The Institute

BASIL HETZEL INSTITUTE
RESEARCH REPORT 2021

Translational health research
at The Queen Elizabeth Hospital

The Hospital Research
Foundation Group

ON THE COVER

To help celebrate the 30th TQEH Research Expo and 60 years of research at TQEH, logos were created by THRF Group Graphic Design Volunteer Piper White, under the supervision of THRF Group Creative Lead, Siri Bakke. Inspiration was taken from the original TQEH Coat of Arms, granted in 1964, with particular reference to the shield and the Tudor Rose.

Photography: Photographs taken at the gala dinner and of many of the research groups by Andrew Beveridge from ASB Creative Professional Photography.
▶ **asbprophoto.com**

Graphic Design: Icarus Design.
▶ **icarus.com.au**

BASIL HETZEL INSTITUTE FOR TRANSLATIONAL HEALTH RESEARCH

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▶ **basilhetzelinstitute.com.au**

The Basil Hetzel Institute, TQEH, forms part of the Central Adelaide Local Health Network (CALHN), one of ten local health networks within SA Health.

The Institute
basil hetzel institute for translational health research

SUPPORT

PRODUCTIVITY

THEMES

AGEING

CANCER

CARDIOVASCULAR DISEASE

CHRONIC DISEASE

CLINICAL SCIENCES, HEALTH SERVICES AND POPULATION HEALTH

DRUG AND VACCINE DEVELOPMENT

INFLAMMATORY DISEASE

CELEBRATING 60 YEARS OF TQEH RESEARCH

60 YEARS TQEH RESEARCH

30 YEARS TQEH RESEARCH EXPO

DIRECTOR'S REPORT 2021

THE YEAR MARKED TWO IMPORTANT MILESTONES FOR THE BHI, TQEH; 30 YEARS OF TQEH RESEARCH EXPO, AN EVENT HELD ANNUALLY IN OCTOBER, AND 60 YEARS OF RESEARCH AT THE QUEEN ELIZABETH HOSPITAL SITE.

Many had hoped that 2021 would see a return to a more normal existence after the pandemic-related disruptions of 2020. This was not the case. Although South Australia was largely spared the direct impact of COVID due to the isolationist approach of the State Government, the inability to attend face-to-face meetings, attract overseas students and network effectively with national and international research communities impacted the ability of the Basil Hetzel Institute for Translational Health Research to perform at prior levels.

This was, in some measure, reflected in the Annual Assessment of Research Productivity undertaken at the end of the 2020-2021 financial year [▸ **www.basilhetzelinstitute.com.au/latest-news/research-reports**]. Although the results showed our funding had slipped, our research publications were maintained and the number of grants on which BHI, TQEH researchers were investigators increased. Of some concern was the reduction in higher degree completions. Understanding the impact of the COVID crisis on performance is challenging, and it is highly likely some of the aberrations we are seeing, positive and negative, can be ascribed to the current pandemic and its impact on our local health networks.

2021 has not been without many significant successes, as you will see in the pages of this report and in the award of Investigator, Ideas, and MRFF grants to our research teams.

The year marked two important milestones for the BHI, TQEH; 30 years of TQEH Research Expo, an event held annually in October, and 60 years of research at The Queen Elizabeth Hospital site. These milestones were celebrated with a Gala dinner held at the National Wine Centre. We were joined by our guest-of-honour, the recently installed Governor of South Australia, the Honourable Frances Adamson AC, as well as many BHI, TQEH alumni and staff, and a large cohort of young, dynamic scientists and students currently engaged with the activities of the institute. They mixed with leaders of the South Australian scientific and political communities who were, without exception, impressed by the history, performance and dynamic approach displayed within the BHI, TQEH over the last 60 years and today.

