Sir Charles Hercus Health Research Fellowship Evaluation

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Executive Summary

Established in 2003 to support the future leaders of health research in New Zealand, the Sir Charles Hercus Health Research Fellowship (SCHF) has supported 33 Fellowships since its inception, with the majority (90 percent) of these fellowships in biomedical research. The evaluation of this advanced Postdoctoral Fellowship has been carried out to provide an understanding of whether the goal of the HRC to support New Zealand's future health research leaders - with the ability to contribute to health and economic gains for New Zealand - has been met, and to identify how this goal could be better supported.

Past Fellowship holders were asked through an on-line survey to identify the impediments for career progression and ways in which emerging and mid-career research fellows could be better supported in the research environment, and where they thought the gaps in career support lay. Adding to this information was an analysis of contractual data contained in the HRC’s contract management database (RATA) and Fellows’ final reports submitted into the HRC’s online research contract reporting database (HEARD), which provided information on research advancement and impact.

The last evaluation of the SCHF was carried out in 2009, and since then, 14 SCHFs have been completed and final reports submitted. Of these Fellows, 10 completed the on-line survey (a 71 percent response rate), all were biomedical researchers, and six were women. Of the 119 applications received for the SCHF, 64 percent have been from women. However, overall women have had a low success rate (19 percent) for attaining a SCHF since the inception of the award, compared to the success rate for men (42 percent). In the last five years the overall success rate for the award has been 25 percent.

Over the five-year period (2010/11 – 2014/15), SCHFs made up 16 percent of the HRC’s salaried postdoctoral workforce, with 50 percent of these contracts being in the areas of cardiovascular disease (24 percent); CNS/neurological disorders (21 percent) or oncology and cancer (15 percent).

The following are the key findings from the evaluation:

- Nearly all Fellows had advanced their research careers since the inception of their Fellowship, and had established themselves as independent researchers leading research teams responsible for staff and students. On completion of the Fellowship, 13 Fellows were in more senior positions, one of whom had progressed to Head of Department;
- All 14 Fellows secured further research funding, with half being named investigators on both HRC Projects and Programmes;
- All ten survey respondents are now leading their own research teams, and were positive of the value the Fellowship provided in terms of the freedom it allowed them to establish themselves as independent researchers, forming a research team to support their research, and establishing relationships with collaborators without the pressure of teaching and faculty responsibilities;
- Training and mentoring emerging researchers was seen as a major part of the Fellow’s role, with all supervising students (42 in total), of whom 30 are undertaking a PhD;
- Fellow’s research had contributed to expanding knowledge in their field, with the translation of this knowledge into clinical settings, the generation of intellectual property, as well as the development of new and improved techniques and methodologies. The uniqueness of these methods and techniques were attributed to attracting both national and international collaborators to their research, which had brought new expertise and resources to their programs of research;
Fellows received significant recognition of their work through Awards and Prizes, including the Zonta Science Award for an emerging woman scientist; the Prime Minister's Prize for Science Media communication; the Royal Society's Callaghan Medal, and the HRC's Liley Medal. One Fellow attended the Science Foo Camp – organized annually by Google, Nature, Digital Science and O-Reilly Media. This event is by invitation only and brings together 250 people from around the world identified as conducting ground-breaking work;

Fellows were prolific in the dissemination of their research findings through academic avenues, producing an average of 13 peer reviewed publications per Fellow, which is equivalent to the average output from an HRC programme contract in the HRC’s recent bibliometric survey;

While traditional academic avenues of dissemination were high, the majority of Fellows did not report activities which had engaged the public in their research;

While Fellows had been successful in advancing their research and careers, they highlighted significant barriers that faced emerging and mid-career researchers. The significant stumbling blocks to career progression were identified as a lack of tenured positions and an over-subscription for these positions, as well as limited research funding in a highly competitive environment;

Of the ten Fellows surveyed, five had secured tenured positions at a university, while the remaining five Fellows were reliant on external funding to support their salary, and their research;

Fellows were aware of other postdoctoral fellows having to leave research careers to pursue other professions, or pursuing their research career overseas. Two of the four Fellows repatriated through the Hercus fellowship were investigating research opportunities overseas, given the austere funding environment;

Mid-career was identified by Fellows as where the biggest gap in career support appeared, with the mid-career researcher no longer eligible for postdoctoral funding, but without the track record of the senior researcher for whom they must compete for funding;

Mentors were identified as important in fostering and supporting researchers career progression. As such, mentorship programs - which include career planning and succession planning for researchers, as well as the development of the skills required to be a successful research leader - were viewed as one means of supporting Fellows in their career progression;

Other suggestions for support were an increase in funding to support mid-career researchers, and to ensure that the Fellowship keeps up with the costs of inflation, and that the workplace is a flexible environment supportive of researcher’s responsibilities outside of work.
Introduction

The Sir Charles Hercus Health Research Fellowship is an advanced post-doctoral fellowship which was established by the Health Research Council in 2003 to support up to three outstanding emerging researchers (4-8 years post-PhD) each year who are committed to a health research career in New Zealand. The intent of the award is that it will contribute to the retention and repatriation of New Zealand’s future health research leaders, those with the capability to conduct world-class research. Funding of up to $500,000 is available to recipients over four years.

Hercus Fellows are assessed by a Career Development Awards Committee, which selects Fellows on the basis of their application, referee reports, supervisor’s report, and a telephone interview during the committee meeting. The assessment process places greater emphasis on the candidate, rather than the outlined research project, with 60 percent of the criteria score attributed to ‘person characteristics’, which include the assessment of the applicant’s: value of service to the New Zealand academic and research community; their research experience and achievement; and the potential for development/future vision. The remaining 40 percent of the criteria score assesses the suitability and quality of the research environment and the potential for training and collaboration (20 percent); and research characteristics, which assess the potential for health and economic gains, and the design and methods of the research (20 percent).

An evaluation of Sir Charles Hercus Health Research Fellowships was last undertaken in 2009. This evaluation was focused on the six contracts that had reached completion since the commencement of the Fellowship in 2003. The evaluation was based on information obtained from: the HRC’s research contract management database (RATA); the HRC’s contract reporting database (HEARD) and Fellows’ final reports submitted at the conclusion of the Fellowship; as well as an email survey of Fellows.

Evaluation Methodology

The overall intention of the evaluation of the Sir Charles Hercus Research Fellowship is to provide the HRC with an understanding of whether the goals of the Fellowship are being met, and how these goals could be better supported within the research environment. The evaluation sought to identify:

- Career progression of Fellows and their establishment as independent researchers;
- Barriers to career progression and identified gaps in career support within the research environment;
- The development and progression of the Fellows research and evidence of research advancement and the potential for research to contribute to health and economic gains for New Zealand.

Information was obtained through: an analysis of contractual data contained in the HRC’s contract management database (RATA); Fellows’ final reports submitted upon conclusion of the fellowship into the HRC’s online research contract reporting database (HEARD); and an online survey sent to all Fellows who had completed their Fellowship and submitted a final report. The evaluation excludes those Fellows included in the 2009 evaluation.

The online survey asked Fellows to provide information and feedback in a number of areas, including: their current employment status and the staff and students they are responsible for; their career progression (the barriers they or colleagues had encountered at postdoctoral level;
where they believed the biggest gap existed in career support, and how postdoctoral fellows could be better supported in their career progression; whether they had progressed the research supported through the Hercus Fellowship; the personal value of the Fellowship to themselves and their institution; and if leadership development or media training would have been valuable skills to develop as part of their Fellowship.

Since 2009, 16 Hercus Fellowships have been awarded and reached completion. Of these 16 Fellowships, two will submit final reports outside of the evaluation timeframe, with the remaining 14 Fellows having submitted final reports between 2009 and 2015. The time elapsed since the expiry date of each Fellowship ranges from 5 months to 6 years.

Of the 14 Fellows who received the online survey, 10 completed the survey, a response rate of 71 percent, with a relatively even gender split (men (n=4) and women (n=6)). Of these 10 respondents, all were in the area of biomedical research. The four Fellows who did not participate in the survey were also biomedical researchers.

Overview of the Sir Charles Hercus Postdoctoral Fellowship

Over the five-year period (2010/11 to 2014/15) postdoctoral fellows\(^1\) made up 12-14 percent of the total HRC supported research workforce (excluding those who were identified as time only), with Sir Charles Hercus Health Research Fellowships accounting for 16 percent of this postdoctoral workforce.

Since the inception of the Sir Charles Hercus Health Research Fellowship in 2003, 33 contracts have been awarded and 23 Fellowships have reached completion, 7 triaged and 79 declined. Successful contracts have been awarded predominantly to biomedical researchers (30 biomedical, 3 public health) with a relatively even split across genders (men (n= 18) and women (n=15)).

While a broad range of health issues has been addressed over the years by awardees (see figure 1), half of this research has been in the area of Cardiovascular/cerebrovascular disease (24 percent) or relating to the central nervous system and neurological functions (21 percent); with Oncology and Cancer (15 percent) the third largest health issue addressed by awardees.

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\(^1\) The HRC classifies postdoctoral fellows as researchers who have held a PhD for less than six years
Success Rates for the Sir Charles Hercus Health Research Fellowship

Since the award of the Fellowship in 2003, a total of 119 applications have been received, with the majority of these applications (86 percent) in the area of biomedical and clinical research, and the remaining 15 percent, public health. Of these applications 29 percent of biomedical and clinical applications, and 19 percent of public health applications have been successful.

Of these 119 applications, 64 percent have been received from women, of whom 19 percent have successfully gained a Fellowship. Of the 43 men who have applied for a Fellowship, 42 percent have been successful in attaining one. In the area of public health, in which 63 percent of applications were received from women, no women were successful in receiving a Fellowship. In the area of biomedical and clinical research, in which 64 percent of applications were from women, only 23 percent of applications were successful, compared to men, of whom 41 percent were successful in gaining a Fellowship.

In the last five years the number of applicants for the Fellowship has increased, with 2015 seeing the largest number of applications (14 in total) (see figure 2). Since the inception of the Fellowship, an average of 8 applications have been received per year, with a success rate of 38 percent (3 applications per funding round). Forty-two percent of Biomedical researchers have been successful in attaining funding (30 funded fellows out of 72 applications), with 23 percent of public health researchers’ applications successful (3 funded fellows out of 13 applications).

Over the 5-year period since 2011, an average of 12 applications per year have been received by the HRC, with 3 of these applications being successful in gaining funding, a success rate of 25 percent, lower than the overall success rate for applications (38 percent).
Fellowship applications are scored out of a total score of 21, and those deemed fundable receive a score of 16.5. In the 2015 funding round, only three applications out of the 15 received were considered fundable.

Figure 2. Number of Sir Charles Hercus Fellowship applications and success rates, 2003-2015

Outcomes of the Sir Charles Hercus Health Research Fellowship Evaluation

Career Pathways – Where are Fellows now?

An intention of the Sir Charles Hercus Health Research Fellowship is to repatriate New Zealand researchers based overseas and to retain and support the capacity and capability of the New Zealand health research workforce. Of the 14 Fellowship recipients, 4 were repatriated from academic posts in the USA (3) and the UK (1). Of those who received the Fellowship, all have remained in research and have continued to progress their research careers at universities in New Zealand.

On completion of their Fellowship, 13 of the Fellows are in more senior positions at universities in New Zealand, than when they first applied for their Fellowship. Five of these Fellows are Senior Research Fellows, five are Senior Lecturers, and three are at the level of Associate Professor, with one Fellow progressing to Head of Department (Figure 3).

Of the 10 Fellows who responded to the survey, half had secured tenured positions at their universities, with the remaining 5 Fellows reliant on external grants to support their research. All of the respondents considered it a challenge to secure research funding or an academic position, as funding was highly competitive and positions were extremely limited and applications for them heavily oversubscribed.
“Very difficult as there is still a lack of middle/senior positions and new academic positions are few. Most recent lectureship positions in biology or biomedical science at Auckland have had more than 50 applicants.”

“I gained an academic position in the same year I was awarded the Fellowship. So that was not challenging per se. Securing funding for our research is extremely difficult, and the lack of money, particularly for salaries, is a real and constant constraint.”

**Figure 3.** Current academic position and academic position at the time of application for the 14 Sir Charles Hercus Health Research Fellows.

![](chart.png)

**Career Progression – Are Fellows Independent Researchers?**

An objective of the Fellowship is to provide emerging researchers with the time and financial support that enables them to establish themselves as independent researchers with their own research team capable of exploring and advancing new research avenues. Fellows surveyed highlighted the freedom the Fellowship awarded them to focus on establishing themselves as research leaders, with the time and resources to: attract students to their research team; strengthen collaborative relationships which for many played a key part in the success of their research; attract funding; build their reputation as leaders in their field within their department; and contribute to their institution as a core faculty member.

“It provided me with job security, the time to focus on research and research outputs, enabled me to be more productive by growing my lab through the recruitment of new students, it allowed me to strengthen relationships with clinical staff and finally, it helped me to develop into an independent scientist capable of leading a productive team.”

All those surveyed were now leading their own research teams, and were responsible for 38 staff in total, ranging from one to eight staff members per research team. The Fellows were also supervising students (42 students in total), with the majority of these students being PhD candidates (71 percent). Training and mentoring emerging researchers was identified by Fellows as being of high importance during the tenure of their fellowship.
“It has always been a key aspect of supervisory remit to provide my students with world class resources and training, and a skill set that will make them highly employable. Every single one of my students has obtained a job (or PhD position in another lab) quickly after graduating from my lab.”

Eight of the Fellows surveyed felt that their fellowship had impacted on their career progression in a positive way, while 2 did not believe the award of the fellowship had had an impact on their career progression. For one of these respondents, while they didn’t consider the fellowship to have made an impact on their formal progression through the academic system, they did however see the fellowship as enabling them to establish a research program: “In terms of actually enabling me to initiate a viable research program - absolutely.”

Barriers to Career Progression

When survey respondents were asked whether they or any of their colleagues had encountered barriers to the progression of their career at postdoctoral level, eight out of ten respondents said that they or others they knew had encountered barriers. Researchers were aware of postdoctoral fellows moving away from research careers to other professions, with others seeking opportunities overseas.

“NZ has very few avenues of independent support for postdoctoral researchers. Beyond the Rutherford scheme and the Hercus there’s very little. That’s certainly making the careers of many talented people extremely precarious.”

Common barriers to career progression were cited as an inability to secure funding and a dearth of permanent postdoctoral and early mid-career positions. Funding was seen as difficult to obtain for researchers at postdoctoral and early mid-career level as they were competing against established senior researchers and their research teams for a limited pool of funds.

One respondent cited growing a research team as essential to career progression, but that this is difficult to do without a tenured position, and that other factors such as maternity leave for women, make it difficult when it comes to growing a team. “Growing your team is essential to progression, this is difficult until you get tenure. Maternity leave is also really difficult if you are funding a team.”

A lack of a tenured position and a defined career structure for non-tenured researchers was cited by one researcher as creating a high level of risk and a lack of security, which in turn impacts negatively for these non-tenured researchers with regards to students choosing them as supervisors.

“The main barriers early on relate to the eligibility to supervise students and to apply for certain types of grants that naturally affect career progression and productivity. New Zealand lacks a defined career structure for research scientists who are not tenured. This creates a very high level of risk in the research environment and this risk is assessed by potential students who are aware of a supervisor’s Academic position. I have been told by several potential PhD students that they would only consider a Professor as a supervisor due to prestige and security. I understand the security perspective and this is certainly an area we could improve.”
Gaps in Career Support

Researchers were asked to identify where they saw the biggest gap in career support along the career spectrum. The majority of respondents (9 out of 10) considered that the biggest gap in career support was the one that they were experiencing now, mid-career. Mid-career researchers no longer qualify for the Fellowships available to emerging researchers, but they are having to compete with senior researchers with their established research teams and better track records, for a limited pool of funding.

“I have not been able to secure an academic position yet, and as a researcher - 10 years post PhD I am no longer eligible for fellowships e.g. Rutherford, to help cover my salary and research expenses. Instead, I not only have to apply for extremely competitive HRC or Marsden project grants which I have been close, but not yet successful in attaining.”

“The biggest gap in career support is the lack of structured funding targeted specifically at mid-career researchers. New Zealand, unlike many other countries, does not have any fellowships for individuals for senior fellows >9 post PhD. This would not be an issue if the rate of new research leaders and retiring academic staff were in equilibrium. But this is clearly not the case and New Zealand is exceptional at producing highly capable highly productive researchers through the Hercus and Rutherford, but has no real answer post these positions. We are increasing funding in the realm of post graduate students and as a group leader I want this to happen and want my students to be well funded. But I am also mindful that unfortunately most of them will not get a fellowship or job in New Zealand after they graduate.”

Researchers who did not have tenured positions were reliant on continuous funding to support themselves, with one researcher finding it impossible to support themselves on just one grant and being in the current position of receiving the support for their salary from two countries...

“I’m currently funded salary-wise between two countries.”

Career Progression Support

Respondents raised a number of ways by which researchers could be better supported in their career progression, including: effective mentoring programs; discussions around career planning at the outset of their postgraduate career; succession planning during their fellowship; leadership programs to help develop leadership skills; making sure the workplace is a flexible environment that is supportive of researcher’s responsibilities outside of work; and ensuring that costs keep up with inflation.

“There needs to be some serious career planning between the Fellow and their senior Academic mentors as early as possible.”

One respondent considered that it was as an obligation of the universities that those who received fellowships have their positions made permanent, with the majority of respondents noting a need for more support of non-tenured research staff, given the issues they faced around a lack of job security. Respondents suggested more funding to support emerging and mid-career researchers was required, which would allow researchers to establish their own research teams and put them in a more favorable position to acquire external funding. A lack of external funding was identified by one researcher as a stumbling block to gaining promotion.

“There is a lack of support for research only academic staff at all levels within the university. This needs to be addressed. I also have not gone for promotion as I always get asked do you have funding to support this. No funding = no promotion.”
Support from Host Institutions

When researchers were asked whether their host institution provided support to foster their research career, 3 of the 10 respondents said that they had been supported, but did not elaborate on what this support had been, while 7 said the support they had received had been minimal or "a little bit". Four of the respondents cited individuals, and in particular an individual mentor as having been supportive and helping foster their career, rather than their host institution.

One respondent who said they were ‘pretty neutral’ on the support provided by their institution to foster their career, felt there weren’t a lot of initiatives that were practically useful, such as ready access to travel support, or financial support to meet publication charges offered by their institution.

"... this (support) has been provided more from the recognisance of my mentor and head of department. Rather than a direct of the faculty or my School. That is to say that not everyone would be provided with the same level of support."

Perceptions of the Value of the Sir Charles Hercus Health Research Fellowship to the Fellow and the Fellow’s Host Institution

Personal Value of the Sir Charles Hercus Health Research Fellowship

The value of the Fellowship for the majority of Fellows was the freedom it allowed them to develop into independent researchers capable of leading their own research program, and progressing to a senior researcher role, as well as the freedom it gave Fellows to explore and establish new initiatives. The prestige of the Fellowship was acknowledged by two respondents, with the standing of the Fellowship being attributed in part to two Fellows securing permanent academic posts.

"I was and I am still very proud of the achievement of being awarded a Hercus. It is to me the most prestigious fellowship for research fellows in New Zealand. It also provided me with the freedom to develop real independence."

For two respondents who had been repatriated from overseas, the Fellowship allowed them to return to New Zealand and establish a career and develop a research program and research team. However, of note, is that of the four Fellows who returned to New Zealand as a result of the Fellowship, two are exploring overseas career opportunities because of the constrictions on funding and lack of mid-career opportunities in New Zealand.

"This allowed me to return to NZ and establish my own laboratory. However, due to the lack of options here in NZ we are also exploring options about moving back overseas."

Value of the Sir Charles Hercus Health Research Fellowship to the Host Institution

Fellows were asked what they believed the value of the Fellowship was to their institution, with 9 out of 10 Fellows responding to this question. A number of Fellows cited that the Fellowship was highly regarded by their institution and in this sense contributed to the research excellence of their department and the university, as well as their PBRF ranking.

The Fellowship was seen as contributing financially to institutions, both in the sense of the salary support provided by the fellowship and the equipment and resources the fellow was able to purchase through the fellowship budget. The Fellowship resulted in expertise being retained
at institutions, with Fellows bringing new techniques and expertise that they have shared with other research groups within the institution.

“The value could be measured financially whereby since my Hercus I have brought in more than $2M in research funding, supported > 10 post graduate research students and was awarded a PBRF score of B in the last round. There is also a follow on legacy to my Hercus due to all of the equipment and resources I have helped established which will have a benefit to all the research in my team now and in the future.”

While the majority of Fellows considered the Fellowship to be of value to their institution, one Fellow, who did not hold a tenured position at his institution, considered that the Fellowship presented a double-edged sword for his institution. On the one hand, it brings exposure to the university, but his feeling is the university would prefer to support staff who hold permanent academic positions.

“This is a love hate relationship. The university loves having you as you bring exposure to the university, however, the overall feel is they wish to support research only staff. I have personally experienced staff going out of their way to prevent you from submitting grants and also changing research tracks to compete against you for funding.”

Development of Skills

An expectation of the Hercus Fellowship is that it will support emerging researchers to establish themselves as independent mid-career research leaders with the ability to supervise a research team and undertake the activities that are the role of a team leader. Survey responses identified that mentors played a key role in providing support and advice to Fellows with regards to their career. The value of having an effective mentoring program was seen as important to fostering career progression, and supporting Fellows to develop the skills required of a research leader.

“I think much could be learned from the Rutherford Discovery Fellowship model which builds a cohort of fellows who meet several times a year and are mentored by those who have come before them.”

The majority of Fellows (n=7) felt that leadership or media training would have been helpful, with one researcher citing the importance of … “leadership programmes to help develop leadership skills, [as] despite what people think, scientists do need to be communicators and leaders”.

Other potential career development opportunities raised by researchers included greater opportunities for postdoctoral fellows to contribute to teaching; support enabling Fellows to become primary supervisors of students; and opportunities for Fellows to sit on grant panels.

