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: Dr Simran Maggo	
Department - UOC &/or CDHB (if applicable): Pathology (UOC)	
First Supervisors Phone: 03 378 6268	First Supervisors Email: simran.maggo@otago.ac.nz
First Supervisors Mailing Address: Department of Pathology, University of Otago Christchurch, P.O. Box 4345, Christchurch 8140	
Co-Supervisors Name and Title(s): Professor Martin Kennedy	

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

Project Title (20 words MAXIMUM):

HLA-Typing of Patients with Severe Adverse Drug Reactions

Project Description:

Introduction:

Our laboratory is interested in understanding the impact of genetic variation on response to drugs, and in particular on liability to severe adverse drug reactions. Adverse drug reactions (ADRs) cause significant morbidity and mortality and pose a major socioeconomic burden on the health system. Some ADRs are immunological in nature and can be severe enough to warrant admission to hospital. Genetic variation in the Human Leukocyte Antigen (HLA) genes may be able to predict these ADRs. This summer studentship project will investigate the type and prevalence of these variants in patients with severe ADRs.

Aim:

Severe hypersensitivity ADRs associated with specific HLA-alleles are now well characterized for the drugs flucloxacillin (HLA-B*57:01), carbamazepine (HLA-B*15:02), and allopurinol (HLA-B*58:01), and mandatory testing is required prior to prescription of abacavir (HLA-B*57:01). Our hypothesis is that patients who have suffered severe hypersensitivity ADRs to commonly prescribed medication such as statins for hypercholesterolemia, or ACEi for hypertension have an underlying genetic variation in the HLA gene locus.

Our specific aims are to profile HLA-variants in patients who have had

- Repeated statin muscle ADRs i.e statin-intolerant patients
- Severe ACEi-induced angioedema (requiring hospitalisation)

This will enable us to look for patterns of HLA-variation that may confer a risk for that ADR.

Possible impact (in lay terms):

We are actively investigating the application of genetic knowledge to reduce harms (ADRs) and improve benefits of commonly used medication. ADRs are commonly cited as the main reason for poor compliance, and in patients prescribed antihypertensive and/or statin medication, compliance is reported to be as low as 25%. The HLA genes are located within one of the most complex regions of the human genome and encode proteins that have a critical role in the immune response and ADRs. The outcomes of this project will help in understanding the genetic basis of adverse effects to prescribed medication, and ultimately may help predict individual risks of suffering an ADR.

Method:

The methods to be used will be predominantly polymerase chain reaction (PCR), real time PCR (RT-PCR) and Sanger sequencing. HLA-typing will be conducted using a kit sold by Linkage Biosciences, San Francisco, USA. Kits available from this company are able to assess participant DNA samples for variant HLA alleles using the LightCycler 480 instrument which is available for use at UOC. We have several consented DNA samples from cases in our ADR biobank (UDRUGS - Understanding Drug Reactions Using Genomic Sequencing) that are appropriate for this work. In addition to participant samples, positive controls, i.e. DNA samples with known HLA variants have been previously purchased from the Coriell Institute for Medical Research, and will be used to validate and confirm the results of this study.

Student Prerequisites (eg. Medical Student) if applicable:

Prior laboratory and/or bioinformatic experience would be valuable

Administration Details

1. Is ethical approval required? Yes

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

   a) Approved (attach a copy of the letter of approval from the ethics committee or application #)

   HDEC approval number: URA/11/11/065

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.

   Canterbury Health Labs, HRC, CMRF

   If Yes: You will be sent a request for more information.

3. Medical Records or Decision Support accessed No

4. Health Connect South or other DHB records No

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):	Date:

- 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: (Print Name)	Date:
Signature of Clinical Director: (if applicable) (Print Name)	Date: