2016 ANNUAL REPORT

OTAGO
MEDICAL RESEARCH FOUNDATION

CONTENTS

01 OBJECT OF THE FOUNDATION

CHAIRPERSON'S REPORT 02

03 FUNDS GIVEN

FOUNDATION SUPPORTING ON-GOING SUCCESS 05

07 UNDER THE MICROSCOPE

REPORT FROM THE DIRECTOR OF DEVELOPMENT 08

09 FUNDS RAISED

EVENTS 10

12 CLUB OTAGO

LIST OF MEMBERS 13

14 THE FOUNDATION COUNCIL

SCIENTIFIC COMMITTEE REPORT 17

27 FINANCIAL HIGHLIGHTS

AUDITOR'S REPORT 28

29 INFORMATION ABOUT THE FOUNDATION

OBJECT OF THE FOUNDATION

There is not one person alive today who has not benefitted from medical research.

The Object of the Otago Medical Research Foundation: the furtherance of medical research in Otago.

We fund world class research, equipment and facilities for Otago's highly talented medical community of scientists, students, practitioners and lecturers.

Our recipients contribute invaluable medical knowledge that can be applied to medicine and prevention in the future, and in doing so we also retain top medical talent and intellectual property in Otago.

MEDICAL RESEARCH IS A LIFE CHANGER. YOU'RE A LIFE CHANGER.

The answers unearthed through medical research irrefutably lead to greater quality of life for society – through earlier diagnosis and treatment. Since the Foundation was established in 1967, it has identified and funded close to $8 million worth of grants and scholarships, with much of the work undertaken now acclaimed around the world.

The lives of tens of millions of people have ultimately been improved by the research funded by the Otago Medical Research Foundation, made possible by you, our generous supporters.

IT ALL STARTS SOMEWHERE.

The Foundation helps to fund medical research projects and scholarships which are highly novel and scientifically worthy, but due to their early exploratory nature don't attract the interest of larger funding agencies.

However, in the world of medical research what the Foundation launches cannot be underestimated. Once that initial research has been completed and the answers reported, it often opens up new areas of investigation for bigger entities to develop.

So the research never stops and many of our esteemed alumni are now global leaders in their medical fields.

EVERYONE BENEFITS FROM MEDICAL RESEARCH.

There is not one person who has not benefitted from answers found through medical research. Whether that be personally, through parents or children, partners or siblings, work mates or their friends. We will all know many who wouldn't be with us had it not been for the discoveries made and the earlier diagnosis and less invasive treatment that research unveils.

It is irrefutable that from medical research we all benefit.

Charities Registration Number CC33444

CHAIRPERSON'S REPORT

48TH
ANNUAL REPORT
YEAR
2016

$439,960
Increase of
$41,746
Since 2015

Total amount funded
Since the Foundations inception
$8,061,173

It is with pleasure that I present the 48th Annual Report on the Otago Medical Research Foundation's activities for the 2016 financial year. During the year under review, the Foundation approved Grants totalling $439,960, an increase of $41,746 on last year's total of $398,214. Since the Foundation's inception; $8,061,173 has been spent on Medical Research in Otago.

The extract from the Financial Statements, as published elsewhere in the Annual Report, shows a surplus for the year of $80,903 which is $10,348 less than last year. Although the surplus is less than last year it should be noted that Research Grant expenditure increased by $41,746. As the Foundation endeavours to invest surpluses in project grants rather than build up funds, this is not a bad result, but it would be pleasing if we could obtain further injections of capital for investment to help counter the reduced investment rates that we earn on our conservatively invested funds.

The Investment Sub-Committee has continued to face the challenge of finding suitable low risk investments while acknowledging that income and growth are also important. It is pleasing to report that at balance date, the market value of our Company Securities and Shares shows an unrealised gain on cost of $519,623, which is 11.59% of cost.

At 31 March, 2016, Accumulated General Funds total $523,089, and Accumulated Special Funds $4,427,599, a total of $4,950,688, both these figures comprising Capital and Income.

This year marked the 19th year in which the Otago Community Trust awarded an Annual Grant to the Foundation with the details of grants awarded from this year's funding being published in the Scientific Committee Report. This brings the total grants received from the Otago Community Trust to $1,351,000, a truly generous contribution. On behalf of all members of the Foundation and all Researchers based in Dunedin I would like to sincerely thank the Otago Community Trust for its very generous, and much needed, contributions.

The Foundation is deeply indebted to those people who have named the Foundation as a beneficiary in their wills. Medical research is a never ending activity and the role of the Foundation will continue as long as there are medical scientists willing to ask critical questions and people willing to help fund these researchers in their quest for the vital answers. I would ask members to consider the Foundation when preparing their wills. A bequest to the Foundation will be effectively used and your influence will be felt beyond your lifetime.

Council Membership

At present, Membership of Council remains unchanged from the last Annual Report. However, Mr Richard Bunton is standing down as the representative of the Southern District Health Board and is to be replaced by Mr Nigel Millar. We thank Richard for his contribution to Council since he was welcomed to his first Council meeting on 1 June, 2006 and look forward to welcoming Nigel to his first Council meeting in due course.

Thanks

- Firstly, to all those Trusts, Companies, Individuals, Members and Non–Members listed in this Annual Report who have supported the Foundation in the year under review. The Foundation is very grateful that it has continued to receive the support that it has in these difficult economic times.
- To Steve Davie, our Director of Development, for yet another year of commitment and belief in the work of the Foundation, continuing to raise funds for our work, and, just as important, continuing to raise the profile of the Foundation. The Foundation was exceedingly fortunate when Steve accepted the position of Director of Development and commenced working for the Foundation in 2010. Personally, I am amazed at the new innovations and fundraising activities that Steve comes up with and for A Night to Remember to be a sell-out even before a date is announced is testimony to the regard in which an event run by Steve is held. Steve's report can be found on page 8.
- To my fellow Investment Sub-Committee members, Mike Horne, Ron Lewis and Jenny McMahon for their wise counsel, advice and time so willingly given to serve on this Sub-Committee, I thank you most sincerely.
- On reading through my previous Chairperson's Reports I note that I seem to say almost the same thing each year regarding the Scientific Committee, led by their longstanding and dedicated Chairperson, Associate Professor Patricia Cragg. But it is hard to find new words to express my own, Council's and indeed the Foundation's thanks to this group who continue to find the time to provide professional assessment and advice on applications submitted for funding, so I will just say a huge THANK YOU, your work is greatly appreciated. Without you all we would not be able to achieve the object of the Foundation, "The Furtherance of Medical Research in Otago".
- To all Council Members, for your contribution and support, my sincere thanks for your continued interest in, and work done, for the Foundation.
- To the Deloitte team of Mike Horne, Megan Vintiner, Trudy Corbett and Josh Cumming for continuing to provide very professional, friendly and efficient administration services for the Foundation. Mike and Megan are the face of Deloitte for the Council while Trudy and Josh are the backroom team, ensuring that the Foundation's day to day requirements are completed as required.

The year 2017 marks an important milestone for the Foundation as on 14th March, 1967, a preliminary meeting was held which was for the "Proposed Otago Medical Research Foundation". It will be Council's intention to mark this significant occasion in an appropriate manner.

On behalf of the Council

Ken Dempster

Chairperson

FUNDS GIVEN

OF SCHOLARSHIPS, GRANTS, TRUST GRANTS, LAURENSON GRANTS AND JACK THOMSON GRANTS 1ST SEPTEMBER 2015 – 31ST AUGUST 2016

Summer Scholarships

Cancer
$12,000

Pregnancy
$4,000

Heart
$8,000

Drug Development
$16,000

Gut Heath
$8,000

Aging
$4,000

Asthma
$4,000

Future Health Planning
$8,000

Diabetes
$8,000

Obesity and Nutrition
$8,000

Immune System (Garth McQueen)
$5,000

Dentistry
$8,000

Kidney
$8,000

Neuro /Brain
$13,000

Annual Grants

CANCER	GUT HEALTH	WOUND HEALING	HEART
$25,800	$25,600	$28,000	$23,300

Otago Community Trust

NEURO /BRAIN	CANCER	HEART
$23,350	$23,500	$19,500

Laurenson

DRUG DELIVERY	HEART
$60,149	$29,965

Jack Thomson

OSTEO-ARTHRITIS	NEURO-PATHIC PAIN	DRUG THERAPY
$27,228	$29,121	$16,500

FOUNDATION FUNDING FUELLING RESEARCH INTO KIDNEY DISEASE

Over the years, Professor Rob Walker has been a recipient of 13 Otago Medical Research Foundation grants, totaling over $270,000 and we are delighted he was recently awarded the prestigious Dunedin School of Medicine Dean's Medal for Research Excellence, and the Research Development Investment award.

The Dean's Medal is presented for exceptional and sustained work in research, including research publications in high ranking national and international journals, and also recognises researchers making significant contributions to the Dunedin School of Medicine and the wider Otago University Health Campus research environment.

Prof Walker said the medal recognises the work of many people, not only himself.

"This medal goes to a large number of people that I work with," he says in crediting clinicians, pharmacists, those involved with both national and international trials, and people who worked in laboratories.

"This medal is recognition of all these wonderful people, not just me." he says.

Rob is not only a highly prolific research scientist (an author on 16 academic publications in the past two years alone) but also the Head of the Department of Medicine, a Clinical Nephrologist (kidney specialist) in the Southern DHB and a member of a number of national and international societies engaged in research on kidney function. His research focuses on kidney function and disease, 'bench to bedside', and ranges from studies of kidney development and physiology, to clinical investigations and trialing therapies, to prevention of kidney injury or in determining how to slow the progression of kidney disease.

As a newly qualified doctor, Rob became interested in nephrology from contact with the consultants he worked for in Christchurch, particularly the eminent nephrologist Ross Bailey who was very keen on clinical research.

This interest led to his first publication in 1982, reporting three different families in Christchurch with a form of kidney disease, not previously thought to have any genetic basis. He subsequently collaborated with colleagues in the USA, and from one particularly large family (of that group of three), the actual gene defect was identified.

"So that was a pretty cool progression of science from observation to identification," Rob says.

Kidney disease is frequently called the 'silent killer' because of its gradual and insidious onset. In New Zealand, about one person in 11 has kidney disease with half unaware of their illness.

Kidney and heart function are linked. Consequently, patients with chronic kidney disease have a 3-to-5-fold higher risk of cardiovascular events while diabetic sufferers with chronic kidney disease have up to a 20-fold higher risk of early death. As the population ages and rates of those conditions rise, understanding how the aging kidneys handle and excrete medications is increasingly important.

In a recently published study, supported by a Foundation Laurenson grant, Rob showed that there are currently drug treatment inaccuracies as a result of how kidney function is measured with this potentially a major problem in people with complicating conditions such as diabetes.

In the future Rob's discovery will help inform doctors on how to best prescribe medication for such patients, significantly improving clinical practice and drug effectiveness.

Rob says he has been extremely lucky to have both basic science (laboratory-focused) and clinical research interests and he thinks "it is the opportunity to continue as a clinician scientist that is the greatest part of this".

He reiterated the importance of Foundation funding to his work with pilot studies not funded by large external funding bodies.

"The Otago Medical Research Foundation funding allows focussed studies on key areas of interest and the results of that research can then inform larger funding applications. Without funding from the Foundation, vital research might not be carried out."

UNDER THE MICROSCOPE

Summer Scholarships 2015/16

The Foundation awarded a total of 28 Scholarships for Summer 2015/16. Students carry out ten weeks of research, a few of these fascinating studies have been hand-picked for stories below:

Bad habits not so bad

Although parents are often aghast to find their child biting their nails or sucking their thumbs, there might be a bright side to these unwanted childhood habits.

Using data from the Dunedin Multidisciplinary Health and Development study which has followed the progress of 1037 participants born in 1972-1973 into adulthood, Stephanie Lynch working with Assoc. Prof Bob Hancox in the Department of Preventative and Social Medicine, found that 31% of children were frequent thumb-suckers or nail-biters.