The dinner provided an opportunity for our community to recognise the outstanding contributions to the BHI, TQEH made by Professor Dick Ruffin, Dr Prue Cowled, and Mr Paul Flynn and The Hospital Research Foundation Group. The tradition of providing recognition for outstanding service is one that has been perhaps ignored by the BHI, TQEH over the years and hopefully this new category of award will see this recognition become a regular feature of TQEH Research Expo. *[Editor's note: A fourth award that recognised Excellence in Research Leadership at the BHI, TQEH was presented to Professor Guy Maddern, Director of Research BHI, TQEH].*

▸ **More details on the dinner and the awards**

A video created in collaboration with THRF Group to celebrate 60 years of TQEH research can be viewed on the BHI website and provides context to the role that the BHI has played over the last 60 years.

▸ **www.basilhetzelinstitute.com.au/research/information-for-researchers/bhi-activities/tqeh-research-dinner**

The end of 2021 saw the departure of Kathryn Hudson, the BHI Facility Manager. Kathryn joined the BHI, TQEH 14 years ago, at the time of the transition from the old converted nurses' home, which housed much of our laboratory research, into the new purpose-built TQEH research facility opposite The Queen Elizabeth Hospital. Her leadership, guidance and enthusiasm has been a hallmark of her 14 years of service. Kathryn has accepted the role of Institute Manager of SAiGENCI [South Australian Immunogenetics Cancer Institute]. Kathryn has left the BHI in an excellent condition, having provided strong but rational leadership to the activities conducted within the research building. We wish her well and look forward to obtaining a similarly excellent appointee going forward.

The challenges of 2020 and 2021 have been considerable for the research community. The BHI, TQEH has reacted with agility and flexibility to seize opportunities, stay positive and motivated, and respond to changing circumstances.

There can be little doubt that without the ongoing support of The Hospital Research Foundation Group the BHI, TQEH would not be in the strong and stable position it is as it heads into the uncertainty of 2022. The funding obtained by THRF Group comes largely from the South Australian community, and we recognise it is the obligation of the BHI, TQEH to use this funding wisely to support the health and well-being of South Australians through innovative health and medical research.

GUY MADDERN
Director of Research

Basil Hetzel Institute for Translational Health Research
THE QUEEN ELIZABETH HOSPITAL
January 2022

SUPPORT STRUCTURES 2021

The translational health research program of the Basil Hetzel Institute, TQEH, is underpinned by a well-established Committee structure. The BHI Policy Committee, chaired by the Director of Research, BHI, TQEH, has a membership drawn from the research leadership of the BHI, the BHI research community and key stakeholders.

The committee provides strategic counsel for the operation of the BHI, support for the Director of Research and advice on available support for the BHI's research programs. The BHI Policy Committee is assisted by a number of sub-committees, with membership drawn from the BHI and stakeholders, and with defined areas of expertise: the BHI Research Advisory Committee, the BHI Management Committee, BHI Scholarship Selection Committee and the organising committee for the annual TQEH Research Expo.

BHI POLICY COMMITTEE REPORT

2021 has provided no shortage of challenges for the Policy Committee. Meetings have been largely conducted by Zoom with an engaged but detached membership. The Committee has been challenged with the difficulty in obtaining overseas students to the BHI, difficulties in obtaining sufficient funding to maintain the research groups that currently exist within the organisation and a need to demonstrate its importance to the Central Adelaide Local Health Network, as well as the broader research community.

The Committee has, however, dealt with these challenges, been able to fund all the students felt worthy of support, and with the sustained efforts of the Scientific Director, A/Professor Joy Rathjen, we have been able to see through the year with a firm footing going into 2022.

Professor Guy Maddern
Chair

BHI RESEARCH ADVISORY COMMITTEE REPORT

The BHI Research Advisory Committee functions to ensure that research undertaken at the BHI is of high scientific merit and aligns with the purpose of the BHI, a purpose that can be found in the name of the institute – Translational Health Research – and that aims to produce high quality health and medical research outcomes that will benefit the health and wellbeing of people in South Australia, Australia and internationally.

