OTAGO
MEDICAL RESEARCH FOUNDATION

Otago Medical Research Foundation Inc.

Annual Report to 31st March 2012
& Notice of Annual General Meeting

CONTENTS

NOTICE OF MEETING

The Forty Fourth Annual General Meeting of Members
will be held on Tuesday, 11 December 2012 at 5.15 pm
at Deloitte, Level 13, Otago House, 481 Moray Place, Dunedin

Members, and all interested in the work and objects of the Foundation, are invited to attend.
All current grant recipients have been invited to attend the meeting.

BUSINESS

1. To receive the Reports of the Council, the Scientific Committee and the audited Financial Statements for the year ended 31 March, 2012.

2. To record the reappointment of the Auditors, WHK, and authorise the Council to determine their remuneration.

3. Election to Council of five members of the Foundation (see notes).

4. To approve changes to the rules which have been considered by Council and recommended for submission to the AGM. The recommended changes have been made to reflect changes in the University and Health sectors, changes in technology, and to fine tune some administration matters. There has been no change to the object of the Foundation which remains as "The Furtherance of Medical Research in Otago" nor is there any change proposed in the method of this furtherance (as shown on Page 5). There will also be no noticeable change in the way the Foundation will continue to operate under the proposed new Constitution. Members who would like to receive a copy of the proposed Constitution should contact the Secretary.

5. To transact any other business for which notice has been given in writing to the Secretary in terms of Rule 8(d) not less than one week before the date of the meeting and any other matters which may be brought forward by the Council.

Deloitte
Secretaries
P.O. Box 1245, Dunedin

NOTES

a) Retiring elected members; Dr M Coleman, Mr K G Dempster, Mr R P Lewis, Dr J McMahon and Ms S Saunderson-Warner are eligible for re-election.

b) Rule 5(b) provides that nominations for other than current elected members of Council should be received by the Secretary, in writing, 7 clear days before the Annual General Meeting. Such nominations to be signed by the nominator (who shall be a financial member of the Foundation) and by the nominee.

Nomination forms are available at the office of the Secretaries. (Level 13, Otago House, 481 Moray Place, Dunedin).

YOU CAN HELP THE FOUNDATION

By: * joining as a new member * making a bequest * recruiting new members
* using an OMRF fuel card * making a donation

OTAGO MEDICAL RESEARCH FOUNDATION INCORPORATED

To: The Secretary
Otago Medical Research Foundation Inc.
PO Box 1245, DUNEDIN

Name: (Mr/Mrs/Miss/Ms/Prof/Dr or Company) .....

.....

Address: .....

.....

(Please show department address if employed at the University of Otago,
Dunedin School of Medicine or School of Medical Sciences)

E-mail address: .....

ANNUAL SUBSCRIPTION (1/4/12-31/3/13)

I/We wish to join the Otago Medical Research Foundation Inc. as:

☐ An Ordinary Member
(minimum subscription $30 p.a.) $.....

☐ A Research Patron (Business Firm or Corporate Body)
(minimum subscription $100 p.a.) $.....

☐ A Life Member
(minimum subscription - Individuals $500) $.....

(minimum subscription - Corporate Bodies $1,000) $.....

☐ A donation of $..... is enclosed in lieu of
membership application $.....

☐ Please send me information on the Foundation's Fuel Card

TOTAL $.....

I/We agree to be bound by the rules of the Foundation.

Signed .....

☐ Cheque attached
☐ Funds direct credited to the OMRF bank account number 03 0903 0381844 00

Note: Subscriptions or donations of $5 or over qualify for a tax exemption

You may wish to have your contribution take the form of a legacy or bequest in which case you will no doubt obtain proper advice.

FORM OF BEQUEST

A suitable clause in a Will to provide for a bequest would be on the following lines:
"I give and bequeath (free of all duty) to the Otago Medical Research Foundation (Inc) the sum of $ ..... (or description of other property or assets) for research purposes that may relate to a diverse range of health problems including cancer and heart disease, AND I DECLARE that the receipt of the Secretaries or other proper officer thereof shall be a full and sufficient discharge to my Trustee for the said Legacy nor shall my Trustee be bound to see the application thereof

OBJECT OF THE FOUNDATION

EXTRACTS FROM RULES

The object of the Otago Medical Research Foundation Inc. shall be:

THE FURTHERANCE OF MEDICAL RESEARCH IN OTAGO

To this end the Foundation shall have power to carry out the following functions:

- To seek, accept and receive donations, subsidies, grants, endowments, gifts and bequests designed in any way to further the object of the Foundation, and to realise on real estate and personal property received by gift or bequest and apply the proceeds to the furtherance of the object of the Foundation.

- To establish and provide bursaries and scholarships tenable either in New Zealand or abroad and make grants of money to persons, organisations or institutions for the purpose of initiating, aiding or furthering medical research by any such persons or institutions.

- To appoint lecturers and demonstrators, to support the holding of lectures, tutorial classes and demonstrations as will contribute to the instruction of persons interested in any medical or allied subject under investigation or enquiry.

- To provide, equip and maintain laboratories, offices and other buildings, including the provision of materials, chemicals, animals for research purposes, and other equipment, books, journals and apparatus of all types.

ASSISTANCE IN FURTHERING THE OBJECT OF THE FOUNDATION
AND EXPANDING THE SUPPORT OF MEDICAL RESEARCH IN OTAGO
WOULD BE APPRECIATED, AND WILL BE ACKNOWLEDGED
IN FUTURE ANNUAL REPORTS

Please contact the Secretaries: Deloitte , Otago House
PO Box 1245, Dunedin

Telephone: (03) 474-8630
Facsimile: (03) 474-8650

or use the membership/donations form included in this publication.

OMRF COUNCIL

Dr J Adams
Dean Dunedin School of Medicine
- ex-officio

Prof H Nicholson
Nominee of Vice-Chancellor University of Otago
- ex-officio

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

Dr S Bunn
Otago Medical School Research Society

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)

Prof J Highton
General Medical Staff, Otago District Health Board

Mr R Bunton
Otago District Health Board

Dr M Coleman
Elected by Members of the Foundation

Mr K G Dempster
Elected by Members of the Foundation

Mr R P Lewis
Elected by Members of the Foundation

Dr J McMahon MBE
Elected by Members of the Foundation

Ms S Saunderson-Warner
Elected by Members of the Foundation

EXECUTIVE
Mr K G Dempster - Chairperson
Assoc Prof P A Cragg - Deputy Chairperson
Deloitte representative - Secretary/Treasurer

SCIENTIFIC COMMITTEE
Assoc Prof P A Cragg - Chairperson
Physiology Department, Otago Medical School
Members (see report on page 11)

DIRECTOR OF DEVELOPMENT
Mr S. Davie

SECRETARIES
Deloitte

HONORARY SOLICITOR
Mr J Anderson
(Gallaway Cook Allan)

AUDITORS
WHK

PATRON
Emeritus Professor Barbara Heslop

OMRF GRANTS AWARDED JUNE 2011 AND DECEMBER 2011

OTAGO MEDICAL RESEARCH FOUNDATION

Prof M Eccles & Dr S Young (Pathology) - $15,500
Development of a new microparticle vaccine adjuvant with the ability to deliver siRNA to Dendritic cells

Dr S Hughes (Biochemistry) - $19,454
Emptying the rubbish bin – Lysosome function and childhood brain disease

Dr S Taurin & Assoc Prof R Rosegren (Pharmacology & Toxicology) - $32,025
Optimising raloxifene as an effective treatment for triple negative breast cancer tumour: mechanisms and gene expression

OTAGO COMMUNITY TRUST

Prof P Glue (Psychological) & Assoc Prof D Perez (Medicine) - $6,500
Rapid acting antidepressant treatment for depressed patients with cancer in palliative care

Dr G Hammond-Tooke (Medicine) - $9,247
Modification of TMS-evoked cortical potential by repetitive TMS

Prof H Nicholson & M Gould (Anatomy) & Dr I Abraham (Physiology) - $21,245
The role of the cell membrane in prostate cancer progression

Assoc Prof M Thorn
(Surgical Sciences) - $23,679
T-cell trafficking in Crohn's disease

Prof A van Rij
(Surgical Sciences) - $17,347
Circulating microRNAs as indicators of remote ischaemic preconditioning for cardio-protection in surgery

LAURENSON GRANTS

Dr R Lamberts & Dr P Jones
(Physiology) - $16,505
Effects of beta-2-adrenoceptor function in the diabetic myocardium

Dr K Greish & Assoc Prof R Rosengren
(Pharmacology & Toxicology) - $18,018
Utilising Nanotechnology for producing effective anticancer therapy against breast cancer

Dr K Coppell (Medicine) - $27,738
The epidemiology of obesity related liver damage and hyperuricaemia in the NZ adult population

Dr A Bahn (Physiology) & Assoc
Prof L Stamp (Medicine) - $27,738
Regulation of urate synthesis (xanthine oxidase) and renal urate transport (AMP kinase) by furosemide

JACK THOMSON GRANT

Prof J Highton (Medicine), Dr P Hessian
(Physiology) & Assoc Prof L Stamp
(Medicine) - $34,970
Identification of subtypes of Rheumatoid Arthritis through joint and serologic characterization

RENSHAW PRIZE

The Renshaw Prize is named after one of the founders of the Otago Medical Research Foundation Inc., the late Dr P.K. Renshaw. The prize of $250 is awarded to the Summer Research Student, who in the opinion of the Scientific Committee, amongst the Research Scholars supported, has made the most worthwhile contribution to medical research in that particular year.

In recognition of their contribution, prize winners' names are listed below:

1970 - Mr A.G. Yule
1971 - Mr K.J. Davey
1972 - Mr F.M. Patrick
1973 - No Award
1974 - Mr J.C. Montgomery
1975 - Mr A.S. McLean
1976 - Mr N.K. Given
1977 - Miss F.M.F. McQueen
1978 - Mr K.D. Jolly
- Mr J.P. Scott
1979 - Mr R.A. Henderson
1980 - Mr D.W. MacFarlane
- Mr D.W. Shaw
1981 - Mr N.E. Dickson
- Mr Wong Ooi
1982 - Miss C. Page
1983 - Mr I.L. McLean
1984 - Mr I.L. McLean
1985 - Miss B.C. Galland
1986 - Mr R.G. Snell
1987 - Mrs T.E. Inder
1988 - Miss M. Kuipers
1989 - Miss E.R. Dennett
1990 - Miss A. Charlton
1991 - Mr B. McKenzie
1992 - Mr J.W. Corboy
1993 - Ms S.M. Dillon
1994 - Ms N. Dalbeth
1995 - Mr T Zaharic
1996 - Mr M Morrison
1997 - Mr A Brown
- Ms S Safari
1998 - Mr J Mangum
1999 - Ms J Pitchforth
- Ms A Steyn
2000 - Mr J Wales
2001 - Mr M Rahimi
2002 - Ms S Jordan
2003 - Ms E Szymlek-Gay
2004 - Mr D Kieser
2005 - Mr C Young
2006 - Mr C Young
2007 - Mr S Smart
2008 - Ms S Saunderson
2009 - Ms J Lee
- Ms E Winsley
2010 - Mr J Zhang
2011 - Miss E Gavey
- Mr E Ottley
- Mr W Parkyn
2012 - Miss Su Zhou

CHAIRPERSON'S REPORT

It is with pleasure that I present the 44th Annual Report on the Otago Medical Research Foundation's activities for the 2012 financial year. During the year under review the Foundation funded medical research in Otago to the value of $349,226 which was an increase of $21,351 on last year. This brings the total amount funded since the Foundations inception to $6,342,353.

The extract from the Financial Statements, as published further on in the Annual Report, shows a surplus for the year of $74,195. Last financial year a bequest of $2,000,000 was received. If we exclude this for comparison purposes our surplus for last year would have been $42,500 so the increase of $31,695 this year partly reflects the extra income earned from the legacy. The Foundation endeavours to invest surpluses in project grants rather than build up funds but further injections of capital to be invested are needed if the Foundation is to continue supporting research at a minimum of the same level that we have been.

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 $102,741, which is just under 4% of cost, with the New Zealand and Australian investments being the main contributors. Forward commitments for grants approved but not yet paid at balance date total $197,987, compared with $227,867 last year.

At 31 March, 2012 Accumulated General Funds total $353,061 and Accumulated Special Funds $4,439,788; both these figures comprising Capital and Income.

This year marked the 15th 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 further on in the Scientific Committee Report. This brings the total grants received from the Otago Community Trust to $1,155,000, 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 their very generous continuing 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.

CHANGE OF RULES

Those attending the Annual General Meeting will be asked to vote in support of changing the rules which were adopted on 17 November, 1993. The changes have been made to reflect reorganisation in the University and Health sectors, updates in technology, and to fine tune some administration matters.

There has been no change to the object of the Foundation which remains as "The Furtherance of Medical Research in Otago" nor is there any change proposed in the method of this furtherance as shown on Page 5. There will also be no noticeable change in the way the Foundation will continue to operate under the proposed new Constitution.

DAN PEARCE

I am sorry to record the passing of Dan Pearce, who died on the 5th July, 2012. Dan was associated with the Foundation's Auxiliary for many years as Secretary-Treasurer and he was a truly dedicated and efficient person in that role. On behalf of the Foundation I offer our sincere sympathy to Dan's family.

THANKS

- Firstly, to all those Trusts, Companies, Individuals, Members and Non –Members listed further on 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 his commitment to the Foundation. Previous reports have mentioned the work of Steve whose report can be found on page 9. Steve is continuing to generate great publicity for the Foundation with a resultant increase in funds raised through his many fund-raising initiatives and the effort he puts into these is very much appreciated by Council. Thank you Steve.

- To my fellow Investment Sub-Committee member- Mike Horne, Ron Lewis and Jenny McMahon - for their wise counsel, advice and time so willingly given to serve on this Sub-Committee. Thank you most sincerely.

- Special thanks must be recorded to the members of the Scientific Committee, under their long-standing and dedicated Chairperson, Associate Professor Patricia Cragg. Although all busy with their own career activities, the Scientific Committee members still continue to find the time to provide professional assessment and advice on three rounds of Grant applications and then make their recommendations to the Council. Without this group of dedicated people 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.

- Last year's report noted the retirement of Geoff Adams as an elected member of Council. His place was taken by Sarah Saunderson-Warner and she has proved to be a valuable member of Council.

- To the Deloitte team of Mike Horne, Louisa Homersham and Trudy Reveley for continuing to provide very professional and efficient administration services for the Foundation.

On behalf of the Council
Ken Dempster
Chairperson

REPORT FROM THE DIRECTOR OF DEVELOPMENT

If the Foundation's fundraising momentum was viewed as sluggish in the early stages of 2010, it could now be fairly described as gathering pace.

Since the Foundation took its first tentative steps on a concerted funding campaign in early-2010 almost $400,000 has been generated with the Jack Thomson Arthritis Fund, established through a $2 million bequest, additional to that.

So we're out of the blocks now and picking up speed.

As the Foundation's profile builds, so does its ability to generate funding opportunities.

A number of individuals are now regular benefactors, a growing base of business owners lend their support through 'sponsoring' annual summer research scholarships, several gaming machine trusts have made more than one donation, and many within the charitable industry are financially supportive of the Foundation's vision.

The Foundation's annual golf tournament, with OceanaGold partnering up as the major naming rights sponsor, is now seen as a 'must play' event and raises significant funds in its own right. Use of the Foundation's fuel card is on the increase, the Otago Medical Fund – a conduit through which those in the medical industry can make specific and targeted donations – is creating interest, and Club Otago – a lunch club open to individual and corporate supporters alike – has proven especially successful.

A successful movie premiere was staged early in the financial year, as a way of thanking our benefactors, and this will be repeated on an annual basis.

Best of all, the funds raised are making a tangible difference to the Foundation's ability to identify and nurture world-class medical research – and from that we all benefit.

My thanks go to all supporters and friends of the Foundation. Your generosity and foresight in supporting the terrific work our scientists and researchers undertake is very much appreciated.

Steve Davie
Director of Development

OMRF ANNUAL GOLF TOURNAMENT

The Foundation's second annual golf tournament was hosted in association with OceanaGold on the St Clair course in Dunedin in perfect conditions in early October.

OceanaGold, a supporter of the summer research scholarship programme in 2010/2011, strengthened its alignment with the Foundation's work by taking on the tournament's naming rights' sponsorship for an initial period of three years. That financial backing, aligned with the involvement of individual team entries and the hole and prize sponsors ensured a profit of almost $14,500 from the day.

Those funds will be directed into the OceanaGold research grant, identified and allocated in May 2012.

A full field assembled for the tournament which is now viewed as one of the best on the local calendar.

Supporting the OceanaGold commitment were our hole sponsors and the Foundation acknowledges their enthusiasm. Our thanks to Silicon Coach, Orbit Corporate Travel, Dr John Greaves and Keith Newton (Mornington Health Centre), Speight's Brewery, Dr Patrick Dawes, Harcourts Highland Group, Dr David Peart, Forsyth Barr, Mitchells Tavern, Safety Sipper Ltd, Deloitte, Dr Alan Wright, Dunedin Venues, Palmers Mechanical, Body Synergy Gym, Sport Otago, Mr Simon McMahon, Southern Colour Print.

A number of our hole sponsors are also early supporters of the Foundation by way of a financial backing of research grants or summer research scholarships and we are doubly grateful for their additional involvement.

There were also a number of team entries and their support is also appreciated. Our thanks are extended to Ken and Liz Dempster, Arron Campbell, Dave Sharp, the Cameron Brothers, and to Paul Barlow and his team.

Our prize and refreshment sponsors and a number of others also played a part in the success of the day. Our thanks go to Dr Brian McMahon, Dr Jenny McMahon, Wattyl New Zealand, Aravin Central Otago, Dunedin Venues, Perseverance Estate, Speight's Brewery, Liquor King Hillside, Sky Television's Rugby Channel, Southern Honda, Sport Otago Golf Academy, Cadbury Confectionery and Cadbury World, Usher Group Holdings, Rialto Cinemas Dunedin, Neil Metcalfe and the St Clair Golf Club, and Beer Wines and Spirits.

The day's results were –

Closest to the pin – 4th; Steve Todd, 7th; Steve Todd, 13th; Kevin Galliven, 16th; Damian O'Neill.

Longest drive – 9th; Jason Hughes

TEAM RESULTS:

10th – playing off a team handicap of 8.625, net score of 56.375 – Deloitte

9th – 8, 56, Mornington Health Centre

8th – 6.125, 55.875, Palmers Mechanical

7th – 9.25, 55.75, Mr Simon McMahon

6th – 4.625, 55.375, Orbit Corporate Travel

5th – 6, 55, Whatsoever Ltd

4th – 10.125, 54.875, Oceania Gold # 2

3rd – 5.5, 54.5, Cameron Brothers

2nd – 8.625, 54.375, Mitchells Tavern

1st – 8.75, 53.35, Arron Campbell

Ken Dempster, Chairperson of the Otago Medical Research Foundation (right), congratulates Aaron Campbell, Captain of the winning team at the 2011 Otago Medical Research Foundation golf tournament.

SCIENTIFIC COMMITTEE REPORT
1 OCTOBER 2011 TO 31 AUGUST 2012

1. MEMBERSHIP

Assoc Prof Pat Cragg

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

Dr Stephen Bunn
(President Otago Medical School Research Society, ex officio)

Dr Tamlin Conner (Co-opted)

Dr Greg Giles (until March 2012);
Dr Ivan Sammut (from March 2012) (Co-opted)

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

Dr Bob Hancox (Nominee Dunedin School of Medicine)

Dr Nick Heng (Co-opted)

Associate Professor Greg Jones
(Nominee Otago Medical School Research Society)

Dr Beulah Leitch (Co-opted)

Dr David Markie (Co-opted)

Associate Professor Russell Poulter (Co-opted)

Professor Thomas Rades (until end of 2011)(Co-opted)

Professor Clive Ronson (Co-opted)

Dr Paula Skidmore
(Nominee 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 subdisciplines of medical research.

In late 2011 there was one retirement from the committee, Professor Thomas Rades, and we thank him for all his contributions since early 2003 when he became a co-opted member to represent the School of Pharmacy. In March 2012 Dr Greg Giles, a co-opted member representing the Department of Pharmacology & Toxicology, also retired from the committee after two years. For 2012 we welcomed Dr Ivan Sammut from that Department.

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 Scientific Committee's Chairperson of a letter from the University of Otago Animal Ethics Committee, the University of Otago Human Ethics Committee or the Ethics Committee of the 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://omrf.otago.ac.nz/*

2. SUMMER RESEARCH SCHOLARSHIPS 2011/2012

One hundred and forty-one applications (compared with 137 the previous year) were received from the University of Otago in early September 2011, of which 20 were recommended for funding by the OMRF (and 74 gained scholarships from other funding bodies). Of the 20 students funded by the OMRF, ten were studying medicine, five science, two biomedical science, two dentistry and one masters in 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, eleven of the other 16 OMRF scholarships were funded by: Deloitte Touche Tohmatsu Limited, Foodstuffs Community Trust, HealthCare Otago Charitable Trust, Kingston Sedgfield Charitable Trust, Lions Club of Dunedin South, OceanaGold, Otago Service Clubs Medical Trust, St Kilda Community Sports Society (3) and WHK. The involvement of Otago commercial companies and the Otago community for a second year in supporting summer research by tertiary students is much appreciated.

All scholars returned good to excellent reports by the end of February 2012. The Renshaw Prize ($250) for the best report was awarded this year to: Su Zhou, who worked under the guidance of Associate Professor Greg Jones of the Department of Surgical Sciences. This year there were a further four reports that were also excellent and they have been awarded Commendations: Brigitta Connochie, who worked under the guidance of Dr Lisa Houghton of the Department of Human Nutrition; Fiona Firth, guided by Professor Tom Kardos and Dr Lara Freidlander of the School of Dentistry; Rebecca Grattan, guided by Professor Cliff Abraham and Dr Sarah Hulme of the Department of Psychology; and Jordan Vincent, guided by Professor Andre van Rij of the Department of Surgical Sciences.

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 Chairperson of the OMRF Scientific Committee or from the supervisor concerned.

Su Zhou

(Associate Professor Greg Jones, Department of Surgical Sciences)
Title: Micro-RNA levels in patients with varicose veins
(St Kilda Community Sports Society Scholar and Renshaw Prize Winner)

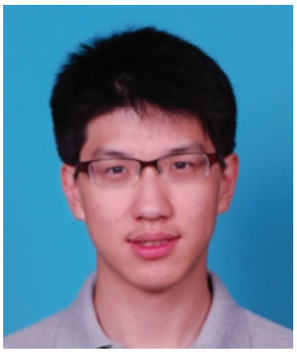
Micro-RNAs (miRNA) are a newly identified class of small non-coding RNAs that play an important role in regulation of gene expression. Circulating miRNAs have been found to be highly stable in plasma, which provides a potential role for miRNAs as plasma biomarkers for disease. By comparing the expression of all known miRNAs in patients with varicose veins, with healthy controls, we identified differences in miRNA expression in both the plasma and tissue samples. These miRNAs were associated with vessel wall homeostasis, angiogenesis and inflammation. This is consistent with prior knowledge of varicose vein pathogenesis, and creates the possibility of miRNAs as biomarkers for venous disease.

Wee Choen Ang

(Professor Mark Stringer, Department of Anatomy)
Title: An analysis of two major abnormalities of the lower body's largest vein

The inferior vena cava (IVC), a large vein that drains the lower half of the body, has two major anatomical variants namely the left-sided and double IVC. Four clinical cases were presented in the report to illustrate these variations, and provide novel data on venous dimensions. A systematic review of the recent literature (2000-2011) was conducted focusing on the anatomy, epidemiology and associated pathology of both malformations.

These variants are clinically important for three reasons: the potential for misdiagnosis on imaging; technical difficulties during abdominal surgery; and their significance in relation to the clinical management thrombosis and embolism.



Sabastian (Wee Choen) Ang

Stella Cameron

(Associate Professor Dorothy Oorschot and Dr Rachel Sizemore, Department of Anatomy)
Title: Mesenchymal stem cells: A possible treatment for cerebral palsy
(St Kilda Community Sports Society Scholar)

Third trimester hypoxic-ischaemic (H/I) injury causes a substantial loss of striatal medium-spiny neurons. Neuronal numbers are restored following delayed administration of mesenchymal stem cells (MSCs). A potential source of these new neurons is the adjacent subventricular zone (SVZ). This project investigated the effect of treatment with MSCs on the proliferation of progenitor cells in the SVZ following H/I injury. Ki-67, a specific label of proliferating cells, was utilised. Results demonstrated a decreased number of proliferating cells in the SVZ following treatment. It is proposed that MSCs serve to increase the migration and differentiation of progenitor cells into the striatum.

Brigitta Connochie

(Dr Lisa Houghton, Department of Human Nutrition)
Title: The perspectives and practices of New Zealand midwives regarding nutrition recommendations during pregnancy
(Commendation)

The New Zealand Ministry of Health recommends supplementation with iodine during pregnancy and lactation but adherence to this guideline is low. Midwives are the preferred source of information for pregnant women however little is known about their opinions on the guidelines. Semi-structured interviews were carried out among Dunedin midwives to explore their opinions, implementation practices, and barriers to adherence. Results showed that midwives were implementing the guideline for iodine, but the majority did not have a good understanding of the supporting evidence behind it. Increased communication and education for incoming guidelines may therefore be beneficial.

Jasper Diong

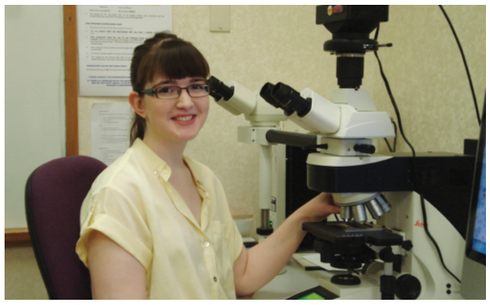
(Associate Professor Rhonda Rosengren and Dr Khaled Greish, Department of Pharmacology & Toxicology)
Title: Improving the nanoparticle encasing the anticancer drug RL71 and testing its ability to kill breast cancer cells
(Lions Club of Dunedin South Scholar)

Triple negative breast cancer (TNBC) is an aggressive subset of breast cancer lacking targeted drug treatments. To effectively deliver the novel drug RL71 to tumours, nanomicelles were constructed. Two micelle constructs were synthesised containing either a low or high concentration of RL71. Both micelle constructs were large enough to provide targeted delivery to tumours. Micelles were highly water soluble and stable, gradually releasing RL71 across 84 hours in conditions that mimicked blood and tumour environments. Micelles with a high RL71 concentration killed TNBC cell lines more efficiently than RL71 alone. Micelles synthesised possess ideal characteristics for further studies in animals.

Fiona Firth

(Professor Tom Kardos and Dr Lara Friedlander, School of Dentistry)
Title: Regulation of immune cells in lichen planus
(Commendation)

This study aimed to investigate the role of two T-helper cell subsets: T regulatory cells (Tregs, FoxP3+) and Th17 cells (IL-17+) in the regulation of the immune response in oral mucosal lichen planus (OMLP) using immunohistochemistry and immunofluorescence. OMLP displayed significantly more FoxP3+ cells and fewer IL-17+ cells than non-specific inflammatory cases. Double-labelled immunofluorescence showed that FoxP3+ cells co-localised with T cells, while the IL-17+ cells did not. These results support the proposition that Tregs are involved in immune control in OMLP, while the role and nature of IL-17+ cells should be further investigated.



Fiona Firth

Midori Fujino

(Dr Jim Faed, Department of Pathology)
Title: Review of experience with introduction of anticoagulant medicine, dabigatran, in Otago

The aim of the project was to evaluate the attitudes and responses by General Practitioners (GPs) and patients in Dunedin to the introduction of dabigatran. GPs and patients were interviewed, and a review of patient clinical records was undertaken. Response rate was 78% for patients and 26% for GPs. 83% of GPs had one or more reservations about dabigatran, however patients had a high satisfaction rating. Issues with a low level of reporting of side effects are highlighted, and it was also found that 16% of patients had ceased to take this agent during the study period.

Midori Fujino

Mayad George

(Dr Andrew Bahn, Department of Physiology)
Title: Influence of urate on transporter protein expression in MIN-6 mouse pancreatic cells
(Otago Diabetes Research Trust Scholar)

Urate, the molecule that causes gout in humans, causes reduced insulin sensitivity. The aim of the project was to determine the effect of urate on the expression of the glucose transports, GLUT2 and GLUT9, in mouse pancreatic “MIN6” cells. No change in gene expression was seen after urate was administered to the cells for both GLUT2 and GLUT9. Low expression of both genes was observed leading to insufficient evidence to support the claim that urate reduces GLUT2 and does not change GLUT9 expression.

Caitlin Glue

(Associate Professor Tony Merriman, Department of Biochemistry)
Title: Genes, fructose and the risk of gout
(Garth McQueen Summer Scholarship)

Gout is a form of arthritis most common in Maori and Pacific Island populations. High serum uric acid levels and fructose intake are risk factors for gout. Single nucleotide polymorphisms (SNPs) associated with high serum uric acid levels in the "Atherosclerosis Risk in Communities" population were identified, and the role of sugar sweetened beverage intake as a marker of fructose intake further investigated. The rs7598433 SNP of the glycerol-3-phosphate dehydrogenase 2 (GPD2) gene was identified as being of interest. In a New Zealand population the correlation between fructose intake and serum uric acid was significantly different between rs7598433 genotype groups.

Caitlin Glue

Rebecca Grattan

(Professor Cliff Abraham, Owen Jones and Dr Sarah Hulme, Department of Psychology)
Title: Neuroprotection mechanisms in an oxygen-glucose deprivation model of ischaemic stroke
(Commendation)

Ischaemic stroke is a leading cause of death in older humans. Recent evidence has emerged suggesting the brain has a coping mechanism named "ischaemic preconditioning" in which short sub-lethal strokes provide neuroprotection against a subsequent lethal stroke. The present study aimed to investigate the mechanisms of a previously established model of "ischaemic preconditioning" using oxygen-glucose deprivation in brain tissue. A preconditioning effect was not found using this model despite numerous methodological trials. Thus, the experiment has highlighted important methodological concerns for developing a clinically appropriate model of ischaemic preconditioning in brain tissue.

Rebecca Grattan

Sarahmarie Innes

(Dr Paul Hessian, Department of Physiology)
Title: Reasons why smoking increases the risk of rheumatoid arthritis
(WHK Scholar)

Smoking increases the risk of developing rheumatoid arthritis (RA). Smoking also causes changes to DNA methylation that affects gene expression. Such changes could explain the increased risk of RA. This study investigated expression of F2RL3, a gene hypomethylated by smoking. Subcutaneous nodule and joint synovial tissues were examined from RA patients who smoked or were non-smokers. F2RL3 was expressed in rheumatoid nodule and synovial tissues seemingly independent of smoking. The methylation status of a further 24 inflammation-related genes was compared in rheumatoid synovium from a smoker and non-smoker. The results suggest reduced methylation is a feature in rheumatoid synovium from smokers.

Marina Kamel

(Associate Professor Alison Rich and Dr Jonathan Broadbent, Department of Oral Diagnostic & Surgical Sciences)
Title: Outcome of potentially malignant oral mucosal lesions: a follow-up study
(Otago Service Clubs Medical Trust Scholar)

The aim was to define clinical characteristics and behaviour of leukoplakia, the commonest potentially malignant oral lesion, in patients diagnosed histologically with epithelial keratosis (with or without dysplasia) from 1997 to 2006. For cases (565) that fulfilled the inclusion criteria, the male:female ratio was 1.23:1, and the average age was 54 years. Progression to a higher degree of dysplasia was observed in 4/107 (4%) of initially non-dysplastic lesions. Malignant transformation occurred in 5/169 (3%) of lesions; 3 previously diagnosed with mild and 2 with moderate dysplasia. None of the severely dysplastic lesions progressed. The absence of dysplasia in an initial biopsy did not preclude later progression.

Marina Kamel

Beom Jun Lee

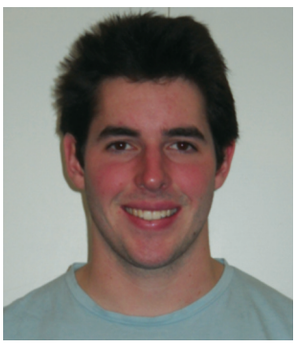
(Dr Mary Jane Sneyd and Associate Professor Brian Cox, Department of Preventive & Social Medicine)
Title: Seasonal variation in incidence of malignant melanoma in New Zealand
(Healthcare Otago Charitable Trust Scholar)

The mechanism of seasonal variation in cutaneous melanoma incidence is poorly understood. We analysed the characteristics of incident cases of cutaneous melanoma by season of diagnosis in the population of New Zealand from 1996 to 2007. Incident melanoma cases were grouped into one of four seasons by month of diagnosis defined in the study. The incidence rates among the seasons were compared using summer:winter ratios as well as negative binomial regression for several characteristics of melanoma. We found significant seasonal variability in melanoma diagnosis with the highest months from November through to March for both men and women. It is most likely that the phenomenon of seasonality in melanoma incidence is multifactorial including the effects of sunlight as well as behavioural factors that differ between seasons.

Michael Milne

(Dr John Ashton, Department of Pharmacology & Toxicology)
Title: Pain in the spinal Cord
(St Kilda Community Sports Society Scholar)

Calcitonin gene-related peptide (CGRP) is located in many areas throughout the body and has been shown to have a variety of roles. In the spinal cord, studies suggest CGRP has a role in the production of neuropathic pain and generation of tolerance towards neuropathic drug treatments. We conducted an experiment to first determine the level of CGRP released in the presence of capsaicin. We then determined whether the opioid, DAMGO, could reduce CGRP release in the presence of capsaicin. Results showed that DAMGO had no effect over CGRP release alone or with capsaicin, suggesting opioid receptors in the spinal cord have no control over CGRP release.



Michael Milne

Rachel Moir

(Dr Alan Carne, Department of Biochemistry, and Dr Aladin Bekhit, Department of Food Science)
Title: Analysis of proteins with health properties in sheep milk
(Foodstuffs Community Trust Scholar)

Recognition of the health properties of milk has stimulated interest in the potential medical value of milk whey proteins that are generated as a side-product fraction of cheese manufacture by dairy companies.

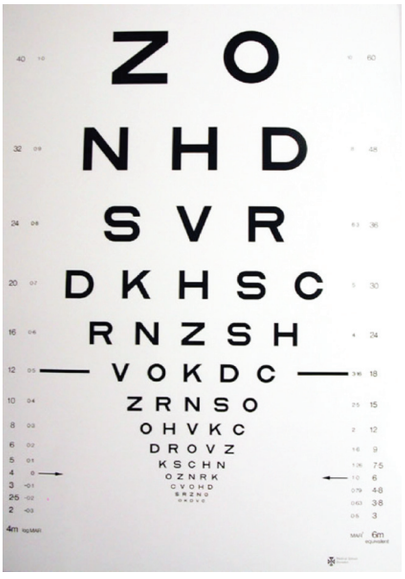
There is interest in evaluating the protein composition of sheep milk generated by Blue River Dairy for its medical and health value and it is known that sheep milk is beneficial to people allergic to cow's milk. This project achieved preliminary fractionation and characterisation of whey proteins in sheep milk for subsequent evaluation of the potential to develop health-promoting whey products.

Rachel Moir

Nishanthan Ramachandran

(Associate Professor Gordon Sanderson, Department of Medicine)
Title: Is your vision tested accurately in New Zealand?
(Deloitte Touche Tohmatsu Limited Scholar)

Twenty-six eyes were tested for visual acuity in 17 Dunedin 'Primary Healthcare' centres (including the Emergency Department) and compared to the Dunedin Hospital Eye Department. Lighting, distance and other variables were also measured. On average 12 centres produced inconsistent visual acuity scores (11 were worse than the Eye Department's and one was better). This could lead to unnecessary referrals or unfair withdrawal of a driver licence, and poor grading of suitability for surgery. Incorrectly measured visual acuity may also mean loss of independence for the elderly. We conclude that inconsistencies in visual acuity scores are easily modifiable by following lighting and distance standards.