These children who were nail biters or thumb suckers, had a lower risk of allergies at ages 13 and 32; children with both habits had the lowest risk.

Stephanie's results agree with other research in the field indicating that the lack of exposure to bacteria and

other infectious agents can increase allergic diseases and introduction of bacteria into the body by thumb sucking helps develop a child's immune system and decreases the risk of future allergies.

Could this be a cure for bad breath?

Up to 30% of people experience halitosis (bad breath) at some point but for certain people this can be an ongoing problem and have a negative impact on their day to day lives.

The tongue provides a large area for the bacteria that cause halitosis to thrive and it's thought that probiotics could be used to increase the levels of good bacteria in the mouth, like they do in the gut. It has also been shown that tongue brushing can decrease the tongue coating of bacteria and minimise bad breath.

During her summer research project, Fay Yan, working with Prof Richard Cannon in the Faculty of Dentistry, recruited people with halitosis to investigate if taking probiotic (good bacteria) lozenges over four weeks could help to reduce it. Some participants were asked to also carry out tongue brushing to discover if the combination of both interventions could improve breath further.

Measuring volatile sulphur compounds and tongue coating, Fay's analysis showed that four weeks of tongue brushing and/or sucking probiotic lozenges decreased the volunteer's volatile sulphur compound levels by 30%, and in the future could be used to help reduce halitosis.

Warm baths a solution to increasing vein size

For people with kidney failure, dialysis is an important procedure, replacing the kidney's work of removing waste products and excess fluid from the blood. During dialysis, a needle is inserted and blood leaves the body to pass through a dialyser, which filters out the toxins. The process of dialysis needs to happen at least three times a week and good access to the veins of a patient can make a huge difference to dialysis.

An arteriovenous (AV) fistula is formed by surgically connecting an artery to a vein. Over time this connection increases the size of the vein, providing a vascular access with good blood flow, suitable for the repeated needle insertions required for dialysis. The initial vein diameter and the ability of a vein to dilate is important for the formation of a successful AV fistula, and patients with a vein diameter of less than 2mm are rarely considered. Tourniquets are normally used to dilate veins for assessment, however studies have shown that other types of interventions to dilate the vein might be better.

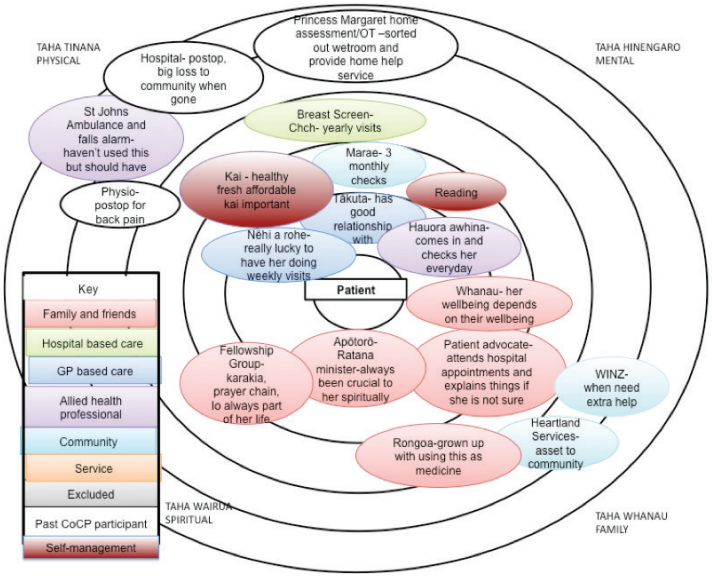
Lauren Smith (Southern Victorian Charitable Trust Scholar), working with Mrs Jo Krysa in the Department of Surgical Sciences, aimed to determine if three different types of interventions were more effective at dilating veins than a tourniquet: warm water bath; warm air; handgrip exercise.

Lauren found that people who put their forearm in a 40°C water bath had the largest vein dilation in the shortest time (10 minutes). For several participants, using the water bath produced a vein dilation required for AV fistula, whereas the current protocol of tourniquet did not.

Lauren's summer project shows that a water bath is a more successful method of veno-dilation and in the future when it is used in clinical practice, more patients will be eligible for AV fistulas, improving their dialysis outcome.

Mapping as a way to understanding people living with diseases

Every day New Zealanders are diagnosed with diseases such as diabetes or asthma. These people normally need life-long support from a lot of places, including the person's family, their GP, the nurse at the practice, a specialist at the hospital or government organizations such as Work and Income. One way of seeing how important all these different things are to the person's wellbeing is by mapping them from interview data. Ursula Poole was the Otago Service Clubs Medical Trust scholar, and with four supervisors from the Department of General Practice and Rural Health, she worked to map what is important to rural people living with life-long diseases. The person is put into the centre of the map. The different sources of care are put into circles that are closer or further away from them to show importance to the person. This project studied what these maps looked like in people living in a small rural town. It found that people with family support, a sense of belonging to the community or who have ways of managing their disease by themselves, felt well looked after. The maps help GPs understand their patients in a broader way and identify gaps in their care.



REPORT FROM THE DIRECTOR OF DEVELOPMENT

I am constantly humbled by the generosity of the growing number of individuals, business and firm owners, chief executives, the gaming machine industry trusts and charities in supporting the Otago Medical Research Foundation and its mission of identifying and establishing world-class, ground-breaking, life-changing research projects and scholarships.

That support lifted again during the last 12 months – as it has each year since the Foundation launched a structured profile and fundraising campaign in early 2010 – with the funds generated through an expanding calendar of events, individual and corporate gifting, bequests, and charity and trust grants accruing almost $4 million in new revenue over that period.

As a result, the Foundation's capacity to set alight the very highest calibre research at a catalyst level is again enhanced. While not every research grant or scholarship creates stellar recognition or uncovers the ultimate answer, the fact that a significant amount of the work instituted by the Foundation is internationally acknowledged, is testament to its value and on-going place in securing a greater quality of life for hundreds of millions of people around the globe.

My thanks to all of our supporters for their tangible show of faith in the Foundation's vision.

The Foundation's calendar of events continues to enthuse with the undoubted highlights being the annual dinner '*A Night to Remember*', the *Club Otago* lunch series and the annual golf tournament. Other functions and concepts through the year included the launch of the *C'mon OTAGO* $1 a point scheme (in association with the Otago Rugby Football Union), a terrific sell-out night with celebrity cook Chelsea Winter and a second successive partnership with the Zonta Club of Metropolitan Dunedin and its *Extraordinary Fashion Show*. The annual movie night for our supporters, featuring the first New Zealand screening of the latest James Bond epic *Spectre* was also a hit.

The Foundation continues to strengthen its partnerships with RD Petroleum in offering a fuel card to supporters and with Payless Energy, which donates funds as residential and business account holders switch their electricity needs. And late in the year we also developed a partnership with accommodation booking site Kiwi Karma.

The Foundation's Bequest Society is also gaining a greater awareness.

The Foundation prides itself on its ability to nurture research which, although highly scientifically worthy, does not attract attention from larger funding bodies. However, without the Foundation showing belief and acting as a stimulus for these grass roots investigations to be established, more in-depth study simply wouldn't occur. Medical research funding from further north is an important contributor to the province's economy and the Foundation's foresight plays a major role in founding that process.

Again my thanks go to all supporters and friends of the Foundation. Your generosity and belief in supporting the terrific work our scientists and researchers undertake cannot be underestimated and is genuinely and gratefully appreciated.

It is irrefutable that from medical research we all benefit.

Steve Davie
Director of Development

FUNDS RAISED

A Night to Remember
$77,013

Golf
$19,179

Community Grants & Donations
$307,686

Club Otago
$70,847

C'mon OTAGO
$7,269

GRANTS AND DONATIONS

A special thank you to our very generous donors who contributed $307,686

Payless Energy
Paper Plus Dunedin
Kingston Sedgfield Charitable Trust
Southern Victorian Charitable Trust
RD Petroleum
Crowe Horwath
Jan Warburton
MM & JH Hughes Family Trust
Otago Service Clubs Medical Trust
Deloitte
Lion Club of Dunedin South
PricewaterhouseCoopers Foundation
Southern Trust
Dr Ailsa Goulding
Dunedin Venues
Kelliher Charitable Trust
Healthcare Otago Charitable Trust
OceanaGold NZ
Zonta Club of Metropolitan Dunedin
JN Lemon Charitable Trust
St Joan's Charitable Trust
Otago Community Trust
William Downie Stewart Charitable Trust
JAD Iverach Memorial Fund
Otago Diabetes Trust
Spec Savers

Figures produced are net values from the End of Year Financial Report to March 31 2016.

EVENTS

A Night to Remember 2016

In Billy Birmingham's best Richie Benaud impersonation – marvellous!

That was the summation after our fourth annual black tie fundraising dinner – *A Night to Remember* –in late-February, which again raised the bar. Such was the success of the night, the 460 seat 2017 event was a sell-out just two weeks after this year's function. *A Night to Remember* is now seen as the best night of entertainment, emotion, story-telling, fine wining and dining, and singing and dancing in Dunedin each year.

More than $87,000 was raised through sponsorships, ticket sales, auction items, the raffle and donations. Funds generated go directly to the Foundation's work of establishing world-class, life-changing medical research in Dunedin... for the benefit of tens of thousands of New Zealanders and hundreds of millions more around the globe.

Our keynote speaker was Australian raconteur and cricket satirist Billy Birmingham, aka The 12th Man. In his first-ever live appearance in New Zealand after 30 years as the 12th Man, Billy brought to life the Channel 9 commentary team of Richie Benaud, Tony Greig and Bill Lawry. His parody of rugby league commentator Ray 'Rabs' Warren and his announcing of the New Zealand rugby league side reduced the audience to tears and there were calls for more at the end of his 45-minute performance.

Also featuring on the night was internationally-acclaimed cellist Heleen du Plessis who played Led Zeppelin and Michael Jackson as we'd never heard them before; Miss World New Zealand, the inspiational Dr Deborah Lambie; and we were also able to acknowledge the presence of Amanda McKewan, who was battling a virulent cancer. The crowd was enthralled and humbled by Amanda's story, all of us shocked to learn she passed away less than three weeks after the dinner.

Shane Cortese and his 8 Track Band, back for a second straight year, had the dance floor packed in a two-hour non-stop grand finale.

This year's naming rights' sponsor was Oyster Executive Recruitment which was joined by OceanaGold NZ and Vero Liability as Associate sponsors, Armstrong Prestige, Forsyth Barr, NZI, QBE, Misha's Vineyard and Crombie Lockwood as supporting partners.

Foundation's annual golf tournament

The annual Otago Medical Research Foundation golf tournament, hosted on the St Clair course in early-October, was played in warm but blustery conditions – with the field of 100 back in the clubhouse less than an hour before a southerly storm hit and the temperature dropped 10 degrees.

Using a twist to the normal ambrose rules – where all players drove from the tee before a dice was thrown to determine which shot would be taken – the tournament was again a popular inclusion in the Foundation's growing calendar of events with just over $19,000 raised on the day.

OceanaGold's naming rights' partnership extended into its fifth year, all 18 holes were sponsored and there was an increase in team entry numbers. The generosity of our sponsors along with a number of individual benefactors and prize donors further cemented the value of the tournament.

The funds generated were directed into a research grant and awarded in May 2016.

Several break-through projects have been established through the $100,000-plus raised since the tournament was first staged in 2010.

Supporting the OceanaGold commitment were our hole sponsors and the Foundation acknowledges their enthusiasm. Our thanks to Bracken Learning, Orbit World Travel, Unichem Mornington Pharmacy and the Mornington Health Centre, Dr Alan Wright, Dr Patrick Dawes, Dr David Peart and Mr Andrew Swan (all Marinoto Clinic), Deloitte, Palmers Mechanical, Sport Otago, Southern Colour Print, Craigs Investment Partners, HSBC, Armstrong Prestige, Stonewood Homes, McDonald's Dunedin, Payless Energy, Agility Logistics and Body Synergy.