A key theme of the discussions in the committee in 2021 was that of attracting research students to the BHI, TQEH. The positive outcomes of developing a strong undergraduate research program were clear to all – students gain a rich understanding the research undertaken at the BHI and can undertake projects within the institute that are clinically-focused. Successful students are likely to return for further research training opportunities and to act as BHI ambassadors in the student community. The committee recognised that there was good student engagement and recruitment in some teams at the BHI, TQEH but this was patchy.

Strategies to be implemented to encourage more groups to engage with undergraduate students included developing a shared induction framework to facilitate undergraduate student onboarding, a plan to ensure all researchers are being notified of research training opportunities, and forging stronger links with course coordinators to enhance student placement with groups at the institute. A small sub-committee will be formed in 2022 to progress this agenda.

The call for a Michell McGrath Fellow to join the BHI was discussed at RAC, specifically to provide advice from the research community on a position description for the role. What emerged from these discussions was that the ideal candidate would need to integrate well into the BHI, be able to capitalise on current research and clinical opportunities at the institute and be an enabling force to build the research ecosystem.

Associate Professor Sarah Vreugde
Chair

BHI MANAGEMENT COMMITTEE REPORT

In 2021 the BHI Management Committee continued to support staff and students to operate in a COVID-19 friendly environment. The Seminar Series included internal staff and student presentations, external speakers, and researcher development 'hot' topics. The popular "Off the Clock" student activity merged with the Games sessions, and provided a popular, well attended social container for the students.

The Committee allocated a total of $200,000, generously provided by THRF Group, to fund equipment at the BHI. This included significant acquisitions of a spectral flow cytometer and high-performance microplate reader. These big-ticket items were part funded by The University of Adelaide Faculty of Health and Medical Sciences.

After cancellation in July, the Longest Table lunch went ahead on 14th September and raised over $1,800 for cancer research. Lastly, 2021 was a year of 'flexing' for long-standing BHI Facility Manager and Committee Member, Kathryn Hudson, dividing her time between the BHI and SAiGENCI.

The Committee warmly welcomed Imogen Bell as the interim Facility Manager supporting the BHI's activities, staff and students during this transition. Speaking for many BHI researchers, I express much gratitude and appreciation for Kathryn's work at the BHI over many years. I look forward to continuing to work with Imogen and the Committee in supporting all researchers at the BHI.

Associate Professor Rosanna Tavella
Chair

BHI SCHOLARSHIP SELECTION COMMITTEE REPORT

In 2021 two calls for applications to THRF Group BHI TQEH Research Scholarships were made to coincide with the mid-year and October calls by the Universities. The Scholarship Selection Committee considered in all 32 applications for funding in 2021, and recommended for funding 2 PhD students, 1 Masters student, 1 Honours student and 8 Vacation students. Our thanks go to those who support this important program at the BHI, TQEH. The awards were generously supported by a $125,000 allocation from THRF Group, and co-funded with support from The University of Adelaide, the University of South Australia and TQEH researchers.

Professor Guy Maddern
Chair

TQEH RESEARCH EXPO ORGANISING COMMITTEE REPORT

This year was an important year for this committee. It was the 30th year a TQEH Research conference had been held to encourage research trainees working at the hospital to present the results of their research. Originally known as TQEH Research Day, the growth of the research training programs at TQEH led to the conference being held over two days, the third Thursday and Friday of October, and a change of name to TQEH Research Expo.

It was a great relief that we were again able to hold the expo as a COVID safe, face-to-face event in the Seminar rooms of the BHI Research Facility. It was a fabulous event, and a full report can be found on page 24.

▸ 30th TQEH Research Expo 2021

Associate Professor Joy Rathjen
Chair

RESEARCH SUPPORT SERVICES

Operations at the BHI are supported and enriched by the following services. The on-site, face-to-face service of previous years was again interrupted by COVID-19, but support continued throughout the year supplemented with Zoom and email.

Statistical support

Dr Suzanne Edwards of the Data, Design and Statistics Service, Adelaide Health Technology Assessment (AHTA), School of Public Health at The University of Adelaide provides support and training to staff and students in statistical methods. This support, of one day a week, is co-funded by the BHI and the Faculty of Health and Medical Sciences at The University of Adelaide.