Nishan Ramachandran

Shin Seong

(Professor Helen Nicholson, Department of Anatomy)
Title: The role of the cell membrane in prostate cancer progression
(OceanaGold – Prostate Cancer Scholar)
Hormone refractory (HR) prostate cancer is the most commonly diagnosed cancer in NZ men and yet the prognosis is poor. It is unclear what drives growth in HR diseases, but recent findings suggest that it may be related to changes in the structure of the cell membrane. Thus, this study investigated how these changes in the membrane promote cell proliferation to identify potential targets for treatment. However, this study failed to produce any significant results and a number of possible reasons have been discussed, so that future studies can be conducted in a more effective manner.

Jordan Vincent

(Professor Andre van Rij, Department of Surgical Sciences)
Title: Detecting reflux into the small veins of the skin in the leg using contrast enhanced ultrasound
(Allan Wilkinson Summer Scholarship and Commendation)

This study investigates a new method to test the function of the small veins just under the skin in the leg. These veins have valves within them that are thought to keep blood moving towards the heart. If these valves stop working people may be more susceptible to developing leg ulcers. We have used traditional ultrasound scanning combined with an injection of a contrast agent that shows up on the scan to image these small veins. The contrast agent only shows in the small veins if their valves are not working. We were able to demonstrate dysfunction of these valves in both healthy people and in those with ulcers. However the test needs to be developed further to be able to see if there is a difference between these two groups.

Jordan Vincent

Gavin Yeh

(Associate Professor Sally McCormick, Department of Biochemistry)
Title: Identifying genetic variation in the LPA gene
(Kingston Sedgfield Charitable Trust Scholar)

Lipoprotein(a) [Lp(a)] is a cholesterol transport molecule found in blood and a risk factor for cardiovascular disease if elevated. Some individuals, however, have virtually no Lp(a) and this is thought to have a genetic basis. In this study we have identified 27 genetic variants within the LPA gene that result in amino acid changes in the glycoprotein component of Lp(a). One particular variant has previously been shown to impair Lp(a) synthesis and another variant shown to result in a complete inability to form Lp(a). Together, these genetic variants could help to explain the lack of Lp(a) in such individuals.

Gavin Yeh

Stephanie Yung

(Dr Nick Cutfield, Department of Medicine)
Title: Head-eye reflex function in Parkinson's disease
(J.A. Iverach Summer Scholar)

The vestibulo-ocular reflex (VOR) is thought to be normal in patients with Parkinson's disease (PD). Due to technical limitations only low frequency VORs have previously been tested. Twenty-three patients with PD were compared to age-matched older and young healthy control groups. Older healthy controls showed a trend to a lower VOR gain with a further trend to reduction in the PD group. The trend to a mild reduction in the high frequency VOR gain in older age may be relevant for imbalance in elderly populations and is worthy of further study. High frequency VOR is unlikely to be a reliable biomarker in PD.

Stephanie Yung

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 2011 there were 27 applications from the University of Otago (cf 34 the previous year) totalling $579,801 and eight of these were funded at a total expenditure of around $145,000 of which $75,000 was provided most generously by the Otago Community Trust. These grants commenced between July and September 2011 and are nearing completion with full reports due 3 months after the one-year grant ends. Progress as at the end of July 2012 is summarised below:

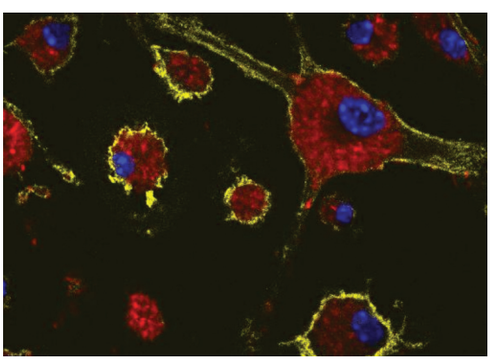
(I) ANNUAL GRANTS

Professor Mike Eccles And Dr S Young

(Department of Pathology)

Development of a new microparticle vaccine adjuvant with the ability to deliver siRNA to Dendritic cells – AG 303

Dendritic cells (DCs) are an important component of the immune system; they possess the unique ability to facilitate immune responses (especially T-cell mediated immunity). This raises the possibility of using DCs to trigger specific anti-cancer immunity. Cancers usually evade the immune system, but occasionally the immune system spontaneously rejects cancer, which can lead to a complete or partial cancer remission in a cancer patient. Therefore, it may be possible to "instruct" DCs to fight cancer cells, which might then potentially represent a new and promising immunotherapeutic approach for treatment of advanced cancer, as well as for the secondary prevention of cancer. In this proposal we aim to boost the survival of DCs and so increase the chance of instructing DCs to mount an immune response against cancer cells. Our strategy for boosting DC survival involves inhibition of the DCs own pathways that normally induce cell suicide (or apoptosis).
To achieve this our strategy is to "vaccinate" DCs with a specialised particle on which we have engineered an inhibitory tag, called an "siRNA". However, firstly we needed to work out exactly how to attach an inhibitory tag to the specialised particle, and then show that this tag enters the DCs along with the particle and is released from the particle once inside the DC. All work towards this goal has been carried out by a PhD student in my lab, Francesco Mainini. Francesco has attached a fluorescent tag (not an siRNA in the first instance, because of the high cost of siRNAs) to the specialised particle (coloured red in the attached image), and this tag/particle combo was then shown to be taken up into the DCs (which here are characteristically labeled cells with yellow margins and blue nucleus). Francesco has further shown that this tag is released inside DCs.
At present he is now beginning to attach the inhibitory tag (siRNA) to the specialised particle, in order to show that we can now boost the DC survival. Once this is shown, we plan to show that this increases DCs survival in vitro and in vivo. In future we would use this strategy to show that this increases the immune response of DCs against cancer cells in mice.



Dr Stephanie Hughes

(Department of Biochemistry)

Emptying the rubbish bin – Lysosome function and childhood brain disease – AG 304

In order to maintain health, cells must constantly renew used components. This is achieved primarily by the lysosome, an acidic organelle containing over 50 enzymes which digest and recycle used cellular waste. Dysfunctional lysosomes contribute to a wide variety of diseases including a group of childhood brain disorders known as Batten disease. Children suffer progressive blindness, cognitive deficits, vegetative state and premature death and there are no effective treatments currently available. In this study we are determining the effects of one common mutation on lysosomal function using neuronal cells from a naturally occurring sheep model. During this study we have shown that the mutation does not affect the stability of the protein suggesting instead an alteration in protein function. Cells from sheep affected by Batten disease have defective lysosome function and changes in the structure of another cellular structure (the endoplasmic reticulum). These changes are being used as markers to monitor the effectiveness of gene therapy strategies.

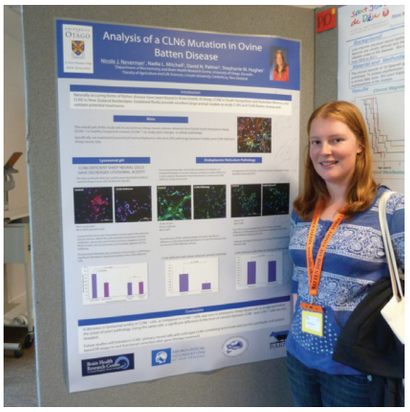


Photo of Hughes lab member Nicole Neverman presenting OMRF funded work at the 13th International Congress on Neuronal Ceroid Lipofuscinosis (NCL 2012). London March, 2012.

Dr Sabastien Taurin and Associate Professor Rhonda Rosegren

(Department of Pharmacology & Toxicology)

Optimising raloxifene as an effective treatment for triple negative breast cancer tumour: mechanisms and gene expression – AG 305

Triple negative breast cancer represents nearly 15% of all breast cancers and is characterised by a lack of expression of three proteins used for targeted therapies namely the oestrogen receptor (ER), progesterone receptor and Her2. Our data have shown that raloxifene, a drug used to treat certain ER expressing breast cancers, is also potently toxic against several ER-negative breast cancer cells. Furthermore, a daily dose of raloxifene is sufficient to decrease the cell proliferation and promote cell death in an animal model of ER-negative breast cancer. The effect of

raloxifene appears to be mediated through a reduction in epidermal growth factor receptor (EGFR) signaling, a protein essential for ER-negative breast cancer growth, migration and invasion, hallmarks of tumour development and metastasis. Additional experiments performed in vitro showed that raloxifene treatment also decreases cell migration and invasion. Overall, these data demonstrated the potential of raloxifene for the treatment of ER-negative breast cancers.

(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 five projects selected were:

Professor Paul Glue

(Department of Psychological Medicine) and Associate Professor David Perez (Department of Medicine)
Rapid acting antidepressant treatment for depressed patients with cancer in palliative care – CT 298

During the course of this project, we performed two detailed literature analyses, the first to evaluate the effects of ketamine in patients with unipolar and bipolar depression, and the second to examine the evidence for antidepressant treatments working on depression in cancer patients. We finalised a treatment protocol, and enrolled one patient. This patient with metastatic ovarian cancer had severe major depression, which responded rapidly and completely to ketamine 1 mg/kg intramuscularly. She requested to remain on treatment and received repeated weekly treatments. During this time her depression was kept in remission, despite the progression of her cancer. As a result of her improved mood, she reported a better relationship with her daughter, and improved functionality. Low-dose intramuscular ketamine may be a useful option for treating depression in patients with end-stage cancer. These data have now been published (J Pall Med 2012, 15:400-403). Dr Grott-Zanicotti, a collaborator, was also invited to present these data at two national research meetings (at the RANZCP Conference in Queenstown, and at a Medical Congress in Sao Paulo, Brazil).