Our prize and refreshment sponsors, and others who played a part in the success of the day, are also warmly acknowledged: Dr Brian McMahon, Dr Jenny McMahon, Aravin Estate Central Otago, Valspar New Zealand, Rialto Cinemas (Dunedin), Rockburn Wines, Gardens New World, Craft Bar, Otago Cricket, Stu McCullum (Wilson Staff Golf), Suits on Wall Street and Armstrong Prestige.

There were also a number of team entries and their support was also appreciated: Ken & Liz Dempster, Whatsoever Ltd (Dave Sharp), Lab Supply Ltd (Adam Spurway), Kiel Sheridan, Dean Delaney and Steve Davie's golfing mates who represented the Foundation.

The day's results were:

Closest to the pin – 4th; Alan Carne, 7th; Callum Stringer, 13th; Jamie Adamson, 16th; Kiel Sheridan, novelty hole; Graham Wyllie

Team results:

1st playing off a team handicap of 5.75, net score of 56.25 – Palmers Mechanical

2nd 7.625, 56.375 – OceanaGold # 1

3rd 3.75, 58.25 – Sport Otago

4th 8.625, 59.375 – Craigs Investment Partners

5th 7.25, 59.75 – Gardens New World (on countback)

6th 9.25, 59.75 – Agility Logistics

7th 9, 60 – Dr Alan Wright (Southern Neurology)

8th 6.875, 60.125 – Body Synergy

9th 8.25, 60.75 – Stonewood Homes

CLUB OTAGO

Established in early-2012, Club Otago continues to bring together the very best in speakers, camaraderie and charity.

This lunch club has been enthusiastically embraced by the region's corporate sector and individual enthusiasts alike and is a high profile component of the Foundation's calendar of events.

Four lunches are hosted each year with these featuring the topical speakers of the moment. All funds raised are directed towards the Foundation and its on-going mission of identifying and nurturing world-class medical research in the city.

Tyler Hamilton – May 2015

Tyler Hamilton, a former Tour de France team-mate of Lance Armstrong and a twice-convicted drugs' cheat himself, bared his soul at April's Club Otago lunch.

Hamilton was immersed in depositions hearings against Armstrong, his US Postal Service team and the UCI (cycling's international governing body) and was in New Zealand to speak at a Drug Free Sport New Zealand conference in Auckland. His address in Dunedin to a record Club Otago attendance was his only other official public appearance in the country.

He spoke about riding clean (on 'bread and water') for two and a half years against those boosted by performance-enhancing testosterone and EPO (erythropoietin, a naturally occurring hormone which boosts red blood cell production which was injected into riders' systems); about how he succumbed to his first doping episode in 1997 (taking a 'red egg', aka a testosterone pill) and how his life then spiralled downhill from there.

Governor-General Sir Jerry Mateparae - October 2015

The year's final Club Otago lunch featured the Governor-General Sir Jerry Mateparae as guest speaker – and what an impression he left.

In both addressing an audience of 170 and in answering questions on a variety of topics, Sir Jerry opened his heart to members and guests in a humble, candid 35 minutes on stage.

Sir Jerry spoke about his own values and what he hopes to leave as a legacy from his five years in the role. He then answered a variety of questions, ranging from the work of New Zealand peace-keeping forces around the world ("you only have to look in the children's eyes to see just how valued our forces are"), his own children's reaction to him being the Governor-General to his current reading and music tastes.

His Excellency also discussed what he and Lady Janine would do once his term ended in August 2016– most probably time overseas – but deftly declined to talk about the flag referendum and the ISIS issue.

OUR MEMBERS ARE:

Patrons

Fellow

Allied Press
Carpet Court Dunedin
Crombie Lockwood
Deloitte
Dunedin City Motors
Farmlands Co-operative
Fitzgerald Family Trust
Fulton Hogan
McMahon Investments
Orbit Corporate Travel
RD Petroleum
Stu Stevenson

Associate Fellow

Asteron Life
Body Synergy
Dunedin Casino
Dunedin Airport
Forays Consulting Ltd
Forsyth Barr
Harvie Green Wyatt
HSBC
Immersion Marketing
Jenepher Glover
Kiwibank
Living Corporation
Octagon Dental Suite
Opus International Consultants
Otago Cricket
Otago Orthodontics
Reid, Paterson, Scully, Cassidy syndicate
Richard Joseph & Associates
Sassanachs RFC
Seperex Nutritionals
SF Waller Family Trust
Southern Wide Real Estate
This Way Ltd

Individual

Sarah Anderson (Regent Theatre)
Peter & Paula Anstey (Progressive Plastics)
Martyn Ballantyne, John Larsen (Suits on Wall Street)
Hudson Biggs (Keogh McCormack)
Adam Binns (PRP Barlow Justice Binns Ltd)
Michael Bird (Storesafe Ltd)
Steve Brocklebank (PWC)
Paul Buckner (Downie Stewart)
Dave Callon (Share NZ)
Andrew Campbell (Wattyl NZ)
Andrew Carmody (Brooker Travel)
Bruce Carvell (Williams Signs & Graphix)
Grant Chirnside (Southern Realty)
Garry Clarke (Arbi Monograms)
Malcolm Dore (Magoo Auto Dunedin)
Malcom Farry (Farry Group)
Dr Norman & Mrs Barbara Fitzgerald (NW Fitzgerald Family Trust)
John Freeland (AON, Mosgiel)
Adam Gain (Metro Realty)
Donna Gale (NZI)
Ross Gamble (Roslyn Storage)
Bill Haydon (Roman Catholic Diocese of Dunedin)
Ian Hogg (ANZ Bank, Commercial)
Murray Hughes (Aotea Electric Group)
Sharon Hyndman (Metro Realty)
Dr Rod Keillor (Keillor Opthalmology)
Adam La Hood (Cook Brothers Construction)
Ron Lewis (Craigs Investment Partners)
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Neil & Jamie Lyons (Signature Property Ltd)
Amy McFadzien (Cook North & Wong)
Stuart McLauchlan (GS McLauchlan & Co)
Mr Will McMillan (McMillan Medical Specialist)
Dave McPhedran (YBT)
Bill Marshall (ASB Commercial)
Nadene Moore (International Freight Logistics)
Alan Nicholls
Simon Parker (Parker Warburton Team Architecture)
Mike Pearce (Strawberry Sound)
Russell Quin (Quintessentially Financial Services)
Jules Radich (ActionCOACH)
Richard Roberts (Dunedin Airport)
Sergio Salis (London Street Specialists)
Sarah Saunderson-Warner (Barrister & Solicitor)
Dr Michael Schultz (Gastroenterology Otago Ltd)
Carl Spruyt (10X)
Justin & Eterei Stonelake (McDonald's Dunedin)
Peter Taylor (Peter J Taylor & Associates)
Dr Paul Templer (Sandman Anaesthesia Services)
Mark Thompson (Thompson Accounting)
Barry Timmings (Timmings Partners)
Chris Timms (Craigs Investment Partners)
Michael Turner (Polson Higgs)
Sherman Weatherall (Agility Logistics)
Tom West (Tom West Risk Advisors Ltd)
John White (Telfer Electrical Otago Ltd)

THE OTAGO MEDICAL RESEARCH FOUNDATION COUNCIL

Professor Barry Taylor
Dean Dunedin School of Medicine
ex-officio

Assoc Prof P A Cragg
Chairperson of Scientific Committee
ex-officio

Mr M C Horne
Deloitte (Secretaries)
ex-officio

Prof A van Rij
Otago University Faculty of Medicine

Dr P Gootjes
N.Z. Medical Association (Otago Division)

Mrs. Sarah Ramsay
Co-opted

Assoc Prof Greg Jones
Co-opted

Prof Vernon Ward
Dean of the Otago School of Medical Sciences

Prof J Highton
General Medical Staff, Otago District Health Board

Mr R Bunton
Otago District Health Board

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Deloitte representative - Secretary/ Treasurer

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Assoc Prof P A Cragg - Chairperson

Physiology Department, Otago Medical School

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Mr Steve Davie

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(Gallaway Cook Allan)

AUDITORS

Crowe Horwath

PATRON

Emeritus Professor Gil Barbezat

BEHIND THE FOUNDATION

Pat Cragg is a very busy woman.

In addition to being an Associate Professor in the Physiology Department, the Divisional Associate Dean (Academic) of Health Sciences and the Deputy Dean of the Otago School of Medical Sciences, she also has professional affiliations with more than 10 societies, and this impressive list doesn't even come close to covering all the invaluable work she does for the Otago Medical Research Foundation.

Pat's interest in biological sciences began in school, leading her to major in Zoology at the University of Bristol. After finishing her degree, Pat knew she wanted to continue studying and she completed a PhD in comparative anatomy and physiology. In 1976, Pat moved to New Zealand and the University of Otago to take up a teaching fellow position in the Department of Physiology, becoming a lecturer in 1979, senior lecturer in 1984 and the Head of Department in 2001. Pat's research interests include both cardiac and respiratory physiology, and she is the author of numerous journal articles and book chapters in these areas.

Pat recognises the importance of training new generations of researchers and has been involved in supervising more than 40 post graduate students. Her involvement in cultivating research is also evident from all the work she does for the Foundation which she joined in 1989, both as a Councillor and as a member of the Scientific Committee of which she became chair three years later.

Pat says she regards this position as an "honour", and although it takes up a significant amount of her time, she says it is extremely worthwhile and, importantly, keeps her up to date with research being carried out in the university.

The Scientific Committee comprises individuals from different university departments, providing a good mix of scientific expertise. Pat says the Foundation isn't short sighted about research, understanding that clinical projects can be equally important as epidemiological or molecular projects. It is also a high priority for the committee to evaluate how projects fit with the sub-sponsors. The Otago Community Trust is a good example of this, as it is keen for its funding to be spent in Otago and provide salaries to people living within the area. So when reading applications, the committee bears this in mind.

Pat is pleased the Foundation recognised the need to enhance its public profile and increase its funding stream, and says Steve Davie (Director of Development) has done a superb job in creating an awareness and in raising funds. She is proud to be part of the Foundation and is excited to see how it continues to progress in the future.

The Foundation is extremely grateful to Pat for all her hard work and in recognition of her contribution, the Council last year announced that the best Summer Research Scholarship presentation awarded by the Foundation at the Otago Medical School Research Society would be named The Pat Cragg Prize in perpetuity.

LIST OF MEMBERS

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SCIENTIFIC COMMITTEE REPORT

1 September 2015 to 30 June 2016

1. MEMBERSHIP

Chair: Associate Professor Pat Cragg
(Nominee of the Otago School of Medical Sciences)

Deputy Chair: Associate Professor Greg Jones
(Co-opted)

Dr Andrew Bahn
(2016 Nominee Otago Medical School Research Society)

Dr Chris Brown
(Co-opted)

Dr Heather Cunliffe
(Co-opted)

Dr Peter Gootjes
(Nominee Otago Branch of the NZ Medical Association)

Associate Professor Bob Hancox
(Nominee Dunedin School of Medicine)

Dr Nick Heng
(Co-opted)

Associate Professor Gill Johnson
(Co-opted)

Dr Reuben Johnson
(2015 Nominee Otago Medical School Research Society)

Dr Joanna Kirman
(Co-opted)

Associate Professor Beulah Leitch
(Co-opted)

Associate Professor Russell Poulter
(Co-opted)

Associate Professor Ivan Sammut
(Co-opted)

Dr Damian Scarf
(Co-opted)

Dr Jon Schemmell
(2016 Nominee Otago Medical School Research Society)

Dr Paula Skidmore
(2015 Nominee Otago Medical School Research Society)

Associate Professor Joel Tyndall
(President Otago Medical School Research Society)

Professor Rob Walker
(Co-opted)

The Scientific Committee is primarily concerned with adjudicating on applications for Research Grants and on applications from students for Summer Research Scholarships. To cover the breadth of topics submitted, the committee is relatively large to ensure it has representatives from all the major sub-disciplines of medical research.

At the end of 2015 or end of March 2016 there were four retirements from the committee: Dr Reuben Johnson, Associate Professor Beulah Leitch, Associate Professor Russell Poulter and Dr Paula Skidmore who joined the committee, respectively, in March 2015, 2007, 2006 and 2009. All have provided excellent input to our deliberations and in particular we thank the latter three for 9, 10 and 7 years of exceptional service. For 2016 we welcome Dr Chris Brown and Dr Joanna Williams as co-opted members from the University of Otago representing the Departments of Biochemistry and Anatomy, respectively, and Dr Andrew Bahn and Dr Jon Schemmell as nominees of the Otago Medical School Research Society.

Note: Most, but not all research projects, have protocols that require approval by the appropriate Ethics or Safety Committee prior to commencement of the research. Agreement by the Foundation to fund research projects is thus subject to receipt by the Chair of the Scientific Committee of a letter from the University of Otago's Animal Ethics Committee, Human Ethics Committee or Human Ethics Committee (Health) (or the Ethics Committee of a Health Funding Authority) indicating that the research has received full ethical approval. Work involving genetically modified organisms requires evidence of approval from ERMA or from the University of Otago's Institutional Biological Safety Committee.

The scientific activities of the Foundation (advertising of up-coming grants and listings of awards) can be found on the following web site http://www.omrf.org.nz

2. SUMMER RESEARCH SCHOLARSHIPS 2015/2016

One hundred and ten applications (compared with 113 the previous year) for an OMRF summer research scholarship were received from the University of Otago in late August 2015, of which 28 (cf 22 last year) were recommended for funding by the OMRF (and at least 65 of the other applicants gained scholarships from other funding bodies or the Division of Health Sciences and its Schools or departments). Of the 28 students funded by the OMRF, five were studying biomedical science, four dentistry, twelve medicine, one pharmacy and six science. It should be noted that the ten-week summer research is not part of the study required in a student's tertiary qualification and any data obtained during the summer research cannot contribute to the dissertation or thesis of such a qualification.

Each scholarship was worth $4,000 except for the two students with the highest scores who were awarded named Summer Research Scholarships ($5,000) – named in honour of the late Allan Wilkinson and the late Emeritus Professor Garth McQueen. Allan was Secretary of the Foundation from its inception in 1967 until his retirement in 1993 and Garth was a foundation member of the Foundation and one of the instigators of the formation of the Foundation's Auxiliary. One of the projects was funded from the Foundation's Iverach Fund and another was administered by the OMRF but sponsored by the Otago Diabetes Research Trust.

Due to the continuing sponsorship drive of the OMRF, all the other 24 OMRF scholarships were funded by: Ailsa Goulding, Crowe Horwath, Deloitte, Healthcare Otago Charitable Trust, Hughes Family Trust, International Freight Logistics NZ Ltd, Jan Warburton, Kelliher Charitable Trust (2), Kingston Sedgfield Charitable Trust, Lions Club of Dunedin South, Otago Service Clubs Medical Trust, Paper Plus Dunedin, PricewaterhouseCoopers Foundation, Southern Trust (2) and Southern Victorian Charitable Trust (5). The involvement of Otago commercial companies and the Otago community for a fifth year in supporting summer research by tertiary students is much appreciated.

All scholars returned good to excellent reports by the end of February 2015. The **Renshaw Prize** ($250) for the best report was awarded this year to two students: **Nigaah Khan**, who worked under the guidance of Dr Jeff Erickson of the Department of Physiology, and **Isabelle van Hout** under the guidance of Associate Professor Grant Butt of the Department of Physiology and Associate Professor Michael Schultz of the Department of Medicine.

The following is a list of the summer scholars and summaries of the projects undertaken – additional information on these projects can be obtained from the Chair of the OMRF Scientific Committee or from the supervisor concerned.

NIGAAH KHAN (Dr Jeff Erickson, Department of Physiology, Otago School of Medical Sciences)

Title: Effects of stress signaling on a key cardiac signaling protein in the diabetic heart

(Otago Diabetes Research Trust Scholar and Renshaw Prize Winner)

Diabetes Mellitus (DM) is a highly prevalent disease which can result in cardiovascular outcomes that may be fatal. CaMKII is a protein that shows increased activity in DM-associated cardiovascular outcomes and in response to *a*-adrenergic receptor (*a*-ADR) stimulus. It can increase and decrease activity of downstream proteins that are involved in the normal contraction and relaxation of the heart. Our aim was to determine whether *a*-ADR stimulus in the presence or absence of CaMKII contributes to the cardiovascular pathology seen in DM. Our results show that heart rate is lower in DM hearts but can be increased by CaMKII inhibition, CaMKII is needed for a response to *a*-ADR stimulus, and that CaMKII may be overexpressed in DM hearts as inhibiting it showed a normal response to *a*-ADR stimulus in DM hearts.

ISABELLE van HOUT (Associate Professor Grant Butt, Department of Physiology, Otago School of Medical Sciences, and Associate Professor Michael Schultz, Department of Medicine, Dunedin School of Medicine)

Title: The effects of bacteria on colonic cell division and cell death

(Southern Victorian Charitable Trust Scholar and Renshaw Prize Winner)

The colon is home to trillions of bacteria, which are prevented from entering the body by the epithelial lining that forms a physical barrier. The barrier is constantly renewed, with a balance between cell proliferation and cell death maintaining its normal structure. Consequently, alterations in either cell proliferation or death can affect the barrier function and allow bacteria to enter the body. This can result in inflammation, leading to pathologies such as Inflammatory Bowel Disease. Here human colonic organoids, an *in vitro* model of the colonic epithelium, have been used to investigate the impact of growth factors and bacteria on the rate of proliferation and cell death in the epithelium. This will help us to better understand how the cellular proliferation and death is controlled in the colon.

CARA ADOLPH (Professor Catherine Day and Dr Anita Dunbier, Department of Biochemistry, Otago School of Medical Sciences)

Title: Investigating the role of two proteins (Arkadia and RNF12) in breast cancer

(MM & JH Hughes Family Trust (Cancer) Scholar)

The purpose of this project was to knockdown the expression of two proteins, Arkadia and RNF12, in breast cancer cells. These proteins are of interest as they enhance the activity of a molecular pathway that promotes metastasis, the main cause of mortality in breast cancer. Knockdown was achieved using shRNA which cause degradation of the target mRNA and hence reduce the overall level of the protein in the cell. Five different shRNA constructs targeting Arkadia and three different constructs targeting RNF12 were tested to determine which was the most effective at reducing the expression of each gene. The best constructs gave 40 and 60 % knockdown of Arkadia and RNF12, respectively, at the mRNA level. These findings will allow the use of these shRNA in future investigations to determine how important these proteins are in metastasis and other breast cancer cell behavior.

BETH DENNIE (Associate Professor Colin Brown, Department of Physiology, Otago School of Medical Sciences)

Title: Receptor expression in hormonal related brain cells in pregnancy and breast feeding

(Crowe Horwath Scholar)

Certain brain cells have been shown to change their signalling activity to other brain cells during pregnancy and breast feeding. A molecule called kisspeptin is thought to be the main factor in causing these changes. We looked to see if these brain cells expressed a certain receptor and whether this was increased during pregnancy and breast feeding, to show a mechanism of how kisspeptin could cause the changes seen in these brain cells. We used the brains of female mice either non-pregnant, pregnant or breast feeding and stained for the brain cells and secondly for the receptor. We found that these brain cells did express this receptor however there wasn't an increase in its expression during pregnancy and breast feeding.

This suggests that kisspeptin may be acting via another receptor or via a larger pathway via other cells to cause the changes seen in pregnancy and breast feeding.

SOPHIE GANDHI (Dr Rajesh Katare, Department of Physiology, Otago School of Medical Sciences)

Title: Micro-molecules mediate cell-to-cell communication within the heart

(International Freight Logistics NZ Ltd Scholar)

Following a heart attack it has been observed that the amount of certain small molecules, termed microRNAs (miRs) is altered in the heart. One such molecule, known as miR-34a, has been shown to increase in the heart and blood. Release of miRs is speculated to be a mechanism of communication between different cells. In this study, we measured the effect of miR-34a released from cardiomyocytes (HL-1) on cardiac stem cells (CSCs). CSCs and HL-1 cells under high glucose stress (20 mM) were found to release more miR-34a into the media than in normal glucose conditions. Following treatment of CSCs with the conditioned media we observed no significant change in miR-34a within the cells, cell death or cell replication. However, the CSCs demonstrated reduced expression of senescence marker when treated with 20 mM glucose media or 30 mM HL-1 conditioned media suggesting high concentrations of glucose reduces the senescence characteristic of the cells (i.e. an inability to replicate).

DANYON GRAHAM (Associate Professor Brian Monk, Department of Oral Sciences, School of Dentistry and Dr Rajni Wilson, Faculty of Dentistry)

Title: The molecular basis of triazole inhibition of an antifungal target

(Healthcare Otago Charitable Trust Scholar)

Mutations in yeast lanosterol 14*a*-demethylase (Erg 11p) can reduce the susceptibility of pathogenic fungi to the well-tolerated and widely-used triazole drugs, limiting therapeutic options. A *Saccharomyces cerevisiae* hyperexpression system was used to investigate the effects of two common, clinically relevant mutations (Yl40H and I1471T) in Ergllp. Cell-based and molecular analysis revealed that the Y l40H + I1471T double mutation conferred resistance to short-tailed but not medium or long-tailed azoles. The chemistry of the linkage between the haem-bound triazole head group and the rest of the drug, together with a medium length tail, may stabilise the drug in the binding cavity and limit the desensitising effect of the double mutation. Improved design of medium tailed azole drugs may lead to a new generation of antifungals that will circumvent the resistance problem.

SHIRLEY KIM (Dr Kristen Coppell, Department of Medicine, and Dr Kristen Kenrick, Department of General Practice & Rural Health, Dunedin School of Medicine)

Title: Has coeliac disease become more common in the Otago region between 1981 and 2010?

(JA Iverach Scholar)

Coeliac disease (CD), an increasingly common disorder, is a chronic small bowel gut disease precipitated by eating dietary gluten. Over the last 50 years, the incidence of CD has increased worldwide. The changing epidemiology of CD in NZ has not been well documented. The aim of this study was to describe the characteristics of CD in the Otago population from 1981 to 2010. A list of possible CD cases was obtained from multiple databases at Dunedin Hospital. Diagnosis was confirmed by checking small bowel biopsy results. Lists for each year were incomplete, except 2005. For this year the age-standardised incidence rate was 16.8 per 100,000 persons, which was higher than reports from Canterbury, the UK and Italy at a similar time, suggesting the incidence of CD in Otago has increased. Practitioners must consider the diagnosis of CD in patients seen with varying presentations.

NAVNEET LAL (Associate Professor Phil Sheard, Department of Physiology, Otago School of Medical Sciences, and Dr Tania Slatter, Department of Pathology, Dunedin School of Medicine)

Title: Examination of the processes involved in human muscle fibre death

(Deloitte Scholar)

Muscular weakness is a hallmark of aging and occurs through loss of skeletal muscle mass, by loss of muscle cells (myofibres; myofibre death) or by a reduction in their diameters (myofibre atrophy). Dying myofibres were only recently discovered by our lab, in mice, and appeared strikingly similar to myofibres in diseases where autophagy (process of self-eating to remove damaged proteins) had become insufficient. Here, I aimed to describe changes in autophagy within dying human myofibres and whether autophagy was effective, by quantifying the autophagic substrate, p62. I also compared these results with my findings from murine models. Consistent with previous findings, autophagic activity was increased in dying versus normal myofibres. However, p62 was not elevated, but accumulated within identical autophagic structures, in similar proportions, as those identified in dying mouse myofibres. These results suggest that autophagic dysfunction in human myofibres occurs in the same autophagic structures as dying mouse myofibres.

STEPHANIE LYNCH (Associate Professor Bob Hancox, Department of Preventive & Social Medicine)

Title: Is there a relationship between nail biting and/or thumb sucking and the development of asthma?

(Kelliher Charitable Trust Scholar)

The Hygiene Hypothesis suggests that exposure to bacteria decreases the risk of allergies. Childhood thumb-sucking and nail-biting introduce bacteria into the mouth. It is not known whether these habits influence allergy development. Using data from the Dunedin Multidisciplinary Health and Development Study we assessed whether children who sucked their thumbs or bit their nails were less likely to have allergies and asthma when they grew up. We found that 31% of children were frequent thumb-suckers or nail-biters. These children had a lower risk of allergy at ages 13 and 32; children with both habits had the lowest risk. Thumb-sucking and nail-biting were not associated with asthma at either age. These findings show that thumb-sucking and nail-biting are associated with a lower risk of allergy.

SIMONETTE MALLARD (Associate Professor Lisa Houghton and Professor Rosalind Gibson, Department of Human Nutrition, Division of Sciences, and Andrew Gray, Department of Preventive & Social Medicine)

Title: The nutritional adequacy of the diets of HIV-exposed and -unexposed infants in urban Zambia in relation to subsequent growth

(Jan Warburton (Nutrition) Scholar)

Dietary diversity, defined as the number of food groups consumed, is used by the WHO as a proxy measure of the adequacy of vitamin and mineral intakes in the monitoring of infant feeding. However, the relationship between dietary diversity and vitamin and mineral adequacy may have weakened with the growing popularity of fortified infant foods. We assessed whether dietary diversity was associated with vitamin and mineral adequacy in HIV-exposed and -unexposed Zambian infants at 6 months of age, and also whether dietary diversity and vitamin and mineral adequacy were linked to growth to 18 months. Consumption of iron-rich, fortified, animal-source, and dairy foods showed better correlation with vitamin and mineral adequacy than did dietary diversity. Nonetheless, dietary diversity had a positive effect on subsequent growth in height that was separate to that

of vitamin and mineral adequacy, warranting its continued monitoring and further investigation into the mechanisms underlying this finding.

ERIN McKERGOW (Dr Lianne Parkin, Department of Preventive & Social Medicine, and Dr Ben Wheeler, Department of Medicine, Dunedin School of Medicine)

Title: Patterns of insulin pump utilisation in New Zealand: A population-based study

(Kelliher Charitable Trust Scholar)

Type 1 Diabetes Mellitus (T1DM) is lifelong disease requiring insulin delivered by injection or a pump. Some patients find pumps more convenient and blood glucose levels may be better controlled, reducing the risk of complications. PHARMAC has funded pumps since 2012, but there has been no research into the impact this has had on pump use. Our aim was to estimate the proportion of New Zealand patients with T1DM who used pumps in the years 2012 to 2014, overall, and according to patient demographic characteristics and region. Proportions were calculated using anonymised patient information provided by the Ministry of Health. Pump use increased annually, with almost 10% of patients using a pump by 2014. The greatest increases were seen among females, children, New Zealand Europeans, higher socioeconomic groups, and in some specific regions. We conclude that here are demographic and regional disparities in pump use which require further investigation.

JAMES NEVILLE (Dr Euan Rodger and Professor Ian Morison, Department of Pathology, Dunedin School of Medicine)

Title: Investigating gene expression changes in a family with an inversion on chromosome 5 associated with myelodysplastic syndrome

(Kinston Sedgfield Charitable Trust Scholar)

Myelodysplastic syndrome (MDS) is a set of cancer like conditions within the blood, the severity of which can range from anaemia to an impaired immune system. The aim of this research was to investigate possible genes involved in the development of MDS using a family with a predisposing genetic abnormality. We predicted that one or more of the genes around this abnormality would be affected and display abnormal levels within blood cells. In order to investigate this we separated the blood into neutrophils and other white blood cells. These were broken down and specific candidate gene expression levels within the cell were measured using a technique called RT-qPCR. Specific primers were designed and evaluated prior to being used to investigate the family's neutrophils and white blood cells. No significant results were obtained from this analysis.

MATTHEW PAGE (Dr Emma Wyeth, Department of Preventive & Social Medicine, and Professor Rob Walker, Department of Medicine, Dunedin School of Medicine)

Title: The accuracy of ethnicity data reporting

(Lions Club of Dunedin South Scholar)

Differing methods and inaccuracies of ethnicity data collection pose issues for planning and provision of healthcare and monitoring of health outcomes for various ethnic groups. This study used self-reported ethnicity data collected in the 'Dialysis Outcomes in those aged ≥65years' (DOS65+) study, to investigate the accuracy of two other sources of ethnicity data: the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), and DOS65+ participants' clinical records. This study found high levels of agreement between self-reported ethnicity in DOS65+ and ethnicity recorded in both ANZDATA and clinical records. This has positive implications for future health planning and analyses.

URSULA POOLE (Dr Martyn Williamson and Dr Jim Ross, Department of General Practice & Rural Health, Dunedin School of Medicine)

Title: Mapping what is important to rural people with long-term diseases

(Otago Service Clubs Medical Trust Scholar)

Everyday New Zealanders are diagnosed with diseases such as diabetes or asthma. These diseases normally need life-long support from a lot of places, including the person's family, their GP, the nurse at the practice, a specialist at the hospital, organisations like the Blind Foundation or Work and Income. One way of seeing how important all these different things are to the person's wellbeing is by mapping them from an interview. The person is put into the centre of the map. The different sources of care are put into circles which can be closer or further away from them. This project studied what these maps looked like in people living in a small rural town. It found that people with family support, a sense of belonging to the community or who have ways of managing their disease by themselves, felt well looked after. The maps help GPs understand their patients in a broader way and identify gaps in their care.

BHAMINI RANGNEKAR (Dr Shyamal Das, School of Pharmacy)

Title: Inhalable multi-drug powder for treating pulmonary tuberculosis

(Paper Plus Dunedin Scholar)

The aim was to create a formulation for tuberculosis that infected the lungs. Pyrazinamide and moxifloxacin hydrochloride were combined to create a powder that could be inhaled. These drugs were aided by two excipients, L-leucine and 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine. The powders were created using the BUCHI B-290 Mini Spray-dryer which produces the dry powder from a solution by continuously spraying the solution into smaller droplets followed by drying. An *in vitro* lung model called the next generation impactor was used to test the ability of the powders to reach the deeper lung. The results showed that after spray-drying the particles are spherical in shape with a size of <5 µm indicating suitability for deep lung delivery. The powder composed of both the drugs and 10% L-leucine showed effective delivery with approximately 70% of the inhaled drug reaching to the deeper regions of the lung.

DARREN RITCHIE (Professor Barry Taylor, Dr Gloria Dainty and Associate Professor David Reith, Department of Women's & Children's Health, Dunedin School of Medicine)

Title: The value of a childhood obesity assessment tool

(Dr Alisa Goulding Scholar)

New Zealand is facing a childhood obesity epidemic, with approximately 33% of children being classified as overweight or obese. This is a significant public health issue due to obesity being a major determinant of childhood health, quality of life, and well-being. However, despite the evidence concerning the outcomes of childhood obesity, there has been a lack of research into tools that support appropriate assessment and management as part of routine care. Our research tested the value of such a tool developed in Dunedin. We found that our tool leads to an improvement in the completeness of assessment in over half of the categories we tested against. Additionally, our research suggests improvement in the patterns of lab-test ordering, and clinical management, which may have additional benefit. This is an important finding as it shows that standardised tools have a role in supporting the high quality assessment and management of childhood obesity.

CHANTELLE ROSSOUW (Professor Mauro Farella and Dr Joseph Antoun, Department of Oral Sciences, School of Dentistry, and Associate Professor Tony Merriman, Department of Biochemistry, Otago School of Medical Sciences)

Title: Finding the genes that cause open bite of the teeth

(Southern Trust Scholar)

The purpose of this study was to investigate the association between anterior open bites (AOBs) and genetic factors and to determine the facial traits of AOB patients. Nineteen AOB patients and 73 control patients were identified using radiographic tracing techniques. DNA was then extracted from existing blood samples of each patient and genetic analysis was completed on the growth hormone receptor (GHR) gene. A significant preliminary association between AOBs and the GHR gene was discovered from the genetic analysis. Further, it was found that the gonial angle and overbite depth indicator were characteristic facial traits of open-bite patients. Although individual facial traits are the result of many small underlying factors, a significant association between such AOB cases and the GHR gene may provide predictive measures for such patients in the future.

SARAH SANDFORD (Dr Joanna Kirman, Department of Microbiology & Immunology, Otago School of Medical Sciences)

Title: Which lung immune cell subsets activate mycobacteria-specific adaptive immune responses?

(Garth McQueen Scholar)

Tuberculosis (TB) is the leading cause of death by an infectious agent *(Mycobacterium tuberculosis)*. Understanding the immune response following infection is essential to develop new immunemodulating treatments. Dendritic cells (DCs) activate important cells to initiate immune control of TB infection. There are many different DC subtypes and little is known about their role in the early response to TB. The aim of this project was to establish a method to detect whether DCs infected with mycobacteria (a model for TB) could activate other immune cells (T cells). DCs isolated from infected lungs were cultured in the laboratory with T cells, and activation and proliferation of T cells were measured by flow cytometry. We found that DCs isolated 7 and 14 days after infection cause T cell activation and proliferation, and therefore we can use this method to determine which DC subset activates T cells after TB infection.

BRIAN SHIN (Dr Andrew Bahn, Department of Physiology, Otago School of Medical Sciences)

Title: Is the onset of type-2 diabetes the result of iron-dependent cell death due to high plasma uric acid levels?

(Southern Trust Scholar)

Insulin producing pancreatic P-cell death and dysfunction are hallmarks of type 1 and 2 diabetes. Studies show circulating urate level is high (hyperuricemia) in people with diabetes. It has been observed that hyperuricemia alone can cause pancreatic P-cell death, but exact cell death pathways involved are unknown. Therefore, our project aimed to observe if the novel cell-death pathway, ferroptosis, is involved in hyperuricemia-induced human pancreatic P-cell death while exploring the involvement of other novel cell-death pathways such as necroptosis. We found hyperuricemia induced significant cell death but use of ferroptosis and necroptosis inhibitors did not significantly rescue the cells from cell death. Therefore the cell death pathways of ferroptosis and necroptosis may not be directly linked to hyperuricemia-induced pancreatic P-cell death.

LAVAN SIVARAJA (Dr Heather Brooks and Dr Michelle McConnell, Department of Microbiology & Immunology, Otago School of Medical Sciences)

Title: Does the probiotic Infloran inhibit growth of harmful gut bacteria through acid production?

(Southern Victorian Charitable Trust Scholar)

Necrotising enterocolitis (NEC) is one of the most common and severe diseases in low birth-weight, preterm infants. It is believed to be caused by certain commensal gut bacteria which have become harmful due to the absence of probiotic bacteria. In Dunedin Hospital, the probiotic Infloran is used as prophylactic for NEC. This study aimed to investigate the action of Infloran on the bacteria that are involved in NEC. It was hypothesised that Infloran creates an acidic environment that inhibits the growth of NEC bacteria. The bacteria were cultured alone and together with Infloran in PreNan formula milk and the growth was measured over 24 hours. The results showed a significantly decreased growth in the presence of Infloran and significantly increased growth in the absence of Infloran. Also a change in pH was detected. In conclusion, Infloran does inhibit the growth of bacteria caused by NEC, and acid production is a likely mode of inhibition. Further investigation is required to fully understand the mechanism of inhibition.

AIMEE SMITH (Professor Cliff Abraham, Department of Psychology, Division of Sciences, and Dr Joanna Williams, Department of Anatomy, Otago School of Medical Sciences)

Title: Understanding enzymes to find Alzheimer's cure

(Southern Victorian Charitable Trust Scholar)

Stable memories require the creation of new proteins to strengthen neuronal connections in the brain. In healthy brains, histone deacetylase enzymes (HDACs) regulate this process to stop the memory system becoming overloaded, but an abnormal increase in HDAC activity has been linked to disorders like Alzheimer disease. Researchers seeking a cure for Alzheimer's need to understand how, and when, HDACs are at work. We used immunohistochemistry to investigate HDAC activity, by looking at the level of histone acetylation, 12 hours after a learning event. Interestingly, despite successful learning in the test group, we did not find a difference in histone acetylation between groups, despite prior evidence that HDACs are more active at this time point. This suggests that other enzymes may be activated to stabilise histone acetylation. Further studies are needed to understand the complex inter-relationships between these molecules as memories stabilise over time.

LAUREN SMITH (Dr Jo Krysa, Department of Surgical Sciences, Dunedin School of Medicine)

Title: Vein dilation mechanisms to improve prediction of vein suitability for arteriovenous fistula

(Southern Victorian Charitable Trust Scholar)

Arteriovenous (AV) fistula, formed by connecting a vein to an artery, allows vascular access for haemodialysis in patients with kidney failure. Vein suitability is determined by a patient's vein diameter and ability to dilate. This project aimed to determine whether 1) warm water bath, 2) warm air, or 3) handgrip exercise, was most efficient at dilating the cephalic vein, compared to current practice in the Otago Vascular Lab which is a tourniquet. The warm water bath was the most efficient and effective mechanism, and caused the highest percentage of participants to reach the threshold diameter of 3 mm. If used in clinical practice to measure vein suitability before surgery, the results suggest it would increase the number of patients put forward for AV fistula. AV fistula has a lower rate of complications than other forms of haemodialysis

therefore the warm water bath could improve overall outcomes if these patients go on to form successful fistulae.

ROBERT SMITH (Dr Bill Hawkins Department of Chemistry, Division of Sciences, and Professor Parry Guilford, Department of Biochemistry, Otago School of Medical Sciences)

Title: Synthesis of possible anticancer compounds

(PricewaterhousCoopers Foundation Scholar)

The E-cadherin protein acts as a tumour suppressant, the down regulation of which has been associated with the formation of metastatic cancers. The treatment options for these cancers are currently limited and the development of selective treatments is difficult due to the lack of a clearly defined intracellular target. Work by Professor Parry Guildford's research group has identified several compounds *via* a high throughput screen that selectively target E- cadherin deficient tumour cells. Synthesis and biological evaluation of analogues of a specific compound was performed during the summer scholarship. The information gathered will aid in the development of a chemotherapeutic agent selective for E-cadherin deficient tumours.

ANNAMARIE van WICHEN (Dr Erwin Lamping and Dr Hi Ji Lee, Department of Oral Sciences, School of Dentistry)

Title: Understanding the structure of the multidrug efflux pump Cdrlp in the fungal pathogen Candida albicans

(Southern Victorian Charitable Trust Scholar)

Over-expression of the model fungal multidrug efflux pump Cdrlp, found in the major opportunistic fungal pathogen *Candida albicans*, causes multidrug resistance. This has the potential for serious consequences such as prolonged treatment or even death for the infected patient. The aim of this project was to determine whether we could employ the novel NanoBRET™ technology developed by Promega Corporation, Wisconsin, USA, to investigate possible homo-dimerisation of Cdrlp in live cells. For this purpose we created a genetically modified yeast strain that over-expressed Cdrlp to which a NanoBRET molecule was physically linked. The results from these experiments confirmed, for the first time, that the highly sensitive and robust NanoBRET technology could be used in yeast cells. We also confirmed that Cdrlp function was not significantly altered by the NanoBRET extension. We can now proceed to investigate Cdrlp homo-dimerisation in live yeast cells.

FAY YAN (Professor Richard Cannon, Dr Li Mei and Professor Mauro Farella, Department of Oral Sciences, School of Dentistry)

Title: Overcoming bad breath with good bacteria

(OMRF Scholar)

Bad breath is a significant social stigma for many people. Good bacteria called probiotic have been used to treat diseases in the mouth like tooth decay. The tongue's rough surface provides a large area on which bad breath-generating bacteria can live. Tongue brushing can reduce bacteria on the tongue. The purpose of this study was to investigate the effect of tongue brushing and /or taking lozenges of good bacteria on reducing bad breath. Volunteers (35) either did tongue brushing and/or took good bacteria lozenges or nothing for 4 weeks. Various measures of bad breath were recorded 3 times (at the start, after 4 weeks and after 8 weeks). Bad breath was reduced by 31% 26% or 30% in the groups using tongue brushing, probiotic or the combined treatment, respectively. Our preliminary results suggest that tongue brushing and/or use of good bacteria may reduce the level of bad breath.

JADE YIP

(Dr Stephanie Hughes, Department of Biochemistry, Otago School of Medical Sciences)

Title: The effect of drug therapy on brain pathology in the mouse model for Batten disease

(Allan Wilkinson Scholar)

Batten disease is a group of lysosomal storage disorders that result in visual impairment, loss in cognitive function and premature death. Mutations in CLN6 gene cause one form of Batten disease. Pre-clinical testing of a drug called NDD-1 has been carried out on a mouse model of this Batten disease, and a previous study has shown that it decreases neuroinflammation in the cortex. In this project, a focussed analysis of three chosen regions using markers of inflammation was carried out to see if the same result was observed. This study however could not conclude a significant effect of NDD-1 in these regions which suggests that more animals/ sections need to be analysed or different regions of the cortex contributed to results previously established.

JADE YORK (Associate Professor Stephen Bunn and Professor Dave Grattan, Department of Anatomy, Otago School of Medical Sciences)

Title: Hormone actions in the brain

(OMRF Scholar)

One of the brain's important roles in the body is regulation of hormone production, including that of prolactin, which has many roles, essentially the production of milk after childbirth. In order to monitor the changes in the brain that occur when increased prolactin secretion is required, technology involving genetically modified rats has been used to monitor the specific neurons involved. The objective of this project was to assess the appropriateness of this rat model for future experiments. It aimed to determine whether it is possible to accurately target the right neuron population using specific staining techniques looking at these neurons under the microscope. The findings of this report indicate the model to be appropriate and effective for further research.

MICHAEL YUAN (Dr Cherie Stayner and Professor Mike Eccles, Department of Pathology, Dunedin School of Medicine)

Title: How do mutations in meckelin cause polycystic kidney disease?

(OMRF Scholar)

Autosomal recessive polycystic kidney disease (ARPKD) is an inherited disorder that results in significant enlargement of the kidneys. It is caused by defects in the primary cilia, a sensing organelle on the cell surface. One form of ARPKD, called Meckel syndrome, can be due to mutations in the *MKS3* gene. This codes for the protein meckelin which is required for primary cilia function. We investigated the effect that mutations in *MKS3* have on the distribution of meckelin in human kidney HEK293 cells. Each *MKS3* mutant construct was introduced into HEK293 cells. This was then passed through a laser to determine the percentage of meckelin within the cell and on the cell surface. Meckel in was found to have a greater accumulation within the cell in the *MKS3* mutations when compared to the *MKS3* WT. As a consequence there is disruption in the meckelin mediated signalling pathways that regulate primary cilia formation.

3. RESEARCH GRANTS AWARDED

(A) ANNUAL GRANTS AND OTAGO COMMUNITY TRUST GRANTS

These one-year grants are for research concerned with human health and the scientific basis of medicine. In June 2015 there were 33 applications from the University of Otago (cf 38 the previous year) totalling $796,944 and seven of these were funded at a total expenditure of around $171,000 of which $70,000 was provided most generously by the Otago Community Trust. These grants commenced between August and October 2015 and are nearing completion with full reports due 3 months after the one-year grant ends. Progress as at the end of May 2016 is summarised below:

(I) ANNUAL GRANTS

Dr Sarah Baird (Department of Pharmacology & Toxicology)

Mesenchymal stem cell-based therapy for aggressive paediatric brain tumours – AG 341

Sponsored by the Southern Victorian Charitable Trust

We are working on a new therapeutic approach to childhood brain cancer. Unfortunately, the average survival time of a child with brain cancer is 11 months. This is largely a result of differences between adult and childhood brain cancers, which have led to a lack of research specifically for children. We are developing a new treatment strategy targeting this childhood cancer with cells derived from the bone marrow. The bone marrow cells have been shown to track down the cancer cells in a patient, and we are altering them in the laboratory so that they will not only find the cancer, but also kill it and stop it moving around the body. We are making the new cells and testing them in the laboratory as well as in mouse models of this cancer.

Associate Professor Grant Butt (Department of Physiology)

Modulation of colonic epithelial proliferation and differentiation by commensal bacteria – AG 342

Sponsored by Foodstuffs Community Trust (South Island)

The lining of the intestine creates a selective barrier between the body and the luminal contents, which allows the intestine to absorb the nutrients, salts and water from the ingested food and, at the same time, prevents bacteria entering the body. This is particularly important in the colon, where there are as many commensal bacteria in the lumen as there are cells in our body. Recently it has been shown that disruption of this barrier and the development of a "leaky gut" results in exposure of the immune system to the commensal bacteria. This plays an important role in a range of intestinal and systemic diseases, such as inflammatory bowel disease and rheumatoid arthritis. Ironically, interaction between the commensal bacteria and the cells in the intestinal lining is important for the development of the intestinal barrier and, in this study, we are using colonoids or "mini guts" to investigate how Crohn's disease affects the way in which the bacteria regulate the growth and development of the intestinal barrier. The "mini guts" are grown in a dish from adult intestinal stem cells isolated from colonic biopsies collected from healthy patients and Crohn's disease patients. Using this model, we have shown that in the intestine from healthy patients, commensal bacteria induce the development of goblet cells, but this is compromised in the intestine of Crohn's disease patients. This is a result of defective regulation of the Notch signalling pathway, which is responsible for determining which of the different cell types in the intestinal lining the stem cells develop into. Goblet cells in the intestine secrete mucus, which is an important part of the intestinal barrier. Therefore, this defective development of goblet cells in the intestine from Crohn's disease patients is likely to contribute to the "leaky gut" seen in these patients and the development of Crohn's disease.

Associate Professor Merilyn Hibma, Dr Heather Cunliffe (Department of Pathology) & Dr Lyn Wise (Department of Microbiology & Immunology)

Understanding regulation of wound closure by skin Langerhans cells – AG 343

Sponsored by the JN Lemon Charitable Trust

Chronic wounds are a major cause of morbidity in New Zealand, especially in those over 60. Understanding wound closure is a critical step towards improving healing. We have identified a suppressive role for a cell type not previously considered to be important during wound healing, the Langerhans cell. We are in the process of investigating the mechanism by which Langerhans cells regulate skin repair using our well-established wound healing model. Our main experiment is in progress and we are planning to submit samples within the next 8 weeks for RNA sequencing so that we can measure the changes in gene expression that are caused by Langerhans cells during wound healing. We will then proceed with the analysis of the data, which will help us understand the role and importance of these cells when wounds heal. We anticipate that the knowledge gained from this research will form the foundation therapies that regulate Langerhans cells to enhance wound repair, which will have broad application for the treatment of unresolved wounds.

Dr Rajesh Katare (Department of Physiology)

Cardiac specific restoration of Pim-1 kinase to prevent cardiomyopathy in female diabetics – AG 344

Sponsored by the Zonta Club of Metropolitan Dunedin

Cardiac complications associated with diabetes are prevalent in women. Our recent study (funded by OMRF – AG307) showed deregulation of a pro-survival protein Pim-1 kinase in the female diabetic heart as the major mechanism for this female disadvantage in diabetes. Importantly, over expression of this protein in the *in vitro* cultured female diabetic cardiomyocytes markedly improved the survival of cells. Based on this evidence the current project aims to determine the effect of cardiac specific overexpression of Pim-1 kinase in reversing the female disadvantage in diabetic heart. So far using the *in vitro* culture of adult mouse cardiomyocytes, we have identified that Pim-1 can be restored in the cardiomyocytes through modulation of a microRNA (miR). miRs are endogenous, short (20-22 nucleotides) non-coding RNA molecules that regulate gene expression at the post-transcriptional level. miRs negatively regulate gene expression by promoting degradation of target mRNA or preventing them from translated into protein, and play an important role in a wide range of physiological and pathological processes. In the current study, we confirmed that female diabetic cardiomyocytes showed marked increase in the expression level of miR-1, which is associated with increased cell death. Importantly, this increase was associated with a significant down-regulation of Pim-1. Further, knockdown of miR-1 using synthetic miR inhibitors restored the level of Pim-1 and hence improved cell survival. Noteworthy, miRs are also released into the circulation which can be measured with the aid of a simple blood test. Therefore, our results suggest that serial monitoring of miR-1 could also serve as a valuable diagnostic biomarker to identify the disease at an earlier stage. Currently, we are planning for the *in vivo* experiment in which miR-1 will be modulated to restore Pim-1 level in the heart.