Suggestions for Improvement of the Fellowship Scheme

Of the ten Fellows who completed the survey, seven provided suggestions for improving the fellowship scheme. A recurrent theme throughout the survey was the challenging research environment and the lack of job security following the completion of the Fellowship, with Fellows vying for limited academic positions and highly competitive pools of funding. In light of the tenuous job security of emerging and mid-career researchers, one Fellow suggested career planning between Fellows and Academic mentors as early as possible, as well as a system of succession planning post completion of the fellowships.
"I would like to see some kind of system of succession planning post completion, especially where tenured positions are few. Currently, there is no obligation for the host institution towards the fellow post completion of the Hercus. Although this is a very complex financial matter I would like to see some kind of system of succession planning post completion especially where tenured positions are few."

Two Fellows felt that an increase in funding was required to support the costs of travel and to meet the costs of inflation over the duration of the fellowship, and that the fellowship should extend to 5 years fully funded... “in line with the Rutherford and similar initiatives offered by Wellcome”. Extending the Fellowship to slightly more senior researchers, ten years out from their PhD was also suggested, as was the need for more Postdoctoral Fellowships to support emerging researchers.

Research Progression and Evidence of Advancement and Impact

All the Fellows had stayed within the broad theme of the research area that had been the focus of their Hercus Fellowship, and were progressing this research or exploring new avenues that had opened as a result of their Fellowship research. However, for one researcher who said that they had stayed within the broad theme of their fellowship, they had had to change to using a different organism in their studies, in part out of necessity to secure a tenured position.

"Since the inception of this project, the scope and value of this research has expanded considerably through several new national and international collaborations and invitations to join international genetics consortia. Aspects of this project have now been expanded into stand-alone research projects that are ongoing and supported by new research funding and additional research staff."

The 14 Fellows included in this evaluation had successfully met the objectives outlined in their Fellowships, with the findings from their research having made significant contributions to their field of study through advancements in knowledge, the development of new technologies and methodologies, and the resultant improved understanding of health conditions and diseases, and their potential management and treatment. In summary, these included:

- the establishment of an internationally recognised animal model of acoustic trauma-induced tinnitus (the only tinnitus model in New Zealand);
- preclinical testing of varenicline (Champix), a smoking-cessation medication, to assess its effectiveness as a potential therapeutic strategy for patients with Huntington’s disease. The results from these studies supported the progression to a randomized controlled trial to investigate the efficacy in symptomatic patients. The clinical trial is supported by two external grants and will investigate whether this smoking-cessation medication is able to improve the cognitive and psychiatric symptoms suffered by patients with Huntington’s disease;
- results which identified for the first time that the elevated risk of stroke associated with smoking is likely to be mediated through changes in baroreflex function (the body's mechanism for helping to maintain blood pressure at constant levels), rather than cerebral autoregulation;
- the establishment of cutting edge technologies in New Zealand through the development of: multiplex cytokine arrays; RTCA xCELLigence biosensor technology; and ECIS technology for measuring endothelial barrier strength which is the first of its kind in New Zealand;
• the identification of 71 risk genes for Crohn’s disease and 47 risk loci for ulcerative colitis, as well as parallel genetic studies in a number of other chronic inflammatory diseases revealing a strong degree of inter-relatedness between Inflammatory Bowel Disease and these other inflammatory diseases that was not previously known;
• contributing to the understanding of viral capsid architecture which is present in retroviruses such as Human Immunodeficiency Virus (HIV) and is key to the success of therapeutic approaches that target the viral capsid (the shell of protein that protects the nucleic acid of a virus). Research for the first time helped to visualize the pentameric building block of the capsid;
• identifying an increase in renal sympathetic nerve activity during the development of hypertension, which is the first study to show an increase in activity in a chronic model of hypertension and provides further support for targeting specifically renal nerves in the treatment of hypertension, which is gaining traction in clinical practice;
• the creation of patient-specific heart modelling methodologies that allows for potential treatments for managing cardiovascular disease in ICU patients to be trialed on a model prior to being administered to the patient. This allows clinicians to be able to get closer to an optimal treatment without having to work through a process of ‘trial and error’ on the patient;
• the development of a virus-like particle (VLP), based on the empty virus shell of rabbit calicivirus, and an understanding of how it acts to induce an anti-tumour response. In vivo studies that were carried out showed that the VLP could be used to deliver a variety of different peptides which can induce a cytotoxic T cell response against tumours. A vaccine strategy that works both in a prophylactic and therapeutic setting;
• the provision of a more complete picture of the spectrum of the cognitive deficits and the mechanisms underlying these deficits following vestibular damage, with the continuation of this research through a Marsden grant;
• research that has shown that certain cellular pathways within the heart may be activated in individuals who carry genetic risk factors for heart disease. This information is being used to identify new candidate biomarkers in blood that can signal the very early stages of heart disease in genetically susceptible individuals who do not yet have symptoms;
• the assessment of BNP signal peptide in a hospital emergency department based study that has indicated that BNP’s potential clinical utility may lie in the determination of cardiac ischemia that may not result in myocardial infarction. This finding presents a major potential clinical advancement as there are no accepted biomarkers that can reliably detect cardiac ischemia symptoms, such as unstable angina;
• establishing the use of Galleria mellonella (greater wax moth) caterpillars as a model for non-tuberculosis mycobacteria, which has opened up a new avenue of research for these neglected pathogens;
• demonstrating that after stroke there is an increase in tonic GABA currents that is contributing to an impairment of motor recovery. This research has shown that there are three key windows where drug treatments can be targeted to aid in the recovery following a stroke.

Researchers were asked if following the submission of their final research report there had been other research impacts to report on. Two researchers said that there were papers in progress that were a result of their Hercus Fellowship, with one researcher saying that post their final report they had produced 5 publications that were a direct result of this research. This researcher believed that an interim report at the end of the grant and then a follow-up report 12-18 months later would give a much better indication of research impact. A report at this date would also capture the attainment of objectives that had occurred beyond the completion date of the contract, as was the case for one Hercus Fellow, who had not met all of their objectives at the time of final reporting.
In one instance, a PhD student supervised by a Fellow, had continued to work in the research area of the Hercus Fellowship and had successfully published 5 research papers with more in the pipeline. This PhD student was the first student that the Fellow had solely supervised and had progressed the research with funding secured post-completion of the Fellowship:

“Since submission of my final Hercus report I have had at least 1 student continue to work on the research project area with support obtained from other sources. This includes (name) who is my very first PhD student where I am the primary supervisor. (Name) is reaching the end of her PhD and I am very proud of her achievements. I am extremely pleased as she already has 5 published research papers with at least 6 more to come before she finishes this year. I think this is excellent and some of this work is a direct consequence of the Hercus fellowship and has been made possible by the Hercus funding.”

Development of new methodologies and techniques

The development of new methodologies and techniques by Fellows had been cited as an incentive for other researchers to form collaborations with their team, as well as playing a part in attracting students to the Fellow's research program. Of the 14 final reports submitted by Fellows, 10 of the 14 Fellows had developed new methodologies and/or techniques as part of their research program. These methodologies and techniques were being published and shared with other researchers and included:

- Methods for sampling and quantification of nerve activity;
- The development of chronic renal sympathetic recordings in the rabbit and rat;
- The establishment of new training protocols to allow established functional tests such as T maze and novel object recognition to be carried out in impaired and aged animals;
- The development of an HPLC assay to measure varenicline concentrations in brain and plasma;
- Establishing a whole lens culturing system under hypoxic conditions which mimics the "normal" environment of the lens, and the development an assay to measure lens viability;
- The development of immunoassays to multiple signal peptides;
- Analytical techniques that will form the basis for future studies seeking to understand the role that baroreflex and cerebral auto regulatory impairment has on the risk of adverse cardiovascular events such as ischaemic and haemorrhagic strokes;
- The development of virus-like particle (VLP) for use as an effective tumour therapy, with the VLP capable of being used as an antigen delivery platform for delivery of peptides, proteins and whole cell lysates to the immune system.