Library support

Anna Holasek and Rachel Davey from the SA Health Library Service help staff and students at the BHI, TQEH with literature and database searches and accessing relevant material from libraries and publishers. They also provide training in the use of online resources and bibliographic tools. The librarians provide the research support team at the BHI with publication lists that document the outputs of TQEH-based researchers which are used in all our reporting processes.

TQEH Institutional Biosafety Committee

TQEH Institutional Biosafety Committee, chaired by Dr Eric Smith, ensured that the PC2 laboratory spaces of the BHI Research Facility comply with the Office of the Gene Technology Regulator PC2 licence requirements.

Operational Support

Many people give of their time to support the researchers and the BHI Facility Manager with procedural compliance, research services and grant applications. Their service to our community is greatly appreciated.

- Mr Serge Stebellini, Faculty Health, Safety and Wellbeing (HSW) Coordinator, Faculty of Health and Medical Sciences, The University of Adelaide.
- Dr Tony Cambareri, Research Development Manager, Faculty of Health and Medical Sciences, The University of Adelaide and his team.
- Dr Cadence Haynes, MRFF Opportunities Manager, Office of the Deputy Vice-Chancellor (Research), The University of Adelaide.
- Professor Amanda Page, Director of Research Education, Faculty of Health and Medical Sciences, The University of Adelaide.
- Mr Martin Hutchens, Team Leader Research Operational Support, Faculty of Health and Medical Sciences, The University of Adelaide.
- Ms Helen Lineage and the TQEH Biomedical Engineering team.
- Mr Matthew Smith, Mrs Bronwyn Hutchens and Mrs Michelle Slawinski from TQEH Experimental Surgical Suite.

CALHN HREC and Research Office Support

The BHI has a dedicated office for use by CALHN Research Services. Research Services staff members provide essential ethics and governance support to all researchers working at TQEH. The office is continually seeking ways to streamline and simplify the provision of this support to BHI, and all sites of CALHN. Research Services staff members also provide help with grant submissions and post-approval and reporting requirements. Many thanks to Bernadette Swart (CALHN Research Office Manager) and Ian Tindall (CALHN HREC Chair), and their teams, for their ongoing support of BHI staff and students.

Current and future leaders at the BHI, TQEH attended workshops by Hugh Kearns from ThinkWell thanks to funding from THRF Group.

THRF GROUP CEO REPORT

The Hospital Research Foundation Group

IN 2021, WE WERE PLEASED TO SUPPORT 52 NEW AND ONGOING GRANTS AND FELLOWSHIPS AT THE BHI, TQEH.

The generosity and support we receive every day from the community enables The Hospital Research Foundation Group to advance world-leading research and improve the health and wellbeing of every South Australian. If the past two years have taught us anything, it is how much the community needs to value peer-reviewed medical research, such as that done by the BHI, TQEH, to guide our public health response and keep Australians safe.

In the fight against COVID-19, we were proud to continue our support for the BHI's Viral Immunology Group, led by Dr Branka Grubor-Bauk. Together with global collaborators, the Group was one of the first in the world to discover that the body's immune system remembers the COVID-19 virus long after infection. They also gathered critical insights into the long-term impacts of the virus and continued the development towards a DNA-based vaccine.

While this work related to the pandemic is imperative, we know that other diseases and illnesses do not take a back-seat. In 2021, we were pleased to support 52 new and ongoing grants and fellowships at the BHI, TQEH. We continued our investment into critical research in the areas of cancer, cardiovascular disease, aged care, rheumatology, ENT, infectious diseases, diabetes, inflammatory bowel disease, and other health issues that impact our community. For example, we saw Associate Professor Wendy Ingman, who leads the Breast Biology & Cancer Unit, using her THRF-funded research to influence policy changes in breast cancer screening, raise community awareness about breast density, and discover risk factors which stem from girls' development during puberty and women's menstrual cycles.

We were proud to nurture the next generation of researchers through many PhD, postgraduate, honours and vacation scholarships. This support plays an important role in progressing projects and bringing outcomes to patients sooner, such as the project by PhD student Alex Minopoulos, supervised by Professor John Beltrame AM within the Translational Vascular Function Research Collaborative, which will help to deliver a less invasive diagnosis method for coronary artery spasm. We've also observed with interest the important work of Professor Tim Price (Solid Tumour Group), Professor Renuka Visvanathan (Adelaide GTRAC Centre) and Professor PJ Wormald, Associate Professor Sarah Vreugde and Professor Alkis Psaltis (ENT Surgery group).

We were also proud to help commemorate 60 years of life-changing research at TQEH at a special event which paid tribute to the many researchers who've made such significant contributions to health science and therapeutic care. It was humbling to accept an award on behalf of The Hospital Research Foundation Group that recognised our exceptional support of research over the years.

Another hugely significant milestone in 2021 was the 30th anniversary of TQEH Research Expo. It is always a highly anticipated event on the industry calendar and showcases some of the outstanding research achievements of the BHI, TQEH. The plenary presentation by Dr Michael Cusack, the state's Chief Medical Officer, was extremely well-received, highlighting the safety, quality and use of data to drive improvements within clinical settings and empower patients.

Congratulations to all the research groups on your outstanding efforts during such a difficult period in global history! We are proud to help facilitate much of your work through funding equipment, fellowships, and other grants. As mentioned from the outset, it would simply not be possible without the generous support of our donors, fundraisers, lottery ticket buyers, community, and corporate partners. It is only together with community support that we can help you progress lifesaving research and improved patient care for every South Australian.

PAUL FLYNN
CEO

THE HOSPITAL RESEARCH FOUNDATION GROUP

The role and value of Aboriginal Health Workers and Practitioners in providing Type 2 diabetes mellitus (T2DM) care in the primary health care setting; a qualitative study

Lauren Vu, Vacation Student
Endocrinology Unit

A substudy of an MRFF funded project, this project aims to contribute to defining the scope of practice of Aboriginal Health Workers and Practitioners in delivering diabetes care within a multidisciplinary team in a primary health care setting. This work will improve the delivery of diabetes care and optimise outcomes for Aboriginal patients with Type 2 diabetes mellitus (T2DM).

Liposomal-based delivery of phosphoantigens as sensitisers for adoptive gd T cell anticancer immunotherapy

Professor Andreas Evdokiou, Research Leader
Breast Cancer Research Unit

The aim of this research is to train a patient's own immune system to recognise, attack and eliminate breast cancer. We developed a world first approach of delivering chemical sensitisers packaged in lipid carriers for transportation directly into cancer cells. Circulating cancer fighting T cells recognise these chemical sensors, bind to and eliminate cancer cells while leaving normal cells unharmed.

Investigator led study exploring the role of microbiome in Parkinson's Disease

Dr Sam Costello, Research Leader
Inflammatory Bowel Disease Research Group

The aim of this trial is to meet an unmet medical need, exploring whether our microbial therapy is safe and tolerable in people with Parkinson's disease. The study will also provide some preliminary information on whether FMT might improve motor and non-motor symptoms of Parkinson's, including constipation. Results of this pilot study will inform the design of future larger studies.

The role of endothelial dysfunction and the expression of rho-kinase in coronary artery spasm

Alex Minopoulos, PhD Student
Translational Vascular Function Research Collaborative

Coronary artery spasm (CAS) is a specific type of cardiovascular disease where the arteries supplying the heart with blood become temporarily narrowed, resulting in chest pain and over time causing parts of the heart muscle to die. People with CAS have poor health outcomes and impaired quality of life, but currently it can be difficult to diagnose because a diagnosis relies on invasive provocative spasm testing. The primary aim of this project is to see whether a marker of CAS, called 'rho-kinase', is measurable in venous blood. If successful, this may lead to improvements in the diagnosis and management of CAS, improving patient outcomes.

The development of a novel multi-antigenic DNA-based vaccine against SARS-CoV-2

Zahraa Al-Delfi, PhD Student
Viral Immunology Group

Most SARS-CoV-2 vaccines in use or in development include the spike (S) protein as an immunogen and aim to elicit neutralizing antibody (NAb) against the virus. The emergence of SARS-CoV-2 variants may reduce the efficacy of S-based vaccines. The aim of this study is to develop a DNA vaccine to elicit NAb to the receptor binding domain (RBD) in the S protein AND cell-mediated immunity against other SARS-CoV-2 proteins, namely the N protein and a truncated version of non-structural protein 3 (tNSP3). As the latter proteins are more highly conserved than the S protein, this vaccine will confer protection against infection with emerging variants of SARS-CoV-2 and will also likely elicit long term immunity.

Novel Nanodrug Delivery Systems to treat Biofilm associated infections in the Vaginal Mucosa

Lana Matteucci, Honours Student
Therapeutics Research Centre

An imbalance of bacteria within the vagina causes an infection known as bacterial vaginosis (BV), which affects 15-50% of all women of reproductive age. If left untreated BV can increase the risk of contracting and transmitting sexually transmitted diseases such as HIV, cause pelvic inflammatory disease, and increase risk of late-stage miscarriage, preterm births, and low weight babies. Despite BV being so clinically important for women's health and their pregnancies it is currently unknown why BV returns so frequently after treatment and critically we do not have any novel therapeutic strategies for dealing with recurrent BV. We will develop a new biofilm penetrating antibiotic delivery system with an additional wound healing compound incorporated to treat BV.

COVID-19 SA

Dr Branka Grubor-Bauk (with Professor Simon Barry, The University of Adelaide & WCH)
Viral Immunology Group

As vaccination rolls out in South Australia and the state prepares to open borders a number of people in high-risk groups will remain vulnerable, as they will in other Australian jurisdictions. We urgently need to identify risk factors for these groups (long COVID patients, transplant recipients, immune compromised people and people living remotely), and strategies for better protection. Using tools and analytics applied to the healthy population, we will test the response of these groups to current vaccination regimes (vaccination efficacy) and test alternate vaccination strategies to improve efficacy.

BHI RESEARCH EQUIPMENT

The Hospital Research Foundation Group

THRF Group is proud to fund state-of-the-art medical research equipment each year to support BHI researchers in their work. In 2021, THRF Group provided over $180,000 for equipment to keep BHI technology at the cutting edge, and to enable researchers to continue their vital work with updated equipment.