(ii) OTAGO COMMUNITY TRUST GRANTS

The Otago Community Trust supports biomedical research in the Otago area with the proviso that the research is selected on topics that can relate well to issues understandable by the layperson. The three projects selected were:

Professor Cliff Abraham & Dr Owen Jones

(Department of Psychology)

Synaptic homeostatic mechanisms in vivo – CT 345

Memories are stored by changes in the strength of communication at the synaptic connections between nerve cells. Such synaptic plasticity needs to be kept within homeostatic limits or else risk neurological impairments. Previously we discovered mechanisms by which this can be accomplished in a brain area important for memory, the hippocampus, using tissue culture techniques. Interestingly the plasticity regulation was triggered by inputs arising from outside the hippocampus. And even more intriguingly, the effect was mediated by non-neural cells called astrocytes. In this grant we are testing whether these plasticity-regulating mechanisms are equally functional in the brains of live animals. To date we have established a reliable method for inducing synaptic plasticity in the hippocampus of awake, freely moving rats. Our initial hypothesis was that activating a brain region that sends inputs to the hippocampus, the medial septum, would recapitulate the down-regulation of plasticity in the hippocampus. However, this hypothesis has not been confirmed. Now we are testing our second main hypothesis, namely that activating hippocampal astrocytes will be sufficient to produce the plasticity regulation. We are doing this by injecting chemicals, known to activate astrocytes, into the brain near to the hippocampus using very fine injection needles. This work is ongoing. We are pleased to have been joined recently by Ms Aline Blistein, a medical student from Frankfurt who is spending 5 months in the Abraham lab to work on this project. In the end, if we are able to confirm a role for astrocytes in the homeostatic regulation of synaptic plasticity in live animals, this will confirm the effect's biological significance and pave the way for understanding how its disruption could contribute to neurological disorders.

Dr Heather Cunliffe (Department of Pathology)

Targeting the androgen receptor in triple negative breast cancer – CT 346

Triple negative breast cancer (TNBC) is an aggressive form of the disease diagnosed in approximately 12% of New Zealand women with invasive breast cancer. There are currently no established options for systemic therapy for these patients other than chemotherapy. This study builds on our published finding that 23% of TNBC tumours are likely fuelled by circulating androgens (from the ovaries or adrenal glands). Growth of laboratory models of TNBC with androgens confirms this likelihood, however the degree to which these tumours rely on androgens depends on whether they carry markers of being 'luminal' or 'non-luminal' in origin. The first aim of this study seeks to define a robust method to identify patients whose TNBC can be characterised as 'luminal' or non-luminal, as a differential diagnosis of luminal tumours is important for identifying TNBC patients likely to respond to treatments involving androgen blockade. In progress to date, we have defined optimal conditions for diagnostic detection of five out of five key biomarkers we believe is sufficient to define luminal-like from non-luminal-like TNBCs (all share positivity for the androgen receptor). Our next step is to apply our optimal conditions defined for each diagnostic antibody to a series of patient tumour samples. The second aim of this proposal is to identify what is likely fuelling the growth of TNBCs that are diagnostically positive for the androgen receptor, but are not luminal. While this particular subtype of TNBCs show enhanced growth in the presence of androgens, unlike luminal TNBCs, they do not *require* androgens, and continue to grow in their absence, albeit at a reduced rate. The cancer biology underpinning this continued growth is not understood, and the objective of our second aim. We have successfully achieved blockade of androgen-mediated growth at physiologically sub-toxic levels in three laboratory models of non-luminal TNBC, and we are currently profiling the molecular characteristics of how these tumour cells are surviving in the absence of androgen. This will facilitate our ability to unmask new vulnerabilities to for targeted attack in non-luminal TNBCs. Once candidate vulnerabilities are identified, our next step will be to combine androgen blockade with blockade of what we propose to be the remaining 'default' survival and growth pathway(s) in this aggressive subtype of breast cancer.

Dr Regis Lamberts (Department of Physiology) & Dr Chris Baldi (Department of Medicine)

Unravelling the secrets of the beta-adrenoceptors in the human diabetic heart – CT 347

β-adrenergic regulation (the fight-or-flight response) is essential for function of the heart. Dysfunction of β-adrenergic regulation of the heart is an undervalued cause of cardiovascular complications in diabetes, and the underlying mechanisms are poorly understood. Traditional treatment of diabetic patients with β-adrenoceptor (β-AR) blockers is of benefit, however to a lesser extent than to non-diabetic patients. β-AR blockers alter the expression and function of these proteins and consequently the function of the heart. Therefore, we aim to determine the expression of β-AR subtypes and their downstream proteins in the human diabetic heart. To this end, we have used fresh human epicardial left ventricular biopsies from coronary artery disease patients with or without type-2 diabetes mellitus. The availability of small pieces of fresh left ventricular heart tissue (see figure) is very exclusive, and made possible through collaboration between clinicians and researchers from HeartOtago. We successfully set up the western blot techniques to assess the expression levels of β_1- and β_2-AR, and one of their downstream proteins GRK2. We found that the expression of β_2-AR and GRK2 was increased in samples from diabetic patients compared to non-diabetic patients, with no difference in β_1-AR expression. Currently, we are setting up the protocol for determination of the expression of β_3-AR and downstream proteins G_i and G_s. Here after the expression profiles of all proteins will be correlated with general patient characteristics (such as age, blood glucose, body mass index), and also with cardiac functional parameters obtained by echocardiography (such as heart rate, stroke volume, ejection fraction). Our results will contribute to the knowledge on changes in β-adrenergic regulation in diabetes, which is vital to understand the cardiovascular complications that occur in the human diabetic heart.

(iii) RECENT ANNUAL GRANT ROUND

In **June 2016** there were 24 applications from the University of Otago totalling $566,489. Five of these applications were funded by the Foundation and their sub-sponsors: Zonta Club of Metropolitan Dunedin, JN Lemon Charitable Trust, OceanaGold, St Joan's Trust/Southern Trust and Southern Victorian Charitable Trust, (~$142,000), and three by the Otago Community Trust (~$67,000). Abstracts of the proposed work can be found on the following web site www.omrf.org.nz

(B) LAURENSON AWARDS

Laurenson Awards are one-year grants for research concerned with the effects of diet and/or drugs on human health. In **December 2015** there were 12 applications (compared with 18 the previous year) from the University of Otago totalling $317,832 and three of these were funded at a total expenditure of around $90,000. All grants commenced between 1 January and 1 March 2016 and final reports are due at the end of March to May 2017. Work in progress, as at the end of May 2016, is summarised below:

Dr Shyamal Das & Professor Ian Tucker (School of Pharmacy)

Pulmonary delivery of kanamycin dry powder for treating tuberculosis – LA 351

We have conducted a review of relevant literature, purchased chemicals and developed powders suitable for inhalation by spray drying method. The spray-dried powders were characterised for physical properties such as particle size, surface morphology, moisture content, glass transition temperature and crystallinity and identified a formulation which provides high deep-lung delivery capacity as determined by an *in vitro* test. Now we are working on the first aim of the project i.e., characterising the surface of the particles to understand the mechanism of increased aerosolisation. We are investigating the composition of the spray-dried powders using several techniques: X-ray fluorescence, Energy dispersive X-ray Scanning Electron microscopy, Raman spectroscopy and X-ray Photo Electron Microscopy. In addition, we are conducting preliminary experiments for the second aim of the project: determining dissolution, alveolar macrophage uptake and cytotoxicity of the powders.

Dr Daryl Schwenke, Dr Regis Lamberts & Dr Pete Jones (Department of Physiology)

Ghrelin dilates human mammary arteries; implications in heart failure – LA 352

We have previously shown that the hormone ghrelin improves heart function following a myocardial infarction, although the underlying mechanisms remain unclear. Evidence has emerged which suggests that ghrelin may directly dilate arteries to improve blood flow. Accordingly, we aimed to assess whether ghrelin could dilate isolated human mammary arteries and potentially identify that the mechanism by which ghrelin ameliorates damage to the heart following acute myocardial infarction is by way of improving coronary blood flow. We are currently utilising the technique of vessel myography to assess the functional integrity of an isolated artery, based on dilatory or constrictor responses to select vasoactive modulators; in particular, the response to ghrelin. Following on from the functional measurements, we will utilise the technique of fluorescence myography to identify whether the mechanism underpinning ghrelin's vasoactive properties is linked to disruption of the intracellular calcium-signaling pathway, since calcium signaling is vital for vascular smooth muscle contraction and, thus, vessel function.

Professor Rob Walker, Dr Mat Bailey & Dr Craig Carr (Department of Medicine) & Associate Professor Natalie Medlicott & Dr Dan Wright (School of Pharmacy)

The impact of intensive care unit (ICU)-based sustained low efficiency hemodiafiltration on the pharmacokinetics of meropenem and tazocin – LA 353

Powerful antibiotics such as meropenem and piperacillin/tazobactam (Tazocin) are required to treat severe infections in patients in the intensive care unit (ICU). Many of these patients develop acute kidney injury (AKI) and will require renal replacement therapy with sustained low efficiency dialysis (SLED) plus haemodiafiltration (HOF). SLED-HOF is very effective in removing substances from the blood stream in the acutely unwell patient and it is therefore probable that antibiotics will also be removed. This may result in sub-therapeutic antibiotic concentrations and failure to adequately treat the life-threatening infection and possible death of the patient. By measuring how these antibiotics are removed by SLED-HOF, we aim to develop an appropriate dosing regimen to maintain appropriate therapeutic concentrations of the antibiotics for patients requiring SLED-HOF treatment. There was initially an issue related to a Crown law ruling related to observational studies in the intensive care setting. As a consequence the study was modified to undertake the drug clearance studies in stable haemodialysis patients who, instead of their usual dialysis session, would undertake a standard SLED-HDF as used in the ICU for 4 hours. This required a second ethics approval (duly obtained). The study is currently underway with 2 subjects out of 6 having completed both a session investigating meropenem clearance and a session investigating Tazosin clearance. As per the protocol, a total of 6 individuals will be studied. We expect to have the studies completed by the end of August and analyses completed by December 2016.

(C) JACK THOMSON ARTHRITIS FUND

This OMRF fund was made possible by a bequest from the late Jack Thomson and commenced in 2011. In **December 2015** there were four applications (compared with three in the previous year) from the University of Otago totalling $94,835 and three of these were funded at a total expenditure of ~$73,000. All grants commenced on 1 February or 1 March 2016 and final reports are due at the end of April or June 2017. Work in progress, as at the end of May 2016, is summarised below:

Dr Prasath Jayakaran, Dr Meredith Perry, Dr Cathy Chapple, Professor David Baxter & Professor Leigh Hale (School of Physiotherapy), Professor Jean-Claude Thesis (Department of Surgical Sciences) & Dr Gareth Treharne (Department of Psychology)

Sensitivity, specificity and accuracy for early detection of hip/knee osteoarthritis in the community – JT 348

Osteoarthritis (OA) of hip/knee is a highly prevalent non-communicable disease. The requirement for joint replacement has increased exponentially in the last decade, costing NZ$200 million annually. Early identification and targeted intervention may slow down the disease progression and thereby improve quality of life. However, there is no effective tool available to identify early OA symptoms among people living in the community. This study will determine the accuracy of a screening questionnaire (survey), by following-up the survey respondents with clinical examination and diagnostic investigations. If the method is determined to have acceptable level of precision, it will be tested at primary care level. The final ethical approval for the project was obtained on the 24th May 2016. The private organisations (Otago Radiology; Southern Community Laboratories) have been approached for study set up and sub-contract. The participants of the survey from the Dunedin study will be approached soon after the sub-contract/MOU has been agreed with these external organisations.

