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 Rachel Purcell		
Department - UOC &/or CDHB (if applicable): Department of Surgery, UOC		
First Supervisors Phone: 021 02476749	First Supervisors Email: Rachel.purcell@otago.ac.nz	
First Supervisors Mailing Address: Dept of Surgery, University of Otago, PO Box 4345, Christchurch 8140		
Co-Supervisors Name and Title(s): Dr John Pearson		
Research Category (Choose one category only **– to be used for judging the students' presentations):**		
Clinical	Laboratory X	Community
Project Title (20 words MAXIMUM):		
Project Description:		

Title: Comparing the colorectal cancer microbiome of stool and tissue samples

Introduction:

Our guts are home to trillions of bacteria, and their vital roles in human health and disease have put the gut "microbiome" firmly in the spotlight. Changes in the microbiome, or dysbiosis, have been linked with inflammation, cancer, obesity and even mental disorders, to name but a few diseases, but despite the intense interest in the field, our exploration of this vast and complex system is only in its infancy, and the potential for microbiome-related diagnostics and treatments is, as yet, untapped. Very recently, we have started to question the role of the microbiome in influencing the onset, progression and outcomes of colorectal cancer (CRC). We have carried out the first analysis of CRC tumour microbiomes in the New Zealand (NZ) setting, seeking to establish whether the subtype of cancer is associated with/influenced by the composition of its own microbiome. In our initial analysis of 34 CRC tumours we have found that tumour microbiomes vary quite dramatically between patients. Using three different types of sequencing technologies, we found significant differences in phylum-level abundance associated with different tumour characteristics and differences in abundance of particular bacterial strains with putative roles in CRC development, such as *Fusobacterium nucleatum*, *Parvimonas micra* and *Solobacterium moorei*. However, testing of tumour tissue is not ideal, due to the cost involved and impact on the patient. Developing stool-based tests to use for screening, prognosis and following response to therapy is the "holy grail" in CRC. In this project we will use a newly developed hand-held sequencer to determine whether bacterial communities in stool samples from CRC patients are comparable to previously determined microbiomes from corresponding CRC tumour samples.

Aim:

To determine the utility of stool samples as a proxy for detecting pathobionts associated with colorectal cancer, using next-generation sequencing.

Possible impact (in lay terms):

Changes in gut microbial composition have been linked to the development of CRC, as a result of recent advances in culture-independent techniques to measure microbial communities. However, the causality and mechanisms involved remain unclear. We have recently shown that specific tumour tissue microbiome patterns are associated with CRC subtypes. Data from this study will reveal whether bacterial targets identified in our ealier study, could have clinical utility as stool-based screening tools, either alone or in conjunction with currently used screening tests.

Method:

We have previously determined the microbiomes of a cohort of 34 CRC tumours using 16S rRNA sequencing, RNA-sequencing and metagenomic DNA sequencing using the MinIon sequencer (Oxford Nanopore). We have extracted genomic DNA from corresponding stool samples from these CRC patients, taken prior to surgery.

The student will carry out metagenomic sequencing using the MinION sequencer on a subset of these stool DNA samples (n = 6), using the protocol that we developed for the tumour DNA samples.

We will use the 'What's in my pot' (WIMP) bioinformatics workflow that enables us to identify bacteria in complex samples in real time. Analysis begins as soon as sequence data starts being streamed (a few seconds after the experiment starts). Each read of streamed sequence data is compared against a database of microbial species, and an identification is made. At the same time, WIMP plots and updates a taxonomic tree of all microorganisms found in the sample.

We will then compare the bacterial composition of the stool samples to that of the corresponding tissue samples at different taxonomic levels, from Phylum to Species. This will allow us to determine differences and similarities in the overall microbiomes of tumour and stool samples.

We will also analyse the presence and abundance of specific bacterial species that we have previously found to be associated with CRC, such as *F. nucleatum, P. gingivalis* and enterotoxigenic *Bacteroides fragilis* and compare our findings to that of tumour tissue.

Finally we will validate a small number of these bacterial targets using quantitative PCR on stool DNA, using a protocol already in use in the laboratory.

Student Prerequisites (eg. Medical Student) if applicable:

Administration Details

1. Is ethical approval required? Yes

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

   a) Applied for (provide application #)

   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.

   Bowel and Liver Trust or Gastrointestinal Cancer Institute of NZ (GICI)

   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: