension to that study, we will carry out arrayCGH using Agilent 180k oligo arrays to detect CNVs and LOH in newly presenting Kaikoura earthquake **related SCM cases. Data will be analysed using PerkinElmer's Genoglyphix software**, and candidate copy number variants compared to various disease and control databases including DECIPHER, ClinVar, DGV and our in-house patient database.

Electrocardiogram Study

There are a number of electrocardiogram (ECG) abnormalities that commonly occur in stress cardiomyopathy (broken heart syndrome). One of them is QT prolongation. QT prolongation is also the substrate for torsades de pointes. Torsades is a form of ventricular tachycardia that can be fatal. It is recognised from case reports that QT prolongation can occur in stress cardiomyopathy but the pattern has not been documented across large case series.

Since the September 2010 Christchurch earthquake Cardiology Department has maintained a log of stress cardiomyopathy cases. We have earthquake related cohorts and also sporadic cases. In the electrocardiograph part of the summer studentship the student would be measuring QT intervals both before, when available, and during the patient's index admission. They would be expected to construct an Excel spreadsheet to allow us to analyse the relationship between QT prolongation and patient factors such as age, echocardiographic takotsubo variant and genetic abnormality. This may lead to abstract presentation through a poster at the 2018 New Zealand Cardiac Society Annual **Scientific Meeting in Christchurch. The student would be reviewing the ECG's in both the Health Connect South software platform and from hard copy paper ECG's and clinical notes. Dr Paul Bridgman will be the lead supervisor for this part of the project.** His publication record since the Christchurch earthquake is attached as an appendix. When working on the clinical part of the studentship the student would be expected to attend Cardiology Department clinical meetings and some ward rounds and clinics.

Appendix.

Stress cardiomyopathy publications since 2011 for the first supervisor.

Bridgman, P. G. and Chan, C. W. (2017), The fifth takotsubo variant. *Echocardiography*, 34: 122–123. doi:10.1111/echo.13405

Chan CW, Bridgman PG, Troughton RW. Favorable 5-Year Outcome of 21 Takotsubo Stress Cardiomyopathy Cases Triggered by an Earthquake. *J Am Coll Cardiol*. 2016;68(8):877-877. doi:10.1016/j.jacc.2016.05.074

Bridgman PG, Finsterer J, Lacey C, Kimber B, Parkin PJ, Miller AL, Kennedy MA. CTG-repeat expansions in the DMPK gene do not cause takotsubo syndrome. *Int J Cardiology*. 203 (2016) 107-8.

Chan CW, Troughton RW, Elliott JM, Zarifeh JA, Bridgman PG. One-year follow-up of the 2011 Christchurch Earthquake stress cardiomyopathy cases. *NZMJ* 2014 127 1396.

Bridgman, P.G. Chan, C.W. Takotsubo syndrome: Lessons from the Christchurch earthquakes. *Dialogues in Cardiovascular Medicine*, vol. 19 (2014).

Lacey C, Mulder R, Bridgman PG, Kimber B, Zarifeh J, Kennedy M, Cameron V. Broken heart syndrome – Is it a psychosomatic disorder? *J of Psychosomatic Research*. 2014. 77(2): 158-160

Chan C, Elliott J, Troughton R, Frampton C, Smyth D, Crozier I, Bridgman PG. (2013) Acute Myocardial Infarction and Stress Cardiomyopathy following the Christchurch Earthquakes. *PLoS ONE* 8(7): e68504. doi:10.1371/journal.pone.0068504

Elliott JM, Chan CW, Daly MG, Chan CW, Saireddy RR, Milburn KAM, Troughton RW, Bridgman PG. When the earth quakes the heart breaks: Stress Cardiomyopathy after a 6.3 earthquake. *Heart Lung Circ* 2011;20 (6): 379.

Zarifeh JA, Mulder RT, Kerr AJ, Chan CW and Bridgman PG. Psychology of earthquake-induced stress cardiomyopathy, myocardial infarction and non-cardiac chest pain. *Intern Med J* 2012; 42: 369-373.

Bridgman PG, Chan CW, Elliott JM. A case of recurrent earthquake stress cardiomyopathy with a differing wall motion abnormality. *Echocardiography*. 201110.1111/j.1540-8175.2011.01568.x

Student Prerequisites (eg. Medical Student) if applicable:

Medical student.

Administration Details

1. Is ethical approval required? Yes

If Yes: please circle or tick one of the following:

- a) Applied for See text above, Dr Cameron Lacey has contacted the committee to reactivate our ethics approval
- b) Approved (attach a copy of the letter of approval from the ethics committee or application #)
- c) To be done

2. Are you able to provide the funding for this project (ie. \$5,000 for the student, incidental expenses should be met from departmental or research funds) No

If Yes: Please provide name of the funder _____

If No: Please provide ideas of possible funding sources, including past funding agents and topics often associated with this research area, for the Research Office to contact.

Materials for the array CGH will cost \$4000, this will be seen as incidental expenses and will be met from Cardiology and Pathology department funds.

3. Medical Records or Decision Support accessed Yes

4. Health Connect South or other DHB records Yes

5. Signatures:

- I have read the 2017/2018 Summer Studentship programme handbook.
- I am prepared to supervise the project and will be available to the student during the studentship (including Christmas/New Year break if the student is working during this time).
- I agree to assume responsibility for the submission **of the student's reports to the Research Office** by the due date 29 January 2018.
- I agree that the project lay report may be available to local media for publicity purposes.

Signature of Project Supervisor(s): Paul Bridgman

Date:26/06/17

- I understand that I am responsible for hosting the Summer Student chosen for this project and will meet any costs incurred. I agree that incidental expenses will be met from departmental or research funds.

Signature of Head of Department: Lutz Beckert
(Print Name)

Date:26/06/17

Signature of Clinical Director: David Smyth
(Print Name)

Date:26/06/17