The 2017 John Chalmers Oration

Crisis or opportunity? A new era for medical research funding in Australia

Professor Anne Kelso AO
CEO, National Health and Medical Research Council
Health in Australia – a good news story

Life expectancy has increased 3 months per year since the late 1800s:

- clean water and food
- immunisation
- water fluoridation
- tobacco control
- reduced salt intake
- blood pressure control
- cancer screening
- antibiotics
- acute care
Health in Australia – present and future challenges

More complex and chronic conditions:
- dementia
- obesity, diabetes
- mental illness
- asthma

Emergencies:
- antimicrobial resistance
- pandemics
- climate change
Health in Australia – opportunities

• Higher burden of disease in lower socioeconomic groups and more remote areas

• At least 31% of burden of disease is preventable, due to modifiable risk factors, especially:
  o tobacco use
  o high body mass
  o high blood pressure
  o high alcohol use
  o physical inactivity

• Most will require other approaches
Crisis or opportunity? Health and medical research
Crisis or opportunity? Health and medical research

- Demand >> supply
- Too tough for early and mid-career researchers
- Not enough jobs
- Writing grants takes too much time for low return
- Great ideas not funded
Crisis or opportunity? Health and medical research

- New rules: NHMRC grant reform
- New funding: Medical Research Future Fund
- Government’s innovation and science agenda
- Opportunities of modern biology
What do we want from research today?

- Solutions to our problems
- A better life for everyone
- Discovery and translation
- Creativity and innovation
- Collaboration and global connectedness
- Efficiency and speed
- Value for money

How should we support health and medical research to meet these needs?
Medical research is changing

• Teams have replaced the lone scientist – shared leadership

• Research teams need access to diverse skills:
  o animal, cellular, molecular, informatics, modelling, clinical, population..

• Research networks are global and multicultural

• Everyone is digitally connected:
  o data are shared
  o ideas spread fast

• Technology has replaced the traditional lab assistant:
  o kits, high-throughput robotics, data
  o outsourced specialist services
Louis Pasteur (Albert Edelfelt, 1885)  
Peter Doherty and Rolf Zinkernagel (1996)

http://mdhs.unimelb.edu.au
Whole-genome characterization of chemoresistant ovarian cancer

Ann-Marie Patch1,2*, Elizabeth L. Christie3*, Dariush Etemadmoghadam3,4,5*, Dale W. Garsed3*, Joshy George5, Sian Fereday3, Katia Nones1,2, Prue Cowin3, Kathryn Alsop3, Peter J. Bailey1,7, Karin S. Kassahn1,8, Felicity Newell1, Michael C. J. Quinn1,2, Stephen Kazakoff1,2, Kelly Quek1, Charlotte Wilhelm-Benartzi9, Ed Curry9, Huei San Leong3, The Australian Ovarian Cancer Study Group†, Anne Hamilton3,10,11, Linda Mileshkin3,5, George Au-Yeung3, Catherine Kennedy12, Jillian Hung12, Yoke-Eng Chiew12, Paul Harnett13, Michael Friedlander14, Michael Quinn22, Jan Pyman11, Stephen Cordner15, Patricia O’Brien15, Jodie Leditschke15, Greg Young15, Kate Strachan15, Paul Waring4, Walid Azar3, Chris Mitchell5, Nadia Traficante3, Joy Hendley3, Heather Thorne3, Mark Shackleton3,5, David K. Miller1, Gisela Mir Arnau3, Richard W. Tothill3,5, Timothy P. Holloway3, Timothy Semple3, Ivon Harliwong1, Craig Nourse1, Ehsan Nourbakhsh1, Suzanne Manning1, Senel Idrisoglu1, Timothy J. C. Bruxner1, Angelika N. Christ1, Barsha Poudel1, Oliver Holmes1,2, Matthew Anderson1, Conrad Leonard1,2, Andrew Lonie16, Nathan Hall17, Scott Wood1,2, Darrin F. Taylor1, Qinying Xu1,2, J. Lynn Fink1, Nick Waddell1, Ronny Drapkin18, Euan Stronach9, Hani Gabra9, Robert Brown9, Andrea Jewell19, Shivashankar H. Nagaraj1, Emma Markham1, Peter J. Wilson1, Jason Ellul2, Orla McNally22, Maria A. Doyle3, Ravikiran Vedururu3, Collin Stewart20, Ernst Lengyel19, John V. Pearson1,2, Nicola Waddell1,2, Anna deFazio12§, Sean M. Grimmond1,7§ & David D. L. Bowtell3,4,5,9,21§
Antagonism of B cell enhancer networks by STAT5 drives leukemia and poor patient survival