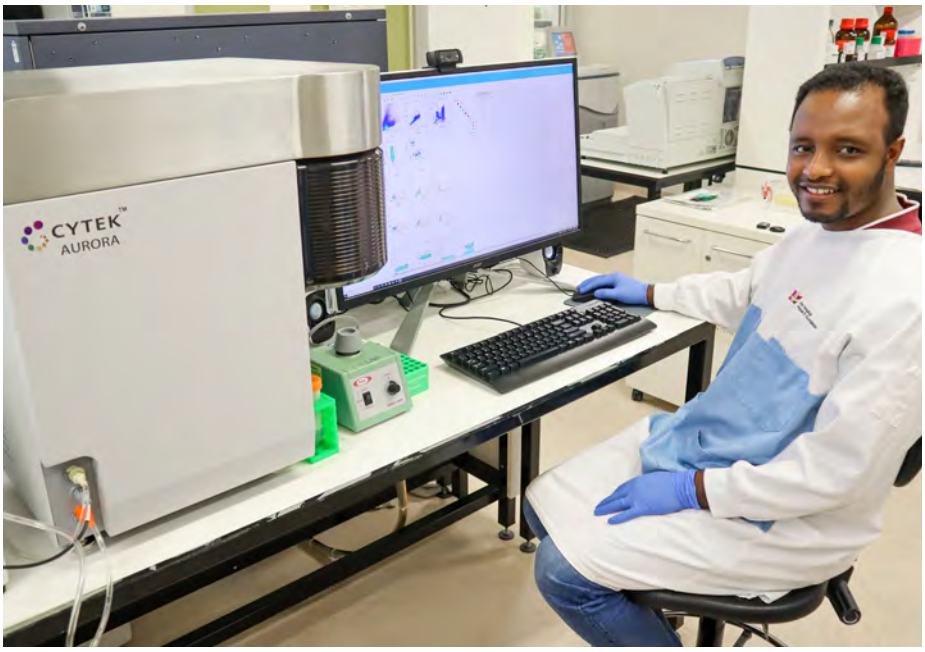
Cytek® Aurora 3L Flow Cytometer

In 2006, THRF Group supported the purchase of a FACSCanto™ II Flow Cytometer. This instrument has served its purpose for 15 years; however, it only detects eight colours and current flow cytometry techniques require increased colour detection. In 2021, THRF Group, in conjunction with The University of Adelaide, funded the Cytek® Aurora 3 Laser system (the Aurora), a flow cytometer capable of detecting 24 colours and with the capacity to increase to 40 colours.

The Aurora will impact the research of multiple groups at the BHI, TQEH. It will be used by:

- the Surgical Science Research Group, who will use this technology for the development of immune-based cellular therapy for metastatic colorectal cancer by characterising cells used in cellular therapy and identifying critical factors responsible for tumour clearance.
- The Solid Tumour Group, who will use this technology to determine how delivery of anti-cancer drugs can affect the tumour microenvironment. These insights will lead to a better understanding of how novel and current anti-cancer therapies can synergise with immunotherapy.
- The Viral Immunology Group, who will use this technology in their vaccine development programs and for characterising the body's immune response to COVID-19.
- The ENT Surgery group, who will use this technology to characterise the different cellular components found in chronic rhinosinusitis. This will give insights into potential new targets for treatments for this disease.

We expect this piece of equipment to find multiple other uses by groups at the BHI, TQEH in the years to come.



BMG CLARIOstar® *Plus* Plate reader

The BMG CLARIOstar® *Plus* is a multi-mode plate reader that detects sample fluorescence, absorbance and luminescence, and that has multiple uses in cell biology research. The CLARIOstar® will allow:

- Professor PJ Wormald and his ENT Surgery group to assess the effects of various antimicrobial products on cultured bacterial biofilms, supporting research into Chronic Rhinosinusitis.
- Dr Branka Grubor-Bauk and her Viral Immunology Group to determine immunogenicity of vaccines, including vaccines for COVID-19, in pre-clinical models, as well as characterising the immune response of patients with COVID-19 serology. The information gained will advance vaccine design, treatment options, and develop diagnostic reagents.

Essential Equipment

THRF Group have funded several other essential pieces of equipment that will support all laboratory research groups at the BHI, TQEH. These include the SARTORIUS-arium© water purification system, which will provide ultrapure water for research use, a thermocycler used to perform PCR experiments in routine molecular biology, a refrigerated centrifuge and rotors to increase sample preparation and processing capacity, and an antigen retriever for use in histology and immunology techniques.

Dr Zelalem Mekonnen, Viral Immunology Group, using the new Cytek® Aurora Flow Cytometer.