Dr Ramakrishnan Mani (School of Physiotherapy) & **Professor Dirk de Ridder,** (Department of Surgical Sciences)

Central nervous system mal-adaptations in individuals with arthritic pain – JT 349

The brain and the spinal cord respond adversely to ongoing unpleasant sensory stimuli from chronic painful arthritic joints. The adverse changes are considered to be a key contributor of persistent pain. The extent of these changes may be influenced by factors including: body weight, psychological state, physical function, and associated comorbidities. This research aims to identify subgroups of middle-aged, and older adults, with arthritis (of the hip, knee, low back, neck and shoulder), and group them according to distinct mal-adaptive nervous system profiles. This subgrouping approach will help develop a better management framework incorporating nervous system profiles and the factors influencing them, thereby helping to facilitate treatment specificity.

Associate Professor Sarah Young (Department of Pathology), **Dr Greg Walker** (School of Pharmacy), **Emeritus Professor John Highton,** (Department of Medicine) **& Ms Estelle Peyroux,** (PhD student, Department of Pathology)

Development of a novel anti-inflammatory therapy for ankylosing spondylitis using nanofibre technology incorporated with the neuropeptide vasoactive intestinal peptide (VIP) – JT 350

Overcoming inflammation in an arthritic joint requires sustained delivery of a therapeutic compound to break the destructive cycle of inflammation and tissue damage. The purpose of this study is to develop a novel anti-inflammatory targeted therapy effective for ankylosing spondylitis (AS) patients. We are dampening-down this response using the vasoactive intestinal peptide (VIP), as it is capable of down-regulating immune responses. In order to determine the anti-inflammatory potential of the VIP for an AS therapy, we have assessed its capacity to suppress inflammation in a cell culture model. We have observed that VIP can reduce the activation of dendritic cells, the orchestrator of the immune response. Furthermore, our VIP-treated dendritic cells can reduce the generation of inflammatory effector cells (T cells), both in number, activation markers and soluble messenger molecules. Currently we are in the process of optimising the measurement of surface markers on immune effector cells and determining VIP's toxicity. Once this is achieved we will be assessing VIP's stability in nanofibre formulations.

4. OTHER ACTIVITIES OF THE SCIENTIFIC COMMITTEE

OMRF Student Speaker Awards at the Otago Medical School Research Society:

The Student Speaker awards are given to the student speakers who, in the opinion of a panel of three to four judges, gives the best and second best oral presentation – based on both the components of the presentation and its scientific merit. To be eligible the candidates must report work that has been performed under the auspices of the University of Otago.

(1) At the **September 2015** scientific meeting of the Otago Medical School Research Society (OMSRS) there were 10 doctoral candidates (selected from 21 applicants based on their submitted abstracts). The first Prize ($1,000) funded by Otago Postgraduate Medical Society was awarded to **Andrew Reynolds** (supervised by Dr Bernard Venn & Professor Jim Mann, Department of Human Nutrition, and Associate Professor Sheila Williams, Department of Preventive & Social Medicine) on the topic of "Impact on glycaemia of walking after eating and standard physical activity advice in type 2 diabetes: a ramdomised crossover trial". The second prize ($500), which was funded by the **OMRF**, was awarded to **Kate Thomas** (supervised by Professor Andre van Rij, Department of Surgical Sciences, and Dr Sam Lucas and Associate Professor Jim Cotter, School of Physical Education, Sport & Exercise Sciences) on the topic of "Hot-water immersion increases popliteal artery shear stress in peripheral arterial disease".

(2) At the **May 2016** scientific meeting of the OMSRS there were 10 candidates (selected from 25 applicants based on their submitted abstracts). All were **summer research scholars** and 6 of the 10 (and 11 of the 25) had been sponsored by the OMRF. **The first prize** ($500) funded by the **OMRF** was awarded to **Danyon Graham** (supervised by Associate Professor Brian Monk & Dr Rajni Wilson, Department of Oral Sciences, School of Dentistry, sponsored via the OMRF by the Healthcare Otago Charitable Trust) on the topic of "The molecular basis of triazole inhibition of an antifungal target". The **second prize** ($250) funded by the **OMRF** was awarded to **Isabelle van Hout** (supervisors Associate Professor Grant Butt, Department of Physiology, and Associate Professor Michael Schultz, Department of Medicine, sponsored via the OMRF by the Southern Victorian Charitable Trust) for "The effects of bacterial components on colonic stem cell proliferation".

The OMRF summer research prizes from 2015 onwards are now called *"The Pat Cragg Summer Scholar Speaker Prizes"* in recognition of the long-standing involvement by Associate Professor Pat Cragg in the summer research scholarship assessing committee.

OMRF-sponsored Invited Speaker for the Otago Medical School Research Society:

The opportunity for such sponsorship did not occur in 2015.

OMRF-sponsored prizes at the Otago School's Science Fair:

The Foundation sponsors four prizes ($50 each) each year in the Special Prize category at the **Otago Aurora Science & Technology Fair** for secondary schools for projects involving medically orientated topics. The **August 2015** recipients were "Problems under pressure" by Nuala O'Malley-King & Charlotte Hewson (Year 7), "Zap that zit" by Meg Christophers (Year 7), "Brain o"Clock" by Emma Wilson (Year 8) and "Boose versus Baby" by Ruby Grave (Year 9). The Foundation's judges were Associate Professor Greg Jones, Dr Nick Heng and Dr Paula Skidmore.

ACKNOWLEDGEMENTS

The Foundation continues to play an ever increasing role in funding Medical Research in Otago – may I thank the Scientific Committee for its dedicated efforts in the arduous, though satisfying, work of assessing the scholarship and merit of the many summer research projects and grant applications that it receives. We thank the Council of the Foundation for the support, advice and enthusiasm with which our funding recommendations are endorsed and the many Benefactors and Sponsors of the Foundation whose financial support has made all this possible.

- Associate Professor Patricia A. Cragg
Chair, OMRF Scientific Committee
30 June 2016

FINANCIAL HIGHLIGHTS

Otago Medical Research Foundation Inc.

This summary financial report has been authorised for issue by the Chairperson of the Council Mr Ken Dempster . The results presented in the summary financial report have been extracted from the full financial report for the year ended 31 March 2016. As such, this summary report cannot be expected to provide as complete an understanding as provided by the statements of financial performance, financial position and movements in equity of the Otago Medical Research Foundation Incorporated. A full copy of the audited financial report for the Otago Medical Research Foundation Incorporated for the year ended 31 March 2016 is available from the office of the Foundations administrators - Deloitte, Otago House, 481 Moray Place, Dunedin.

Statement of Financial Performance

For the Year ended 31 March 2016

	2016 $	2015 $
Operating Income		
Donations, Bequests, Subscriptions	642,828	572,780
Investment Income	276,231	288,536
Profit (Loss) on Disposal of Investments	(1,652)	(16,811)
	917,407	844,505
Less Expenses		
Administration	84,919	83,418
Promotion Costs	311,625	271,622
Total Expenses	396,544	355,040
Net Surplus before Research Grants	520,863	489,465
Research Grants - Current year	439,960	398,214
Net Surplus for the year	80,903	91,251

Statement of Financial Position

As at 31 March 2016

	Market Value	2016 $	2015 $
Current Assets		203,829	137,857
Investments	5,675,896	5,156,274	5,099,392
Total Assets		5,360,103	5,237,249
Current Liabilities		409,415	367,464
Total Liabilities		409,415	367,464
NET ASSETS (EQUITY)		4,950,688	4,869,785

Statement of Movements in Equity

For the Year ended 31 March 2016

	2016 $	2015 $
Revenue		
Net Surplus	80,903	91,251
Total Recognised Revenues and Expenses	80,903	91,251
Equity at the Beginning of the Year	4,869,785	4,778,534
Equity at the End of the Year	4,950,688	4,869,785

Statement of Cash Flows

For the Year ended 31 March 2016

	2016 $	2015 $
Net Cash Flows from Operating Activities	128,204	75,278
Net Cash Flows from Investing Activities	(58,534)	(143,381)
Net Increase / (Decrease) in Cash Held	69,670	(68,103)
Cash at the Beginning of the Year	38,721	106,824
Cash at the End of the Year	108,391	38,721

Statement of Service Performance

For the Year ended 31 March 2016

The Foundation aims to establish world-class medical research for the benefit of local, national and international health.
The Foundation has provided a calendar of events in which members, supporters and the public were invited to participate - the Club lunches, annual dinnner, annual golf day, and various other one-off events.

Grants and scholarships approved during the year:

	Number	Actual ($)	Budget ($)
Annual Grants	7	171,050	152,000
Special Fund Grants	6	162,963	165,000
Summer Research Scholarships	28	114,000	90,000
Otago Medical School Research Society Award Sponsorship	2	450	450
Total	43	$ 448,463	$ 407,450

The full financial report of the Otago Medical Research Foundation for the year to 31 March 2016 were authorised for issue by the Chairperson of the Council. The full financial statements applied Public Benefit entity reporting (not for profit) standards. The auditor expressed an unqualified opinion. The summary financial report has been examined by the auditor for consistency with the full financial report. The auditor has expressed an unqualified opinion.

Deloitte

CROWE HORWATH NEW ZEALAND

AUDITOR'S REPORT

Crowe Horwath

Crowe Horwath
New Zealand Audit Partnership
Member Crowe Horwath International

44 York Place
Dunedin 9016 New Zealand

PO Box 188
Dunedin 9054 New Zealand

Tel +64 3 477 5790
Fax +64 3 474 1564

www.crowehorwath.co.nz

REPORT OF THE INDEPENDENT AUDITOR ON THE SUMMARY FINANCIAL STATEMENTS

To the Council of the Otago Medical Research Foundation

The accompanying summary financial statements, which comprise of the summary statement of financial position as at 31 March 2016, the summary statement of financial performance and the summary statement of movements in equity for the year then ended, and related notes, are derived from the full audited financial statements of the Otago Medical Research Foundation for the year ended 31 March 2016. We expressed an unmodified audit opinion on those financial statements in our report dated 29 July 2016. Those financial statements, and the summary financial statements, do not reflect the effects of events that occurred subsequent to the date of our report on those financial statements.

The summary financial statements do not contain all the disclosures required for full financial statements under generally accepted accounting practice in New Zealand. Reading the summary financial statements, therefore, is not a substitute for reading the full audited financial statements of the Otago Medical Research Foundation.

Council's Responsibility for the Financial Statements

The Council are responsible for the preparation of a summary of the audited statements in accordance with PBE FRS-43: *Summary Financial Statements.*

Auditor's Responsibility

Our responsibility is to express an opinion on the summary financial statements based on our audit procedures, which were conducted in accordance with International Standard on Auditing (New Zealand) (ISA (NZ)) 810, "Engagements to Report on Summary Financial Statements".

Other than in our capacity as auditor we have no relationship with, or interests in, Otago Medical Research Foundation.

Opinion

In our opinion, the summary financial statements derived from the audited full financial statements of the Otago Medical Research Foundation for the year ended 31 March 2016 are consistent, in all material aspects, with those financial statements, in accordance with PBE FRS-43.

Crowe Horwath

Crowe Horwath New Zealand Audit Partnership
CHARTERED ACCOUNTANTS
29 July 2016

OTAGO
MEDICAL RESEARCH FOUNDATION

OTAGO MEDICAL RESEARCH FOUNDATION

Annual Report to 31st March 2016 & Notice of Annual General Meeting