The methods and techniques that were developed by researchers in one laboratory had led to a world leader in their research area collaborating with the research team and presenting their data as part of a key-note lecture at the American Heart Association's High Blood Pressure Research Scientific Sessions in Florida.

“The techniques developed throughout this project have proven to be of great interest to other researchers around the world. A number of collaborators have visited the lab specifically to learn the chronic recording techniques, and through both direct visits and the published papers describing the techniques, members of the research sector are already adopting the techniques used in this research project.” (Final report excerpt)

As well as attracting international collaborators to research teams, new methodologies and techniques developed by researchers also attracted national collaborators. One Hercus Fellow cited the development and expansion of their expertise in methodologies and techniques
required for specific technologies during the course of their research as having enabled collaborations with fellow colleagues in the Centre for Brain Research.

Knowledge Translation – the Path to Clinical Application

The research carried out by Fellow’s has contributed to the evidence base for clinical practice and there are examples of Fellow’s research leading to commercialisation of products and clinical trials, with the potential for knowledge translation. The survey of Fellows identified four researchers whose research had impacted on clinical practice, and a further four researchers who believed that their research had the potential to influence clinical practice in the future. The knowledge gained from the fellow’s programs of research had:

- led to two new candidate biomarkers for diagnosis or prognosis in heart attack patients, with the granting of a provisional patent, “MicroRNAs as diagnostic and prognostic biomarkers for atherosclerotic conditions”;
- resulted in research that has shown that there is an increase in renal sympathetic nerve activity during the development of hypertension. A finding that is important as it is the first study to directly show an increase in activity in a chronic model of hypertension and provides further support for the clinical use of renal nerve ablation as a treatment strategy for hypertension;
- led to new technologies that were being explored in an MBIE Smart Ideas grant awarded in 2015. This funding will support the development of a portable device to monitor the brain’s metabolism. The device will enable clinicians to assess the brain’s metabolic activity and improve the management of brain injuries;
- shown that there are three key windows in which drug treatment can be targeted to aid recovery following a stroke. The researchers are working with industry (Roche) and leading medicinal chemists to develop novel drug treatments that they aim to take through to the clinic;
- resulted in the development of patient-specific heart modelling methodologies for the improved diagnosis and treatment of cardiac conditions experienced by individual Intensive Care Unit (ICU) patients. Successful clinical trials in New Zealand have led to further clinical trials in Europe;
- led to the development of the world’s first immunoassays to multiple signal peptides which have been patented, with the technology commercialised by Otago Innovation Limited. In late 2015 Upstream Medical Technologies [UMT] was formed by the University of Otago and Powerhouse Ventures Ltd to commercialise the technology developed, including a world-first test to potentially speed up the diagnosis of unstable angina. Investment in this research will led to the refinement of the test and larger clinical trials, steps in the process towards developing a product.

A synopsis of the research programs of six Hercus Fellows which have led to knowledge translation or have the potential in the future to have clinical application are included in Appendix A.

Further Funding of Research

All of the 14 Fellows who were included in this evaluation have been successful in securing further funding, with 7 of the recipients having been named investigators on both HRC projects and programmes post Fellowship award, and three Fellows currently in the process of applying for HRC funding as 1st Named Investigators. Further funding has come from a number of
funding sources, including: Marsden grants; MBIEs’ SmartIdeas Fund; the New Zealand Neurological Foundation; the Auckland Medical Research Foundation; Lottery Health and CureKids Innovation Seed Fund.

Half of the survey respondents said that their funding included research overheads, which are paid to the host institution to maintain research infrastructure. Those whose funding included overheads were three researchers with tenured positions and two researchers who did not hold tenured positions.

Collaboration

Eight Fellows reported a total of 60 collaborative relationships in their annual and final reports, with 40 percent of these collaborations with overseas researchers and 60 percent with New Zealand-based researchers. The top three countries Fellows collaborated with were the UK (9 collaborations), USA (4 collaborations) and Australia (4 collaborations).

Of the 10 survey respondents, nine had continued the collaborations they had formed during their fellowship, with these collaborations considered to be very important to the success of the research. Collaborative relationships had opened up new avenues for researchers and supported the success of research through: the exchange of complimentary expertise; access to external funding; the establishment of links with clinicians; access to new technologies; and the development of compounds.

“(Collaborations were) very important then and they are still. The best advice I could give any new Fellow is to form good collaborations on an equal footing as these are the ones that last the test of time. Single sided collaborations are doomed to fail. All of my collaborations amplify our collective research power and have increased productivity.”

Final research reports showed that Fellows’ collaborations had led to the advancement of the research supported by the Hercus Fellowship. These collaborations had led to contributions towards our understanding of the genetics of disease, the development of compounds to modulate GABA transporters and GABAc receptors, as well as an antibiotic discovery project.

“We are now collaborating with colleagues from Landcare Research in an antibiotic discovery project, screening a unique collection of New Zealand and Pacific fungi for novel antibiotics with activity against three of the four pathogens of great relevance to New Zealand’s future: M.tuberculosis, E.coli and S.aureus.” (Final report excerpt)

Recognition of Research Contribution

An invitation to review grants, membership on editorial boards and the review of peer-reviewed articles are all indicators of a researcher’s ‘esteem’ amongst their peers, as are awards, membership on professional bodies and invitations to present at conferences and scientific meetings.

Awards and Prizes

Over the duration of their fellowship, six Fellows received prizes and awards for their contribution to research and in recognition of the quality of their research. Two Fellows were presented with the University of Otago’s Early Career Award for Distinction in Research, one Fellow was awarded the Zonta Science Award for an emerging woman scientist, another Fellow was presented with the Prime Minister’s Prize for Science Media Communication and the Royal Society of New Zealand’s Callaghan Medal, and one Fellow was the recipient in 2011 of the
HRC’s prestigious Liley medal. Hercus Fellows and the students in their research teams also received prizes at conferences for best posters, oral presentations and abstracts.

**Editorial Boards and Reviews**
Six Fellows were on editorial boards for peer reviewed publications, with one Fellow invited to be Associate Editor for a new journal in the field of Physiology. Five fellows were asked to review grant applications for both national and international funding organisations. National funding organisations included the HRC, Heart Foundation New Zealand, Lottery Health and the Auckland District Health Boards A+ Trust. International organisations that asked Fellows to review grant applications included the Medical Research Council, Wellcome Trust and the Royal National Institute for Deaf People in the UK, the Canada Foundation for Innovation, and the Danish Council for Independent Research.

**Dissemination of research findings**

**Written presentations of research**
All the Fellows had disseminated the findings of their research through one written medium or another. These written forms of dissemination included conference proceedings, editorials and reviews, non-reviewed and peer-reviewed publications, and book chapters (see figure 4).

All Fellows had published in peer-reviewed journals, with a total of 186 peer-reviewed articles published (61 percent of all written outputs), which represented a prolific output rate of 13 articles per Fellow. The number of articles produced by the 14 Fellows is equivalent to the number of articles on average produced by programme contracts in the HRC’s most recent bibliometric report. Researchers had published articles in highly cited journals such as the interdisciplinary science journal *Nature, Nature Genetics*, the cardiovascular journal *Circulation*, the *Pharmacogenomics Journal*, and the *Journal of Neuroinflammation*.

