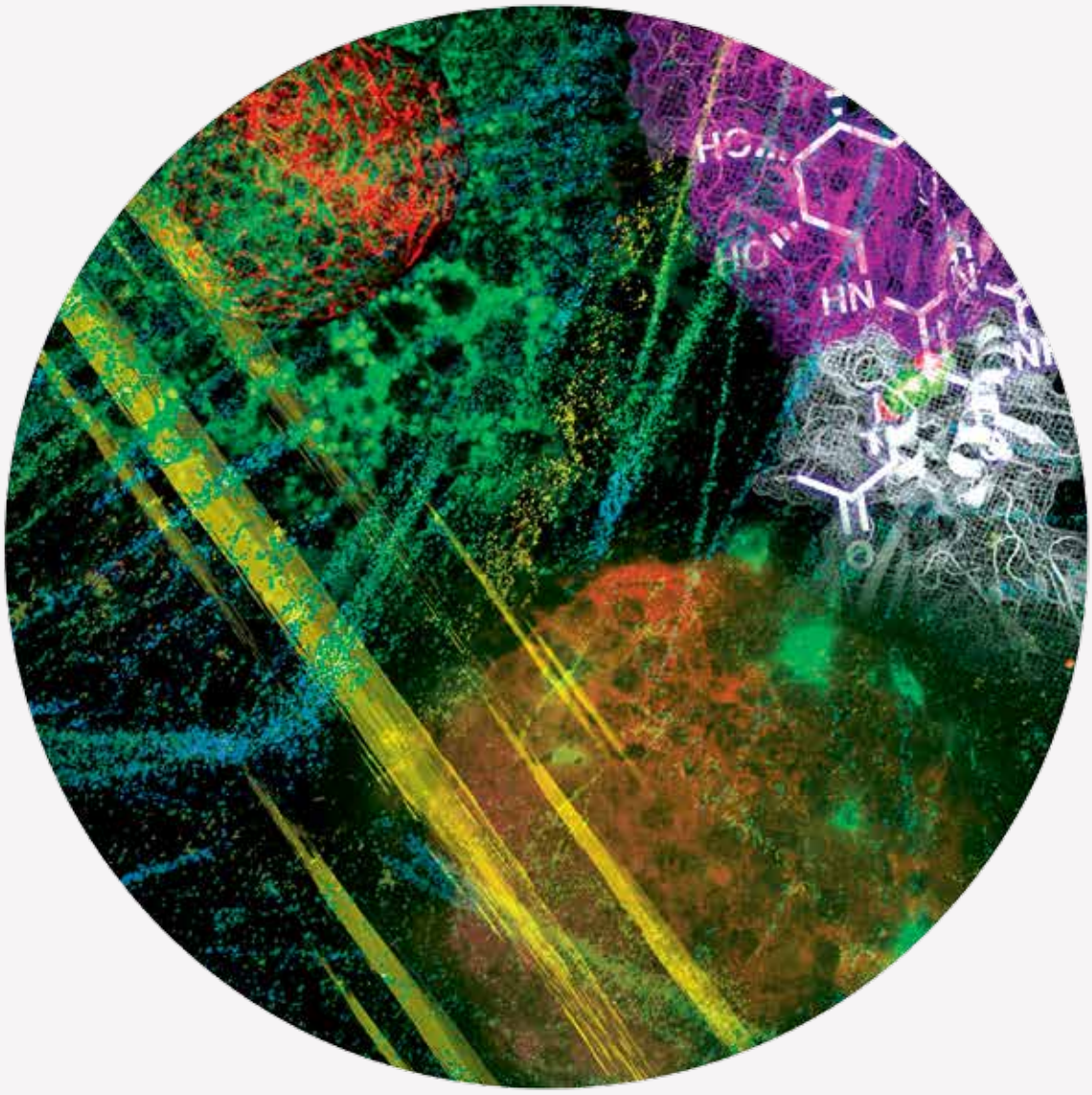
Centre for Advanced Molecular Imaging

AN ARC CENTRE OF EXCELLENCE



ANNUAL REPORT

2014

Funding Body

Australian Government
Australian Research Council

Administrating Organisation

MONASH University

Collaborating Organisations

THE UNIVERSITY OF MELBOURNE

LA TROBE UNIVERSITY

UNSW AUSTRALIA

THE UNIVERSITY OF QUEENSLAND AUSTRALIA

Partner Organisations

ansto

Australian Synchrotron

THE UNIVERSITY OF WARWICK

Leica MICROSYSTEMS

DESY

ZEISS

ARC Centre of Excellence in Advanced Molecular Imaging Annual Report 2014

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Contents

Overview

Our health - our ability to ward off infection and disease - depends on our immune system. The key to the operation of the immune system is how its proteins, cells and other components interact at a molecular level with threats such as toxins and invading microbes. Uncontrolled immune responses can also result in disease - through chronic inflammation, for example.

This is what the Centre for Advanced Molecular Imaging (Imaging CoE for short) is all about - developing and using innovative microscopy and imaging techniques to observe the details of how the immune system functions at the molecular level.

The highly collaborative Centre brings together biologists, physicists and chemists from five Australian universities, the University of Warwick in the UK, the Australian Nuclear Science and Technology Organisation (ANSTO), synchrotrons in Australia and Germany and several high-tech companies.

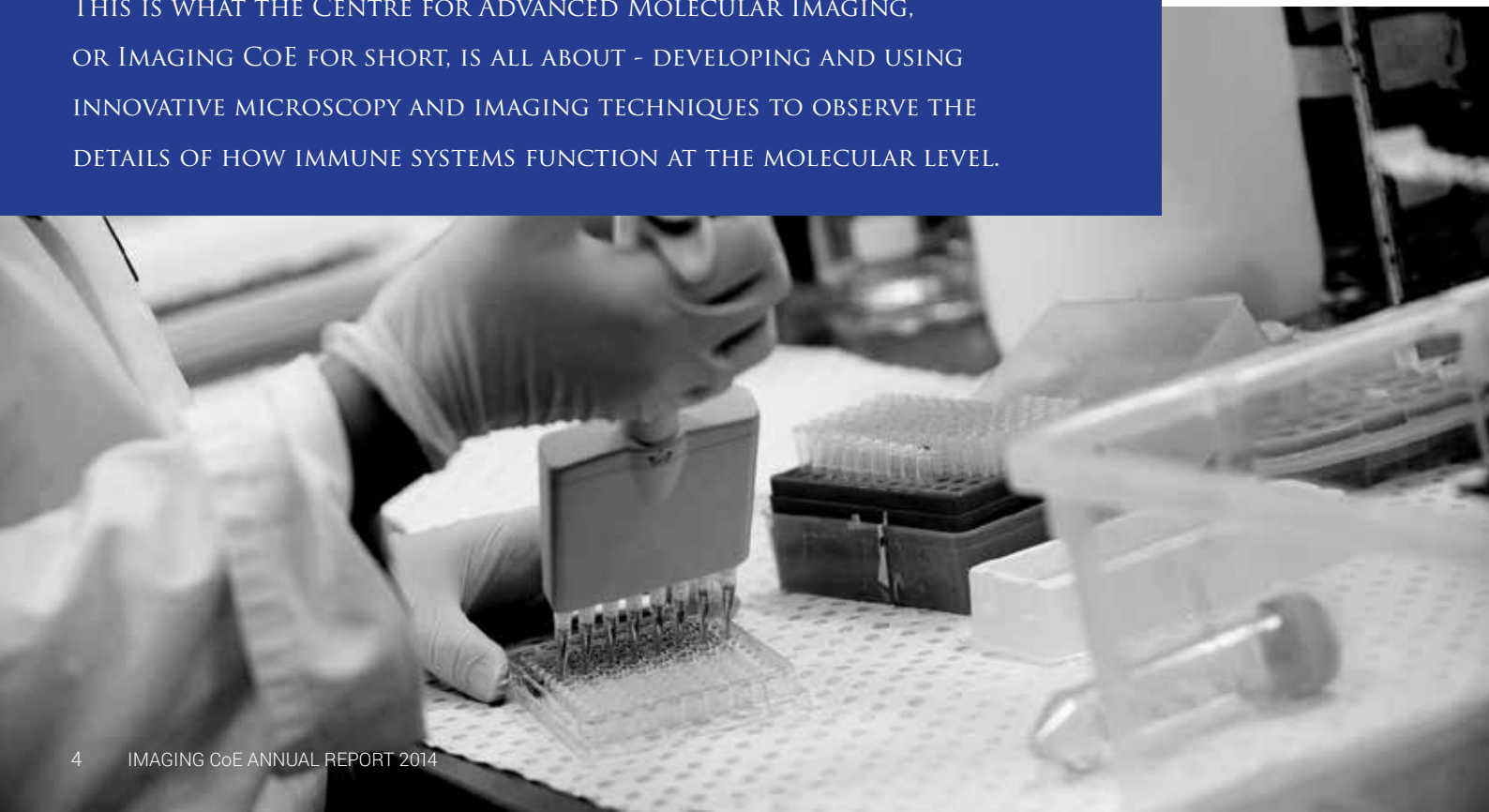
It is an Australian Research Council (ARC) Centre of Excellence and funded with more than $39 million over seven years from 2014—$28 million from the ARC and a further $10 million from its partners.

By building Australia's knowledge, capabilities and capacity in advanced molecular imaging and immunology, the Centre will provide an unprecedented understanding of how immune recognition events result in the appropriate defensive responses. It will also pioneer the next generation of imaging at the atomic, molecular, cellular and whole animal levels.

The objectives of the Centre are to:

- Undertake large scale, transformative, interdisciplinary and collaborative research;
- Develop innovative imaging technologies, products and intellectual property;
- Establish a centre that will link national and international networks of universities, research infrastructure and industry;
- Attract and mentor early and mid-career interdisciplinary researchers; and
- Establish a strong, nationwide, outreach program, with a focus on communicating our scientific discoveries to key stakeholders and the general public.

This is what the Centre for Advanced Molecular Imaging, or Imaging CoE for short, is all about - developing and using innovative microscopy and imaging techniques to observe the details of how immune systems function at the molecular level.



About The Centre

5 collaborating universities

6 partner organisations, including

2 commercial partners

$39 million investment over 7 years

67 researchers

9 world class Chief Investigators across physics, chemistry and biology

21 students

ACHIEVEMENTS/2014

61 publications, including 12 in Nature group journals

130 citations

90 media articles (TV, print, radio and internet) covering the Centre

110 presentations in conferences and meetings in 12 countries

$33.5 million attracted in additional funding and grants

4 new linkages made with external organisations

Director's Message

Why immunity? Scientists have always been fascinated by how the immune system functions; its failure or unwanted activities underpin most of the conditions that beset humans as they age

Throughout the history of biology the questions of "What does it look like?" and "How does it work?" have been inextricably linked. The answer to these questions lies in one word – "imaging". Accordingly, the fields of biology, physics and chemistry have together revealed insights into more and more complex biological problems. These hard-won breakthroughs have often arisen from these fields intentionally working hand-in-hand with one another, spurred on by the serendipity of sudden and unexpected discoveries in the different scientific arenas. Together these communities have achieved more than the sum of the individual parts.

Progress in imaging has been further accelerated through the construction of more powerful supercomputers, sophisticated software and larger and more powerful light sources. In regards to the latter technology, our scientific world has benefited from revolutionary developments in light and electron microscopy, through the construction of multiple generations of synchrotrons around the globe (including in Australia), and, most recently, the development and application of massively powerful X-ray free electron lasers (XFEL). Our new Imaging Centre is the latest exemplar of such international collaborative science, and is applying the full spectrum of microscopy and other imaging technologies to probe the workings of the mammalian immune system.

Why immunity? Scientists have always been fascinated by how the immune system functions; its failure or unwanted activities underpin most of the conditions that beset humans as they age. Accordingly, imaging and immunity have made excellent and productive bedfellows over the development of modern biological chemistry. For example, some of the earliest crystal structures were of immunity-related proteins that could be purified in sufficient quantities to crystallize.

2014 saw the first year of funding our Imaging Centre. During this year, the Centre has established our administrative structures. For this I have to thank Manoj Sridhar, Chantelle Linnett and the Centre team as a whole for their tireless efforts and support. We have further had many important scientific successes – the first paper in Nature from the Centre was published early in the year, featuring two of our CI team. This work detailed how mucosal-associated invariant T cells detect reactive intermediates in the synthesis of vitamin B2.

Our deputy director Kat Gaus attracted the first Centre-associated EMBL-Australia Group Leader to the node she leads. More EMBL-Australia Group Leaders will join the Centre in 2015.

Our physicists and mathematicians based at La Trobe University, the University of Melbourne, the Australian Synchrotron in Monash University and ANSTO have joined forces with our crystallography teams and started to collect data at the Stanford XFEL – this is imaging at its most extreme indeed. Further the Centre and our physics team are now part of the Single Particle Imaging initiative (SPI).

From a personal perspective one highlight of the the year came in December with the delivery (in 31 crates) of the FEI Titan Krios to the new Clive and Vera Ramaciotti Centre for Structural Electron Microscopy at Monash University. This instrument will represent a critical and complementary technology for biologists and crystallographers to understand protein and cellular structures.

What is ahead for us in 2015? The application of new physics and chemistry to understanding immunology will allow us to probe some of the most challenging questions in biology. Further, we will continue to develop new and exciting ways to engage with both the public and our industrial partners. Finally, in early 2015 a new group of PhD and Undergraduate students have joined the Centre; we are all looking forward to working with these young, energetic and imaginative scientists.

Prof. James Whisstock
Director, ARC

Centre of Excellence in Advanced
Molecular Imaging
NHMRC Senior Principal Research Fellow
Department of Biochemistry & Molecular Biology
Monash University

Message from our Governing Board Chair

My Board colleagues and I are really impressed by the confluence of physicists, who are developing new approaches to imaging, with biologists and chemists

I am delighted to serve as the Chair of the Governing Board of the Imaging CoE alongside my fellow Board colleagues, Prof. Ian Smith from Monash University and Dr. Erol Harvey from miniFAB (Aust) Pty Ltd.

As a Board, we are here to ensure that the that the Centre reaches the amazing potential that it holds; that it operates in a way that fulfills all the obligations of its agreement with the ARC; that it maintains its finances well and reports appropriately; and that it maintains a system for controlling risk. I am confident that the broad ranging expertise across academia, industry and stakeholder relations that the Governing Board members possess will enable us to provide valuable insights to James and the Centre Executive.

My Board colleagues and I are really impressed by the confluence of physicists, who are developing new approaches to imaging, with biologists and chemists, who are some of the best people in the country and have an in-depth understanding of how the immune system works.

The Centre got off to a great start in 2014 and this is reflected in the Centre's key performance indicators (tabled in page 52). The highlights of the year for me were the outstanding research outcomes produced in the first year of Centre operations by our Chief Investigators, that has garnered an impressive amount of media coverage, and the success of the Centre in attracting nearly $30 million in additional funding through the EMBL Australia Group Leaders program and the 2014 round of ARC and NHMRC grants.

I share James' enthusiasm for 2015 as the Centre embarks upon a full year of research, training, and outreach programs, and wish James and the Centre all the very best in 2015.

Prof. Frances Shannon

Governing Board Chair
Deputy Vice Chancellor, Research
University of Canberra

BRIEF PROFILE

Frances is Deputy Vice Chancellor, Research, at the University of Canberra and Chair of the Governing Board of the Imaging CoE.

She was educated in Ireland and holds a PhD in Biochemistry from University College Dublin. She then moved to Australia and developed a successful career in biomedical research. Her particular research interest is in how proteins of the immune system are encoded in DNA and she led the Gene Expression and Epigenomics Laboratory at John Curtin School of Medical Research at the Australian National University.

Frances has managed large, complex, multi-disciplinary, multi-institution projects such as the Murray-Darling Basin Futures project, and she brings this expertise, in addition to her research knowledge, to the Centre's Governing Board.

GOVERNANCE

The Imaging CoE is administered by Monash University with day-to-day operations managed by the core administrative team including the Centre Director, Professor James Whisstock, Chief Operating Officer, Dr. Manoj Sridhar, and Centre Administrator, Ms. Chantelle Linnett.

The Centre's current governance structure is shown in the chart on page 9. The Governing Board is at the pinnacle of the Centre's governance structure. Meeting on a biannual basis, the Board's role is to ensure fiscal compliance, good research practice, and alignment of the Centre activities with respect to the goals of the Centre. The Board also provides strategic advice with regards to scientific research directions, commercialisation and industry linkage opportunities, and outreach and advocacy issues.

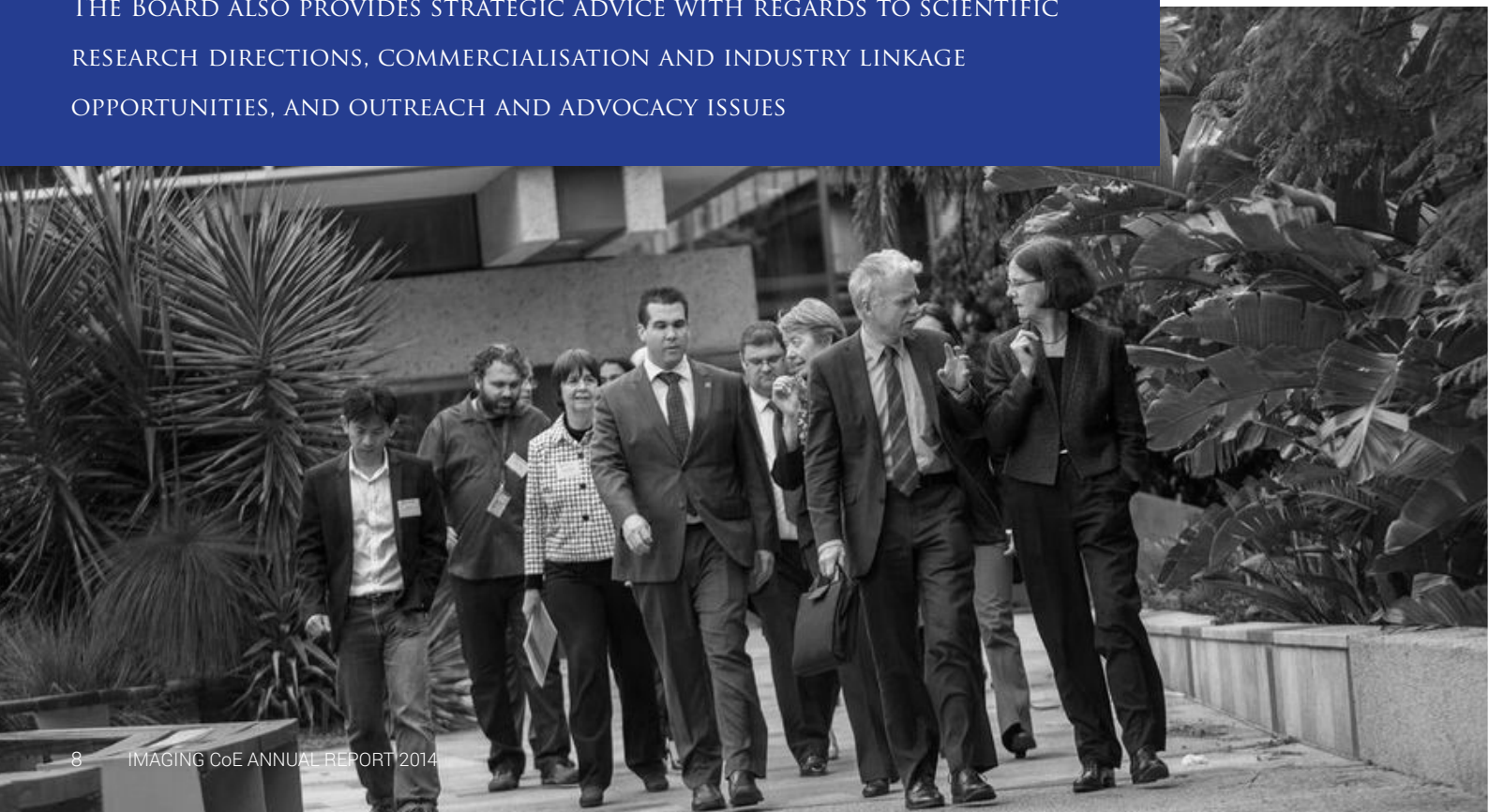
Headed by Professor Frances Shannon, Deputy Vice Chancellor (Research) at the University of Canberra, the Board comprises of Professor Ian Smith (Vice Provost (Research & Research Infrastructure) and Dr. Erol Harvey (Founder & Chief Executive Officer, MiniFAB (Aust) Pty Ltd. In addition to technical expertise in molecular biology and proteomics, Profs. Shannon and Smith bring considerable experience in governing and operating successful, national collaborative projects. Dr. Harvey, a distinguished physicist with expertise in microfluidics and polymer micro engineering, brings a deep knowledge of translational research and commercialisation from his work in industry and academia.

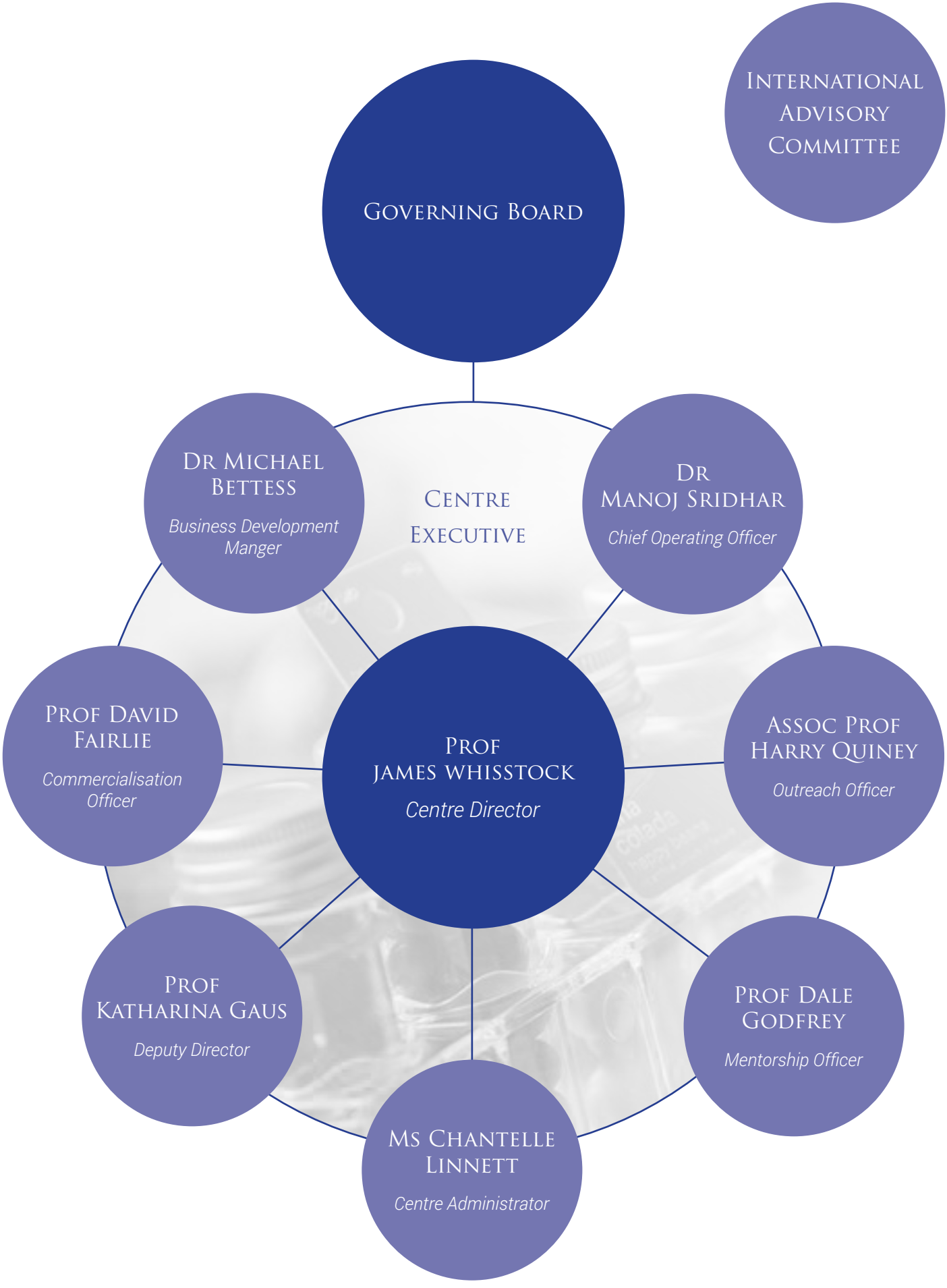
The International Advisory Committee gives independent strategic advice to the Director on the positioning of the Centre with respect to new research directions, international outreach and industry linkage opportunities. The Committee also annually reviews the research, education and outreach programs as well as industry linkages and commercialisation outcomes of the Centre and conveys its findings to the Governing Board for consideration and action.

The Centre Executive oversees the general management and operations of the Centre across each of the five collaborating nodes. The Executive meets on a monthly basis and discuss and solve issues arising on the scientific, financial and commercial arenas.

All Centre CIs meet on a quarterly basis to discuss their research projects, key milestones and achievements, and to discuss potential opportunities for collaboration and problem solving. These quarterly meetings have a strong focus on research progress, key barriers to progress and opportunities for collaboration. They are a vital part of the Centre's operations as it presents the opportunity for all Centre CIs and relevant project members to meet with other Centre staff from different nodes to share ideas and explore new opportunities for growth and development.

THE BOARD ALSO PROVIDES STRATEGIC ADVICE WITH REGARDS TO SCIENTIFIC RESEARCH DIRECTIONS, COMMERCIALISATION AND INDUSTRY LINKAGE OPPORTUNITIES, AND OUTREACH AND ADVOCACY ISSUES




International Advisory Committee
Governing Board
Centre Executive
Dr Michael Bettess
Business Development Manger
Dr Manoj Sridhar
Chief Operating Officer
Prof David Fairlie
Commercialisation Officer
Prof James Whisstock
Centre Director
Assoc Prof Harry Quiney
Outreach Officer
Prof Katharina Gaus
Deputy Director
Prof Dale Godfrey
Mentorship Officer
Ms Chantelle Linnett
Centre Administrator

Imaging CoE Chief Investigators

Prof. James Whisstock
Centre Director

James is a NHMRC Senior Principal Research Fellow at Monash University.

He trained in Bioinformatics and Structural Biology and obtained his PhD from University of Cambridge in the UK in 1996. Since arriving in Australia in 1997, James has established himself as one the leading structural biologists nationally and internationally. He has played a critical role in establishing state-of-the-art research platforms in Protein Production, eResearch and Structural Cryo-Electron Microscopy at Monash University.

His specialty is in decoding the atomic structures of complex protein molecules with a particular interest in membrane attack complex/perforin-like proteins, which play a critical role in immunity and developmental biology.

James has won numerous awards during his career including Science Ministers Prize in Life Sciences (2006), Commonwealth Health Ministers Award (2008) and the Australian Academy of Science Gottschalk Medal (2010).

Prof. Katharina (Kat) Gaus
Deputy Director

Kat is a NHMRC Senior Research Fellow at UNSW and leads the UNSW Centre in Single Molecule Science at the Lowy Cancer Research Centre.

She is a trained physicist with a PhD in biotechnology from the University of Cambridge in the UK. Her specialty is super-resolution microscopy, which she uses to study how T cells make decisions on actions such as moving, secreting signalling compounds such as cytokines or committing suicide. She has been collaborating with renowned German manufacturer of optical systems, Carl Zeiss AG in developing a super-resolution fluorescence microscope that can image molecules within living cells.

Together with Justin Gooding and Peter Reece, colleagues at UNSW, Kat was one of the finalists for the Eureka Prize for Excellence in Scientific Research in 2014. for developing an optical device that can monitor the activity of a single cell. She also won an Elizabeth Blackburn Fellowship in 2014.

Assoc. Prof. Brian Abbey

Brian is an ARC Future Fellow in the Department of Physics and leads the Materials characterisation and XFEL Science group at La Trobe University.

He holds masters degrees from University College London and Imperial College of Science and Technology, and a PhD in Chemistry from University of Cambridge in the UK. An experimental scientist, Brian works along with Centre colleagues, Keith Nugent and Harry Quiney, to develop new X-ray free electron laser imaging technology that will revolutionise the field of structural biology. XFEL-based imaging has the potential to allow structural biologists to determine the atomic structures of single biomolecules with unprecedented resolution without the need to form large crystals.

To develop this cutting edge technology, Brian collaborates with leading scientists and engineers at the Deutsches Elektronen Synchrotron (DESY) in Hamburg, Germany as well as the Stanford Linear Coherent Light Source (LCLS) in California, USA.

Prof. David Fairlie

David is a NHMRC Senior Principal Research Fellow and Head of the Division of Chemistry and Structural Biology at the Institute for Molecular Bioscience, University of Queensland.

David holds a PhD in Chemistry from the University of New South Wales. His research involves chemistry (design, synthesis, structure), biochemistry (enzymology, protein-protein interactions) and pharmacology (molecular, animal).. His focus is on inventing new drugs and in understanding molecular mechanisms of disease development and drug action.

Immune responses and the pervasive influences of chronic inflammation in development and progression of diseases are central in his research.

David has experience in translating laboratory research into commercial successes by forming industry linkages with pharmaceutical companies and brings this experience to the Centre as the Commercialisation Officer for the Imaging CoE.

Prof. Dale Godfrey

Dale is a NHMRC Senior Principal Research Fellow at the University of Melbourne and current President of the Australasian Society for Immunology, a society with over 1,000 members. He also serves as Imaging CoE Mentorship Officer responsible for the development of mentoring and training programs for Centre students.

Holding a PhD in immunology from Monash University, Dale has worked in the field of T cell biology for over 25 years with a focus on T cell development and innate-like T cell biology. Specifically, he has made progress in understanding the roles and functions of two innate T cell subgroups - Natural Killer T (NKT) cells and Mucosal Associated Invariant T (MAIT) cells.

Working together with Centre colleague, Jamie Rossjohn, Prof. James McCluskey at the University of Melbourne and a number of high profile international collaborators, Dale and his group aim to identify and study all the different types of innate T cells, which form between 5% - 20% of the body's overall T cell population.

Dale was awarded the Woodward Medal at University of Melbourne in 2013 in recognition of his research excellence.

Prof. William (Bill) Heath

Bill is a Professor in the Department of Microbiology and Immunology at the University of Melbourne.

An experienced and distinguished immunologist with a PhD in Medicine from the University of Melbourne, Bill uses infectious diseases, particularly malaria and Herpes simplex (the virus that causes cold sores), to study how the immune system functions. Specifically, he focuses on understanding the role and functions of memory T cells, which are critical in the development of vaccines, and dendritic cells, which play a critical role in triggering an immune reaction by presenting antigens to T cells.

Working with Centre colleagues, Scott Mueller, Kat Gaus and Woei Ming (Steve) Lee and Prof. Frank Carbone and the University of Melbourne, Bill uses and develops imaging technology to look at immune responses in tissues and whole animals.

In addition to a long and successful track record in obtaining competitive research funding, Bill was also selected as a Fellow of the Australian Academy of Science and awarded the Burnet Oration and Medal by the Australasian Society for Immunology in 2011.

Imaging CoE Chief Investigators

Prof. Keith Nugent

Keith is currently Deputy Vice Chancellor (Research) at La Trobe University.

He holds a PhD in laser physics from the Australian National University and has previously served as Director of the Australian Synchrotron, Laureate Professor of Physics at the University of Melbourne and Research Director of the ARC Centre of Excellence for Coherent X-ray Science.

Working together with his fellow Centre colleagues, Brian Abbey and Harry Quiney, Keith is developing new X-ray free electron laser (XFEL) imaging technology to determine the structure of single molecules. This is presently not possible with existing X-ray crystallography techniques and requires improved understanding of fundamental physics.

Over a distinguished career, Keith has won numerous awards for his scientific excellence and leadership including the Victoria Prize in 2004, Centenary Medal in 2003 and two R&D100 awards for innovation in 1988 and 2001.

Prof. Jamie Rossjohn

Jamie is a NHMRC Australia Fellow in the Department of Biochemistry and Molecular Biology at Monash University.

He is a world-leading X-ray crystallographer and holds a PhD in X-ray crystallography from Bath University. His expertise is in understanding the structural and biophysical basis for T cell recognition of foreign antigens. Working together with fellow Centre colleagues Dale Godfrey and David Fairlie, Jamie studies the molecular interactions of a number of different classes of immune cells with a view to understanding the role they play in infection and immunity.

Jamie has won numerous awards for scientific excellence including the Prime Minister's Prize for Life Scientist of the Year in 2004, Gottschalk Award from the Australian Academy of Science in 2007, and the Eureka Prize for Scientific Research in 2013. He was also elected as a Fellow of the Australian Academy of Science in 2014.

THE UNIVERSITY OF MELBOURNE

Assoc. Prof. Harry Quiney

An experienced theoretical physicist, Harry holds a Master's degree in Theoretical Chemistry from Monash University and a PhD in Physical Sciences from University of Oxford in the UK, he previously served as Deputy Director of the ARC Centre of Excellence for Coherent X-ray Science. His expertise is in developing computational models of the structure of atoms and molecules, the quantum nature of materials, chemical bonding and the interaction between light and matter.

Working with his experimental Centre Colleagues, Brian Abbey and Keith Nugent, Harry is developing computational algorithms that interpret and translate single molecule diffraction data from X-ray free electron lasers (XFELs) into meaningful atomic structures. Modelling the interaction of molecules with XFELs is complex and involves discovering new physical phenomena because XFELs are a billion times more powerful than the X-rays used in traditional X-ray crystallography.

Harry carries out his computational work on supercomputers such as those available through the Victorian Life Sciences Computational Initiative (VLSCI).

He is also passionate about communicating the excitement and value of science to young students. He is heavily involved with the Growing Tall Poppies Program which provides practical scientific training to secondary school students.

Membership

Partner Investigators

Name	Institution
Prof. Andrew Peele	Australian Synchrotron
Prof. John Davey	University of Warwick, UK
Prof. Henry Chapman	DESY, Germany

Associate Investigators

Name	Institution
Dr. Michelle Dunstone	Monash University
Dr. Ruby Law	Monash University
Dr. Thomas Caradoc-Davies	Australian Synchrotron
Dr. Julian Vivian	Monash University
Dr. Stephanie Gras	Monash University
Dr. Danny Hatters	University of Melbourne
Dr. Till Boecking	University of New South Wales
Dr. Woei Ming (Steve) Lee	Australian National University
Assoc. Prof. Matt Sweet	University of Queensland
Dr. Kate Schroder	University of Queensland
Dr. Shan Shan Kou	University of Melbourne
Dr. Jeffrey Davis	Swinburne University of Technology
Dr. Daniel Pellicci	University of Melbourne
Dr. Scott Mueller	University of Melbourne
Dr. Adam Uldrich	University of Melbourne
Dr. Ranjeny Thomas	University of Queensland
Dr. Michael Jones	Australian Synchrotron
Dr. Benedicta Arhatari	La Trobe University
Dr. Jeremie Rossy	University of New South Wales
Assoc. Prof. Hans Elmlund	Monash University
Assoc. Prof. Dominika Elmlund	Monash University
Dr. Elizabeth Hinde	University of New South Wales

Senior Scientists and Postdoctoral Researchers

Name	Institution
Dr. Philip (Rusty) Nicovich	University of New South Wales
Dr. Sophie Pageon	University of New South Wales
Dr. Elvis Pandzic	University of New South Wales
Dr. Jieqiong Lou	University of New South Wales
Dr. Bo Chen	La Trobe University
Dr. Connie Darmanin	La Trobe University
Dr. Guido Cadenazzi	La Trobe University
Dr. Peter Berntsen	La Trobe University
Dr. Ruben Dilanian	University of Melbourne
Dr. Janice Cheng	University of Melbourne
Dr. Darryl Johnson	University of Melbourne
Dr. Tamara Hilmenyuk	University of Melbourne
Dr. Ali Zaid	University of Melbourne
Dr. Ben Gully	Monash University
Dr. Claudia Del Campo	Monash University
Dr. Andrew Keller	Monash University
Dr. Richard Berry	Monash University
Dr. Victoria Hughes	Monash University
Dr. Siew Siew Pang	Monash University
Dr. Travis Johnson	Monash University
Dr. Paul Conroy	Monash University
Dr. Andrew Ellisdon	Monash University
Dr. Daouda Traore	Monash University
Dr. Ligong Liu	University of Queensland
Dr. Jeffrey Mak	University of Queensland
Dr. Annika Yau	University of Queensland
Dr. Rink-Jan Lohman	University of Queensland
Dr. Jacky Suen	University of Queensland
Dr. Abishek Iyer	University of Queensland
Dr. James Lim	University of Queensland
Dr. Robert Reid	University of Queensland
Dr. Timothy Hill	University of Queensland
Dr. Huy Hoang	University of Queensland

Administrative Staff

Name	Institution
Fabienne Perani	La Trobe University
Dr. Manoj Sridhar	Monash University
Chantelle Linnett	Monash University
Kathy Palmer	University of Melbourne
Dr. Michael Bettess	Monash University

Research Assistants and Laboratory Managers

Name	Institution
Stephanie Pradier	University of Melbourne
Scott Reddiex	University of Melbourne
Zheng Ruan	University of Melbourne
Marcin Ciula	University of Melbourne
Fiona Ross	University of Melbourne
Garth Cameron	University of Melbourne
John Wadington	University of Melbourne
Ming Li	University of Melbourne
Abigail Pollock	University of New South Wales
Margaret Bills	Monash University
Gordon Lloyd	Monash University
Devadharshini Jeevarajah	Monash University

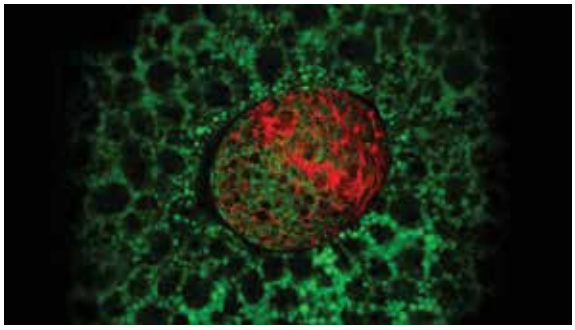
Students

Name	Institution
Yuanqing Ma	University of New South Wales
Yui Yamamoto	University of New South Wales
Nicholas Phillips	La Trobe University
Hannah Coughlan	La Trobe University
Henry Kirkwood	La Trobe University
Salman Maqbool	La Trobe University
Nicholas Anthony	La Trobe University
Catherine Sadatnajafi	La Trobe University
Sophie Williams	University of Melbourne
Rebecca Ryan	University of Melbourne
Daniel Wells	University of Melbourne
Nicholas Gherardin	University of Melbourne
Fern Hui Koay	University of Melbourne
Catarina Almeida	University of Melbourne
Yu (Alex) Kato	University of Melbourne
Jyh Liang Hor	University of Melbourne
Anh Do	University of Queensland
Yuhong Jiang	University of Queensland
Kai-chen Wu	University of Queensland
Lilong Dong	University of Queensland
Weijun Xu	University of Queensland
Huu Thanh Le	Monash University
Bradley Spicer	Monash University

Research program

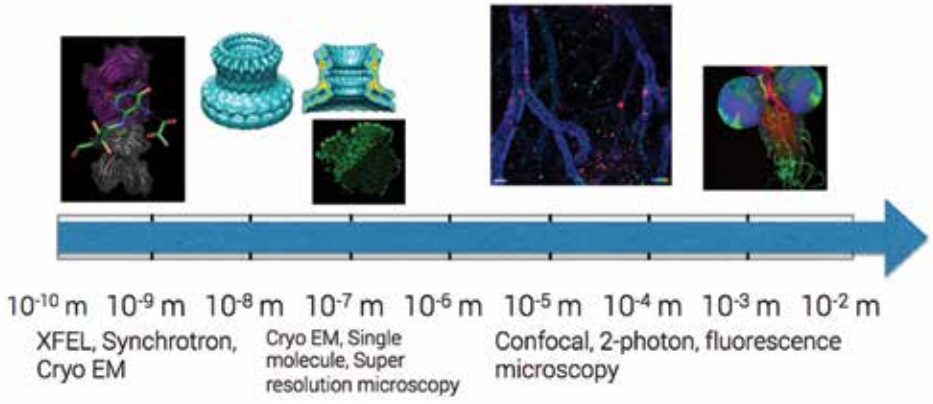
Research Overview

The research program of the Imaging CoE is broadly organised into two key themes - imaging and immunology. The imaging research themes aim to develop new microscopy and visualisation techniques that further the state-of-the-art technology available commercially. The immunology research themes aim to understand the various processes and interactions that underpin immunity by utilising a broad range of imaging techniques and a multi-scale approach to imaging. The figure below illustrates the organisation of our research theme and the range of techniques employed to study the various atomic, molecular and cellular interactions involved in immunity.



Imaging Research Themes

Our imaging research themes are broadly divided into atomic, molecular and cellular imaging. Each of the three imaging research themes focuses on specific imaging technologies and techniques that provide vital information on different length scales. Atomic imaging is primarily focused on determining the atomic structure of proteins that participate in various molecular interactions in the immune system. Molecular imaging seeks to place single molecules, multi-molecular complexes and protein clusters within the cellular context, and cellular imaging will focus on visualising immunological functions at the cell and whole animal scale. This multi scale approach will allow us to determine a holistic view of immune function - from the atomic structure of a key protein to the cellular responses triggered by its interaction with other proteins and molecules in the immune system - giving immunologists an unprecedented view of immunological activity.



Immunology Research Themes

Our immunology research themes will directly harness the new and existing cutting edge atomic, molecular, cellular and in vivo imaging technologies developed by our colleagues and others to address key immune-related themes that are interconnected to provide a comprehensive understanding of innate and adaptive immunity. The three immunology themes encompass:

- Immune recognition of three classes of antigens - peptides, lipids and metabolites (Recognition);
- How recognition events result in T cell activation (Activation); and
- The responses triggered by innate immunity as well as immune effectors (Effector function).

Atomic Imaging

Theme Leaders: Brian Abbey, Keith Nugent and Harry Quiney

Linking atomic structure to function is the key to understanding the molecular interactions and cellular responses that underpin immunity. There are several major technical difficulties in doing this, however. For instance, the principal technique for determining the atomic structure of proteins is X-ray crystallography. It demands large crystals, which diffract light well, however, preparing large crystals of certain functionally important proteins is not practically possible.

To explore protein structures at the atomic level, we develop and use a variety of next generation imaging technologies including:

- Exceptionally intense micro-focused beamlines at 3rd and 4th generation synchrotron facilities in Australia and at our international partners in Germany and the US;
- X-ray free electron laser (XFEL) beamlines at our international partners in Germany and the US;
- State-of-the-art cryogenic transmission electron microscopy and cryogenic focused ion beam scanning electron microscopy.
- The application of single molecule light microscopy-based techniques to progress in vivo structural biology

Using these techniques and theoretical modelling of relevant light-matter interactions, we focus on three specific outcomes:

- Obtaining structural information on challenging proteins using small crystals in Femtosecond nanocrystallography or electron crystallography experiments.
- Determining protein structures and insights into function from single molecule experiments or through TEM analysis of single molecules or complexes in cells or in vitro.
- Obtaining accurate dynamic insights or "Molecular movies" that allow us to visualize how proteins change in shape during biological function.

What we have done so far?

Protein crystals generally exhibit significant deviations from ideal periodic structures. In nanocrystals, there is a presumption that disorder on the surface of the crystal may limit the resolution achievable in crystallographic studies of structure. Such disorder gives rise to deviations from ideal behaviour that become more pronounced as the size of the nanocrystal is reduced. In femtosecond nano crystallography, very small but otherwise perfect crystals generate signals between the Bragg peak positions. Surface disorder of the crystals causes this information to be blurred in a manner that is analogous to the effects of partial coherence in the incident radiation.

By adopting models of the nature of the surface structure relative to the bulk, the partially coherent effects of structural disorder may be completely ameliorated in femtosecond nanocrystallography. We have collected data at LCLS on samples of beta-hematin to test the validity of these disorder models and to develop new methods of structure determination in cases where there is significant inter-Bragg diffraction. We have also developed profile-fitting techniques for powder diffraction studies and have shown that protein structures can be obtained by a "divide and conquer" approach that is minimally biased by molecular modelling strategies.

Partial spatial and temporal coherence can be incorporated within detailed models of the optical wave fields that are incident on a sample, and which exit the sample affected by the time evolution of its scattering characteristics. These effects are particularly important in proposed single-molecule imaging experiments in which Bragg diffraction patterns are replaced by the continuous diffraction patterns that are characteristic of spatially finite objects. The restriction to finite objects can be overcome by the technique known as ptychography, in which exposure positions are overlapped and image information recovered simultaneously from multiple illuminations of the sample.

We have developed an approach to the problem of polychromatic ptychography that represents a significant advance on recent work reported in the literature. We have shown that the use of polychromatic illumination in ptychography has some significant advantages with respect to the stability of the reconstruction algorithms used to obtain structural information. The most obvious application of this approach is to cellular imaging in the water window, which may improve imaging of extended biological objects.

We have also been collaborating closely with structural biologists like Al Ruby Law and Siew Siew Pang to undertake a series of experiments to explore how different methods of protein crystal preparation and presentation, and data collection strategies can make the best of the XFEL to gather high-resolution structural data. These experiments have been run both at the Australian Synchrotron and at LCLS at Stanford University, USA. These national and international collaborations have been vital in speeding up the development of the XFEL imaging technique especially given the current scarcity of XFEL facilities worldwide and the global competition for experimental time on these beamlines.

Where are we going?

Crystallography groups have thus far reported modest improvements in resolution using XFELs of 0.2 - 0.4 angstroms. Led by the La Trobe node, we will participate in a series of single particle imaging experiments scheduled at LCLS in 2015 which will aim to make significant progress in the single molecule imaging program. We will continue to work very closely with our structural biologist colleagues to ensure that we maximise the potential of any experimental time available on the beamlines. We will investigate ways to obtain a greater improvement in resolution by using a variety of clever sample preparation techniques, and also seek ways to exploit the timing resolution of the XFEL which is where there is the greatest potential for breakthrough discoveries.

Our theoretical group will also continue our simulation studies of the effects of structural disorder in XFEL imaging experiments and the phenomenon known as "gating". Gating is characterized by a

PERSONAL SUCCESS - HENRY CHAPMAN

In December 2014, Centre Partner Investigator Henry Chapman was awarded one of the prestigious Gottfried Wilhelm Leibniz Prizes 2015 by the German research foundation Deutsche Forschungsgemeinshaft (DFG). He received the 2.5 million euro prize for his pioneering work in the development of femtosecond crystallography. Henry designed and led the application of the technique, which uses X-ray free electron lasers, to decode the atomic structure of complex biomolecules without having to form regular crystals of these molecules.

sudden transition between the original ordered crystal structure (which generates Bragg diffraction) and a highly disordered structure (the plasma state) which contributes a structure-less background signal to the diffraction. If sufficient Bragg diffraction signal has been collected before gating occurs, then it may be recovered by careful background subtraction if the shape of the background can be determined accurately.

The extent to which is this procedure is valid depends on a number of factors including the pulse fluence, temporal profile of the pulse, size of the crystal and the original degree of order in the crystal. The simulation studies will examine how well the modelling is able to reproduce the observed background signal in existing XFEL Bragg diffraction data, a large amount of which exists now and is publicly available.

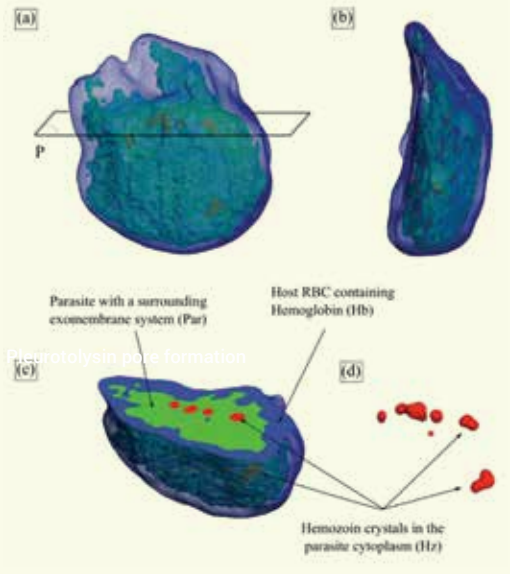
RESEARCH HIGHLIGHT

Centre CIs Brian Abbey and Keith Nugent and Partner Investigator Andrew Peele were part of a team of researchers who developed a new X-ray imaging technique to image whole cells in capillaries in three dimensions. Led by Drs Mac Luu and Grant van Riessen from La Trobe University, a node of the Imaging CoE, the researchers used this high resolution cellular imaging technique to image a red blood cell infected with a malaria parasite.

The experiments were conducted at the Advanced Photon Source in Chicago. Funding for the trip was provided by the International Synchrotron Access Program supported by the Australian Government and managed by the Australian Synchrotron, a partner organisation of the Centre.

Fresnel coherent diffractive imaging tomography of whole cells in capillaries. New Journal of Physics, Sep 2014

Authors: MB Luu, GA van Riessen, B Abbey, MWM Jones, NW Phillips, K Elgass, MD Junker, DJ Vine, I McNulty, G Cadenazzi, C Millet, L Tilley, KA Nugent, AG Peele



(a,b) 3D surface rendering of three recognised features in the reconstructed red blood cell (RBC) at two different views perpendicular to each other; (c) A cross-section through the RBC at the position indicated by plane P in (a); blue features indicate the host RBC, the green feature indicates the parasite and its exomembrane system (Par), and the red features represent hemozoin (Hz) crystals within the parasite cytoplasm; (d) 3D rendering of the Hz as shown in (c)

Molecular Imaging

Theme Leader: Kat Gaus

Understanding molecular interactions and how this translates to cellular activity represents a monumental unmet need in the biological sciences. Hence, it is imperative that structural information is linked to the movements and interactions of single molecules in intact and live immune cells.

We develop and use novel single molecule and super-resolution fluorescence microscopy tools to bridge this gap between structural biology and cellular function.

What we have done so far?

We developed a fluctuation-based approach to quantifying interactions between molecules and applied this technique to link the subcellular translocation, oligomerisation and activation of the GTPase Rac1 (see Research highlight). Further, we extended fluorescence correlation spectroscopy to spectrally resolved data, and demonstrated that it is possible to separate two dyes with highly overlapping emission spectra using six spectral channels of a commercial confocal microscope with an GaAsP detector array. We also developed a method that combines fluctuation analysis with Stimulated Emission Depletion (STED) with Fluorescence Correlation Spectroscopy (FCS) that is auto-calibrated and overcomes issues with photo-bleaching. We used this approach to map the dynamics of two lipids in the plasma membrane of a cell and found regions of high local density correlated with slow molecular diffusion, indicating trapping of these lipids.

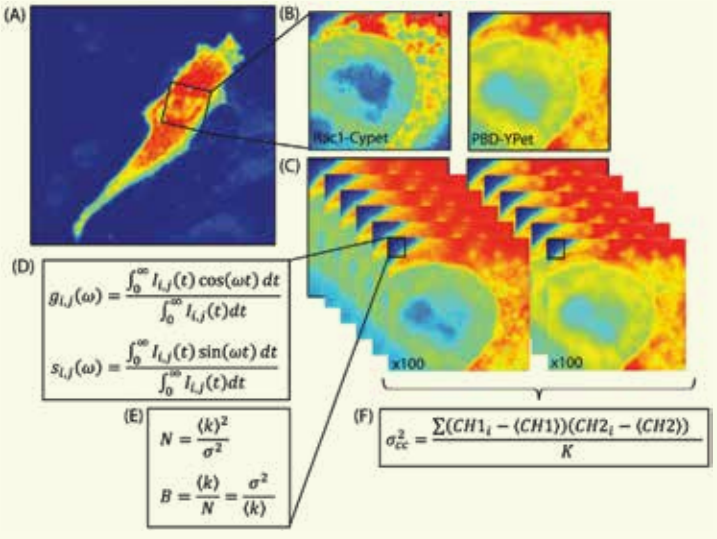
RESEARCH HIGHLIGHT

Centre collaborator Elizabeth Hinde and Deputy Director Kat Gaus were part of a team of researchers who developed a new imaging technique that can quantify the interactions between protein molecules. The technique involves acquiring a time series of images in a particular region of interest of the cell and measuring the fluorescence intensity and lifetime at each pixel in the image. Using this technique, they showed that upon DNA damage, monomeric and active Rac1 in the nucleus was segregated from dimeric and inactive Rac1 in the cytoplasm.

The work was published in Scientific Reports, a Nature group journal, and is a key technique that provides scientists the context in which molecular interactions occur and the ability to follow them in time.

Fluctuation-based imaging of nuclear Rac1 activation by protein oligomerisation. Scientific Reports, Feb 2014

Authors: E Hinde, K Yokomori, K Gaus, KM Hahn, E Gratton



(A) Intensity image of a NIH3T3 nucleus transiently transfected with the Rac1 dual chain FLARE biosensor. (B) Intensity image of Rac1-CyPet (donor) and its binding partner PBD-YPet (acceptor) in a selected region within the NIH3T3 cell shown in (A). (C) Time series acquired of the same region as shown in B in the respective channels of Rac1-CyPet and PBD-YPet. (D) In each pixel of the frame acquisition we obtain a time series of the phasor coordinates (gi,j and si,j) with nanosecond resolution, which determines the pixel lifetime and reflects Rac1 activity. (E) In each pixel of the frame acquisition, we also obtain an intensity fluctuation with second resolution, which has a given average intensity (k) and variance (σ2) that describe the number (N) and brightness (B) of the molecules. (F) By calculating the cross variance in each pixel, we obtain the number of Rac1-CyPet molecules moving together with PBD-YPet.

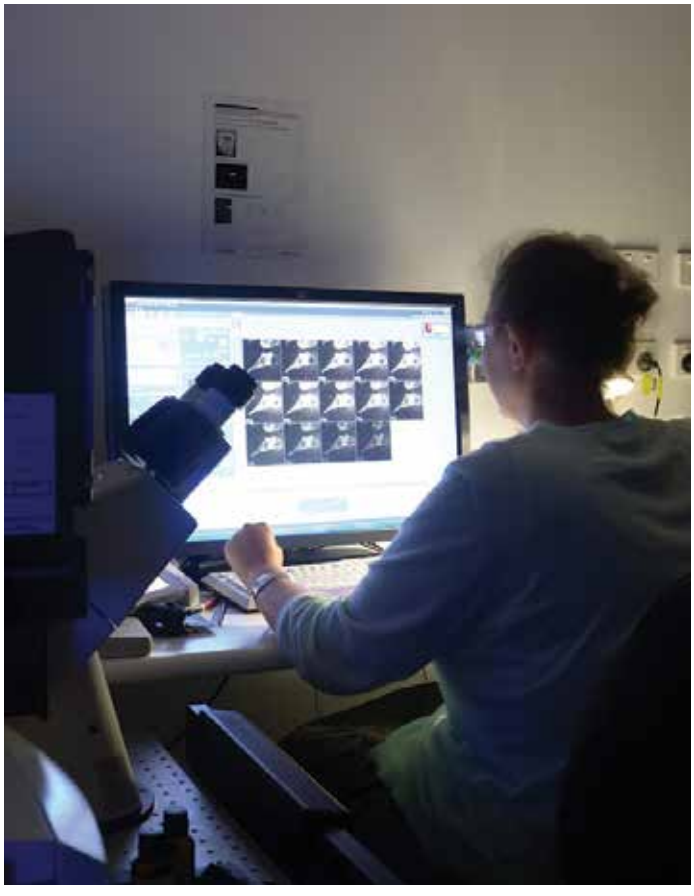
PERSONAL SUCCESS - KATHARINA GAUS

In June 2014, Centre Deputy Director Katharina (Kat) Gaus was awarded an Elizabeth Blackburn Fellowship for biomedical research for her work on super-resolution microscopy that can resolve components within a single T cell that are highlighted by fluorescent markers. She was one three winners of the Blackburn fellowships, which is presented annually to highlight the achievements of women scientists. Kat aims to use this technique to understand how the hundreds of proteins inside a single T cell are involved in the decision-making process that triggers an immune response. Whilst a successful immune response can rid the body of an infection, aberrant immune responses could lead to auto-immune diseases such as multiple sclerosis or Crohn's disease. Her work and award led to a feature article in the Sydney Morning Herald. She also won a $385,000 Australian Research Council Linkage grant to work on generating algorithms to analyse images from her super-resolution microscope together with Swiss microscopy software company Bitplane AG.

Where are we going?

In our quest to develop new tools for single molecule and super resolution microscopy, we are going to focus on developing new hardware with better spatial and temporal resolution, and better software for analysis of single molecule data in 2D and 3D.

We will drive the application of the techniques we develop to interesting biological systems in close collaboration with our immunologists and structural biologists to generate proof-of-principle data, for example, of the complex heterogeneity and assembly in the context of effector functions. Conversely, these experiments will inform and guide our development of suitable microscopy techniques that can enable these biologically important questions to be answered.



Cellular Imaging

Theme Leader: Bill Heath

To understand how molecular mechanisms result in co-ordinated immune responses, it is essential to image and quantify cellular behaviour in living animals. Utilising the facilities available at the In Vivo Imaging Facility (IVIF) at the University of Melbourne, X-ray fluorescence microscopy and the Imaging and Medical Beamline at the Australian Synchrotron, and intravital imaging developed at the Australian National University, we delve into the pathological consequences of disease and mechanisms of immune protection, and bridge the divide between animal models and imaging experiments that ultimately transform the fundamental understanding of how different components of the immune system interact with each other in health and disease.

The two main threads in this theme are in vivo imaging and single cell to animal imaging. In vivo imaging will visualise immune cell trafficking, antigen presentation and immune responses in organs and skin and the interplay of innate and T cell immunity. Single cell to animal imaging will develop protocols that allow immunologically relevant cells to be tagged for X-ray imaging, imaging methods that can track clusters of cells in whole animal imaging experiments, and greater resolution of tissue structure in intravital microscopy.

What have we done so far?

We have established the capacity to image cells in the liver and spleen on an upright two-photon microscope. For liver cells, surgical techniques and customised microscope stages have been developed to enable stable, long-term imaging, and we have demonstrated this by successfully imaging memory T cells within the liver of live mice. We have also established fluorescent mouse models that allow imaging of liver sinusoidal endothelial cells and liver associated T cells, to better define liver architecture and liver-associated T cells.

The stage equipment has been produced to enable spleen imaging, and an approach to introduce fluorescent dendritic cells into the spleen for imaging has been developed. Initial attempts have successfully imaged cells within the spleen but imaging depth has been suboptimal. We are pursuing various methods to improve depth of imaging.

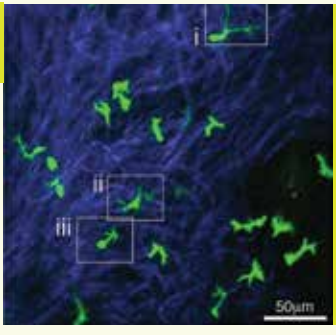
We have also established lymph node imaging of migratory dendritic cells and their interaction with helper and killer T cells during initiation of immunity to HSV. We have also obtained mice to enable imaging of a second important subset of dendritic cells called resident dendritic cells.

Where are we going?

Through 2014, we have hired several Research Fellows and PhD students to work on projects in this theme. With the added manpower and some solid advances made in 2014, we look forward to pushing the boundaries of cellular imaging further in 2015.

RESEARCH HIGHLIGHTS

Centre Research Fellow Ali Zaid, AI Scott Mueller and CI Bill Heath were part of a team of researchers who showed that in the skin, tissue-resident memory T cells, a type of immune cell that contributes to protection from infections, remain preferentially at the site of a prior infection despite having the ability to migrate through the epidermis. Moreover, they also showed that the formation of these memory T cells involved concomitant local reduction in numbers of another type of immune cell, dendritic epidermal γδ T cells, and that the same transcription factor responsible for maintaining dendritic epidermal γδ T cells also contributes to the maintenance of memory T cells. Together, these findings suggest that the epidermal T-cell niche is tightly regulated. The work was published in the Proceedings of the National Academy of Sciences of the United States of America and involved researchers from University of Melbourne and The Babraham Institute in Cambridge, UK.



Fluorescence image of skin resident memory T cells imaged by two-photon microscopy 32 days after HSV infection.

Persistence of skin-resident memory T cells within an epidermal niche. PNAS, April 2014

Authors: A Zaid, LK Mackay, A Rahimpour, A Braun, M Veldhoen, FR Carbone, JH Manton, WR Heath, SN Mueller

PERSONAL SUCCESS - STEVE LEE

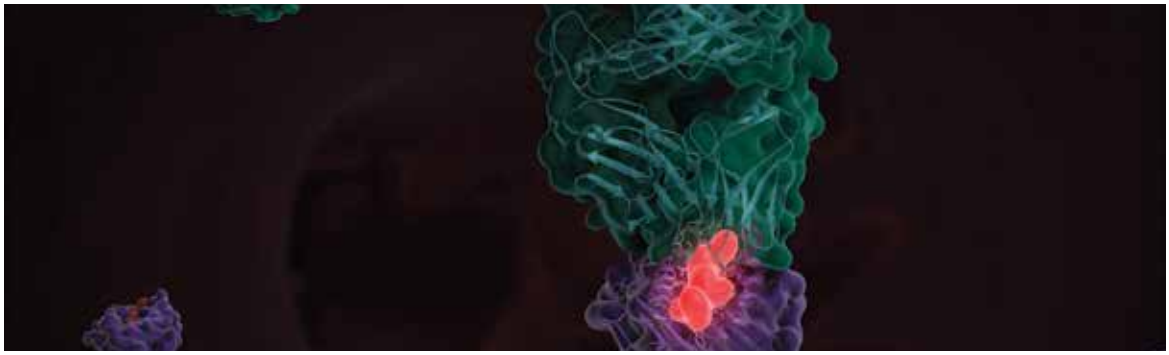
Centre Associate Investigator Woei Ming (Steve) Lee, in collaboration with Dr. Tri Phan from the Garvan Institute of Medical Research, won the Eureka Prize for Innovative Use of Technology for inventing a low-cost technique for making high resolution polymer lenses that could turn your average smartphone into a mobile microscope. The lenses can be made in about 15 minutes using a polymer mix and a standard kitchen oven for less than $2 each. Steve's primary research interest is in developing miniature optical devices that deliver to biologists magnified images of cells from deep inside living tissues. He is looking at using this polymer lens technology to make even more powerful lenses that can be implanted inside tissues and organs. At present, commercial microscope technologies are rarely implanted and their operations are limited to only a millimetre or two beneath the surface. Steve's technology would allow scientists to penetrate deep into the tissues and organs of the body and still resolve images to around a thousandth of a millimetre, small enough to pick out sub cellular structures like mitochondria.

We will be looking to develop rapid, multicolour deep tissue imaging of cells in live mice. To do so, we have ordered a new two-photon microscope with tunable, long wavelength capability through an ARC-LIEF grant in collaboration with fellow Centre CI Jamie Rossjohn. Along with our surgical and stage developments, we will be extending our work to explore the function of the various T cell populations such as memory and effector T cells, NKT cells and MAIT cells within the liver in the steady state as well as during or after infection or vaccination in malaria and viral infections. This work will be done in collaboration with Centre colleagues Dale Godfrey and Jamie Rossjohn.

We will also develop tools for imaging splenic immunity initiated by blood stage infection with malaria and viral infection with LCMV. Another goal is to image T cells, B cells and dendritic cells in the humoral response to antigens targeted to the dendritic cell molecule Clec9A with the aim of understanding how to improve vaccine design.

Centre PhD student Jyh Liang Hor is currently establishing the capacity to image different populations of dendritic and T cells within the lymph node at the same time, and the new two-photon microscope that should enable more efficient multicolour imaging to achieve these aims has just been ordered. This capacity will be used to define the interaction between these cells during initiation of immunity to herpes simplex virus, which infects the skin. We originally reported that an interaction between two DC subsets was required to initiate this response and will now use imaging approaches to decipher this interaction.

CIs Harry Quiney and Brian Abbey have also initiated a pilot study to investigate the feasibility of collecting two-photon emission from organic material and using the methods of coherent diffractive imaging to determine the structure of the material to a resolution that is much higher than by photon counting and scanning techniques. In principle, the emission pattern of such an experiment encodes information about the molecular polarizability of the target, which reflects the local structure and density. In the first instance, we will investigate the emission signals from polymer samples to test the sensitivity of the technique to structural details with the aim of extending our study to tissue samples, in collaboration with CIs Bill Heath and Dale Godfrey, if it proves successful.



Recognition

Theme Leaders: Dale Godfrey and Jamie Rossjohn

Recognising a foreign invader is one of the key functions of our immune system. This role is typically performed by a variety of T cells in our body that are capable of recognising different kinds of antigens. Primarily utilising atomic and molecular imaging techniques, we focus on understanding:

- How peptides are captured and presented to the immune system and aberrant T cell reactivity (Imaging peptide-mediated immunity);
- What specific antigens do lipid-reactive T cells see, and how are they mobilised during infection/disease (imaging lipid-mediated immunity); and
- How metabolites are presented to and detected by our immune system and how this triggers subsequent activation of an immune response (imaging metabolite-mediated immunity).

Peptide-mediated immunity

What have we done so far?

The work on this theme encompasses (i) protective immunity (ii) aberrant T-cell reactivity. Regarding (i), we have investigated immune response to viral mutations and how the T-cell repertoire changes as a result of changes in the polymorphic pMHC landscape. Regarding (ii) we have investigated the molecular basis of DQ2-mediated celiac disease, and provided molecular insight into the genetic association of an HLA class II allele with a commonly used drug.

Where are we going?

Our ongoing work will continue on both these two main themes – by focussing in on:

(i) the protective immune response to: influenza, HIV, Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) primarily, and

(ii) T-cell autoimmunity, including celiac disease, rheumatoid arthritis, psoriasis and T-cell alloreactivity.

Further down the track, we will investigate the structure and dynamics of the peptide-loading complex.

Metabolite mediated immunity

What have we done so far?

We have continued our investigations on the MAIT-MR1 axis. In collaboration with our chemistry colleagues, we established that a transitory intermediate originating from the riboflavin pathway and other metabolites generates a neo-antigen that activates MAIT cells. We also established a molecular basis for MAIT cell heterogeneity and have generated molecular images of a series of MAIT cell TCRs bound to MR1 plus antigen. We have also described a new and more potent MAIT cell inhibitor, demonstrating the effectiveness in activation assays using flow cytometry.

Where are we going?

We have started to actively explore, via the use of the MR1 tetramers we have generated, the role of MAIT cells in disease. We have now thoroughly characterized MAIT cells in mice which serves as the basis for understanding how these cells behave in disease models. We are studying MAIT cells in situ, with a goal to understanding the precise location and trafficking of MAIT cells in the immune system and during immune responses. Our ongoing work will include: looking to understand the range of ligands that MR1 can bind, understand the factors that determine MAIT cell potency, and MR1 trafficking within the cell.

Lipid mediated immunity

What have we done so far?

Our goal here is to understand how T-cell receptors interact with lipid-based antigens that are presented by the CD1 family. The CD1 family is subdivided into two groups – group 1 (CD1a, CD1b and CD1c) and group 2 (CD1d). NKT cells are restricted to CD1d, and we have pioneered the field of NKT TCR recognition of CD1d plus lipid antigens, and will continue to work in this axis.

PERSONAL SUCCESS - JAMIE ROSSJOHN

Centre Chief Investigator Jamie Rossjohn was admitted as a Fellow of the Australian Academy of Science (FAA) in May 2014. Jamie's election by his peers as a Fellow is one of the highest honours Australian science can bestow. His citation recognised "his research into the structural basis for T cell recognition of foreign antigens which has had a profound impact on our understanding of immune recognition, particularly in autoimmunity and drug and food hypersensitivities". Jamie was also awarded the National Health & Medical Research Council 's highest-ranked project grant to further his investigation into mucosal-associated invariant T (MAIT) cells, the sentry immune cells found in abundance in the gastrointestinal system. Capping off an excellent 2014, Jamie, in collaboration with fellow Centre Chief Investigator Dale Godfrey, also won an ARC Linkage grant worth $590,000 to work on developing and testing new synthetic compounds which will enhance our ability to understand the molecular recognition and activation mechanisms of the innate immune system's Natural Killer T (NKT) cells. This project will be done in collaboration with Vaxine Pty Ltd, a South Australian vaccine company.

Where are we going?

Increasingly, we are turning our attention to the CD1 group 1 family –as much less is known regarding TCR recognition of these antigen-presenting molecules. In this light, we provided insight into how natural skin oils, which are presented by CD1a, can serve as antigens for TCR recognition. We have also identified lipid antigens that can support or inhibit autoreactivity by human CD1a-restricted T cells and, using x-ray crystallography at the Australian Synchrotron, determined the molecular basis for how these antigens are recognised. Our work will continue to expand in the CD1 group 1 axis in 2015 and beyond – addressing its role in protective and aberrant immunity.

RESEARCH HIGHLIGHT

Our guts, lungs and mouths are lined with mysterious immune cells that make up to ten per cent of the T cells in our immune system. Last year Australian researchers showed that these cells act as sentinels against invading bacteria and fungi. Now they've identified the precise biochemical key that wakes up these sentries and sends them into action.

The patented work, published in Nature, provides the starting point to understanding our first line of defence, and what happens when it goes wrong. It will lead to new ways of diagnosing and treating inflammatory bowel disease, peptic ulcers and even TB. It could also lead to novel protective vaccines.

The discovery is the result of national and international collaboration between the universities of Melbourne, Monash, Queensland and Cork. It also depended on access to major facilities including the Australian Synchrotron and the Bio21 Institute.

Last year members of the research team won an Australian Museum Eureka Prize for determining that these immune cells, known as mucosal-associated invariant T cells (MAITs), detect reactive intermediates in the synthesis of vitamin B2 (riboflavin) that is made by many invasive bacteria and fungi. The latest discovery narrows the trigger down to a small group of compounds produced by specific bacteria and fungi, which may be associated with several diseases.

The work was conducted by a team of researchers led by Centre CIs Jamie Rossjohn and David Fairlie, and received media coverage in the Australian Life Scientist and Daily Telegraph, alongside a number of online media outlets.

T cell activation by transitory neb-antigens derived from distinct microbial pathways. Nature, Apr 2014

Authors: AJ Corbett, SB Eckle, RW Birkinshaw, L Liu, O Patel, J Mahony, Z Chen, R Reantragoon, B Meehan, H Cao, NA Williamson, RA Strugnell, D Van Sinderen, JY Mak, DP Fairlie, L Kjer-Nielsen, J Rossjohn, J McCluskey.

Activation

Theme Leader: Kat Gaus

Once a foreign invader is recognised by our immune system, the next stage is the activation of an appropriate response to deal with the threat. After a T cell receptor detects an antigen, multi-subunit, membrane signalling complexes translate this antigen recognition into T cell signalling and activation through a signalling apparatus known as the CD3 complex. Using specialised fluorescent T cells and single molecule and super-resolution microscopy techniques, we aim to determine the dynamic spatial organisations of signalling complexes, clusters and vesicles, and link these signalling patterns to downstream activation responses (Imaging of T cell activation networks).

What have we done so far?

We have extended single molecule cluster analysis to two-colour co-clustering analysis, which now allows us to distinguish signalling from non-signalling T cell receptors on the same cell. This is the foundation to determine which antigen recognition event triggers a signalling event. It turns out that not all copies of the T cell receptor – despite being identical genetically and biochemically – are equal.

We have also extended single molecule images to applications beyond T cell signalling, such as integrin clustering (see Research highlight), beyond T cells, such as novel and generic cellular uptake mechanisms, and beyond cells, with recombinant caveolae complexes.

We have also made progress towards the understanding the molecular organisation of the TCR-CD3 complex – this has been a long-standing question in the field. We have, over the last decade, worked out a means to express and purify this integral membrane complex in sufficient quantity and purity to initiate structural studies. We have also engineered various soluble constructs of the TCR-CD3 complex to permit solution-based experiments such as Small Angle X-ray Scattering (SAXS). This work culminated in a collaboration with KC Garcia at Stanford University, where we combined our SAXS data with Garcia's negative stain EM data, thereby providing some insight into the nature of the TCR-CD3 complex.

Where are we going?

We will continue our two-colour clustering analysis work and expect to make further progress in understanding the signalling dynamics and mechanisms of T cell receptors.

To further our understanding of the TCR-CD3 complex, we will pursue cryo-EM using the microscopy facilities available at the newly established Clive and Vera Ramaciotti Centre for Structural Cryo-Electron Microscopy at Monash University.

RESEARCH HIGHLIGHT

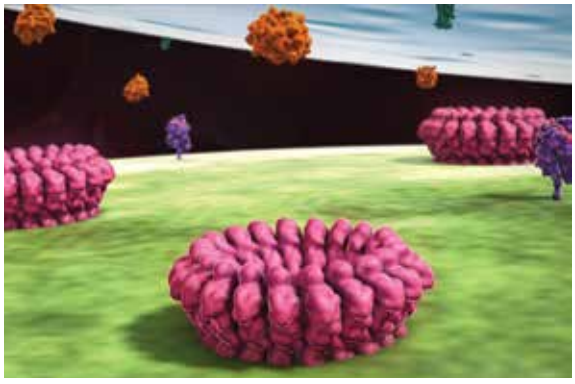
Cell-expressed integrins mediate adhesion with other cells and with extracellular matrix and are essential for embryonic development and for controlling leukocyte migration in later life. Using single molecule techniques, Centre AI Jeremie Rossy and CI Kat Gaus were part of a team of researchers who revealed what controls clustering of integrins on the cell membrane and that the activation state of individual integrins can be switched off. They also found that disruption of this pathway caused autoimmune phenomena.

Dynamic control of β1 integrin adhesion by the plexinD1-sema3E axis. PNAS, Jan 2014

Authors: YI Choi, JS Duke-Cohan, W Chen, B Liu, J Rossy, T Tabarin, L Ju, J Gui, K Gaus, C Zhu, EL Reinherz

Effector Function

Theme Leaders: James Whisstock and David Fairlie



The final step in the process of dealing with a foreign invader is effecting an appropriate lethal response to deal with the threat. How immune recognition events translate into cell fate decisions and the dynamics of the movement of various immune cells in response to "danger" signals within the body are key areas of investigation in this research theme. Specifically, we look at:

- How the innate immune system responds to the detection of pathogens, and ways to target and module the response of specific innate immune cells selectively (Imaging of innate immune responses); and
- The weaponry associated with immune killing, and the roles for complement proteins in immune signalling (Imaging of immune effectors).

Imaging of innate immune responses

What have we done so far?

Different innate immune cells are involved at different stages and in different ways in immune responses to infection, injury and disease. One goal is to track immune cells during acute to chronic inflammation, develop a more sophisticated understanding of their functions, and examine novel effectors of innate immune cells using imaging tools and techniques. For example, we developed new chemicals to activate complement proteins on human immune cell surfaces and in rodent models of human inflammation and disease. This allows us to study the interplay of protein-protein interactions and immune cells in immunity.

Where are we going?

We will continue to develop new chemical reagents and approaches for tracking and modulating innate immune cells such as mast and dendritic cells, neutrophils and macrophages. We will also develop fluorescent ligands selective for innate immune cells and identify key proteins for imaging of innate immune responses both in vitro and, on a temporal scale during progress of inflammation, in vivo.

Another major focus here has been on understanding Killer Immunoglobin Receptor (KIR3DL1)specificity. Arising from our KIR3DL1-HLA-B57 report (Vivian et al., Nature 2011), we have generated a series of testable hypotheses regarding specificity, in which we blend mutational analyses with functional and structural data. We are now progressing towards other KIR3D family members, where ligand specificity is less clear or unknown. We are using KIR3D tetramers to enable this.

Imaging of immune effectors

What have we done so far?

We are studying the structure, function and biology of a large family of pore forming immune effectors. A major focus of our work is Perforin, a protein secreted by cytotoxic T-lymphocytes and Natural Killer cells in order to eliminate virally infected and pre-malignant cells. Once released into the immunological synapse between immune cells and targets, perforin forms pores that permit toxic granzyme proteasess to enter and kill the target.

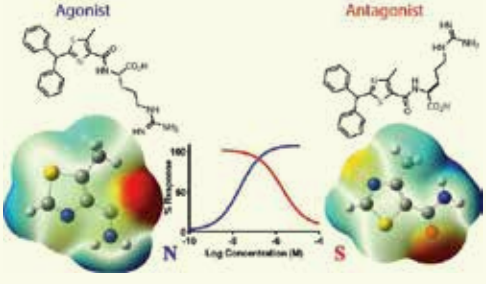
Perforin and related proteins represent challenging targets

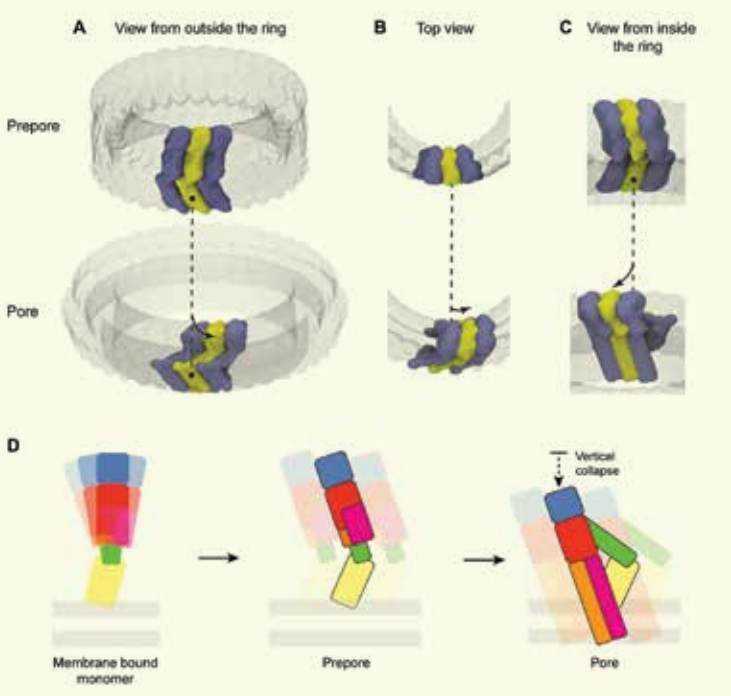
Research Highlight

We have created the smallest known agonists (activators) and antagonists (inhibitors) of human complement C3a protein that act on a receptor on the surface of immune cells to effect degrfaulation and chemotaxis.

Electric Dipole Imaging: "Chemical Structure Imparts Function"

Heterocyclic agonist (left, blue) and antagonist (right, red) that respectively activate or inhibit Complement C3a protein on human macrophages. J Am Chem Soc **2014**, 136, 11914-17.





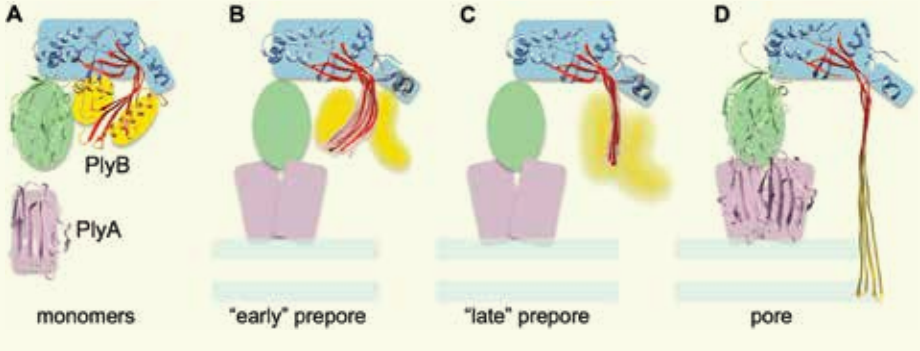
Orchestrated domain movement and proposed mechanism of pore formation.

for structural studies, particularly in the context of the crucial, membrane bound pore form. This is because perforin-pores vary in size (heterogeneity) and shape, precluding a conventional, crystallography-driven approach to understand structure. Understanding the perforin pore structure and the mechanism of pore formation is important, not least in order to derive key knowledge to help drive the development of therapeutically useful immunsupressive perforin inhibitors.

To address this, in work led or co-led by Al Dunstone, we have made two important breakthroughs in our understanding of how perforin-like proteins span membranes.

Firstly, we used structural comparisons, molecular modeling and molecular dynamics to predict how one branch of the perforin superfamily; the cholesterol dependent cytolysins (CDC), may undergo a concerted collapse in order to penetrate the membrane (see above figure). Our data suggested that a major rotation of the central domain of the CDCs was required for proper function. Later experimental studies provided strong support for this idea (Leung et al., 2014, elife).

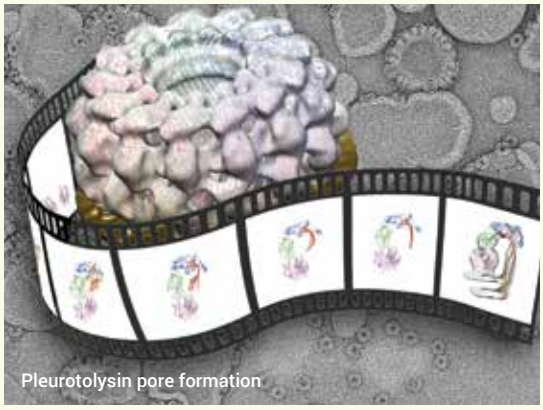
Secondly, by using the model perforin-like protein Pleurotolysin, together with a combination of crystallography, protein engineering and single particle cryo-EM to visualize the



Schematic diagram of sheet opening in pleurotolysin pore formation

RESEARCH HIGHLIGHT

Al's Dunstone, Law and Caradoc-Davies and CI Whisstock were part of a large international team that determined the 11 Å resolution structure of the Pleurotolysin pore form. Crucially, they discovered that the second transmembrane spanning region in concert with a conserved helix-turn-helix motif forms a key role in triggering the conformation changes that culminates in pore formation. It is anticipated that other perforin-like proteins (and perforin itself) are controlled in a similar fashion, thus suggesting a new approach for the development of perforin inhibitors.

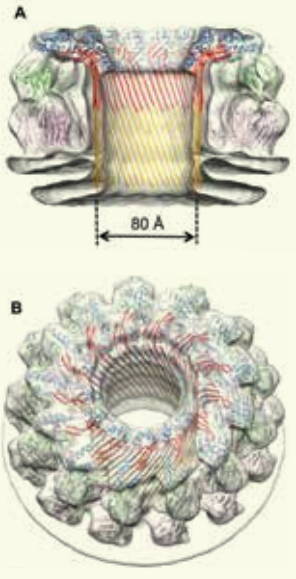


Pleurotolysin pore formation

molecular events that take place during pore formation (Lukoyanova et al., 2015 PLOS Biology; see also research highlight below). In contrast to perforin, Pleurotolysin forms small relatively homogenous pores that are well suited for studying using single particle cryo-EM.

Accordingly, we have been able to determine the highest resolution structure of any perforin-like protein in the pore form to date (see figure above).

Further, through protein engineering and the introduction of disulphide traps, we have been able to capture Pleurotolysin in several intermediate steps en route to the pore form (see figure below).



Cut away side and tilted surface views of the structure of the pleurotolysin pore

Many complement proteins are created on cell surfaces for immediate immunoprotective actions but, when their expression or regulation is uncontrolled, their prolonged actions can cause diseases. While many complement proteins are rapidly degraded in blood, we have been able to downsize them to equipotent plasma-stable small molecules with identical functional profiles. These are being used as tools to mimic or block complement function in immune responses, for identifying mechanisms of immune cell migration (chemotaxis), release of inflammatory mediators from immune cells (degranulation, cytokines) and inflammatory signalling and amplification. We have identified key complement receptors on macrophages, mast cells and T cells.

Where are we going?

We are using our discoveries on Pleurotolysin to develop ways to stabilize the perforin pore (or prepore intermediates) for high-resolution cryo-EM or crystallographic studies.

Using mouse, fish and Drosophila models, we are discovering new roles for perforin-like immune effectors in developmental and neuro-biology.

We are using nanocrystallography to determine structures of important, difficult to crystallise multi-protein complexes that relate to the immune effector program.

We will investigate novel modulators of complement proteins and their fluorescent analogues for future imaging of complement-mediated immunity in vitro and in vivo, tracking ligand fate, interactions with proteins, modulation of intracellular signaling pathways, and probing mechanisms of degranulation and chemotaxis of immune cells.

Media and Outreach

As the Imaging CoE was being established in 2014, we realised the importance of having a professional and effective communications and outreach strategy because this was key to raising awareness about the Centre amongst our key stakeholders and partners, State and Federal government agencies, the broader scientific community and the general public.

To assist in achieving our mission, the Centre engaged Science in Public, a science communication agency based in Melbourne, to assist the Centre with the development of a communications strategy, drafting of media releases and monthly newsletters as well as promotion of Centre activities and key outcomes. The relationship with Science in Public has been extremely productive to date, as you will see from the examples below, as we have been able to attract highly valuable TV, radio and print coverage for some of the outstanding work of our Centre researchers.

Media Coverage

There were five main Imaging Centre stories in the news over the last year—see list below.

These have led to 35 stories in 'traditional' media (TV, print and radio), plus 53 online stories, and another 18 cases of important stakeholders engaging via their own release, or via a link to the Imaging Centre (or University) release.

- Turning on our immune sentries: 4 print stories, 10 other media, 4 stakeholder engagement
- The molecular heart of celiac disease revealed: 10 print & radio, 12 online, 11 other media, 2 stakeholder engagement
- Do you look infected? Should I kill you? No, I'm fine, move along, nothing to see: 1 each of TV, radio, print & online, 7 other, 2 stakeholder
- Steve Lee's DIY droplet lens Eureka Prize: 1 TV, 11 print, 13 other, 5 stakeholder
- Imaging CoE Launch: 3 radio, 4 stakeholder engagement

The media coverage received for our Centre research has given our researchers a vital platform to explain the relevance and significance of their work to both the broader scientific community and the general public.

TURNING ON OUR IMMUNE SENTRIES - APRIL 2014

Paper: T-cell activation by transitory neo-antigens derived from distinct microbial pathways. (Nature, May 2014)

Authors: AJ Corbett, SB Eckle, RW Birkinshaw, L Liu, O Patel, J Mahony, Z Chen, R Reantragoon, B Meehan, H Cao, NA Williamson, RA Strugnell, D Van Sinderen, JY Mak, DP Fairlie, L Kjer-Nielsen, J Rossjohn, J McCluskey.

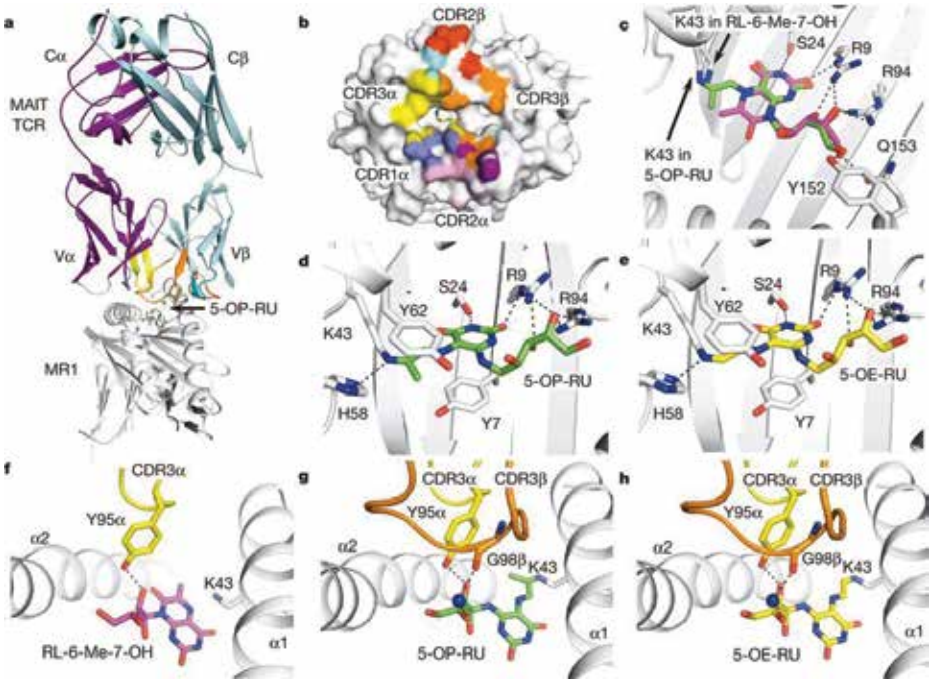
Media release: http://www.imagingcoe.org/news/turning-on-our-immune-sentries

Our guts, lungs and mouths are lined with mysterious immune cells that make up to ten per cent of the T cells in our immune system. Last year Australian researchers showed that these cells act as sentinels against invading bacteria and fungi. Now they've identified the precise biochemical key that wakes up these sentries and sends them into action.

The patented work, published in Nature today, provides the starting point to understanding our first line of defence, and what happens when it goes wrong. It will lead to new ways of diagnosing and treating inflammatory bowel disease, peptic ulcers and even TB. It could also lead to novel protective vaccines.

The discovery is the result of national and international collaboration between the universities of Melbourne, Monash, Queensland and Cork. It also depended on access to major facilities including the Australian Synchrotron and the Bio21 Institute.

This was a complex story and one that could too easily be over-sold and misreported, so we were conservative in our approach to the story. But the paper did receive a bit of media attention.



Traditional media

1. Australian Life Scientist: Microbial signatures provide key to immunosurveillance
2. Business Standard: Switch that awakens immune cells found
3. Medical Xpress: Immune cell defenders protect us from bacteria invasion
4. Daily Telegraph: Your immune system heroes

There was also additional interest from New Scientist and Clifford Fram, Australian Associated Press (AAP)'s national medical writer, but neither went ahead with the story. There were also follow-up requests from the Herald Sun, and Body and Soul.

Other media

1. Science Newsline,
2. myScience
3. Press-News.org
4. Brunch News
5. World News Network
6. Technology.org
7. Red Orbit
8. Immune Regulation News
9. Infection Control Today
10. BioPortfolio

Stakeholder engagement

1. Monash University: Immune cell 'defenders' could beat invading bacteria
2. The University of Melbourne: Immune cell defenders protect us from bacteria invasion
3. The University of Queensland: Immune sentries protect gut from bugs by sensing vitamins
4. Australian Synchrotron: Our immune system's front line

THE MOLECULAR HEART OF CELIAC DISEASE REVEALED - APRIL 2014

Australian, US and Dutch researchers have determined the molecular details of the interaction between the immune system and gluten that triggers celiac disease. Their work opens the way to potential treatments and diagnostics.

Monash, Melbourne and Leiden university researchers, in collaboration with colleagues from a Boston-based company, have described the molecular basis of how most of the immune cells (T cells) that induce celiac disease lock onto gliadin, a component of gluten, thereby triggering inflammation of the lining of the small intestine. This is what gives many celiac sufferers symptoms similar to food poisoning after eating a slice of toast.

"We studied how different T cells bind to gliadin, a component of gluten. And when we looked closely we found the docking mechanism was similar. This provides us with a way to develop drugs that might reduce or turn off the immune response," says Dr Hugh Reid of Monash University. Dr Reid and fellow Australian-based researchers collaborated in the study with Prof Frits Koning from the Leiden University Medical Center in the Netherlands and with US company, ImmusanT.

Celiac disease is an immune system intolerance of gluten, a protein which occurs naturally in grains such as wheat, rye, barley and oats, and therefore is typically found in bread, pastries and cakes. The problem is that certain immune system T cells regard gluten as a foreign and potentially toxic substance, and initiate action against it. This inflammatory process is triggered when these T cells bind to gliadin.

Today's paper, published in Nature Structural and Molecular Biology, explains what's happening in the overwhelming majority of celiac disease sufferers, the ninety-five percent who carry a gene for the particular protein, HLA-DQ2. In 2012, the research team found a similar trigger for the other five per cent who have HLA–DQ8, another celiac disease susceptibility gene.

With the assistance of the Australian Synchrotron, the researchers were able to determine the structure of the molecular complexes that form during the interaction between T cell receptor and gliadin. Armed with this information, they were able to work out what was important in the T cell response.

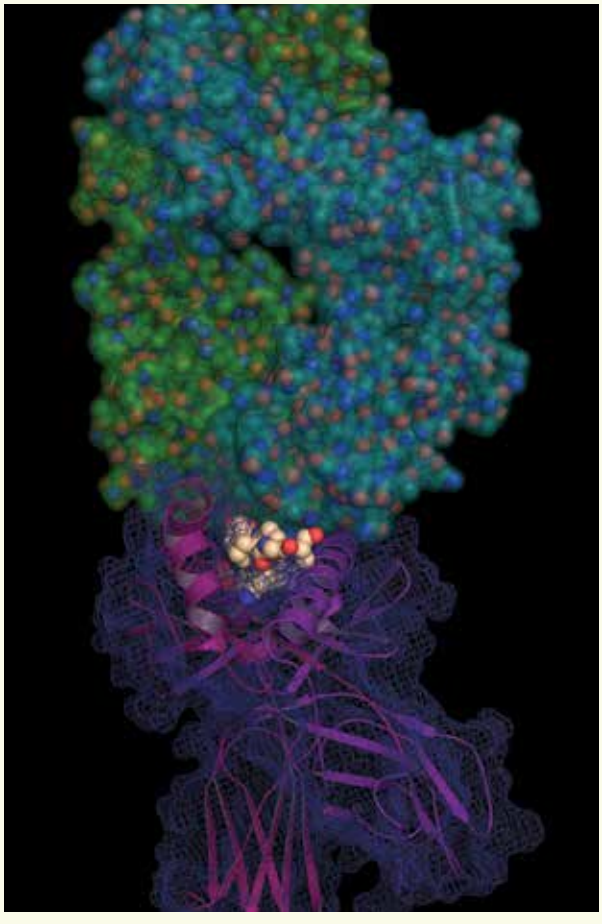
"This research is a classic example of what the new Australian Research Council of Excellence in Advanced Molecular Imaging strives to achieve," says Prof Rossjohn from Monash University, "Using the latest imaging tools - from microscopes to the synchrotron – we can understand and influence the immune recognition events that trigger immune responses, both good and bad."

Ultimately, the insight provided by the research will assist the development of a blood test and a therapeutic vaccine for patients with celiac disease who carry the gene HLA-DQ2.

Abstract and full paper available at: http://www.ncbi.nlm.nih.gov/pubmed/24777060

This paper got a great run in the media. The highlight was an interview with Hugh Reid on ABC Radio's The World Today. He also made it into the Herald Sun, in a story picked up by other in the News Corp stable of papers, and onto 774 with Red.

The story was Editor's Choice on ABC Science and Hugh did a string of morning radio interviews. And AAP's national medical writer put out a story on the wire. NSMB also made the paper a highlight in their Nature weekly email newsletter and on their website.



Paper: T-cell receptor recognition of HLA-DQ2-gliadin complexes associated with celiac disease. (Nature Structural & Molecular Biology, April 2014)

Authors: J Petersen, V Montserrat, JR Mujico, KL Loh, DX Beringer, M van Lummel, A Thompson, ML Mearin, J Schweizer, Y Kooy-Winkelaar, J van Bergen, JW Drijfthout, WT Kan, NL La Gruta, RP Anderson, HH Reid, F Koning, J Rossjohn.

Media release: http://www.imagingcoe.org/news/the-molecular-heart-of-celiac-disease-revealed

Print

1. The Herald Sun: Aussies find trigger for coeliac disease, 29 April 2014, page 7
2. The Advertiser, Adelaide: Key find in gluten reaction battle, 29 April 2014, page 15
3. Townsville Bulletin: Coeliac trigger point, 29 April 2014, page 6

Radio

1. 774 ABC Melbourne: Breakfast with Red Symons
2. ABC The World Today: Melbourne researchers discover coeliac disease trigger
3. ABC NewsRadio: Monash University researcher describes scientific breakthrough for Celiac disease
4. 2UE Sydney (Fairfax Radio News): Mornings with Angela Catterns
5. 92.5 ABC Central Coast: Day Shift with Scott Levi
6. FIVEaa Adelaide: Coeliac disease discovery
7. Student Youth Network (SYN): Panorama

Online

1. The Herald Sun: Melbourne researchers find trigger for coeliac disease
2. ABC Online: The molecular secrets of celiac disease
3. AAP: Aussie scientists reveal coeliac secrets
4. SBS: Aussie scientists reveal coeliac secrets
5. Ninemsn: Aussie scientists reveal coeliac secrets
6. msn NZ: Aussie scientists reveal coeliac secrets
7. The FA Daily: Celiac disease's molecular secrets
8. Business Wire: Wheat Activates the Immune Response to Gluten in Celiac Disease
9. Business Channel: Scientists reveal coeliac secrets
10. Bmag: Coeliac disease, the latest research breakthrough
11. Yahoo Finance: New Research Published in Nature Structural and Molecular Biology Shows How Wheat Activates the Immune Response to Gluten in Celiac Disease
12. Nature Structural and Molecular Biology highlights: Snapshots of celiac disease

Other media

1. Chemical & Engineering News, ChemistryInPictures blog
2. Hot headlines
3. Medical Xpress
4. AllNewsAu
5. ClickSport
6. Australia Glory
7. Veooz
8. RSSNews
9. ThinkGP
10. Yummy Mummy Club
11. IBS Treatment Centre

Stakeholder engagement

1. Monash University: The molecular heart of coeliac disease revealed.
2. ImmusanT: New research published in Nature Structural and Molecular Biology shows how wheat activates the immune response to gluten in celiac disease.

DO YOU LOOK INFECTED? SHOULD I KILL YOU? NO, I'M FINE, MOVE ALONG, NOTHING TO SEE - JULY 2014

Paper: The structure of the cytomegalovirus-encoded m04 glycoprotein, a prototypical member of the m02 family of immunoevasins. (Journal of Biological Chemistry, August 2014)

Authors: R Berry, JP Vivian, FA Deuss, GR Balaji, PM Saunders, J Lin, DR Littler, AG Brooks, J Rossjohn.

Media release: http://www.imagingcoe.org/news/do-you-look-infected-should-i-kill-you-no-im-fine-move-along-nothing-to-see

Some viruses can hide in our bodies for decades. They make 'fake' human proteins that trick our immune cells into thinking 'everything is awesome', there's nothing to see here.

Now researchers at the Imaging Centre of Excellence at Monash and Melbourne Universities have determined the basic structure of one of the two known families of these deceptive proteins, the m04 immunoevasin from mouse cytomegalovirus, a member of the m02 protein family.

Using synchrotron light and working with a common virus that lives in people happily and for the most part harmlessly, they worked out the structure of the fake proteins. This is an important first step towards producing better vaccines and drugs to fight viral disease.

This paper also received TV, print and radio coverage with the highlight being Monash postdoctoral researcher Richard Berry interviewed live on Channel 9's Today Show in Perth.

Traditional media

1. Channel 9 Today Show: Live interview with Richard Berry
2. Sydney Morning Herald Online: Researchers build microscope to view inside workings of a cell
3. ABC radio news midday
4. World News (WN) Online: Viruses use 'fake' proteins to hide in our cells (Monash University)

Other Media

1. Life Extension Foundation
2. Phy.org
3. Asian Scientist
4. Infection Control Today
5. Medical Jobs Australia
6. Science Daily
7. FindKa Online: How viruses use 'fake' proteins to hide in our cells

Stakeholder engagement

1. Monash University: Viruses use 'fake' proteins to hide in our cells.
2. ARC: How viruses use 'fake' proteins to hide in our cells.

STEVE LEE'S DIY DROPLET LENS EUREKA PRIZE - AUGUST 2014

Al Steve Lee, along with collaborator Dr. Tri Phan from the Garvan Institute, won the ANSTO Eureka Prize for Innovative Use of Technology for their invention of a novel polymer droplet lens that can be used to turn a smartphone into a microscope for less than $2.

Media and Outreach

This was one of the most successful of the Eureka press stories, receiving coverage in The Age, Channel Seven News, News24 TV, The Sydney Morning Herald, the Daily Telegraph and other papers (23 media mentions).

TV

1. Channel 7 aired on Today Tonight in Adelaide and Perth (~ 3.5 minutes), and News in Brisbane and Sydney

Print

1. The Canberra Times: The Australian National University is up two places on international rankings (featured in the body of this article)
2. The Age: Smartphones to get smarter with plastic lens
3. The Canberra Times: Smartphones to get smarter with plastic lens
4. The Sydney Morning Herald: Smartphones to get smarter with plastic lens
5. Perth Now (via AAP): Eureka prize for $2 phone microscope
6. The Age (via AAP): Droplet lens that turns smartphones into microscopes for $2 wins Eureka prize
7. The Canberra Times (via AAP): Droplet lens that turns smartphones into microscopes for $2 wins Eureka prize
8. The Courier Mail (via AAP): Eureka prize for $2 phone microscope
9. The Daily Telegraph (via AAP): Eureka prize for $2 phone microscope
10. The Sydney Morning Herald (via AAP): Droplet lens that turns smartphones into microscopes for $2 wins Eureka prize

Other media

1. MX Sydney: Inventors in it to win it
2. Omnichannel Media: How to Turn Your Smartphone into a Microscope for $2
3. Tech Assimilate:Two dollar droplet microscope acccessory for smartphones wins science prize
4. 7 News (via ABC): Scientists who invented a smartphone microscope and a photographer win Eureka science prizes
5. ABC News: Scientists who invented a smartphone microscope and a photographer win Eureka science prizes
6. Australian Geographic (via AAP): 2014 Eureka Prizes for science winners unveiled
7. News.com.au (via AAP): Eureka prize for $2 phone microscope
8. SBS news (via AAP): Eureka prize for $2 phone microscope
9. Sky News Australia (via AAP): Eureka prize for $2 phone microscope
10. Asian Scientist Magazine: Australian Museum Eureka Prize Celebrates 25th Anniversary
11. CityNews.com.au: Canberra boffins take out four of the 15 Eureka Prizes.
12. Guardian: Australian National University moves into top 25 global rankings
13. The Conversation: Hendra virus to basket stars – Eureka Prize finalists announced

Stakeholder engagement

1. UNSW News: UNSW stands out in Eureka Prizes line-up
2. UNSW: Imaging winners at the Eureka Prizes
3. ANU Newsroom: Scientists shortlisted for Eureka Prizes
4. The Australian National University: ANU scientist wins Eureka Prize
5. Garvan Institute News: 'DIY droplet lens' nominated for an Australian Museum Eureka Prize

A NEW WAY OF LOOKING AT THE IMMUNE SYSTEM; IMAGING CENTRE OF EXCELLENCE LAUNCH - OCTOBER 2014

Media release: http://www.imagingcoe.org/news/a-new-way-of-looking-at-the-immune-system-imaging-centre-of-excellence-launch

The $39 million ARC Centre of Excellence in Advanced Molecular Imaging was launched on 15 October 2014 by Mr. Michael Sukkar, MP, Federal Member for Deakin. Among the other dignitaries present at the Centre Launch were Prof. Aidan Byrne, CEO of the ARC, Prof. Edwina Cornish, Provost of Monash University, Prof. Peter Gunning from University of New South Wales, who served as Master of Ceremonies, and Prof. Frances Shannon from University of Canberra, who serves as Chair of the Imaging CoE Governing Board. Attended by around 100 invited guests, the Centre launch featured addresses by Prof. Byrne, Mr. Sukkar and Prof. Cornish, a formal unveiling of the Centre launch plaque as well as brief descriptions of the impact of the Centre by three young scientists.

Speaking at the launch, Prof Byrne explained how the funding security offered by the Centres of Excellence scheme allows research to be nurtured through every stage - from conception through to realisation of benefits. He also described how the longevity of a Centre of Excellence allows good relationships to be built nationally and internationally, and between universities and industry.

"If we can determine at a molecular level how individual immune cells are triggered to respond to a threat, then we can open the door to new drug development and therapies." So said Mr. Sukkar reiterating and stressing the value of the Imaging Centre's core goal before he officially opened the Centre. He also paid tribute to the value of the collaborative partnerships the Centre has built with universities and industries, and expressed confidence in the ultimate success of the Centre's aim, saying that he was certain that the research produced will be rapidly exploited to create new ways of managing auto-immune diseases.

Prof. Cornish pointed out that the Centre had phenomenal links with key research groups around the world and that it was opening up connections with international facilities such as the European synchrotrons and X-ray free electron lasers. She also acknowledged and welcomed the co-operation of all the Centre partners in this world-class initiative.

The Centre launch got picked up particularly by radio with Director James Whisstock interviewed on three radio stations.

Radio

1. Radio National with Fran Kelly, 16 October
2. ABC Hobart with Leon Compton, 16 October
3. ABC Brisbane with Kelly Higgins-Devine, 31 October

Stakeholder engagement

1. ARC: New research centre to use advanced molecular imaging to fight auto-immune diseases.
2. Monash University: New Centre of Excellence to shed light on the immune system.
3. UNSW: Immunity under the microscope at new Centre of Excellence.
4. University of Queensland: Imaging centre to unravel secrets of immune system.

In addition, Deputy Director Kat Gaus was featured in a nice piece in the Sydney Morning Herald in June 2014 entitled "Researchers build microscope to view inside workings of a cell" in conjunction with her winning the prestigious Elizabeth Blackburn Fellowship. CI Jamie Rossjohn's Australian Academy of Sciences Fellowship was mentioned in the Leader.

Website and Social Media

The Imaging CoE website (www.imagingcoe.org) was launched in May 2014 and serves as a vital distribution point for Centre media releases, information regarding events such as launch, workshops etc., and news about the latest publications and presentations of our Centre CIs.

We have been active on Twitter and have integrated our Twitter feed into the home page of our website to provide visitors a real-time view of the latest activities within the Centre. Since establishing our Twitter account in May 2015, we tweeted 317 times and the increasing value and popularity of our tweets has seen our followers grow rapidly to 192 at the end of 2014.

Since the website was launched in May 2014, we have had 3,113 unique visitors to our website who have collectively viewed 15,670 pages on our website. 59% of our visits have been from new visitors and visitors on average have viewed three pages on our website per session. In addition, as a consequence of our strong international relationships with partners and collaborators, 35% of our website visitors have been international, from 79 countries including the United States, the United Kingdom, Netherlands and Germany.

The peak traffic through our website was recorded on 15 October 2014, the day of our official Centre Launch.

The currency that we have achieved with our website and our Twitter feed has been critical in the success we have had thus far in attracting visitors to our website.

Newsletter

As mentioned above, Science in Public prepare a monthly newsletter that is circulated electronically to our internal and external stakeholders to keep them abreast of the Centre's latest activities and successes. The aims of the newsletter are to inform our key stakeholders of the latest advances made by the Centre, celebrate the successes of the Centre and associated staff, and encourage communication among Centre staff across the various nodes.

The Imaging CoE monthly newsletter has been highly successful in achieving its aims. Since we started distributing the newsletter in May 2014, we have received numerous informal and formal messages with positive feedback regarding the usefulness of the articles published in the newsletter. Consequently, we have seen our newsletter subscription list grow from 240 in May 2014 to 520 in December 2014. On average, 50% of our subscribers are active readers of each newsletter meaning that we are effectively reaching an audience of around 250 readers each month.

Each newsletter is also featured and archived on our website each month.

Public Outreach

In addition to reaching out to the broader scientific community and general public via our media opportunities, our researchers were also proactive in taking steps to communicate their work and key insights via public lecture series and specific targeted talks.

In July 2014, CI Harry Quiney and PI Andrew Peele both delivered public lectures at the University of Melbourne as part of celebrations of a century of X-ray crystallography. Harry discussed how the use of new sources of electrons, neutrons and X-rays promises to revolutionise both materials science and biology, and Andrew described how the Australian Synchrotron works, what it does, and how it has accelerated outputs in biotechnology, helped industries of the future and is working to save lives. The lectures were part of a series held at the Carillo Gantner Theatre in the Asia Centre on Swanson Street on Friday evenings in July.

In June 2014, CI Brian Abbey visited Ivanhoe Grammar School and presented a talk entitled "Molecular movies: imaging single molecules using visible light and X-rays". Addressing a group of 60 Year 9 students, he spent an hour describing how Centre researchers were utilising various wavelengths of light to study the structure and dynamics of single molecules.

Also in June 2014, CI Jamie Rossjohn gave a public lecture entitled "Immunity to vitamin B metabolites" as part of the Australian Academy of Science's New Fellows and Medalists Symposium. The symposium was held at the University of Melbourne Auditorium at the Melbourne Brain Centre, Parkville, and featured talks from newly elected Victorian Fellows of the Australian Academy of Science as well as 2014 Australian Academy of Science medal winners.

PI Andrew Peele, who is the Director of the Australian Synchrotron, and Director James Whisstock also spoke to the Science Policy section of the Department of Industry in June 2014. They shared with government officials the significance, outcomes and economic benefits of the Synchrotron and also how synchrotron imaging approaches can be used to revolutionise industrial capability in fields as diverse as medicine, agribusiness and materials science. They were also able to highlight how the partnership between the Imaging CoE and the Australian Synchrotron will be of particular relevance to making discoveries regarding the functions of our immune system.

National and International Linkages

In the first year of operations, our Centre's focus has been on (a) establishing stronger collaborative links with our Partner Organisations, (b) forming strategic national and global linkages that will drive research excellence, and (c) raising our engagement profile with government and industry.

In addition, our researchers and staff visited 12 countries and gave 110 talks at seminars, workshops and conferences nationally and internationally, raising the profile of the Imaging CoE globally. A list of presentations given by our Centre researchers can be found in page 46.

Centre Partner Organisations

In addition, both our Centre Director and Chief Operating Officer personally visited our international partner organisations - University of Warwick and DESY - to consolidate their relationship with the Centre and to work out a strategic plan for their involvement in Centre activities. The visit was immensely valuable and has served as a catalyst for collaborations. The DESY partnership will revolve around development of XFEL technology for imaging single molecules as well as development of sample delivery approaches to improve the efficacy of X-ray and electron beam experiments. The Warwick partnership will revolve around the Warwick Open Source Microscope (WOSM) program and the development of advanced manufacturing techniques to build customised, low cost microscopes and accessories.

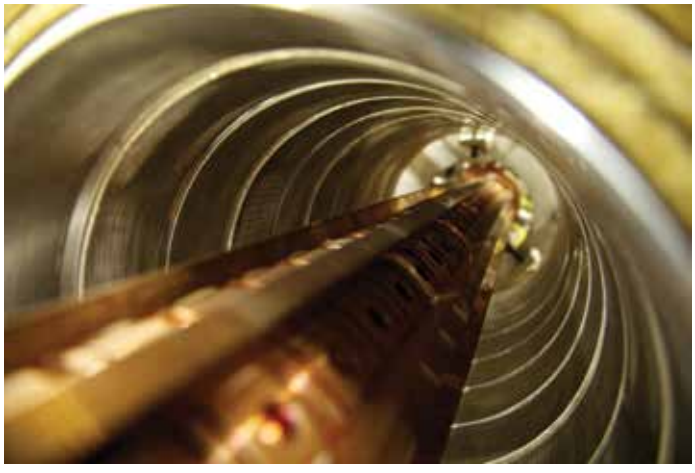
In particular, we are currently investigating ways in which we can embed researchers in our international partner organisations to improve the connectivity and productivity of our collaborations. For example, plans are currently underway to embed a postdoctoral researcher at DESY, and to appoint a joint professorship between Monash University and University of Warwick through the Monash-Warwick Alliance.

The Centre Director and Chief Operating Officer also visited ANSTO, our key national partner organisation who also have operational responsibility for the Australian Synchrotron, and had wide-ranging discussions on how best to leverage the expertise available at ANSTO and the Centre. Both parties realise that the greatest scientific discoveries will only be made through forming strategic relationships with a diverse group of experts who can each bring their respective knowledge bases to bear on a common problem. Hence, we will be utilising the ANSTO-funded Centre postdoctoral fellows to work on strategic projects, particularly involving the Centre's La Trobe University node, the Australian Synchrotron and DESY, around common issues that are critical for the X-ray, electron and neutron imaging communities.

The Imaging CoE has also expanded the partnership with the Australian Synchrotron in 2014 as the Synchrotron will play a critical role in furthering the scientific goals of the Centre as it provides the primary X-ray crystallography facilities to our researchers. The increased partnership will involve a second joint postdoctoral appointment between Monash University and the Australian Synchrotron to work on computational problems, particularly related to the crystallography beamline at the Synchrotron. This position is in addition to the experimental postdoctoral position that was planned for in the original Centre proposal. The recruitment for this position is currently underway and a suitable candidate will be appointed in early 2015.

National Linkages

The Growing Tall Poppies (GTP) program offers authentic science experiences for secondary school students with a particular focus on increasing the number of girls enrolling in the sciences to year 12 and beyond. In 2014, the GTP project, led by Dr. Eroia Barone-Nugent, won a five-year, $727,800 grant from the Department of Education through the Australian Maths and Science Partnership Program (AMSPP) with the Imaging CoE as one of its project partners. The Centre's Outreach Officer, Harry Quiney, will co-ordinate the Centre's involvement with the GTP project which will involve Centre scientists across the various Centre nodes supporting and mentoring students participating in the GTP program.



The linear accelerator at the Australian Synchrotron

NATIONAL LINKAGES: MASSIVE

One of the key elements across all of the various imaging modalities used across the Imaging CoE - be it X-ray imaging, electron or optical microscopy - is data processing and visualisation. Researchers require tremendous computational power to handle the huge datasets, up to several terabytes per experiment, that can be produced by the state-of-the-art imaging/microscopy instruments.

Rather than having researchers develop their own hardware and software to deal with these datasets, the Centre formed a strong working relationship with the Multi-modal Australian ScienceS Imaging and Visualisation Environment (MASSIVE) facility, a specialised national high performance computing facility for imaging and visualisation that provides access to state-of-the-art high performance computing facilities and expertise to Australian researchers.

Currently, MASSIVE provides our X-ray scientists with tailored supercomputing facilities that allow them to process the huge datasets obtained during X-ray diffraction experiments at the Australian Synchrotron and make decisions regarding experimental parameters in real-time, whereas previously scientists had to wait several days after experimental runs to find out whether their experiments were successful. As mentioned above, the Centre will further strengthen the computational capabilities afforded by MASSIVE at the Australian Synchrotron by appointing a Centre postdoctoral fellow jointly across Monash University and the Australian Synchrotron (reflecting the co-location of MASSIVE at both these institutions). We should point out here that the developments made through our Centre researchers' involvement with MASSIVE will be broadly available to all users of the Australian Synchrotron.

The Centre is working closely with MASSIVE to establish a similar supercomputing workflow for processing electron microscopy data that will be generated from the microscopes at the new Clive and Vera Ramaciotti Centre for Structural Cryo-Electron Microscopy. This work will be driven by AI Hans Elmlund, the Director of the new cryo-electron microscopy Centre, and the workflows developed will be made available to scientists all around Australia. In addition, Centre researchers also access and use the high performance computing facilities available through the Victorian Life Sciences Computational Initiative (VLSCI).

National and International Linkages

Beam tunnel @ European XFEL

International Linkages

The La Trobe node of the Centre, led by CIs Keith Nugent and Brian Abbey, are also leading the Centre's strategic involvement in the Single Particle Imaging (SPI) initiative at LCLS (Stanford University). The SPI initiative was launched in 2014 by LCLS in order to identify and solve the main challenges for reaching atomic resolution in single particle imaging experiments using XFELs. The initiative involves 17 institutions internationally, three of whom are Centre nodes (University of Melbourne, La Trobe University and Monash University). In fact, the Imaging CoE is the only Australian partner in this global initiative, that will tackle four key challenge areas identified - sample damage, algorithm development, instrumentation and sample characterization and delivery.

In addition, CI Harry Quiney was appointed a member of the assessment panel that allocates time to users of the LCLS at Stanford University.

In conjunction with the SPI initiative, the La Trobe University node of the Centre, led by CI Brian Abbey, have formed a new collaboration with the Centre for Bio-Imaging Sciences at the National University of Singapore (NUS) to further single particle imaging experiments with the aim of visualising biomolecular structures without the need for crystallisation.

The Centre, through its relationship with DESY which is leading the development of the European XFEL, has been closely involved in the development of the capabilities and expertise that

will be offered at the European XFEL. PI Henry Chapman heads the team designing and constructing the Serial Femtosecond Nanocrystallography (SFX) beam line at the European XFEL in Hamburg, Germany, and Keith and Brian sit on its management board. We will continue to grow our partnership with DESY in 2015 to cement our relationship as one of the key global contributors and users of the European XFEL.

The Centre, led by Director James Whisstock and Deputy Director Kat Gaus, also collaborated with EMBL Australia to the expand the highly successful EMBL Australia Group Leader program at UNSW and Monash University. The program offers a five-year funded research group leader position that can be extended to a maximum of nine years subject to an external review. In all, there will be four new EMBL Australia Group Leaders directly associated with the Centre - two of them will be in areas of light microscopy and single molecule science based at UNSW and the other two in protein crystallography and electron microscopy based at Monash.

Altogether this represents a funding commitment of $25.2 million that the Centre has been able to attract, and will provide us with a major opportunity to recruit the best available talent to our shores. An international recruitment drive is in progress and appointments are expected to be made in early 2015. This has also served to bolster the burgeoning reputation of the Centre as a truly world-leading collaborative research centre, and has provided us with the international networks afforded to us through the EMBL program.

Government and Industry

Imaging CoE Chief Operating Officer, Dr. Manoj Sridhar, was part of a Victorian trade delegation that participated in the Advamed 2014 Conference in Chicago, USA, the largest global medical technology conference, from 5 - 8 October 2014. The delegation comprised of over 30 representatives from across Victoria's medtech community and was led by Dr. Buzz Palmer, CEO of Small Technologies Cluster (STC) Australia, and Dr. Krystal Evans, Chief Executive Officer of the BioMelbourne Network.

The aims of the Centre's participation in this trade delegation were to:

(a) develop closer relationships with the Victorian Government, particularly in the Department of State Development, Business and Innovation (DSDBI), and STC Australia,

(b) explore and form relationships with Australian businesses in the medical technologies space, and

(c) learn about commercialisation pathways for medical technologies and typical challenges faced by startup companies through the educational programs and forums offered at the conference.

The trip was an extremely productive one as all three of these objectives were achieved. The key outcomes that have arisen as a direct consequence of participation in this conference are listed below:

1. In the months since the conference, our friends at DSDBI have helped us identify one new local SME with whom we are presently working to establish a R&D collaboration. We are also in regular communication with both parties to keep abreast of the latest leads and to explore further linkages as appropriate.

2. The Centre made contact with one local SME who was a fellow conference delegate, with whom we will explore possibilities for R&D collaboration in the coming weeks.

3. The Centre has the support of both the Victorian Government and STC in putting together our proposed 'Industry meets Centre' Day in 2015. We will involve them in further planning discussions regarding this event as their involvement will significantly expand our reach to industry and help ensure that we have the maximum exposure for our Centre's research in the commercial and political space.

4. At the conference, the Centre formed contact with the Invest in France Agency, which is a French Government agency aimed at attracting foreign investment and collaborations to France. The Centre is currently exploring possible connections with the Marseille Immunopole cluster and surrounding infrastructure in the areas of imaging and immunology.

5. Manoj also attended several talks and forums at the conference relating to commercialisation of medical technologies, and learnt a lot about the key challenges facing entrepreneurs, commercialisation pathways and funding strategies for startups. Contact was also made with Life Sciences Nation, a Boston-based company that assists entrepreneurs with finding suitable startup funding through an online matchmaking service.

In addition, we will also use the relationships that we have established to continue our involvement in strategic events led by the Victorian Government and STC Australia such as planned trade delegations to relevant, major international conferences such as Bio 2015, and entrepreneurship training programs such as MedTech's Got Talent.

In 2015, we will also be holding a showcase event specifically targeting imaging technology companies and drug development/ pharma companies to explore possibilities for collaboration in areas of mutual interest.

Graduate Training

Attendees of the Crystallography Workshop sponsored by the Imaging CoE holding up letters symbolising the International Year of Crystallography.

The Imaging CoE's overall training mission is to provide our graduate students and postdoctoral researchers with a well rounded experience that enables them to develop their scientific expertise and deliver maximum impact for themselves and to the Centre's broader goals. In particular, the Centre will target three key training areas - technical skills in imaging and immunology, science communication, and entrepreneurship/ commercialisation skills - that will achieve our mission.

In 2014, our primary focus was on technical skills as our key goal was to ensure that our Centre staff had (a) the necessary capabilities to carry out leading edge science, and (b) awareness of the breadth of scientific research that was being carried out across the Centre's nodes. To this end, the Centre sponsored and ran three training workshops for our graduate students and postdoctoral researchers.

The 2nd Australian Advanced Methods in Crystallography Workshop was held at the Australian Synchrotron in June 2014. AI Dr Stephanie Gras was one of the organisers of the two-day workshop, which was attended by a total of 60 students

GRADUATE PROFILE - MS HANNAH COUGHLAN

Hannah is a second year PhD student in CI Brian Abbey's group at La Trobe University. She is working to improve X-ray crystallography so that it overcome the current limitations of requiring large, perfect crystals in order to determine their molecular structure. To achieve this goal, Hannah joins fellow Centre colleagues in working at the Australian Synchrotron as well as international facilities such as the Linac Coherent Light Source (LCLS) at Stanford University, USA and DESY in Hamburg, Germany. She presented her work on coherent biological imaging techniques last year at the JILA Institute in Boulder, Colorado, and was also co-author on a paper reviewing the experimental requirements and basic principles of ptychographic Fresnel diffraction tomography that was published in the International Journal of Materials Research.

and researchers.Key topics explored included the latest modelling and refinements, tricks and traps in data processing, developments in Lipidic Cubic Phase (LCP) crystallisation, and hands-on opportunities to use new methods available on Synchrotron beamlines.

The Centre also conducted the first annual Imaging Symposium which was held at the National Synchrotron Science Building in October 2014. The main motivation for the Symposium was to expose our Centre staff and researchers to areas of research that were outside their specialty so as to promote cross-disciplinary collaborations. The Symposium featured talks from a selection of our CIs and AIs that covered the breadth of expertise present in our Centre, from physics and modelling of molecular interaction with x-ray free electron laser beams to chemistry and targeting immune cells with small molecules to biology and understanding the regulation of T cell immunity after viral infection of the skin. The 42 attendees in the audience had the chance to interact with the presenter both immediately after each talk and also during discussion breaks during and after the event. Feedback collected after the event indicated that attendees found the talks and format of the event very useful and eye-opening.

CI Brian Abbey organised a day-long X-ray Science Workshop at La Trobe University in November 2014. The workshop was organised as a follow-up to the 12th International Conference on X-ray Microscopy which was held at the Melbourne Convention and Exhibition Centre from 26-31 October 2014. The workshop featured three Australian and five international X-ray imaging experts, including Dr. Adrian Mancuso from Centre partners DESY, and was attended by around 50 scientists from across biology, chemistry and physics. The workshop was aimed at introducing the latest developments in X-ray microscopy, X-ray science at the Australian Synchrotron and the advent of the European XFEL facility in Hamburg, Germany. A dozen Centre staff and students participated in the workshop and benefited from the in-depth discussions on this cutting edge subject.

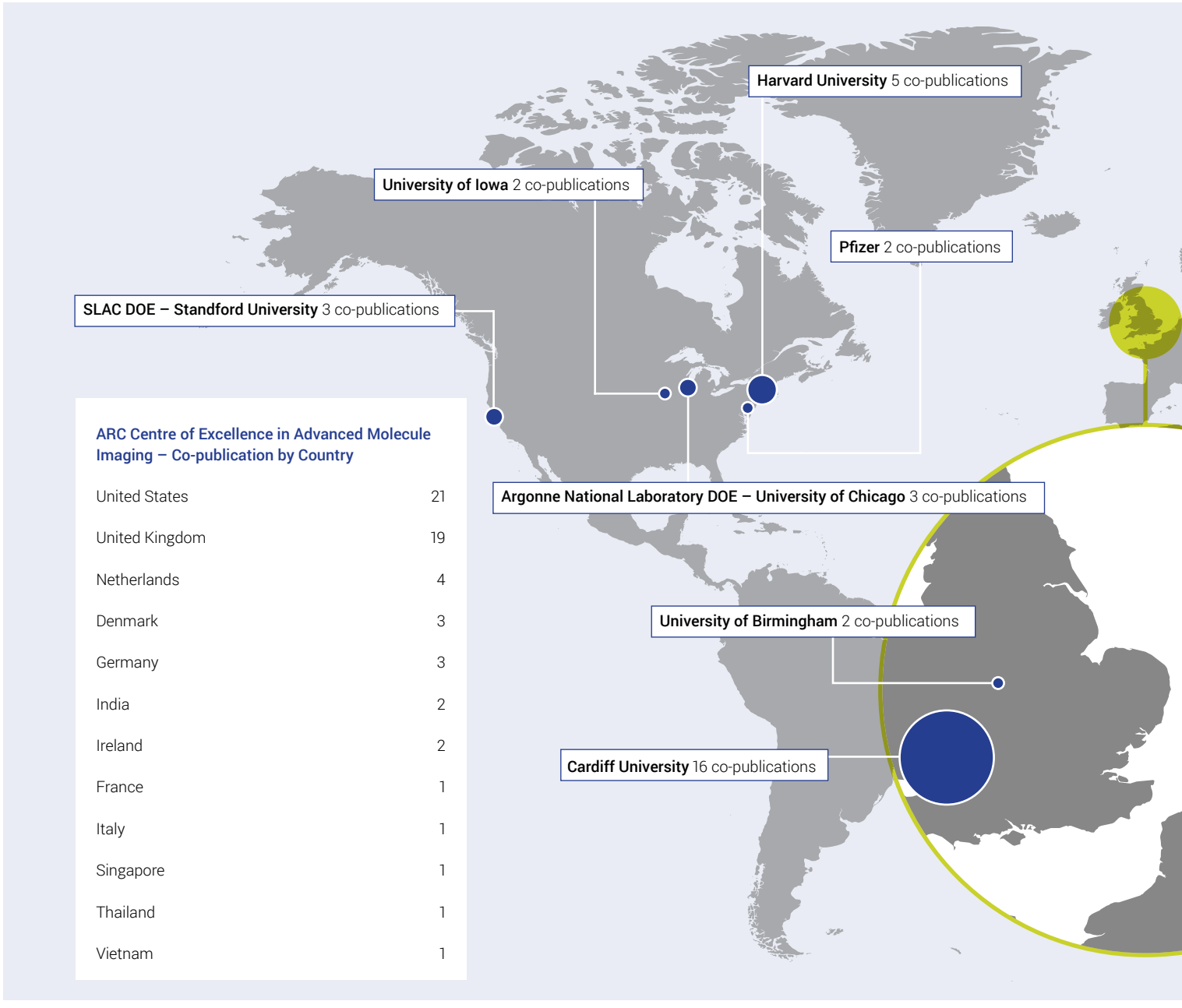
Where are we going?

In 2015, we will expand on the range of technical workshops and symposia that we sponsor and run for our students and researchers. These workshops will primarily be held in conjunction with major national and international conferences such as the International Proteolysis Conference and Australasian Society of Immunology Annual Scientific Meeting.

Plans are also underway for a media training workshop which would provide hands-on training in science communication through a variety of media such as TV, radio and print. We will also be organising and sponsoring a series of workshops to promote entrepreneurship and commercialisation skills to our students and researchers.

Attendees at the X-ray Science Workshop held at La Trobe University

Publications

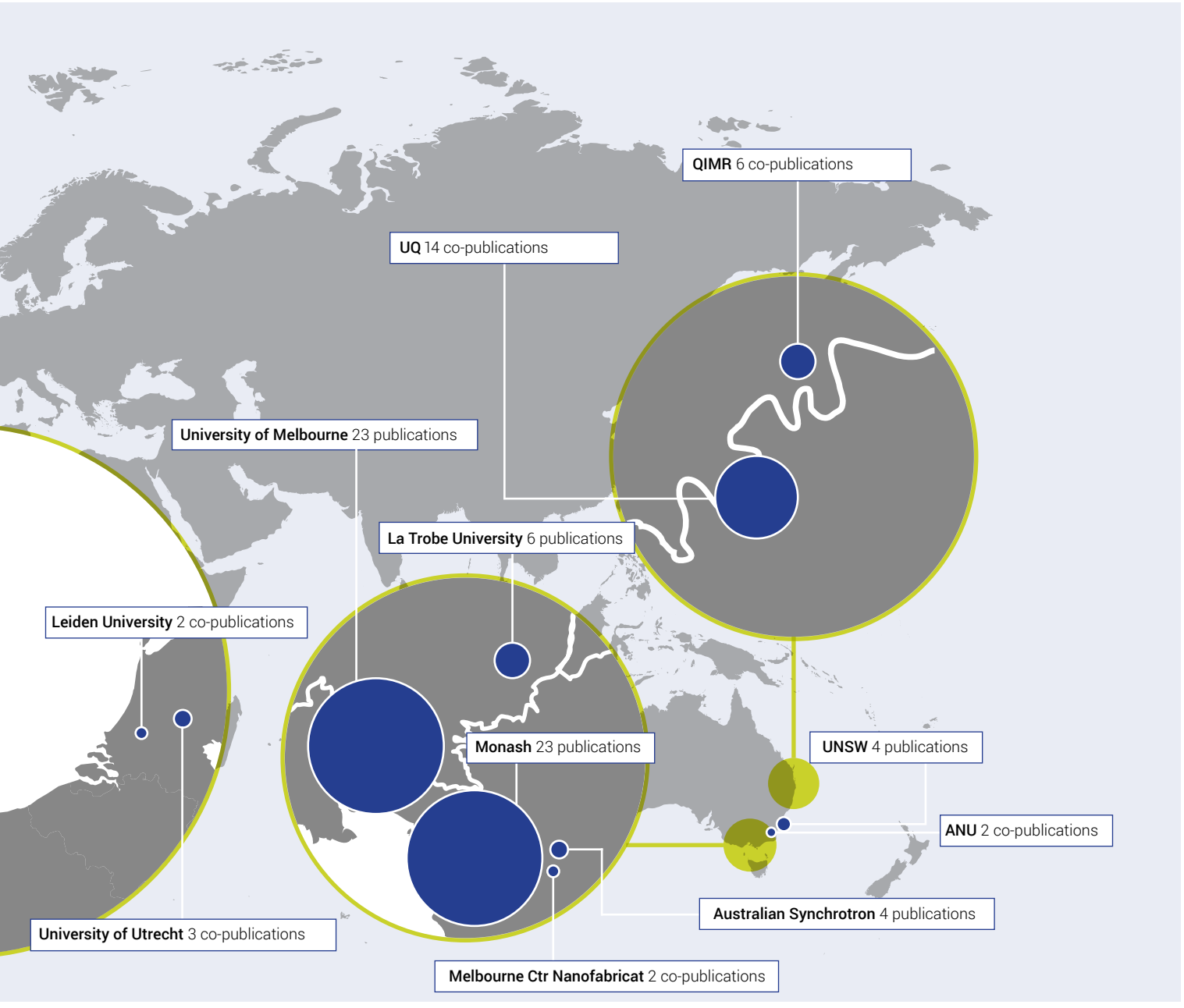


ARC Centre of Excellence in Advanced Molecule Imaging – Co-publication by Country

United States	21
United Kingdom	19
Netherlands	4
Denmark	3
Germany	3
India	2
Ireland	2
France	1
Italy	1
Singapore	1
Thailand	1
Vietnam	1

ARC Centre of Excellence in Advanced Molecule Imaging – Publication Mapping

(map only shows organisations that co-published 2 or more publications with the CoE Advanced Molecular Imaging)


QIMR 6 co-publications
UQ 14 co-publications
University of Melbourne 23 publications
La Trobe University 6 publications
Leiden University 2 co-publications
Monash 23 publications
UNSW 4 publications
ANU 2 co-publications
Australian Synchrotron 4 publications
University of Utrecht 3 co-publications
Melbourne Ctr Nanofabricat 2 co-publications

Publications

January 2014

Dynamic control of ß1 integrin adhesion by the plexinD1-sema3E axis. (Proceedings of the National Academy of Sciences USA, Vol. 111, pg 379-84)

Authors: YI Choi, J Duke-Cohan, W Chen, B Liu, J Rossy, T Tabarin, L Ju, J Gui, K Gaus, C Zhu, EL Reinherz.

Single molecule analysis reveals self assembly and nanoscale segregation of two distinct cavin subcomplexes on caveolae. (eLife, Vol. 3, e01434)

Authors: Y Gambin, N Ariott, KA McMahon, M Bastiani, E Sierecki, O Kovtun, M Polinkovsky, A Magenau, WR Jung, S Okano, Y Zhou, N Leneva, S Mureev, W Johnston, K Gaus, JF Hancock, BM Collins, K Alexandrov, RG Parton.

Maspin is not required for embryonic development or tumour suppression. (Nature Communications, Vol. 5, article 3164)

Authors: SSY Teoh, J Vieusseux, M Prakash, S Berkowicz, J Luu, CH Bird, RHP Law, C Rosado, JT Price, JC Whisstock, PI Bird.

Cascleave 2.0, a new approach for predicting caspase and granzyme cleavage targets. (Bioinformatics, Vol. 30, pg 71-80)

Authors: MJ Wang, XM Zhao, H Tan, T Akutsu, JC Whisstock, JN Song.

Preexisting CD8+ T-cell immunity to the H7N9 influenza A virus varies across ethnicities. (Proceedings of the National Academy of Sciences USA, Vol. 111, pg 1049-54)

Authors: S Quinones-Parra, E Grant, L Loh, TH Nguyen, KA Campbell, SY Tong, A Miller, PC Doherty, D Vijaykrishna, J Rossjohn, S Gras, K Kedzierska

February 2014

Molecular imprint of exposure to naturally occurring genetic variants of human cytomegalovirus on the T cell repertoire. (Scientific Reports, Vol. 4, article 3993)

Authors: C Smith, S Gras, RM Brennan, NL Bird, SA Valkenburg, KA Twist, JM Burrows, JJ Miles, D Chambers, S Bell, S Campbell, K Kedzierska, SR Burrows, J Rossjohn, R Khanna

CD1a-autoreactive T cells recognize natural skin oils that function as headless antigens. (Nature Immunology, Vol. 15, pg 177-85)

Authors: A de Jong, TY Cheng, S Huang, S Gras, RW Birkinshaw, AG Kasmar, I Van Rhijn, V Pena-Cruz, DT Ruan, JD Altman, J Rossjohn, DB Moody

Fluctuation-based imaging of nuclear Rac1 activation by protein oligomerisation. (Scientific Reports, Vol. 4, article 4219)

Authors: E Hinde, K Yokomori, K Gaus, K Hahn, E Gratton

Fluorescence spectral correlation spectroscopy (FSCS) for probes with highly overlapping emission spectra. (Optics Express, Vol. 22, pg 2973-88)

Authors: A Benda, P Kapusta, M Hof, K Gaus

March 2014

Insights into adhesion biology using single-molecule localization microscopy. (European Journal of Chemical Physics and Physical Chemistry, Vol. 15, pg 606-18)

Authors: T Tabarin, SV Pageon, CTT Bach, Y Lu, GM O'Neill, JJ Gooding, K Gaus

Trunk cleavage is essential for Drosophila terminal patterning and can occur independently of Torso-like (Nature Communications, Vol. 5, article 3419)

Authors: MA Henstridge, TK Johnson, CG Warr, JC Whisstock

Local regularization of tilt projections reduces artifacts in electron tomography (Journal of Structural Biology, Vol. 186, pg 28-37)

Authors: M Maiorca, C Millet, E Hanssen, B Abbey, E Kazmierczak, L Tilley

The perforin pore facilitates the delivery of cationic cargos. (Journal of Biological Chemistry, Vol. 289, pg 9172-81)

Authors: SE Steward, SC Kondos, AY Matthews, ME D'Angelo, MA Dunstone, JC Whisstock, JA Trapani, PI Bird.

TCR bias and affinity define two compartments of the CD1b-glycolipid-specific T Cell repertoire (Journal of Immunology, Vol. 192, pg 4054-60)

Authors: I Van Rhijn, NA Gherardin, A Kasmar, W de Jager, DG Pellicci, L Kostenko, LL Tan, M Bhati, S Gras, DI Godfrey, J Rossjohn, DB Moody

Method for co-cluster analysis in multichannel single-molecule localization data. (Histochemistry and Cell Biology, Vol. 141, pg 605-12)

Authors: J Rossy, E Cohen, K Gaus, DM Owen

April 2014

T-cell activation by transitory neo-antigens derived from distinct microbial pathways (Nature, Vol. 509, pg 361-5)

Authors: AJ Corbett, SB Eckle, RW Birkinshaw, L Liu, O Patel, J Mahony, Z Chen, R Reantragoon, B Meehan, H Cao, NA Williamson, RA Strugnell, D Van Sinderen, JY Mak, DP Fairlie, L Kjer-Nielsen, J Rossjohn, J McCluskey

Persistence of skin-resident memory T cells within an epidermal niche (Proceedings of the National Academy of Sciences USA, Vol. 111, pg 5307-12)

Authors: A Zaid, LK Mackay, A Rahimpour, A Braun, M Veldhoen, FR Carbone, WR Heath, SN Mueller

High resolution structure of cleaved Serpin 42Da from Drosophila melanogaster (BMC Structural Biology, Vol. 14, article 14)

Authors: AM Ellisdon, Q Zhang, MA Henstridge, TK Johnson, CG Warr, RH Law, JC Whisstock

T-cell receptor recognition of HLA-DQ2–gliadin complexes associated with celiac disease (Nature Struct. & Mol. Biology, Vol. 21, pg 480-8)

Authors: J Petersen, V Montserrat, JR Mujico, KL Loh, DX Beringer, M van Lummel, A Thompson, ML Mearin, J Schweizer, Y Kooy-Winkelaar, J van Bergen, JW Drijfhout, WT Kan, NL La Gruta, RP Anderson, HH Reid, F Koning, J Rossjohn

Endocytic crosstalk: cavins, caveolins and caveolae regulate clathrin-independent endocytosis. (PLoS Biology, Vol. 12, e1001832)

Authors: N Chaudhary, GA Gomez, MT Howes, HP Lo, KA McMahon, JJ Rae, MM Hill, K Gaus, AS Yap, RG Parton

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Authors: JJ Gooding, SG Parker, Y Lu, K Gaus

May 2014

Complement C5a Receptor Facilitates Cancer Metastasis by Altering T-Cell Responses in the Metastatic Niche (Cancer Research, Vol. 74, pg 3454-65)

Authors: SK Vadrevu, NK Chintala, SK Sharma, P Sharma, C Cleveland, L Riediger, S Manne, DP Fairlie, W Gorczyca, O Almanza, M Karbowniczek, MM Markiewski

The organisation of the cell membrane: do proteins rule lipids? (Current Opinions in Chemical Biology, Vol. 20, pg 54-9)

Authors: J Rossy, Y Ma, K Gaus

Galectin-3 drives glycosphingolipid-dependent biogenensis of clathrin-independent carriers. (Nature Cell Biology, Vol. 16, pg 595-606)

Authors: R Lakshminarayan, C Wunder, U Becken, MT Howes, C Benzing, S Arumugam, S Sales, N Ariotti, V Chambon, C Lamaze, D Loew, A Shevchenko, K Gaus, RG Parton, J Johannes

CD8+ T cells from a novel T cell receptor transgenic mouse induce liver-stage immunity that can be boosted by blood-stage infection in rodent malaria (PLOS Pathogens, Vol. 10, e1004135)

Authors: LS Lau, D Fernandez-Ruiz, V Mollard, A Sturm, MA Neller, A Cozjinsen, JL Gregory, GM Davey, CM Jones, YH Lin, A Haque, CR Engwerda, CQ Nie, DS Hansen, KM Murphy, AT Papenfuss, JJ Miles, SR Burrows, T de Koning-Ward, GI McFadden, FR Carbone, BS Crabb, WR Heath

Reconciling the structural attributes of avian antibodies (Journal of Biological Chemistry, Vol. 289, pg 15384-92)

Authors: PJ Conroy, RH Law, S Gilgunn, S Hearty, TT Caradoc-Davies, G Lloyd, RJ O'Kennedy, JC Whisstock

Versatile "click chemistry" approach to functionalizing silicon quantum dots: applications toward fluorescent cellular imaging. (Langmuir, Vol. 30, pg 5209-16)

Authors: X Cheng, SB Lowe, S Ciampi, A Magenau, K Gaus, PJ Reece, JJ Gooding

June 2014

Structural and functional correlates of enhanced antiviral immunity generated by heteroclitic CD8 T cell epitopes (Journal of Immunology, Vol. 192, pg 5245-56)

Authors: JA Trujillo, S Gras, KA Twist, NP Croft, R Channappanavar, J Rossjohn, AW Purcell, S Perlman

Key interactions for clathrin coat stability (Structure,Vol. 22, pg 819-29)

Authors: T Boecking, F Aguet, I Rapaport, M Banzhaf, A Yu, JC Zeeh, T Kirchhausen

A Molecular Basis for the Interplay between T Cells, Viral Mutants, and Human Leukocyte Antigen Micropolymorphism. (Journal of Biological Chemistry, Vol. 289, pg 16688-98)

Authors: YC Liu, Z Chen, MA Neller, JJ Miles, AW Purcell, J McCluskey, SR Burrows, J Rossjohn, S Gras

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Ultrafast Imaging of Shocked Material Dynamics with X-ray Fee Electron Laser Pulses (CLEO: 2014 Postdeadline Paper Digest, OSA Technical Digest (online) (Optical Society of America, 2014), paper STh5C.8)

RL Sandberg, C Bolme, K Ramos, Q McCulloch, JL Barber, R Martinez, M Greenfield, SD McGrane, B Abbey, A Schropp, F Sieboth, P Heiman, B Nagler, EC Galtier, E Granados

The structure of the cytomegalovirus-encoded m04 glycoprotein, a prototypical member of the m02 family of immunoevasins (Journal of Biological Chemistry, Vol. 289, pg 23753-63)

Authors: R Berry, JP Vivian, FA Deuss, GR Balaji, PM Saunders, J Lin, DR Littler, AG Brooks, J Rossjohn

July 2014

Antibody modified porous silicon microparticles for the selelective capture of cells. (Bioconjugate Chemistry, Vol. 25, pg 1282-9)

Authors: B Guan, A Magenau, S Ciampi, K Gaus, PJ Reece, JJ Gooding

Biointerfaces on indium-tin oxide prepared from Organophosphonic acids self-assembled monolayers. (Langmuir, Vol. 30, pg 8509-15)

Authors: M Chockalingam, A Magenau, SG Parker, M Parviz, SR Vivekchand, K Gaus, JJ Gooding JJ

Missense single nucleotide polymorphisms in the human T cell receptor loci control variable gene usage in the T cell repertoire. (British Journal of Haematology, Vol. 166, pg 148-52)

Authors: RM Brennan, JM Burrows, T Elliott, MA Neller, S Gras, J Rossjohn, JJ Miles, SR Burrows

Ptychographic Fresnel coherent diffraction tomography at the nanoscale (International Journal of Materials Research, Vol. 105, pg 655-663)

Authors: NW Phillips, CT Putkunz, G Van Riessen, HD Coughlan, MWM Jones, B Abbey

Comparative α-Helicity of Cyclic Pentapeptides in Water (Angewandte Chemie, Vol. 53, pg 6965-9)

Authors: AD de Araujo, HN Hoang, WM Kok, F Diness, P Gupta, TA Hill, RW Driver, DA Price, S Liras, DP Fairlie

Imaging Lattice Dynamics in Individual Nanocrystals (9th International Conference on Ultrafast Phenomena, OSA Technical Digest (online) (Optical Society of America, 2014), paper 09.Wed.E.1)

Authors: JN Clark, L Beitra, G Xiong, A Higginbotham, D Fritz, H Lemke, D Zhu, M Chollet, G Williams, M Messerschmidt, B Abbey, R Harder, A Korsunsky, J Wark, I Robinson

Tissue-resident T cells: dynamic players in skin immunity (Frontiers of Immunology, Vol. 5, article 332)

Authors: SN Mueller, A Zaid, FR Carbone

A molecular basis underpinning the T cell receptor heterogeneity of mucosal-associated invariant T cells (Journal of Experimental Medicine, Vol. 211, pg 1585-600)

Authors: SBG Eckle, RW Birkinshaw, L Kostenko, AJ Corbett, HEG McWilliam, R Reantragoon, Z Chen, NA Gherardin, T Beddoe, L Liu, O Patel, B Meehan, DP Fairlie, JA Villadangos, DI Godfrey, L Kjer-Nielsen, J McCluskey, J Rossjohn

The Glucocorticoid Receptor 1A3 Promotor correlates with high sensitivity to glucocorticoid-induced apoptosis in human lymphocytes (Immunology & Cell Biology, Vol. 92, pg 825-36)

Authors: DR Liddicoat, K Kyparissoudis, SP Berzins, TJ Cole, DI Godfrey

August 2014

Cyclic Penta- and Hexa-Leucine Peptides Without N-Methylation Are Orally Absorbed. (ACS Medicinal Chemistry Letters, Vol. 5, pg 1148-51)

Authors: TA Hill, RJ Lohman, HN Hoang, DS Nielsen, CCG Scully, WM Kok, L Liu, AJ Lucke, MJ Stoermer, CI Schroeder, S Chaousis, B Colless, PV Bernhardt, DJ Edmonds, DA Griffith, CJ Rotter, RB Ruggeri, DA Price, S Liras, DJ Cralk, DP Fairlie.

Rapid, low dose X-ray diffractive imaging of the malaria parasite Plasmodium falciparum (Ultramicroscopy, Vol. 143, pg 88-92)

MWM Jones, MK Dearnley, GA van Riessen, B Abbey, CT Putkunz, MD Junker, DJ Vine, I McNulty, KA Nugent, AG Peele, L Tilley

A New Model for Pore Formation by Cholesterol-Dependent Cytolysins (PLOS Computational Biology, Vol. 10, e1003791)

Authors: CF Reboul, JC Whisstock, MA Dunstone

The Cellular Redox Environment Alters Antigen Presentation (Journal of Biological Chemistry, Vol. 289, pg 27979-91)

Authors: JA Trujillo, NP Croft, NL Dudek, R Channappanavar, A Theodossis, AI Webb, MA Dunstone, PT Illing, NS Butler, C Fett, DC Tscharke, J Rossjohn, S Perlman, AW Purcell

Distinct APC subtypes drive spatially segregated helper versus killer T-cell effector activity during skin infection with HSV-1(PLOS Pathogens, Vol. 10, e1004303)

Authors: BL Macleod, S Bedoui, JL Hor, SN Mueller, TA Russell, NA Hollett, WR Heath, DC Tscharke, AG Brooks, T Gebhardt

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Authors: RC Reid, MK Yau, R Singh, J Lim, DP Fairlie

September 2014

Fresnel coherent diffractive imaging tomography of whole cells in capillaries (New Journal of Physics, Vol. 16, 093012)

Authors: MB Luu, GA van Riessen, B Abbey, MWM Jones, NW Phillips, K Elgass, MD Junker, DJ Vine, I McNulty, G Cadenazzi, C Millet, L Tilley, KA Nugent, AG Peele

HLA-DQA1-HLA-DRB1 variants confer susceptibility to pancreatitis induced by thiopurine immunosuppressants. (Nature Genetics, Vol. 46, pg 1131-4)

Authors: GA Heap, MN Weedon, CM Bewshea, A Singh, M Chen, JB Satchwell, JP Vivian, J Rossjohn et al.

Pathway-selective antagonism of proteinase activated receptor 2. (British Journal of Pharmacology, Vol. 171, pg 4112-24)

Authors: JY Suen, A Cotterell, RJ Lohman, J Lim, A Han, MK Yau, L Liu, MA Cooper, DA Vesey, DP Fairlie.

October 2014

Skin DCs cluster for efficient T cell activation. (Nature Immunology, Vol. 15, pg 1004-5)

Author: SN Mueller

Potent Heterocyclic Ligands for Human Complement C3a Receptor. (Journal of Medicinal Chemistry, Vol. 57, pg 8459-70)

Authors: RC Reid, MK Yau, JK Hamidon, J Lim, MJ Stoermer, DP Fairlie.

Mapping biological composition through quantitative phase and absorption and X-ray ptychography. (Scientific Reports, Vol. 4, article 6796)

Authors: MWM Jones, K Elgass, MD Junker, MB Luu, MT Ryan, AG Peele, GA van Riessen.

MAIT cells are depleted early but retain functional cytokine expression in HIV infection. (Immunology & Cell Biology, Vol. 93, pg 177-88)

Authors: CS Fernandez, T Amarasena, AD Kelleher, J Rossjohn, J McCluskey, DI Godfrey, SJ Kent.

An Extensive Antigenic Footprint Underpins Immunodominant TCR Adaptability against a Hypervariable Viral Determinant. (Journal of Immunology, Vol. 193, pg 5402-13)

Authors: UK Nivarthi, S Gras, L Kjer-Nielsen, R Berry, IS Lucet, JJ Miles, SL Tracy, AW Purcell, DS Bowden, M Hellard, J Rossjohn, J McCluskey, M Bharadwaj.

November 2014

Improving on Nature: Making a Cyclic Heptapeptide Orally Bioavailable. (Angewandte Chemie, Vol. 53, pg 12059-63)

Authors: DS Nielsen, HN Hoang, RJ Lohman, TA Hill, AJ Lucke, DJ Craik, DJ Edmonds, DA Griffith, CJ Rotter, RB Ruggeri, DA Price, S Liras, DP Fairlie.

Uptake of the butyrate receptors, GPR41 and GPR43, in lipid bicontinuous cubic phases suitable for in mess crystallization. (Journal of Colloid and Interface Science, Vol. 441, pg 78-84)

Authors: Y-L Liang, CE Conn, CJ Drummond, C Darmanin.

Constraining Cyclic Peptides to Mimic Protein Structure Motifs. (Angewandte Chemie, Vol. 53, pg 13020-41)

Authors: TA Hill, NE Shepherd, F Diness, DP Fairlie.

Molecular architecture of the αβ T cell receptor-CD3 complex. (Proceedings of the National Academy of Sciences of the USA, Vol. 111, pg 17576-81)

Authors: ME Bimbaum, R Berry, YS Hsiao, Z Chen, MA Shingu-Vazquez, X Yu, D Waghray, S Fischer, J McCluskey, J Rossjohn, T Walz, KC Garcia.

December 2014

The molecular bases of δ/αβ T cell-mediated antigen recognition. (Journal of Experimental Medicine, Vol. 211, pg 2599-615)

Authors: DG Pellicci, AP Uldrich, J Le Nours, F Ross, E Chabrol, SBG Eckle, R de Boer, RT Lim, K McPherson, G Besra, AR Howell, L Moretta, J McCluskey, MHM Heemskerk, S Gras, J Rossjohn, DI Godfrey.

Regulatory iNKT cells lack expression of the transcription factor PLZF and control the homeostasis of Treg cells and macrophages in adipose tissue. (Nature Immunology, Vol. 16, pg 85-95)

Authors: L Lynch, X Michelet, S Zhang, PJ Brennan, A Moseman, C Lester, G Besra, EE Vomhof-Dekrey, M Tighe, HF Koay, DI Godfrey, EA Leadbetter, DB Sant'Angelo, U von Andrian, MB Brenner.

Presentations

Name Centre Node	Conference/Meeting	Location
Brian Abbey La Trobe University	Asian Forum for Accelerators and Detectors	Melbourne, Australia
Jamie Rossjohn Monash University	JDRF/ Wellcome Trust Frontier Meeting: The Common Mechanisms of Autoimmune Diseases	London, UK
Ruby Law Monash University	Gordon Research Conference on Plasminogen Activation and Extracellular Proteolysis	California, USA
Dale Godfrey University of Melbourne	Lorne Infection and Immunity Conference 2014	Lorne, Australia
Brian Abbey La Trobe University	The Minerals, Metals and Materials Society Annual Meeting 2014	San Diego, USA
Brian Abbey La Trobe University	Melbourne Centre for Nanofabrication (MCN) Showcase	Melbourne, Australia
Scott Mueller University of Melbourne	Peter MacCallum Cancer Centre Research Seminar	Melbourne, Australia
Stephanie Gras Monash University	ThymOz: An International Workshop on T Lymphocytes	Heron Island, Australia
Dale Godfrey University of Melbourne	ThymOz: An International Workshop on T Lymphocytes	Heron Island, Australia
James Whisstock Monash University	Monash Technology Research Platforms Seminar	Kuala Lumpur, Malaysia
Scott Mueller University of Melbourne	Centenary Institute	Sydney, Australia
Brian Abbey La Trobe University	DSTO invited Seminar	Melbourne, Australia
Scott Mueller University of Melbourne	Dept of Anatomy & Neuroscience, University of Melbourne	Melbourne, Australia
Dale Godfrey University of Melbourne	Seminar, Boston CD1 group, Brigham and Women's Hospital	Boston, USA
Dale Godfrey University of Melbourne	Dana Farber Cancer Institute/Brigham and Women's Hospital joint seminar program	Boston, USA
Dale Godfrey University of Melbourne	Seminar, Harvard University	Boston, USA
Stephanie Gras Monash University	5th Australasian Vaccines & Immunotherapeutics Development Meeting	Melbourne, Australia
Dale Godfrey University of Melbourne	Seminar, La Jolla Institute for Allergy and Immunology	San Diego, USA
Dale Godfrey University of Melbourne	Seminar, Scripps Research Institute	San Diego, USA

Name Centre Node	Conference/Meeting	Location
William Heath University of Melbourne	Tsinghua University	Beijing, China
Scott Mueller University of Melbourne	Tsinghua University	Beijing, China
Jamie Rossjohn Monash University	2014 Science at the Shine Dome	Canberra, Australia
Jamie Rossjohn Monash University	North American Comparative Immunology Workshop	Alberquerque, USA
Scott Mueller University of Melbourne	Gordon Research Conference on Immunochemistry & Immunobiology	Maine, USA
Brian Abbey La Trobe University	Ivanhoe Grammar School	Melbourne, Australia
Jamie Rossjohn Monash University	AAS New Fellows and Medallists Symposium	Melbourne, Australia
Michelle Dunstone Monash University	Microbiology and Infectious Diseases Asia Congress 2014	Singapore
Jamie Rossjohn Monash University	FASEB Immunoreceptors Conference	Colorado, US
Katharina Gaus University of NSW	9th International Weber Symposium on Innovative Fluorescence Methodologies in Biochemistry and Medicine	Kauai, Hawaii
James Whisstock Monash University	Gordon Research Conference on Proteolytic Enzymes and their Inhibitors	Lucca, Italy
Dale Godfrey University of Melbourne	Seminar, Monash University Centre for Inflammatory Diseases	Melbourne, Australia
Katharina Gaus University of NSW	5th International Nanomedicine Conference	Sydney, Australia
James Whisstock Monash University	Infection and Immunity workshop, Jagellonian University	Krakow, Poland
Henry Kirkwood La Trobe University	Chinese Materials Association-UK Conference	Oxford, UK
Praveena Thirunavukkarasu Monash University	13th Melbourne Protein Group student symposium	Melbourne, Australia
Dale Godfrey University of Melbourne	Monash Haematology	Melbourne, Australia
Harry Quiney University of Melbourne	Public Lecture	Melbourne, Australia
Nicholas Philips La Trobe University	Invited seminar, JILA Institute	Boulder, USA
Hannah Couglan La Trobe University	Invited seminar, JILA Institute	Boulder, USA

Presentations

Name Centre Node	Conference/Meeting	Location
James Whisstock Monash University	Peptide Users Group - Winter Symposium	Melbourne, Australia
Jamie Rossjohn Monash University	The 28th Annual symposium of the Protein Society	San Diego, USA
Elizabeth Hinde University of NSW	2014 International Biophysics Congress	Brisbane, Australia
James Whisstock Monash University	Catalyst Seminar Series, Monash University	Melbourne, Australia
Katharina Gaus University of NSW	2014 International Biophysics Congress	Brisbane, Australia
Richard Berry Monash University	2014 International Biophysics Congress	Brisbane, Australia
Stephen Scally Monash University	23rd Congress and General Assembly of the International Union of Crystallography	Montreal, Canada
Jerome Le Nours Monash University	23rd Congress and General Assembly of the International Union of Crystallography	Montreal, Canada
Harry Quiney University of Melbourne	Public Lecture	Melbourne, Australia
Michelle Dunstone Monash University	2014 International Biophysics Congress	Brisbane, Australia
Brian Abbey La Trobe University	Joint Institute for Laboratory Astrophysics (JILA)	Colorado, USA
Stephen Scally Monash University	The Scripps Research Institute	San Diego, USA
Dale Godfrey University of Melbourne	Flinders Medical Centre	Adelaide, Australia
Katharina Gaus University of NSW	Invited seminar, Weatherall Institute of Molecular Medicine, University of Oxford	Oxford, UK
Dale Godfrey University of Melbourne	Perth Immunology Group Annual Meeting	Perth, Australia
Katharina Gaus University of NSW	4th Single Molecule Localisation Microscopy Symposium, King's College	London, UK
James Whisstock Monash University	Deutsches Elektronen Synchrotron Symposium	Hambug, Germany
Dale Godfrey University of Melbourne	24th Annual Combined Biological Sciences Meeting	Perth, Australia
Michelle Dunstone Monash University	Pore-Forming Toxins: a meeting in memory of Gianfranco Menestrina	Trento, Italy
James Whisstock Monash University	Seminar, University of Warwick	Coventry, UK

Name Centre Node	Conference/Meeting	Location
Richard Birkinshaw Monash University	Seminar, Southampton University	Southampton, UK
Nicholas Phillips La Trobe University	International Workshop on Phase Retrieval and Coherent Scattering	Chicago, USA
Brian Abbey La Trobe University	APS Upgrade Workshop on Coherent Imaging	Chicago, USA
James Whisstock Monash University	XIVth International Symposium on Proteinases, Inhibitors and Biological Control	Bernardin, Slovenia
Keith Nugent La Trobe University	20th Users' Meeting & Workshops - National Synchrotron Radiation Research Center	Hsinchu City, Taiwan
Dale Godfrey University of Melbourne	James Cook University	Townsville, Australia
Richard Berry Monash University	Natural Killer Cell Symposium 2014	Hannover, Germany
Scott Mueller University of Melbourne	13th International Symposium on Dendritic Cells	Tours, France
Michelle Dunstone Monash University	8th Asia Oceania Forum for Synchrotron Radiation Research	Hsinchu, Taiwan.
Stephen Scally Monash University	ComBio 2014	Canberra, Australia
Scott Mueller University of Melbourne	ComBio 2014	Canberra, Australia
Stephanie Gras Monash University	GT Bio Conference	Grenoble, France
Stephanie Gras Monash University	Pasteur Institute	Paris, France
James Whisstock Monash University	Garvin Signalling Meeting	Sydney, Australia
Stephanie Gras Monash University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
James Whisstock Monash University	World Health Summit	Berlin, Germany
Michelle Dunstone Monash University	2nd Microbiology @ Monash Plenary Meeting	Melbourne, Australia
William Heath University of Melbourne	1 Day Symposium Immunology 2014: Where to from here? Doherty Institute, University of Melbourne	Melbourne, Australia
Bo Chen La Trobe University	International conference on X-ray Microscopy 2014	Melbourne, Australia
Hannah Couglan La Trobe University	International conference on X-ray Microscopy 2014	Melbourne, Australia
Michael Jones La Trobe University	International conference on X-ray Microscopy 2014	Melbourne, Australia

Presentations

Name Centre Node	Conference/Meeting	Location
Benedicta Arhatari La Trobe University	International conference on X-ray Microscopy 2014	Melbourne, Australia
Benedicta Arhatari La Trobe University	International conference on X-ray Microscopy 2014	Melbourne, Australia
Keith Nugent La Trobe University	X-Ray Science Workshop, La Trobe University	Melbourne, Australia
Michael Jones La Trobe University	X-Ray Science Workshop, La Trobe University	Melbourne, Australia
Brian Abbey La Trobe University	X-Ray Science Workshop, La Trobe University	Melbourne, Australia
Nicholas Philips La Trobe University	X-Ray Science Workshop, La Trobe University	Melbourne, Australia
Brian Abbey La Trobe University	Physics Department, National University of Singapore	Singapore
Brian Abbey La Trobe University	NUS Centre for bioimaging sciences	Singapore
David Fairlie University of Queensland	3rd Annual Conference of the International Chemical Biology Society	San Francisco, USA
Brian Abbey La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Ruby Law Monash University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Julian Vivian Monash University	Synchrotron user meeting 2014	Melbourne, Australia
Jamie Rossjohn Monash University	Cardiff Institute of Infection and Immunity Annual Meeting	Cardiff, UK
Connie Darmanin La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Hannah Couglan La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Michael Jones La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Nicholas Anthony La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Nicholas Philips La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Benedicta Arhatari La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Arhatari La Trobe University	University of South Australia	Adelaide, Australia

Name Centre Node	Conference/Meeting	Location
Henry Kirkwood La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
Bo Chen La Trobe University	Australian Synchrotron User's Meeting 2014	Melbourne, Australia
David Fairlie University of Queensland	Victorian Peptides User Group	Melbourne, Australia
Henry Kirkwood La Trobe University	AINSE-ANBUG Neutron Scattering Symposium	Sydney, Australia
Dale Godfrey University of Melbourne	44th meeting of the Australasian Society for Immunology	Wollongong, Australia
Katharina Gaus University of NSW	44th meeting of the Australasian Society for Immunology	Wollongong, Australia
Dale Godfrey University of Melbourne	44th meeting of the Australasian Society for Immunology	Wollongong, Australia
James Whisstock Monash University	The Third Australia-China Joint Symposium on Energy and Biomedical Materials	Melbourne, Australia
Jeremie Rossy University of NSW	2014 ASCB/IFCB Meeting, Optical Microscopy and Superresolution Imaging	Philadelphia, USA
James Whisstock Monash University	Monash/Melbourne Structural Immunology Meeting	Melbourne, Australia

Key Performance Indicators

Research Findings

Performance Measure	Target 2014	Actual 2014
Number of publications	30	61
Number of citations	50	130
Number of invited talks	10	110
Number of media releases	2	4
Number of media articles	2	90

Research Training and Professional Education

Performance Measure	Target 2014	Actual 2014
Number of professional training courses	1	3
Number of Centre attendees	12	41
Number of new postgraduate students	4	20
Number of new postdoctoral researchers recruited	4	33
Number of new Honours students	5	2
Number of early career researchers	2	11
Number of students mentored	8	21
Number of mentoring programs	2	5

International, National and Regional Links and Networks

Performance Measure	Target 2014	Actual 2014
Number of international visitors and visiting fellows	5	12
Number of national and international workshops held/organised by the Centre	1	3
Number of visits to overseas laboratories and facilities	5	17
Examples of relevant interdisciplinary research supported by the Centre	2	2

End-user Links

Performance Measure	Target 2014	Actual 2014
Number of government, industry and business community briefings	2	3
Number and nature of public awareness/outreach programs	1	2
Number of website hits	2500	5,297
Number of talks given by Centre staff open to public	1	4

Organisational Support

Performance Measure	Target 2014	Actual 2014
Annual cash contributions from Administering & Collaborating Organisations	$1,333,333	$1,266,665
Annual in-kind contributions from Collaborating Organisations	$2,684,041	$2,993,360
Annual cash contributions from Partner Organisations	$195,000	$195,000
Annual in-kind contributions from Partner Organisations	$1,524,572	$253,612
ARC grants secured by Centre staff	$250,000	$3,762,394
Other Australian competitive grants secured by Centre staff	$250,000	$4,627,913
Number of new organisations collaborating with, or involved in, the Centre	1	4

National Benefit

Performance Measure	Target 2014	Actual 2014
Number of projects and publications in relevant National Research Priorities	NRP Areas relevant to the Centre: • Frontier Technologies for Building and Transforming Australian Industries • Promoting and Maintaining Good Health	NRP Areas relevant to the Centre: • Frontier Technologies for Building and Transforming Australian Industries (30) • Promoting and Maintaining Good Health (33)

Financial Statement

Statement of Operating Income and Expenditure for the calendar year ended 31 December 2014

Income	2014 $
ARC Centre Grant	4,000,000
Administering Organisation Cash Support	399,000
Collaborating Organisations Cash Support	866,666
Partner Organisations Cash Support	195,000
Total	**5,460,666**

Expenditure	2014 $
Salaries	1,093,686
Scholarships	8,645
Equipment & Access	162,288
Maintenance and Consumables	202,283
Outreach	119,727
Meetings and Travel	104,238
Centre Administration	26,801
Total	**1,717,668**
Surplus	**3,742,998**

Imaging CoE Grants Success

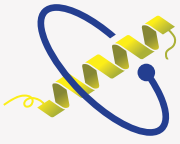
Imaging CoE researchers were very successful in securing competitive funding from both the National Health & Medical Research Council (NHMRC) and the Australian Research Council (ARC) in 2014. Overall, Centre researchers secured over $4.5 million in funding from the NHMRC and nearly $4 million from the ARC).

NHMRC grants

- David Fairlie (University of Queensland) for investigations into downsizing a human protein to modulate inflammatory diseases and targeting protease activated receptor 2 in immunometabolism and obesity.
- Dale Godfrey (the University of Melbourne), for work with Adam Uldrich on MAIT cell development.
- Scott Mueller (the University of Melbourne) for research with Erica Sloan into the neural regulation of T cell functions.
- Daniel Pellicci (the University of Melbourne) for work on the recognition of lipid antigens by CD1d-restricted Type-2 natural killer T cells.
- Ranjeny Thomas (the University of Queensland) for work with Hugh Reid and Hani El-Gabalawy to understand the development of rheumatoid arthritis in response to the presentation to T cells of peptide antigens where the amino acid arginine has been converted to citrulline.
- James Whisstock (Monash University) for research with Terry Kwok-Schuelein on the structural basis for adhesion of the bacterium Helicobacter pylori to host epithelial cells.

ARC grants

- David Fairlie's lab (University of Queensland), which is researching how to engineer peptide surfaces to allow them to be effective in oral treatment.
- Jamie Rossjohn's team (Monash University), which is investigating the impact of post-translational modifications in host proteins. Jamie's lab also received funding to establish a cytometry-by-time-of-flight (CyTOF) facility to determine the properties of cells.
- Kat Gaus (UNSW), with a host of other Centre researchers, to establish a single-molecule imaging laboratory to close the gap between structural imaging and cellular imaging.
- Georg Ramm, James Whisstock, Kat Gaus and others to establish a new cryo-FIB-SEM (focused ion beam scanning electron microscope) facility at Monash University, which will complement the Titan Krios cryo-transmission electron microscope.
- Kat Gaus to work on generating algorithms to analyse images from super-resolution microscopes in collaboration with Swiss microscopy software company Biplane AG.
- Jamie Rossjohn and Dale Godfrey to work with South Australian vaccine company Vaxine Pty Ltd to develop and test new synthetic compounds that will enhance our ability to understand the molecular recognition and activation mechanisms of the innate immune system's Natural Killer T (NKT) cells.



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