Casey S. Katerndahl1,13, Lynn M Hellemans-Harris1,13, Mark J Willet1, Christine M Henzler2, Seth Frietze2, Rendong Yang2, Hilde Schjerven2, Kevin A T Silverstein2, Laura B Ramsey3, Gregory Hubbard3, Andrew D Wells4, Roland P Kuiper4, Blanca Scheinen5,9, Frank N van Leeuwen6, Markus Mišc6,7,8, Steven M Kornblau1,11 & Michael A Ferrara1

The transcription factor STAT5 has a critical role in the development of lymphoblastic leukemia (B-ALL). How STAT5 mediates this effect is unclear. Here, we found that activation of STAT5 cooperates with defects in signaling components of the precursor B cell antigen receptor (p-BCR), including defects in downstream effectors such as BTK, PKCδ, NF-κB and IKAROS, to initiate B-ALL. STAT5 antagonizes the transcription factors NF-κB and IRF, suggesting that STAT5 regulates the expression of shared target genes. Super-enhancers showed enrichment for STAT5 binding and were associated with the STAT5+ enrichment for NF-κB and IRF4 and IKAROS. Patients with a high ratio of active STAT5 to NF-κB or IKAROS had more aggressive disease, highlighting the importance of STAT5 in B-ALL development.Biomedical and clinical

Shared leadership

11 institutions in US and Europe

15 funders

Complex data

A lot of data

Specialist skills

7 figures in main article, 8 supplementary figures on-line
Medical research is changing

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• Research teams need access to diverse skills:
  o animal, cellular, molecular, informatics, modelling, clinical, population..

• Research networks are global and multicultural

• Everyone is digitally connected:
  o data are shared
  o ideas spread fast

• Technology has replaced the traditional lab assistant:
  o kits, high-throughput robotics, data
  o outsourced specialist services

➤ Research is complex and expensive but outcomes are extraordinary
Science is boundless

The Nobel Prize in Physiology or Medicine 2016
Yoshinori Ohsumi

“There is no finish line for science. When I find an answer to one question, another question comes up. I have never thought I have solved all the questions.”
The budget for science is not boundless

Excludes Administered funding of $200 million over 5 years for the Boosting Dementia Research measure in the 2014-15 Budget, that is outside MREA.

* $74.3 million in funding was re-phased from 2012-13 to 2014-15.
How should we support health and medical research?

- Big science or small science
- People or projects
- Basic science or translational science
- Priorities or blue sky
- Investigator-initiated or targeted calls
- Prevention or cure
- Burden of disease or national strengths/weaknesses
People or projects?

What are the best predictors of future scientific success?

- Publication citation rates and various indices (e.g., h-index)
- Number of papers in high-impact journals
- Frequency of collaboration
- Pre-PhD publications
- First-author or high-impact publications in early career
- Gender
- Rank of institution
- Evaluation of research contributions and depth by peers

von Bartheld CS et al, Peer J 3;e1262 (2015)
People or projects?

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- Future success can be predicted (imperfectly)
- Metrics must be used with care
- Metrics drive behaviour
- Expert peer review is critical

von Bartheld CS et al, Peer J 3;e1262 (2015)
Predicting discoveries

- Productivity peaks early for most researchers
- Major discoveries occur at any point in the sequence of a scientist’s publications

Predicting discoveries

Creativity

https://blog.bigml.com/2013/04/19/a-new-way-to-visualize-decision-trees/

Photo by Ken McGregor
Creativity

- Creativity needs trust, flexibility and time to think, talk, try new things (methods, ideas, fields), fail and get feedback.

- Creativity is impeded by excessive competition, insecurity, short review cycles and predefined deliverables.

- Potentially groundbreaking research is characterised by controversy and uncertainty (and serendipity).

- Peer review is inherently conservative:
  - Mario Capecchi’s 2007 Nobel Prize for gene targeting: “We are glad you didn’t follow our advice” (NIH renewal panel in 1984).

WORK CONTEMPLATED FOR 1939.

It is impossible to put forward a detailed plan of research. For the last five years I have followed the course of (a) investigating such local epidemics or epizootics of virus disease as offered useful opportunities for work, and (b) of following up “leads” obtained in current work. (A) It is impossible to predict what virus infections may be prevalent, but both influenza and measles have been absent from Victoria from some years, and on their next appearance I hope to make a study of the viruses responsible. (B) We intend to continue the current investigations on the nature of immunity to viruses of the central nervous system, and on the essentially similar problem of influenza immunity, but what lines the work will take will depend on unpredictable circumstances.

(F.M Burnet)
Priorities or blue sky?

• In defence of blue sky research:
  o Impact of any one project is unpredictable.
  o Investments in basic research are variously estimated to return 20% – 60% per year in the long term, but better methods are needed.
  o Basic research provides new technologies and skills to translate knowledge into practice, solve problems and gain access to knowledge from elsewhere.

• Basic science and applied science are two sides of the same coin.

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➢ Unpredictable outcomes
➢ Unexpected connections
A new drug for chronic lymphocytic leukaemia

**Nature Vol. 335 29 September 1988**

*Bcl-2* gene promotes haemopoietic cell survival and cooperates with *c-myc* to immortalize pre-B cells

David L. Vaux, Suzanne Cory & Jerry M. Adams

The Walter and Eliza Hall Institute of Medical Research, PO Royal Melbourne Hospital, Victoria 3050, Australia

**FDA News Release**

FDA approves new drug for chronic lymphocytic leukemia in patients with a specific chromosomal abnormality

For Immediate Release

April 11, 2016

**The New England Journal of Medicine**

Targeting BCL2 with Venetoclax in Relapsed Chronic Lymphocytic Leukemia

Andrew W. Roberts, M.B., B.S., Ph.D., Matthew S. Davids, M.D., John M. Pagel, M.D., Ph.D., Brad S. Kahl, M.D., Soham D. Puvvada, M.D., John F. Gerecitano, M.D., Ph.D., Thomas J. Kipps, M.D., Ph.D., Mary Ann Anderson, M.B., B.S., Jennifer R. Brown, M.D., Ph.D., Lori Gressick, B.S., Shekman Wong, Ph.D., Martin Dunbar, Dr.P.H., Ming Zhu, Ph.D., Monali B. Desai, M.D., M.P.H., Elisa Cerri, M.D., Sari Heitner Enschede, M.D., Rod A. Hummerickhouse, M.D., Ph.D., William G. Wierda, M.D., Ph.D., and John F. Seymour, M.B., B.S., Ph.D.
Priorities or blue sky: predicting discoveries

*Fig. 1. How unexpected is a discovery?* Scientific discoveries vary in how unexpected they were relative to existing knowledge. To illustrate this perspective, 17 examples of major scientific discoveries are arranged from the unanticipated (like antibiotics, programmable gene editing, and cosmic microwave background radiation) to expected discoveries (like the observation of gravitational waves, the structure of DNA, or the decoding of the human genome).

Priorities or blue sky?

• We need problem-solving and priority-driven research:
  o Meet expectations of community and government for use of public funds
  o Ensure translation of knowledge into improvement of health and wellbeing
  o Attract researchers to questions important to society

• Setting priorities isn’t easy:
  o Burden of disease, emerging threats
  o National strengths versus national needs or gaps
  o Spending money, saving money
  o Who decides?
How should we support health and medical research?

There is no one “best” way to do research or to fund research – we need to support:

• research at different scales
• researchers at all career stages
• free-range research – the engine for future application
• research that addresses the problems of today – local, national, global.
NHMRC funding reforms
NHMRC research funding – the problem

• After strong growth, NHMRC research budget has been on a plateau for the last 5 years.

• Funding rates in some major schemes are now about 15%.

• Excessive competition is damaging our national research effort:
  - researchers are discouraged
  - research is more likely to be risk-averse
  - research time is lost preparing and reviewing grant applications.

➤ Development of NHMRC’s new grant program
The review:

- Examined structure of NHMRC’s current grant program
- Consulted on alternative models
- Develop a preferred new model.

Process (January 2016 – May 2017):

- Expert Advisory Group
- Consultations:
  - national consultation (public forums and written submissions)
  - targeted consultations
  - Government departments
  - Research Committee, Council and other PCs
- Announcement by Minister for Health on 25 May 2017
Objectives of reform

• Encourage innovation and creativity across all fields of health and medical research

• Provide opportunities for talented researchers at all career stages and across all disciplines

• Minimise burden on researchers, freeing up time for research while retaining core focus on improving human health and wellbeing through research
Philosophy underpinning the new grant program

Health and medical research is best supported by a diversified portfolio of schemes that:

• Fund across the spectrum of health and medical research
• Invest in people with outstanding research achievement and promise
• Support the most innovative projects to solve complex problems
• Meet specific strategic objectives.
# NHMRC’s current grant program

<table>
<thead>
<tr>
<th>Fellowships and Scholarships</th>
<th>Program Grants</th>
<th>Project Grants</th>
<th>Strategic and leveraging grants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual researchers:</td>
<td>Teams of high-performing researchers pursuing broad-based, multidisciplinary research activities</td>
<td>Research projects of individuals and teams: • creation of new knowledge • across all fields of health and medical research</td>
<td>Research that responds to national priorities: • Centres of Research Excellence • Partnerships • Development Grants • Targeted Calls • International schemes</td>
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<td>Six per investigator</td>
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NHMRC’s new grant program

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| Support the research program of outstanding investigators at all career stages | Support outstanding multidisciplinary teams to work together to answer major questions that cannot be answered by a single investigator | Support innovative research projects addressing a specific question | Research that responds to national priorities:  
- Centres of Research Excellence  
- Partnerships  
- Development Grants  
- Targeted Calls  
- International schemes  
- Clinical trials and cohort studies |

| | | | |
| Salary + research support package | Research costs ($5 million) | Research costs | Research costs |
| One per investigator | One per investigator | Two per investigator | No caps |
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• Clinical trials and cohort studies |
| 5 years | 5 years | Up to 5 years | |
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... while retaining core focus on improving human health and wellbeing through research
Objectives of reform

• Encourage innovation and creativity across all fields of health and medical research
  - Investigator Grants offer flexibility for strategic, creative, collaborative research
  - Ideas Grants focus on fresh thinking – science rather than track record
Objectives of reform

• Encourage innovation and creativity across all fields of health and medical research

• Provide opportunities for talented researchers at all career stages and across all disciplines
  
  ➢ Investigator Grants will be provided for all career stages
  
  ➢ Synergy Grants will encourage diverse teams, e.g. by discipline, career stage and gender
  
  ➢ Ideas Grants will be an opportunity for those with less-developed track records
Objectives of reform

• Encourage innovation and creativity across all fields of health and medical research

• Provide opportunities for talented researchers at all career stages and across all disciplines

• Minimise burden on researchers, freeing up time for research
  - Investigator Grants consolidate funding and reduce need to apply for Project Grants every year
  - Consolidation plus capping is expected to reduce application numbers in steady state
New grant program – timeline

25 May 2017
Announcement of new grant program

Development of funding rules

August 2017
Webinar

From late 2018
Applications open under new grant program

January 2020
Grants commence under new grant program

Late 2019
First grants awarded under new grant program
New grant program – timeline

- **August – December 2017**
  - Peer review advisory groups
  - National consultation on peer review

- **Late 2019**
  - First grants awarded under new grant program

- **25 May 2017**
  - Announcement of new grant program

- **From late 2018**
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Medical Research Future Fund
Two federal medical research funds: MREA and MRFF

To raise the standard of individual and public health throughout Australia...