Conference proceedings were the second largest category of dissemination outputs, with half of all fellows reporting dissemination through this medium (79 conference proceedings, 26 percent of all outputs).

**Figure 4. Written Dissemination Outputs of Hercus Fellows**
Oral presentations of research
In total, Fellows recorded 169 occasions in which they presented their research to those in the scientific community (see Figure 5). Conference presentations accounted for 55 percent of all oral presentations delivered to the scientific community and were a form of dissemination used by the majority of Fellows, with 93 presentations reported by 12 Fellows. Of these presentations, just over half were international conference presentations (57 percent).

One Fellow was asked to deliver the keynote address at two national conferences in their research area, another had received an award for the top oral presentation at an international conference, and other Fellows had been given the responsibility of organizing and chairing conference sessions. All of these outputs are an indication of the esteem that Fellows are held in by their peers.

Following conference presentations, seminars were the next most common form of oral presentation to peers, closely followed by scientific meetings and presentations at symposia.

A significant coup for one Fellow was the invitation to attend Science Foo Camp, which is an annual event organised by Digital Science in collaboration with Google, O'Reilly Media and Nature. The event is by invitation only and brings together 250 people from around the world who have been identified as conducting groundbreaking work across diverse areas of science and technology. Those attending the event are researchers, technologists, writers, educators, artists, policy makers, investors and other thought leaders, who meet for a weekend of discussion, demonstration and debate.

Figure 5. Oral presentations to the scientific community

Public engagement activities
In total, 63 counts of public engagement activities were recorded by 3 Fellows, of which one Fellow was responsible for 87 percent of these activities (see Figure 6). Dissemination via media articles, television appearances and radio appearances formed a relatively small percentage of all outputs and was only undertaken by 3 of the Fellows, with one Fellow accounting for 81 percent of these outputs. Radio interviews accounted for 24 percent of all
public engagement activities and were the most popular form of media engagement, followed by television interviews (17 percent).

Public engagement through presentations to interest groups, such as Rotary and U3A, was undertaken by relatively few of the researchers, with only 2 presenting their research to those in the wider community; however, this form of dissemination accounted for 32 percent of all public engagement activities. Of the 20 recorded presentations to interest groups, one Fellow was responsible for delivering the majority of these (18 in total).

Other forms of public engagement carried out by Fellows included: videos posted on YouTube; participation in National Science week in Australia; participation in the RSNZ’s Inspiring Science day for school children, and TedX talks.

Figure 6. Public Engagement Activities

Conclusion

It is clear from the findings of the evaluation that the HRC is identifying individuals with the caliber to become independent research leaders in their field. All Fellows were highly productive in disseminating their research through academic mediums, with 13 Fellows having achieved promotion within their institutions, and successfully securing further research funding. The advancement of Fellows in their career was also apparent for the Fellows surveyed in the 2009 Hercus Evaluation, with five of these six Fellows now holding associate professor and professor roles at their institutions.

The contribution of research supported through the SCHFs to health and economic gains for New Zealand was evident in much of the research, with evidence of Fellows achieving knowledge translation of their research, and research resulting in an evidence base to improve the understanding of health conditions and diseases and contribute to their potential management or treatment.

While the Hercus Fellowship evaluation shows we are supporting our future biomedical research leaders, it is evident that an imbalance exists in the areas of research we are
supporting, with only three Fellowships in public health research awarded since 2003. In addition, the gender balance of applications does not match those which are funded, with far more women applying and being declined, than men. Further investigation is required to understand this discrepancy and ensure the HRC supports gender equity throughout researchers’ career paths\(^2\).

At a national and international level there is recognition of gender inequity in the career progression of women into senior research roles in Science, Technology, Engineering and Mathematics (STEM). "Globally, women are the most under-represented not at the entry into science education as children or youth, but starting in graduate studies, with a "leaky pipe" of career development, so that at every step up the level of status and responsibility, women become rarer"\(^3\).

The Human Rights Commission produce a bi-annual report – New Zealand Census of Women’s Participation – which identifies the proportion of women who hold senior academic appointments at New Zealand universities. The most recent 2012 Report\(^4\) identified that across New Zealand universities, 24 percent of women were senior academic staff members, with 19 percent at the level of Professor. These figures for senior female academic staff mirror overseas figures, where women hold, on average, only 20 to 25 percent of full time professor roles. In the US women account for 19 percent of full professors\(^5\), while in the UK women constitute 22 percent of fulltime professors\(^6\). The statistics available for women holding senior positions in academia in Australia are aggregated to positions above the level of senior lecturer. In 2012, 29 percent of Australian women held the position of Associate Professor or Professor at an Australian university\(^7\).

A workforce analysis of HRC-funded research programmes and projects identified that between 2006 to 2015 only 14 percent of programmes were led by women. The imbalance of men as lead investigators is also apparent across biomedical and clinical research projects, with 76 percent of biomedical projects led by men and 69 percent of clinical research projects led by men. In comparison, 61 percent of principal investigators on public health projects are women, while 43 percent of projects in the health services area are led by women. In the area of public health, it is at the programme level that an imbalance between men and women occurs, with women under-represented as principal investigators.

The NHMRC in Australia sees a similar decline in women moving up the career ladder, with women in 2014 accounting for 63 percent of all applications for NHMRC’s early career fellowships, but falling to just 11 percent for NHMRC’s most senior and experienced fellowships.

Internationally, a number of policies and initiatives have been introduced by funding organisations to address gender inequity. These policies and initiatives include: the establishment of advisory committees and working groups on gender equity; assurance from host institutions that they have adequate gender equity strategies in place; re-entry fellowships for

\(^2\) The 2016 Career Development Awards Funding Round did not reflect this pattern, with 73 percent of applications received from women, and the six SCHFs funded being awarded to women (a 100 percent success rate).


\(^4\) https://www.hrc.co.nz/files/2314/2360/5171/web-census.pdf


\(^6\) https://www.hesa.ac.uk/data-and-analysis

those returning from a hiatus in their career; part-time and flexible options for undertaking research grants; and mentorship programmes.

While the HRC is successfully identifying individuals who have the ability to be independent research leaders, there are issues within the research environment that result in a high degree of job insecurity for our Fellows post-completion of their award. Of the five Fellows holding non-tenured positions within their institution, all are reliant on external funding to support their salary, and their research. All of the Fellows surveyed considered funding for research or securing an academic position as incredibly challenging in the present research environment, with funding competitive and Fellows having to compete against established researchers at professorial level. Academic positions in their departments were few, with little turnover in senior staff, and a very high demand for these positions when they became available. Non-tenured positions resulted in a lack of job security, and with the inherent risk this brings, some postdoctoral fellows find their ability to attract students to their research program reduced.

The majority of the Fellows surveyed had encountered barriers in their career progression, with Fellows aware of other postdoctoral fellows having to leave research careers behind to pursue other professions, or pursuing their research career overseas. Two of the four Fellows repatriated through the Hercus fellowship were investigating research opportunities overseas, given the austere funding environment.

The difficulties of pursuing a research career in New Zealand were reflected by Fellows in the 2009 evaluation, with the transition from being an emerging to an independent researcher seen as ‘difficult and frustrating’. The challenges of sustaining a research career were reflected in all of the surveys, with one researcher suggesting that a research career was a ‘very difficult option that requires hard work, good fortune and compromise’.

