2016/2017 Summer Studentship Project Application Form

Send to: Research Office, University of Otago Christchurch, PO Box 4345, Christchurch, by 5pm on **4 July 2016**

Supervisor Information (First named supervisor will be the contact):	
First Supervisor's Name and Title: Associate Professor Gabi Dachs	
Department - UOC &/or CDHB (if applicable): Pathology, UOC	
First Supervisors Phone: 3640544	First Supervisors Email: gabi.dachs@otago.ac.nz
First Supervisors Mailing Address: 2 Riccarton Ave, Christchurch	
Co-Supervisors Name and Title(s):	

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

Project Title (20 words MAXIMUM):

Can we slow down breast cancer in mice using vitamin C?

Project Description:

We are looking for a bright, enthusiastic student to join a multidisciplinary cancer research group. The Mackenzie Cancer Research Group is interested in the cellular and molecular basis of cancer and response to therapy. We have close links with the clinic and the proposed study represents an important part of our ongoing research.

Introduction:
In NZ and worldwide many cancer patients seek high dose ascorbate treatment from complementary medicine providers. This treatment option continues to be controversial, largely due to the lack of an agreed mechanism of action or evidence for clinical efficacy. We have generated significant *in vitro*, *in vivo* and pre-clinical evidence that suggests a link between tumour ascorbate content, activity of the transcription factor HIF-1 and tumour growth and aggression (Vissers 2007, Kuiper 2010, 2014, Campbell 2015, 2016). Our recent data from breast cancer patients (Campbell unpublished) have supported our data in endometrial and colorectal cancer patients, and showed an association between increased ascorbate levels in tumours and a reduced aggressive tumour phenotype. To investigate whether a change in ascorbate supply may alter tumour growth, we have used a knockout mouse model; Gulo$^{-/-}$ mice can't synthesize ascorbate and are therefore similar to humans in this regard. In this mouse model, we have data for lung, colorectal and melanoma tumours, but not of breast cancer tumours.

Aim: To investigate whether increased dietary intake of ascorbate or high dose ascorbate administration can modify breast tumour growth and tumour phenotype in a mouse model of ascorbate dependency.

Possible impact (in lay terms):
The use of vitamin C in cancer remains controversial, yet many cancer patients choose high dose ascorbate treatment provided by alternative providers. This study will provide valuable scientific data for the ongoing debate, and discover whether breast cancer growth can be manipulated with increasing doses of vitamin C in a mouse model. This data is vital for the design of clinical trials in breast cancer patients.

Method:
Animal ethics will be obtained prior to the start of the project. The student will implant breast cancer cells into the mammary fat pad of female Gulo$^{-/-}$ mice maintained on 330mg/L ascorbate in their

drinking water. Once tumours reach treatment size, mice are assigned to either 1) control (no other treatment), 2) change to 3300mg/L ascorbate in their drinking water, or 3) daily injection with 1g/kg ascorbate. Tumour growth will be monitored, and at endpoint, tumours and organs are harvested for biochemical analyses (ascorbate by HPLC, HIF-1 by Western, hypoxia via pimonidazole, and perfusion via Hoechst 33342).