Annual appropriation in Federal Budget

To improve the health and wellbeing of Australians...

Draw-down from projected $20 billion perpetual fund
Projected support from NHMRC and MRFF

MRFF: $1.4 billion draw-down over 5 years

Forward Estimates

2015-16
2016-17
2017-18
2018-19
2019-20
2020-21

Appropriation ($ billion)

Existing NHMRC Funding
$4.9 billion between 2015-16 and 2020-21

MRFF Distributions
$1.4 billion between 2015-16 and 2020-21

Source: 2017-18 Portfolio Budget Statements
Australian Medical Research Advisory Board consults then determines:

- **5-year Strategy:**
  - must ensure coherent and consistent approach is adopted
  - must take NHMRC strategy into account

- **2-year Priorities:**
  - must be consistent with the Strategy
  - must take into account several factors

Minister for Health takes the Priorities into account and may seek expert advice in making decisions on MRFF expenditure.
MRFF: first round of disbursements

• Extensive consultation in 2016.
• AMRAB’s first Strategy and Priorities announced by the Prime Minister on 9 November 2016
• 19 Priorities under six headings:
  o Strategic and international horizons
  o Data and infrastructure
  o Health services and systems
  o Capacity and collaboration
  o Trials and translation
  o Commercialisation
• Investment plan developed by Government taking Strategy and Priorities into account
MRFF: first round of disbursements: $65.9 million

- Preventive health and research translation projects
  - Australian Preventive Health Partnership Centre ($10 million)
  - AHRTCs and CIRHs ($10 million)

- Clinical trials and clinical researchers
  - Clinical trials and registry activities ($13 million)
  - National alliance of clinical trials networks ($5 million)
  - Clinical researcher fellowships ($8 million)
  - Accelerated research investment: CanTeen and MND ($7 million)

- Breakthrough research
  - Antimicrobial resistance ($5.9 million)
  - Pandemic preparedness (CEPI) ($2 million)
  - Proof of concept for new health biotechnology ideas:
    - precision medicine and 3D anatomical printing ($5 million)
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Relationship between MRFF and NHMRC

- NHMRC CEO is an *ex officio* member of Australian Medical Research Advisory Board.

- Advisory Board must take NHMRC strategy into account in setting MRFF strategy.

- MRFF Act enables NHMRC to administer MRFF grant schemes.

MRFF supports research to address national priorities

NHMRC supports activity and capability across breadth of research needs
MRFF

- First disbursements are wide-ranging
- Majority of first disbursements are being delivered through competitive processes, including via NHMRC
- Priorities will change over time
- Available funds will rise very fast – a huge opportunity for the sector
- NHMRC and MRFF offer complementary mechanisms to support Australian health and medical research
Crisis or opportunity? Health and medical research
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- Too tough for early and mid-career researchers
- Not enough jobs
- Writing grants takes too much time for low return
- Great ideas not funded

- New rules: NHMRC grant reform
- New funding: Medical Research Future Fund
- Government’s innovation and science agenda
- Opportunities of modern biology
Opportunities of modern science
The glass is filling

• Health and medical research has a good story to tell and there are opportunities to achieve much more.

• Diverse approaches are needed to fund the best research today.

• There are new opportunities for Australian health and medical research:
  – NHMRC ‘s new grant program
  – Medical Research Future Fund

• Though research we will continue to improve human health and wellbeing.
Thank you