The significant stumbling blocks to career progression – lack of tenured positions and limited research funding - experienced by New Zealand postdoctoral fellows, are not dissimilar to those experienced by postdoctoral fellows overseas. In the US, it was recently estimated that only around 15 percent of US postdocs secure tenure-track jobs, while another survey found that the unemployment rate after completing a postdoctoral fellowship has more than doubled from four percent in 2008 to 10 percent in 20128.

A tracking pilot carried out by the European Science Foundation, which tracked the careers of 499 doctoral holders from five research organisations up to seven years after graduation, identified that while nearly all were in full-time employment, only 35 percent held tenured posts. Of this employment, 88 percent was in research, and predominantly in public sector institutions (82 percent). The most negatively rated factors in the work environment were identified as ‘job security’, closely followed by ‘support for career development’ and ‘organizational culture.’ Unsurprisingly, job security was strongly associated with employment status, with those on temporary contracts more likely than those on permanent contracts to be dissatisfied with their employment situation9.

In light of the barriers that presented themselves to emerging and mid-career researchers, Fellows had a number of suggestions for how they could be better supported in their career progression. Fellows surveyed highlighted the importance of career planning at the outset of a researcher’s career, as well as succession planning post-completion of the Fellowship. Mentors were viewed by Fellows to have played a key role in supporting and fostering their research

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8 http://www.the-scientist.com/?articles.view/articleNo/44874/title/Opinion--The-Postdoc-Crisis/
career, and effective mentoring programs, were seen as important in providing researchers with support in their career progression. Fellows felt that as well as increased funding to support mid-career researchers, it was also important that Fellowships kept up with the costs of inflation, and that the workplace was a flexible environment supportive of researcher’s responsibilities outside of work.

In terms of career development, a number of Fellows saw value in leadership development and media training programs. Mentors were seen by Fellows as being able to provide Fellows with guidance on developing the skills required to be a research leader, and effectively lead a research team, while institutions were seen as having a part to play in providing Fellows with teaching opportunities, and supporting Fellows to become primary supervisors of students.

It is important that we attempt to address the issues that the evaluation has highlighted, particularly those that involve the wider research environment. However, in doing so we must have a sound foundation of evidence to ensure we do not exacerbate existing problems or biases when attempting to address these issues.

Recommendations and Further Actions

In proposing recommendations and further actions, the HRC is conscious that the key barriers identified by Fellows to career progression – lack of permanent academic positions and funding restrictions – require a sector-wide approach. As such, the following recommendations are intended as a way in which the HRC could better support Hercus Fellows and how we could move forward to addressing the bottleneck that exists for early-to-mid-career researchers in their career progression.

1. The HRC should take a leadership role in bringing the sector together to address the drivers of the current early-to-mid-career workforce issues. Ensuring that research workforce capacity and capability is included in the New Zealand Health Research Strategy will be key to creating cross-sector dialogue on the drivers and barriers in the system. A system-wide approach is required to address these, particularly the unintended incentives that arise as a consequence of PBRF funding – such as increasing the number of PhD students;
2. The HRC will work with funders and providers to explore how best to jointly invest in the next generation of health research leaders in New Zealand. This could involve the exploration of a number of different leverage options, such as the employing institution covering a certain percentage of the salary costs for the duration of the Fellowship, to ensure that they are invested in supporting and retaining individuals, if these individuals have been identified as future health research leaders. Further discussion is needed on the issue of research overheads on awards, as the lack of overheads has been cited as a barrier to institutional support of Fellows;
3. Restructuring the Fellowship needs be considered: should we increase the length, offer more (with the potential of decreasing the prestige of the award), or introduce another award that targets mid-career postdocs? Should the Fellowship be tied to capacity gaps identified through our workforce analysis, to target the development of future research leaders? We could also consider areas of national strength, priority and opportunity;
4. Additions to the Fellowship to increase impact:
   a. make Mentoring Plans and Individual Development Plans a core aspect of the award – as is done by the National Science Foundation and National Institutes of Health (USA) and the Wellcome Trust and Medical Research Council (UK);
   b. explore the feasibility of a workshop for past and present Hercus Fellows to present their research and establish networks with other Hercus Fellows, and
discuss any issues they may have; and investigate the cost and feasibility of establishing a mentor database of those willing to mentor Fellows;

c. the HRC could conduct workshops for Fellows interested in being committee reviewers, guiding them through the process of assessing committees and the requirements placed on reviewers. Where possible, and avoiding any perceived conflicts of interest, Fellows could attend an assessing committee meeting to gain a firsthand experience of the process;

d. the HRC should ensure that Fellows are aware of training that is available to them through their institution and workshops that the RSNZ runs on public engagement. A review of available resources should be undertaken by the HRC and made available to Fellows;

5. The HRC receives a low number of applications from public health researchers for the Sir Charles Hercus Health Research Fellowship. The HRC should canvas the research community to better understand the imbalance in applications between biomedical and public health researchers. The HRC should ensure that it is adequately communicating the availability of the Fellowship to public health researchers;

6. A majority of the Sir Charles Hercus Health Research Fellowship applications received are from women, however the success rate for women, as compared to men, is low. The HRC needs to better understand the basis for this gender imbalance, with work required in this area.  

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10 The 2016 Career Development Awards Funding Round did not reflect this pattern, with 73 percent of applications received from women, and the six SCHFs funded being awarded to women (a 100 percent success rate).
Appendix A  Synopsis of Sir Charles Hercus Health Research Fellowship programs which have led to knowledge translation

Dr Ailsa McGregor, *Targeting dysfunctional cholinergic transmission in a model of Huntington’s Disease*, Department of Pharmacology and Clinical Pharmacology, Faculty of Medical and Health Sciences, University of Auckland

Dr McGregor’s research into Huntington’s disease (HD) investigated the mechanisms underlying the disease process and investigated the role that nicotinic acetylcholine receptors play in the pathology of HD with the intention of identifying a potential treatment for the disease. The findings from this pre-clinical research indicated that varenicline, a smoking cessation medication, appeared to delay the onset of cognitive and depressive symptoms in the transgenic mouse model of HD.

“Our results provide proof of principle and support a move to trials in human patients. We have already carried out a small scale tolerance trial in patients with HD. Varenicline was well tolerated and no clinically significant side effects were observed. Preliminary data from cognitive testing carried out before and after varenicline administration in these patients shows improvement in executive function after 4 weeks of treatment. This provides further support for a randomized controlled trial to investigate efficacy in symptomatic patients.” [Final Report excerpt]

In 2014, Dr McGregor successfully secured funding from two organisations to carry out a clinical trial in HD patients. This efficacy trial involves Neurologists and Clinical Psychiatrists from Auckland Hospital. If the trial shows benefit, further studies will be necessary to refine the dosing regimen in patients and to investigate whether treatment can prevent or delay the onset of symptoms in presymptomatic patients. The research has the potential to make a significant difference to HD patients, as at present there are no proven effective treatments for cognitive and affective symptoms of the disease.

Dr Christopher Hann, *Model-based cardiac diagnosis and therapy in critical care*, Mechanical Engineering Department, University of Canterbury, Christchurch

Dr Christopher Hann’s research during his Hercus Fellowship created patient-specific heart modelling methodologies for the improved diagnosis and treatment of cardiac conditions experienced by individual Intensive Care Unit (ICU) patients. This research allows for potential treatments for managing cardiovascular disease in ICU patients to be trialed on a model before being administered to the patient, which means clinicians are able to get closer to an optimal treatment without having to work through a process of ‘trial and error’ on the patient.