Dr Grott Zanicotti, who led this research CT 298 Rapid acting antidepressant treatment for depressed patients with cancer in palliative care.

Dr Graeme Hammond-Tooke

(Department of Medicine)
Modification of transcranial magnetic stimulation (TMS)-evoked potential by repetitive TMS – CT 299

Up to a third of patients with epilepsy are resistant to medication. A potential add-on treatment in this situation is repetitive transcranial magnetic stimulation (rTMS), where the brain is painlessly stimulated with magnetic pulses. We have been using the magnetic stimulation, combined with electroencephalography (EEG), to assess rTMS protocols designed to reduce excitability of the brain and hence control epileptic seizures. Eleven healthy volunteers (mean age 29, 4 male) were tested. In each session a series of electrical responses of the brain to magnetic stimulation were measured by electrodes embedded in a cap placed over the scalp. The participants then received either real or "sham" repetitive stimulation at 1 stimulus per second for 10 minutes and another series of TMS responses was then obtained. The responses were averaged and compared. rTMS changed the size of a negative wave occurring in the brain at 100 milliseconds after the magnetic pulse and therefore called the N100 component. This waveform is thought to represent inhibitory processes in the brain and our findings suggest it is a useful marker of the effects of rTMS. We are now testing epileptic patients to see if they have an abnormality of the N100 and to see whether rTMS can correct that abnormality using rTMS. Ultimately, we aim to use rTMS to reduce the frequency of seizures in patients with drug resistant epilepsy.

Figure: Shows (left to right) Ms Allanah Harrington, research student, holding the magnetic coil, Associate Professor Graeme Hammond-Tooke, the primary investigator and Ms Patsy Mason, EEG technologist.

Professor Helen Nicholson

(Department of Anatomy), Dr Istvan Ábraham (Department of Physiology) and Maree Gould (Department of Anatomy).
The role of the cell membrane in prostate cancer progression – CT 300

Prostate cancer is initially dependent on androgens for growth but in many men, with time, the cancer progresses and becomes hormone refractory (HR). It is unclear what drives growth in HR disease but recent findings suggest that this may be related to (a) changes in the structure of the cell membrane and (b) incorporation of the androgen receptor into the

membrane. Our immunocytochemical studies have confirmed that in prostate cancer cells the androgen receptor is incorporated into the cell membrane where it is co-localised with the lipid raft component of the membrane. We have previously shown that the peptide oxytocin (OT) inhibits cell proliferation while in prostate cancer OT, in the presence of androgen, stimulates proliferation and we have hypothesised that this is due to an interaction of the androgen and oxytocin receptor on the cell membrane. Preliminary data suggest that this is the case. In prostate cancer, but not in normal cells, treatment with OT and androgen results in the OT and androgen receptors co-localising and moving away from the lipid rafts. This movement of receptors may result in the activation of cell signalling pathways that favour cell proliferation.

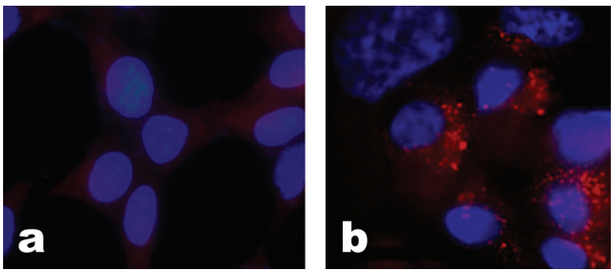


Figure. Co-localisation of oxytocin and androgen receptors using the Duolink system. Prostate cancer cells a) no treatment; b) following treatment with oxytocin and androgen. Blue staining indicates the nucleus of the cell and red where the oxytocin and androgen receptors are co-localised. The role of the cell membrane in prostate cancer progression - CT 300 Professor Helen Nicholson (Department of Anatomy), Dr Istvan Ábraham (Department of Physiology),and Maree Gould (Department of Anatomy).

Associate Professor Magnus Thorn

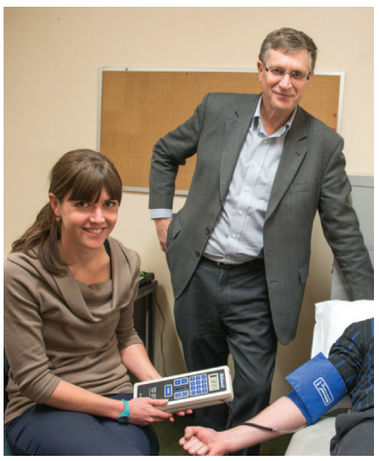
(Department of Surgical Sciences)
T-cell trafficking in Crohn's disease – CT 301

Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gastrointestinal driven by T-cell recruitment and activation in the intestine.
T-cells represent immune cells that mediate defences towards foreign agents present in our body, including molecular components of intestinal bacteria and our food. T-cells can come in different forms, one form presents factors that cause inflammation while another form inhibits inflammation. To affect inflammation or regulation in the intestine, these cells must migrate into the intestine from the blood stream. New treatments for IBD involve pharmacological inhibition of the migration. However, we have found that this specific means of pharmacological blockade may in fact preferentially prevent the beneficial anti-inflammatory T-cell migration to the intestine. We are investigating this further using a combination of advanced surgical immunological techniques.

Professor Andre van Rij

(Department of Surgical Sciences)
Circulating microRNAs as indicators of remote ischaemic preconditioning for cardio-protection in surgery – CT 302

Remote Ischaemic Preconditioning (RIPC) is a phenomenon in which short repeated periods of ischaemia (restriction in blood supply) of the arm provide protection for the heart against prolonged, potentially lethal ischaemia-reperfusion injury (e.g. a heart attack), such as may occur following major invasive surgery. Despite this being a well-accepted occurrence, the way in which it works is not known.
We set out to determine if microRNAs (miRNAs, short pieces of RNA that regulate gene expression) have the potential to give a clue as to how RIPC works.
We measured miRNAs in the blood of 10 healthy, young volunteers, before, 90 min and 24 hours after RIPC was performed. The RIPC protocol simply involved inflating a blood pressure cuff around one arm (as seen in photograph) to 200 mmHg, three times for five minutes each. After 90 min we identified two miRNAs the concentration of which had gone down, and one which had gone up compared to baseline. At 24 hours post-RIPC, two of these initial three were again reduced; in addition there were four other miRNAs whose expression changed. This is a new discovery and now we need to establish what specific gene expression pathways these miRNAs point to. As miRNA analysis is a new and rapidly growing field, the role of our miRNAs of interest unfortunately have not yet been fully worked out. In the meantime we are collecting samples in a patient group, who are undergoing RIPC prior to vascular surgery, to assess if the same miRNAs are expressed in this group. Our aim is to find a specific pattern of miRNA expression that measures the response to RIPC, and use this to help optimise RIPC treatment strategies for multi-organ protection in surgery. The team of investigators are Professor Andre van Rij, Kate Thomas (PhD Candidate), Associate Professor Greg Jones and Vicky Phillips.



Professor Andre van Rij and Kate Thomas. CT 302, Circulating mircoRNAs as indicators of remote ischaemic preconditioning for cardio-protection in surgery.

In June 2012 there were 28 applications from the University of Otago totalling $780,420. Five of these were funded by the Foundation (~$120,000) and two by the Otago Community Trust ($60,000). Abstracts of their proposed work can be found at: *http://omrf.otago.ac.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 2011 there were 13 applications (compared with 16 the previous year) from the University of Otago totalling $305,434 and four of these were funded at a total expenditure of around $90,000. Final reports are not due until the end of March or May 2013. Work in progress is summarised below:

Dr Andrew Bahn

(Department of Physiology) and Associate Professor Lisa Stamp (Department of Medicine, Christchurch)
Regulation of urate synthesis (xanthine oxidase) and renal urate transport (AMP kinase) by furosemide – LA 303

The xanthine oxidase inhibitor allopurinol, or rather its pharmacologically active metabolite oxypurinol, is the most common treatment used to lower abnormally high serum urate (SU) levels in gout patients. Since around 18% of patients with gout suffer from concomitant hypertension, they require additional treatment with diuretics such as furosemide. Surprisingly, it has been reported that patients on furosemide show a significantly higher plasma oxypurinol concentration for any given allopurinol dose compared to patients receiving only allopurinol, whilst requiring relatively higher doses of the xanthine oxidase inhibitor to achieve the target SU of <6 mg/dl. Therefore, it seems that furosemide adversely affects the efficiency of urate regulation by allopurinol. This study aims to identify the molecular basis for this observation. Using a commercial in vitro assay, we determined the effect of various concentrations of both oxipurinol and furosemide (alone and in combination) on xanthine oxidase activity. Results show that under these conditions, the combination of furosemide with oxipurinol does not directly affect xanthine oxidase activity within the examined physiologically-relevant xanthine oxidase activity range of 1-7 mU/ml. These findings imply a more complex drug interaction within the cellular environment. To investigate this further, we grew human liver and kidney cells (HepG2 and HRCE cells) and extracted RNA and proteins. So far, we have analysed the expression level of XO, AMPK and GLUT9 in HepG2 cells in the presence or absence of urate in the culture medium. We have also established the antibodies for XO, AMPK and MRP4 for Western Blot analysis.



From left to right:
Principal investigator Andrew Bahn (Physiology, Dunedin)
Co-Investigator: Assoc. Prof Lisa Stamp (Medicine, Christchurch)
Research Technician: Claudia Knake (Physiology, Dunedin)

Dr Kirsten Coppell

(Department of Medicine)
A description of obesity related liver damage and associated disorders in the adult New Zealand population - Results from the 2008/2009 New Zealand Adult Nutrition Survey – LA 304

Blood remaining from the 2008/2009 New Zealand Adult Nutrition Survey (ANS) provides an opportunity to describe the epidemiology of two increasingly important conditions associated with obesity, that of the metabolic syndrome of non-alcoholic fatty liver disease (NAFLD) and hyperuricaemia (elevated serum urate), both of which are largely silent, yet increase the risk of a number of serious conditions (e.g. cardiovascular disease) and mortality. An ethics application to perform the additional blood analyses was submitted and approved. The laboratory pre-testing for both liver function tests (ALT, AST and GGT) and serum urate have been completed. Although later than planned, the analysis of the 3,100 blood samples at the Diabetes and Lipid Laboratory, Department of Human Nutrition, University of Otago, is well underway, and will be completed by mid-August. The results will be analysed in conjunction with demographic, lifestyle, dietary and anthropometric data collected as part of the ANS.

Dr Khaled Greish and Associate Professor Rhonda Rosengren

(Department of Pharmacology & Toxicology)
Utilising nanotechnology for producing effective anticancer therapy against breast cancer – LA 305

In New Zealand every year breast cancer affects around 2500 new patients and kills > 600 patients. One third of breast tumors lack a protein called the estrogen receptor, resulting in lack of effective management, leading to high mortality. We have synthesised novel curcumin derivatives with high efficacy against this type of cancer. Within the scope of this grant we aim to demonstrate selective delivery of these novel drugs to breast tumor models using nanotechnology. Nanotechnology cannot only increase the efficacy but also the safety of our compounds, and potentially

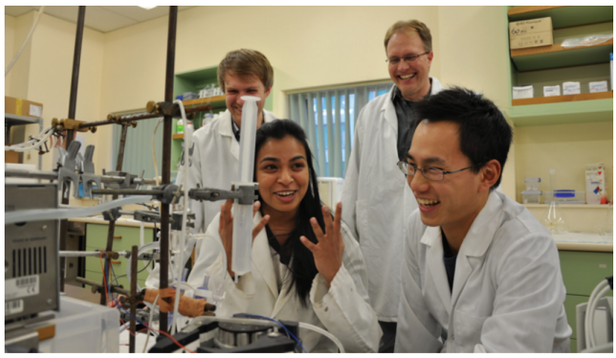
result in a clinical drug for those patients. We have successfully prepared the micelles which made the drug water soluble and therefore can be used clinically. In addition, as expected, the new micelles efficiently killed breast cancer cells. Among the different preparations we developed, we have identified the one with the highest toxicity against tumor cells. Currently we are getting ready to start the use of our novel Nanomicelles in animals with breast cancer, which fulfil the aims of this grant. We have already submitted one abstract based on this data to the Queenstown Chemical Biology and Drug Discovery meeting. We are also preparing a manuscript to publish our data in the international journal of Pharmaceutics.

Dr Khaled Greish
LA 305 - Utilising nanotechnology for producing effective anticancer therapy against breast cancer.

Dr Regis Lamberts and Dr Peter Jones

(Department of Physiology)
Hastened Relaxation in a Non-Failing Diabetic Heart – LA 306

Type-2 diabetes is the most prominent form of diabetes. It is characterised by impaired relaxation of the heart that eventually leads to heart failure. The heart's relaxation pathway is governed by the combined activity of two proteins, SERCA and phospholamban (PLB). SERCA is the major driver of relaxation whilst PLB acts to inhibit relaxation. Several studies of type-1 diabetic patients and animals have shown that SERCA is decreased and PLB is increased, which in combination slows relaxation of the heart. However, little is known about the activity of these two important proteins in type-2 diabetes. To examine the role of these proteins in type-2 diabetes, we collected atrial heart tissue from type-2 diabetic and non-diabetic patients undergoing coronary artery bypass surgery. Only patients without heart failure were included in this study to observe the early effects of type-2 diabetes on a non-failing heart. Using protein analysis techniques we quantified the amount of SERCA and PLB protein in these heart tissue samples. Our current data suggest that in type-2 diabetes the amount of SERCA is unchanged compared to non-diabetics. Unexpectedly our data also show, in contrast to type-1 diabetes, that the hearts of type 2 diabetic patients have less PLB. Combined our data advocate that relaxation of the heart in type-2 diabetes may initially be enhanced. Although unexpected, this could suggest that prior to heart failure the type-2 diabetic heart increases relaxation to counter other changes in an attempt the delay the inevitable decline in heart function and the progression into heart failure. The team of investigators are Shinanjali Lingham (Masters student, Department of Physiology), Pankaj Saxena (Dunedin Hospital), Sean Coffey (Dunedin Hospital) and Dr Chris Baldi (Department of Medicine).



Shivanajali Lingam, Simon Wang, Dr Pete Jones and Dr Regis Lamberts. LA 306 Hastened Relaxation in a Non-Failing Diabetic Heart.

(C) JACK THOMSON ARTHRITIS FUND

This is a new OMRF fund made possible by a bequest from the late Jack Thomson. For the inaugural grant round there were three applications from the University of Otago totalling $102,004 and one of these was funded at a total expenditure of $35,000. Work in progress is summarised below:

Professor John Highton

(Department of Medicine, Dunedin), Associate Professor Lisa Stamp (Department of Medicine, Christchurch) and Dr Paul Hessian (Department of Physiology)
Identification of subtypes of Rheumatoid Arthritis through joint and serologic characterization – JT 01

Different inflammatory pathways contribute to the overall inflammation and destruction of joint tissues in rheumatoid arthritis (RA). The particular focus of this grant is the contribution from an inflammatory pathway, involving the cytokine interleukin (IL)-17A, and the presence of follicular dendritic cells (FDCs).
We establish the presence of this pathway in inflamed joint synovial tissue by measuring expression of the IL17A gene and a gene called CD21L, produced by the FDCs. This aspect of the research work has commenced and we are currently working towards the "typing" of 40 synovial samples for IL17A and CD21L expression. We next propose to measure levels of selected cytokines in "paired" blood samples. We anticipate these will identify the same subgroup of patients in which the IL17A/CD21L pathway contributes to joint tissue inflammation. Using blood samples rather than joint tissue samples brings us closer to clinical application of our research where we can determine if this subgroup of RA patients has more severe disease that requires a different approach to treatment.

Dr Paul A. Hessian and Professor John Highton JT01-Identification of subtypes of Rheumatoid Arthritis through joint and serologic characterization.

4. OTHER ACTIVITIES OF THE SCIENTIFIC COMMITTEE

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

At the May 2012 scientific meeting of the Otago Medical School Research Society (OMSRS) there were ten candidates (selected from 18 applicants based on their submitted abstracts). All were summer research scholars and two of the ten (and four of the 18) had been sponsored by the OMRF. The first prize ($500) funded by the OMRF was awarded to Daniel Sundaresan (supervisor Dr Nick Heng, School of Dentistry) on the topic of "Mummy, Are there bugs in my mouth?". The second prize ($250) also funded by the OMRF was awarded to Samantha Murray (supervisor Dr Christine Jasoni, Department of Anatomy) for "Does the schizophrenia-inducing cytokine IL-6 alter neurite outgrowth in the developing brain?" The OMRF-sponsored summer research scholars presenting at the meeting were: Stella Cameron (supervisors Associate Professor Dorothy Oorschot and Dr Rachel Sizemore, Department of Anatomy) funded by the St Kilda Community Sports Society; and Jasper Diong (supervisors Associate Professor Rhonda Rosengren and Dr Khaled Greish, Department of Pharmacology & Toxicology) funded by the Lions Club of Dunedin South.

The Student Speaker awards are given to the student speakers who, in the opinion of a panel of five 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.

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

The opportunity for such sponsorship occurred in July 2012 when the Annual Review Lecture was given by Professor Melissa Little, University of Queensland, on the topic of "Investigating the kidney: morphogenesis to regeneration". Professor Little not only provided an excellent talk but her visit also the opportunity for extensive research discussions with clinical and basic scientists at the University of Otago.

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

The Foundation sponsors prizes each year in the Special Prize category (four awards at $50 each) at the Otago Aurora Science & Technology Fair for secondary schools for projects involving medically orientated topics. In July 2012 the recipients were "The Tooth Fairy" by Sam Maher (Year 7), "Huh? Is your MP3 player damaging your hearing?" by Arie Nader-Turner (Year 8), "Music & the Heart" by Beth Gray (Year 10), and "Pro? Bio?" by Sarah Graham and Charlotte Paddon (Year 12). The Foundation's judges were Dr Stephen Bunn, Associate Professor Pat Cragg, Associate Professor Greg Jones and Dr Nichola Heng.

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 of the Foundation whose financial support has made all this possible.

Patricia A. Cragg
Chairperson, Scientific Committee

FINANCIAL STATEMENTS

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 on 11 September 2012. The results presented in the summary financial report have been extracted from the full financial report for the year ended 31 March 2012. 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 2012 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 2012

	2012	2011
	$	$
Operating Income		
Donations, Bequests, Subscriptions	309,286	2,272,366
Investment Income	264,469	204,911
Profit (Loss) on Disposal of Investments	1,078	18,085
	574,833	2,495,362
Less Expenses		
Administration	63,241	47,603
Promotion Costs	88,171	77,385
Total Expenses	151,412	124,988
Net Surplus before Research Grants	423,421	2,370,374
Research Grants	349,226	327,874
Net Surplus for the year	74,195	2,042,500

Statement of Financial Position

As at 31 March 2012

	Market	2012	2011
		$	$
Current Assets		100,689	75,769
Investments	4,847,472	4,744,730	4,789,764
Total Assets		4,845,419	4,865,533
Current Liabilities		52,570	146,879
Total Liabilities		52,570	146,879
NET ASSETS (EQUITY)		4,792,849	4,718,654

Forward commitments for grants approved but not yet paid at balance date total $197,987

Statement of Movement in Equity

For the Year Ended 31 March 2012

	2012	2011
	$	$
Revenue and Revaluations		
Net Surplus	74,195	2,042,500
Total Revenue and Revaluations	74,195	2,042,500
Equity at the Beginning of the Year	4,718,654	2,676,154
Equity at the End of the Year	4,792,849	4,718,654

Deloitte

AUDITOR'S REPORT

WHK

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 2012, 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. We expressed an unmodified audit opinion on those financial statements in our report dated 11 September 2012. Those financial statements, and the summary financial statements, do not reflect the effects of events that occured 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 FRS-43: *Summary Financial Statements.*

Auditor's responsibilty

Our responsibilty is to express an opinion on these 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 2012 are consistent, in all material aspects, with those financial statements, in accordance with FRS-43.

WHK OTAGO

11 September 2012

Dunedin
CHARTERED ACCOUNTANTS

INFORMATION ABOUT THE FOUNDATION CHARITIES REGISTRATION NUMBER CC33444

SUBSCRIPTIONS:

Current subscriptions are $30 per annum for Ordinary Members, $100 per annum for Research Patrons (business firms or corporate bodies), and a minimum of $500 paid by individuals, ($1,000 for corporate bodies), applying as Life Members.

Although business firms are welcomed as Ordinary Members, in order to assist in expanding the work of the Foundation, they are invited to consider joining as Research Patrons or Life Members. The Foundation is an approved body for Income Tax purposes, and is registered for GST purposes. The taxation position in respect of donations and subscriptions is as follows:

COMPANIES:

- From 1 April, 2008 a company making cash donations, or paying a membership subscription to any one donee may treat the amount as a deductible item for tax purposes up to the amount of their net income.

MEDICAL PRACTITIONERS:

- Annual subscriptions - claim as a deduction.
- Donations - can be claimed as a rebate as for individual taxpayers.

INDIVIDUAL TAXPAYERS (INCLUDING FULL-TIME SALARIED DOCTORS):

- All taxpayers are entitled to a rebate on subscriptions and donations in excess of $5. Receipts should be attached to the Donations Rebate Form in support of the claim. From 1 April, 2008 taxpayers are able to claim a 33.33% tax rebate on all donations up to their annual net income.

GIFT AND DEATH DUTIES:

- No gift duty is payable by an individual on gifts to the Foundation.

REMEMBRANCE DONATION:

- When you consider this substitute in place of a floral tribute, write or telephone the Secretary giving the name of the deceased, the relationship to the deceased, the relationship to the bereaved, and the name and address of the bereaved. A letter of condolence will be sent to the bereaved notifying them that you have made a donation in place of a floral tribute.
  An acknowledgement, with a receipt for your donation (which may be tax deductible), will be sent to you. This is a dignified and practical way of expressing your condolence, which is invariably appreciated by the bereaved.

MEMBERSHIP:

- A form for membership application or donations is included on page 4 of this report.
  Further information or brochures will be supplied on request to the Secretaries, Deloitte, P.O. Box 1245, Dunedin. Telephone (03) 474-8630.

FUNDING PATHWAY

The Otago Medical Research Foundation made steady progress as it applied a conscious and deliberate funding strategy during the 2011/2012 financial year. A number of charitable Trusts, organisations and companies joined the Foundation in partnership with the details as follows:

Deloitte	$5,000
Dunedin Casino Charitable Trust	$1,000
First Sovereign Trust	$5,000
Foodstuffs Community Trust	$5,000
Dr Ailsa Goulding	$3,000
Infinity Foundation	$5,000
JAD Iverach Memorial Fund	$2,000
Kelliher Charitable Trust	$25,000
Kingston Sedgefield Charitable Trust	$3,200
Lions Club of Dunedin South	$5,000
MM & JH Hughes Family Trust	$2,500
Oceana Gold	$15,000
Otago Diabetes Trust	$4,000
Otago Service Clubs Medical Trust	$5,000
Pub Charity	$10,000
PWC Foundation	$5,000
Southern Trust	$10,000
Southern Victorian Charitable Trust	$45,000
St Kilda Community Sports Society	$12,000
The Community Trust of Otago	$75,000
The Healthcare Otago Charitable Trust	$4,000
WHK Otago	$5,000

During the 2011/2012 financial year, the following individuals have made donations to the Foundation:

Dr F J Austin
Mr M G Bell
Rev Dr J R Brinsley
Mr J Burton
Mr N A Carroll
Dr S O Chin
Mr E J Chronican
Dr M Coleman
Dr A Cook
Mr S Davie
Mr K G Dempster
Mr G G Dunckley
Dr J M Faed
Dr T Fitchett
Prof W Gillett
Dr S J Greaves
Emeritus Prof B F Heslop
Mr & Mrs S D Jones
Assoc Prof I Lamont
Prof R Laverty
Mr R Lewis
S McChesney
Dr B T McMahon
Dr J A McMahon
Prof A C B Molteno
Prof D G Palmer
Prof G B Peterson
Dr E L Phelan
Mr M Rowe
Mr A Swan
Mr I Thomson
Dr M Turner
Dr & Mrs G P White
Mr T J Williams
Mrs S M Willkinson
J C Wilson

LIST OF MEMBERS

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* Dr J. Allison
Mr S.G. Amsden
Mrs S. Armstrong
* Ashburn Hall
Dr F.J. Austin
Assoc Prof M.A. Baird
Dr L D Bascand
Mr M.G. Bell
Dr C.P. Bolter
Rev Dr John R Brinsley
Mr John Burton
Mr N.A. Carroll
Caversham Pharmacy (2005) Ltd
* Dr S.O. Chin
* Mr E.J. Chronican
Dr J.I. Clayton
Dr M Coleman
Dr A. Cook
Assoc Prof P.A. Cragg
Mr K.G. Dempster
* Mr G.G. Dunckley
Dr J.M. Faed
* Fairmaid Chance & Crawford
Mr M Farry
* Prof. F.N. Fastier
Dr B. Galland
Mrs H.L. Gibson
Prof W. Gillett
Dr P R F Gootjes
Prof A. Goulding
Dr S.J. Greaves
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Prof. B.F. Heslop
* Mr J.H. Heslop
Dr M. Hibma
Prof. J. Highton
Dr R.S.J. Highton
Mr M C Horne
Dr C Mck Holmes
* Prof. J.B. Howie
Mr A.K. Jeffery
Prof. D.T. Jones
Mr & Mrs S.D. Jones
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Prof. L.R. Robinson
Mrs M. I. Rowe
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Prof. D.C.G. Skegg
Prof. R.D.H. Stewart
Dr W. Sutherland
Mr M Thompson-Fawcett
Dr M. Turner
Prof. A.M. van Rij
Waihemo Pharmacy Ltd
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Dr & Mrs G P White
Dr S Wilbanks
* Mrs S.M. Wilkinson
Mr T.J. Williams
Prof D. Wilson
Dr R A Wright
Dr M.E. Wyatt
Dr A I Yelavich

* *Indicates Founder Member*

RESEARCH PATRONS

AMI Insurance Limited
Respiratory Research Unit
(University of Otago)
Hope & Sons Limited
Asthma Society Inc.

LIFE MEMBERS

Cadbury Confectonery Ltd
Mrs J Callon
Cerebos Gregg Ltd
Mr L Chronican
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Donaghys Industries Ltd
Dunedin City Council
Mr S Davie
Farra Dunedin Engineering Ltd
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HealthCare Otago Ltd
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Janssen-Cilag Pty Ltd
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Schering (NZ) Limited
Roche Products NZ Ltd
St Margaret's College Council
Mr IA Thomson
Mr HR Wilson & Mrs N Ellis

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Rotary Club of Dunedin South
Mr G T Adams
Mr P C L Gibson
Rotary Club of St Kilda
Prof J I Mann
Dr C N A & Mrs J Trotman

OTAGO
MEDICAL RESEARCH FOUNDATION

Otago Medical Research Foundation Inc.

Annual Report to 31st March 2012
& Notice of Annual General Meeting