Order of the Royal Arch
C/O Mr Geoffrey Coker
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MALAGHAN INSTITUTE OF MEDICAL RESEARCH

1 March 2017

Dear Geoffrey,

Re: Royal Arch Masonic Centennial Award report

I am writing to express my sincere gratitude for the Royal Arch Masonic Centennial Award from 2015-7. By allowing me to establish and conduct a series of immune studies, the Award has been tremendously beneficial in terms of my personal development as a clinician scientist, for the specific project to which the Award contributed, and to provide a lasting dataset to support future research projects and collaborations.

Personal development benefits
I hold a joint role as a doctor (a Consultant Haematologist) at Wellington Blood & Cancer Centre, and as a Clinical Research Fellow at the Malaghan Institute of Medical Research. I am using these joint roles to translate immune therapies into clinical practice, as treatments for cancers and infections. This includes a planned 2018 trial of a new immune therapy for a type of leukaemia.

Science changes rapidly, and one of the more recent developments is use of modern techniques to study the level of many genes at once. 'Nanostring' is one of these techniques, and provides data about hundreds of genes from a single sample of blood cells. This informs us about the detailed behavior of those blood cells when they are exposed to candidate immune treatments in the laboratory. In implementing this technique, and preparing a scientific manuscript for publication that uses these data, I have become familiar with analysis of large datasets, and the interpretation and presentation of such findings. These are key skills applicable to my future research work as well as this specific project.

Project-specific benefits
I used the Nanostring technology to study the effect of new vaccines (produced in collaboration with synthetic chemists at Wellington's Ferrier Institute) on human blood cells. First, I conducted an analysis of the data as a whole, which revealed for the first time that our vaccine drives a set of genes linked to anti-cancer responses ('interferon-inducible genes') in human cells. These data (**Figure 1**) have been incorporated into a draft manuscript for publication, "*Glycolipid-peptide conjugate vaccines stimulate CD8$^+$ T cell responses against human viral peptides*", which I expect to be published in a high-quality peer-reviewed journal during 2017. The paper will acknowledge the support provided by the Royal Arch Masonic Centennial Award. I expect to present the findings at future conferences, at which the importance of the Award will also be recognized.

Benefits for future projects
Because the Nanostring data are so rich, I expect to be able employ the same dataset for additional purposes. I am now supervising a University of Otago medical student, Ellie-May Jarvis, who is examining immune cells in patients treated with immunotherapy for melanoma. I have interrogated the Nanostring data, and found that key genes involved in immune inhibition are increased by our vaccines. This suggests our vaccines may work well alongside new cancer immunotherapies such as Keytruda® (pembrolizumab). Under my supervision, Ellie will conduct additional tests using different

techniques to confirm this. Indeed, I have been able to use the Nanostring data (**Table 1**) to shape and to support a grant application to the Wellington branch of the Cancer Society for Ellie's work. Thanks to your generous support, I expect to use the already-gathered data to determine the effect of our compounds on numerous other immune pathways, and to incorporate additional analyses into my future research projects, each recognizing, of course the role of the Royal Arch Masonic Centennial Award.

Establishment of international collaborations

The award has facilitated my collaborations with other leading scientists in the field – in fact, the draft manuscript mentioned above (of which I am the senior author), is written in collaboration with scientists from the auspicious National Institutes of Health (NIH) in the USA – a world leading research institution. Since the Award was provided, I have also commenced a collaboration with researchers at Guangzhou Institute of Biomedicine and Health in China, with the goal of bringing a new leukaemia immune therapy into a clinical trial in New Zealand. Such collaborations will benefit my current and future research, will raise the impact of the research that I and my colleagues conduct, and should ultimately bring new and effective treatments for New Zealanders.

Again, I thank the Order of the Royal Arch for your generous support, without which this work would not have been possible.

Yours faithfully,

Dr Robert Weinkove MA (Cantab) MBBS (Hons) PhD FRACP FRCPA
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Figure 1: Figure from draft manuscript for publication, showing the degree of enhancement of a subset of the analysed genes with our candidate vaccine (α-GalCer-pp65$_{495\text{-}503}$), and its two constituents, relative to media control (average of four human donors). Brighter red colours indicate a higher degree of enhancement of gene expression (*manuscript in preparation).*

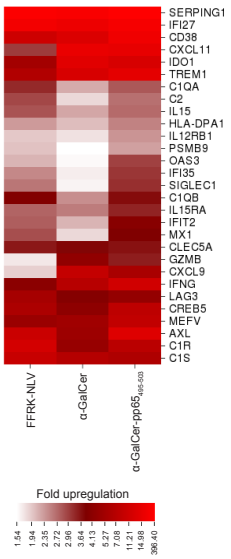

Table 1: Example of an analysis of another subset of the Nanostring data, showing that four out of nine genes of interest (LAG3, CTLA4, PD-L1 and PD-L2) are increased in human cells treated with the vaccine component α-GalCer (average of four healthy human donors). Based on this observation, we have started further work to confirm this finding using complementary techniques, and to explore its implications for combining our vaccines with other immune therapies.

Gene	Fold upregulation*
ADORA2A	1.05
BTLA	1.01
CTLA4	2.08
TIM3	0.90
LAG3	2.28
PD-1	0.70
PD-L1	1.77
PD-L2	1.58
CD137	1.15