Following retrospective animal trials and the gathering of data for the required cardiovascular recordings, human trials were carried out in the Christchurch ICU, with the cardiovascular model correctly predicting the impact of ventilation and adrenaline of several patients. The initial successful results provided the foundation for continuing the trials on a larger scale in the Liege ICU in Belgium, providing access to more data and patients.

The hardware and software involved in the cardiac modelling has been specifically developed by the research team in a format that is suitable for easy transfer to end users, including doctors, nurses and clinical engineers both in Christchurch and in Belgium. Dr Hann’s final report states that a significant part of the progress made by the team was the... “success in explaining algorithms and methods to the nurses and doctors in the Christchurch ICU. As a result, the reputation of the University of Canterbury engineering department has strengthened further, and clinical staff, including biomedical technicians at the ICU, and very forthcoming in providing
The research has successfully engaged clinicians based in the Christchurch ICU and Liege ICU and provided a strong foundation for the forming of engineering and clinical collaborations at both hospitals in the future. A PhD student from Dr Hann’s research team went to Belgium to help with the implementation of the model at the Liege ICU.

**Associate Professor Yu-Chieh Tzeng, ‘Influence of tobacco smoking on dynamic cerebral autoregulation’, Department of Surgery and Anaesthesia, University of Otago, Wellington**

Stroke risk stratification promotes efficient allocation of healthcare resources, yet the identification of high-risk patients remains challenging due to a lack of predictive markers. Cigarette smoking is a major preventable risk factor for both ischemic and haemorrhagic stroke. There are currently no simple markers of its effects on cardiovascular function. During the tenure of Dr Tzeng’s Hercus fellowship his research team developed novel methods for detecting adverse changes in brain blood flow. They showed for the first time that the brain controls its blood supply through a delicate coordination of mechanisms that have traditionally been thought to act independent of each other. They developed methods for quantifying the strength of these interactions, and showed that tobacco smoking can increase stroke risk by impairing the brain’s ability to coordinate these mechanisms. This has led the team to develop novel risk-stratification tools that can allow clinicians to holistically characterise the brain’s ability to regulate blood flow. The team are now testing these tools in people at high risk of stroke such as patients who have suffered a transient ischaemic attack.

In 2013, while undertaking research for his Hercus Fellowship, Dr Tzeng was appointed as the Director of Otago University’s Centre for Translational Physiology in Wellington. The Centre aims to foster interdisciplinary research that accelerates the transfer of clinically-relevant knowledge and technology into the clinical practice. This year the centre completed the construction of New Zealand’s first Calorimetry and Environmental Simulation Suite. This Centre is now supporting HRC funded research in several areas including neurogenic mechanisms of asthma, energy metabolism in different New Zealand ethnicities, and long term cardiovascular consequences of premature birth.

Aspects of Dr Tzeng’s Hercus fellowship research have led to new technologies which are currently being explored through a MBIE Smart Ideas fund awarded in 2015. The collaborative team of clinicians and physicists led by Dr Tzeng, will develop a portable device to monitor the brain’s metabolism. This will allow clinicians to better assess the brain’s metabolic activity and improve brain injury management.

**Dr Andrew Clarkson, ‘Tuning post-stroke cortical excitability: implications for learning and memory’, Department of Anatomy, Otago School of Medical Sciences, Division of Health Sciences, University of Otago**

Dr Andrew Clarkson and his research team have been working with animal models to understand and improve stroke recovery, and are engaged with Industry (Hoffman La-Roche) and medicinal chemists to develop novel drug treatments that they aim to take through to the clinic. ‘Ischaemic stroke is the leading cause of severe long-term disability yet lacks drug therapies that promote the repair phase of recovery. This repair phase of stroke occurs days to months after stroke onset and involves brain remapping and plasticity within the peri-infarct
zone. Elucidating mechanisms that promote this plasticity is critical for the development of new therapeutics with a broad treatment window.11

The research that arose from Dr Clarkson’s Hercus Fellowship demonstrated that after a stroke there is an increase in tonic GABA currents that contributes to an impairment of motor recovery. The findings of this research were published in an article in 2010 in the high impact journal Nature. The researchers have shown that there are several switches on how GABA functioning works after stroke and are targeting a couple of these time points to find novel drug targets, one of which is already in collaboration with Roche Pharmaceuticals.

“Our findings highlight for the first time several key turning points in brain activity after stroke. This is critical and helps us explain why some treatments may work and some may not. A stroke can affect any part of the brain, both sexes, and all races at any time. Yet the chemical makeup in the brain varies between regions, between sexes and with age. Our data is being used to try and understand how some of these changes occurs to better tailor drug treatments.”

The data that has been collected during the Hercus Fellowship and from a research grant from Roche highlight a window and populations that could potentially benefit from this treatment.

“We have continued to engage with Hoffman La-Roche around changes in tonic GABA currents after stroke. We have had significant funding from Roche over the past two years to test some of their compounds in parallel with our studies. Following recent discussion with Roche we are pricing studies to try and translate our preclinical findings into a clinical trial, or at least a proof-of-concept translational research grant.”

Professor Chris Pemberton, ‘BNP signal peptide: a novel, specific marker of acute cardiac Injury’, Department of Medicine, University of Otago, Christchurch

Professor Chris Pemberton’s research has resulted in the development of biomarkers for diagnostic use in cardiac and metabolic disorders, and at the time of his final HRC report 5 patents were in process with the first due to be issued at the end of 2011. These formed the basis of a significant commercial portfolio that at the time was being commercialised by Otago Innovation Ltd. In 2013, Professor Pemberton was awarded the Otago Innovation Proof of Concept grant to further develop a unique biomarker test for predicting those at imminent risk of a heart attack.

In 2015, the University of Otago and Powerhouse Ventures Ltd formed Upstream Medical Technologies (UMT) to commercialise the technology developed by the research team at the University of Otago’s Christchurch Heart Institute, which is led by Professor Mark Richards and Associate Professor Chris Pemberton.

In a news article from the University of Otago’s ‘New at Otago’, Colin Dawson, the Chief Operating Officer of Powerhouse Ventures, is quoted as saying: “Our investment is a critical first step for this development and for UMT, a company that has many more innovations it is working on.” “Our investment will fund further refinement of the test and larger clinical trials,

all of which are important and necessary steps in developing the product."\textsuperscript{12} UMT has developed a world-first test to potentially speed up the diagnosis of unstable angina, a serious cardiac condition that is difficult and time consuming for doctors and is a major area of unmet clinical diagnostics.

**Dr Anna Pilbrow, ‘Blood relations: finding circulating biomarkers for inherited heart disease’, Department of Medicine, University of Otago, Christchurch**

Dr Anna Pilbrow’s research exploring how family history contributes to susceptibility to heart disease, has established genomics and proteomics analysis pipelines for the discovery of novel biomarkers which identify genetic susceptibility to heart disease in individuals who do not yet have any symptoms of heart disease. During the tenure of the Fellowship Dr Pilbrow and her team formed a new collaboration with researchers at the National University of Singapore, which has resulted in two new candidate biomarkers for diagnosis or prognosis in heart attack patients. The team was granted a provisional patent, "MicroRNAs as diagnostic and prognostic biomarkers for atherosclerotic conditions".

Building on this, Dr Pilbrow has recently undertaken a study to predict future heart disease events in people without symptoms or previous history of heart disease. She now has preliminary data to show that some microRNAs can predict who is at risk of having a heart attack within the next 12 months.

\textsuperscript{12} Source: http://www.otago.ac.nz/news/news/otago243001.html