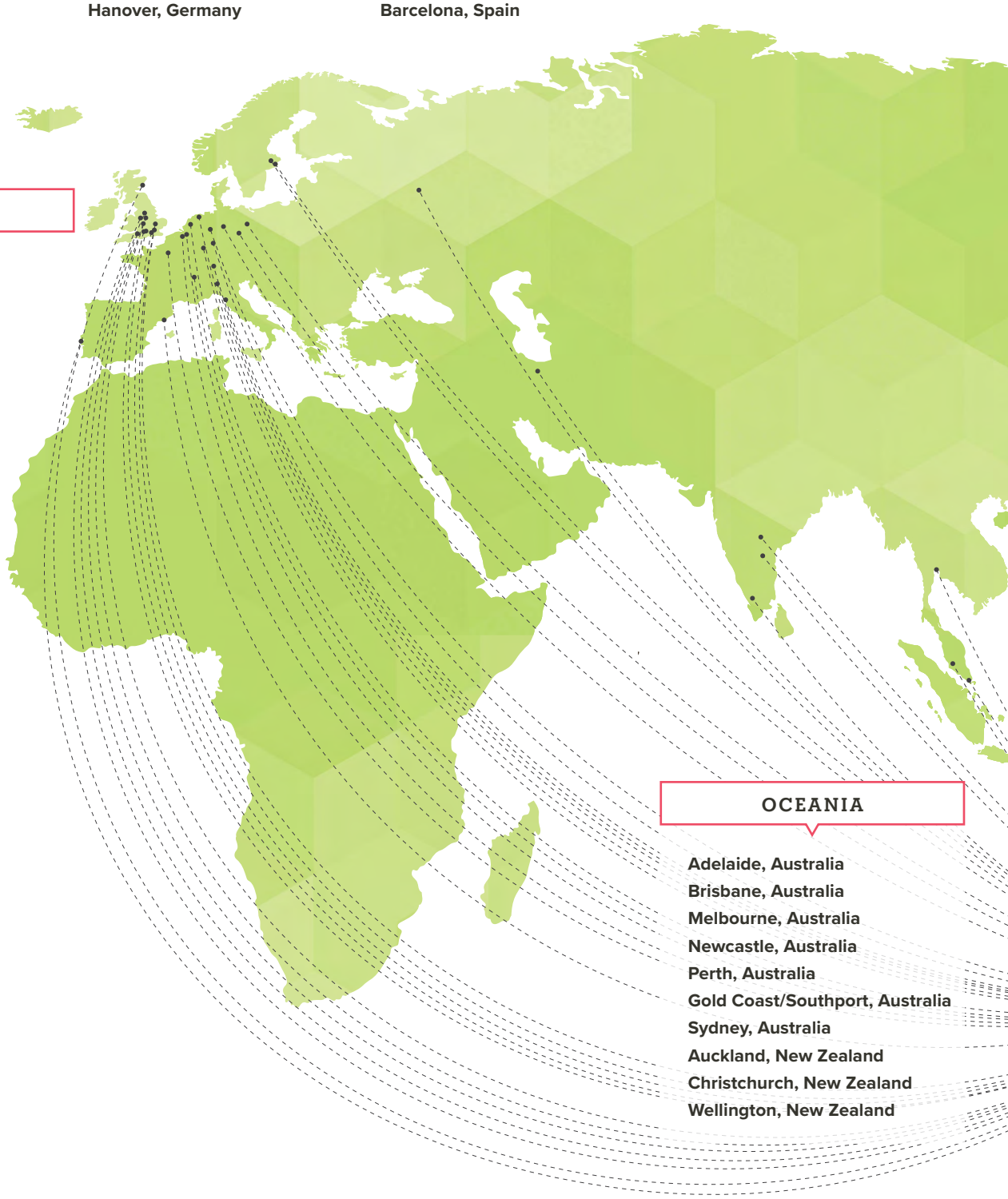
BHI NATIONAL AND INTERNATIONAL COLLABORATORS 2021

EUROPE

Antwerp, Belgium
Ghent, Belgium
Paris, France
Berlin, Germany
Frankfurt, Germany
Halle-Wittenberg, Germany
Hanover, Germany
Münster, Germany
Saarbrücken, Germany
Milan, Italy
Pisa, Italy
Lisbon, Portugal
Moscow, Russia
Barcelona, Spain
Stockholm, Sweden
Uppsala, Sweden
Geneva, Switzerland
Zürich, Switzerland
Amsterdam, The Netherlands
Groningen, The Netherlands

UK

Aberdeen, UK
Abingdon, UK
Bristol, UK
Cambridge, UK
Guildford, UK
Leeds, UK
Leicester, UK
London, UK
Manchester, UK
Oxford, UK
Sheffield, UK



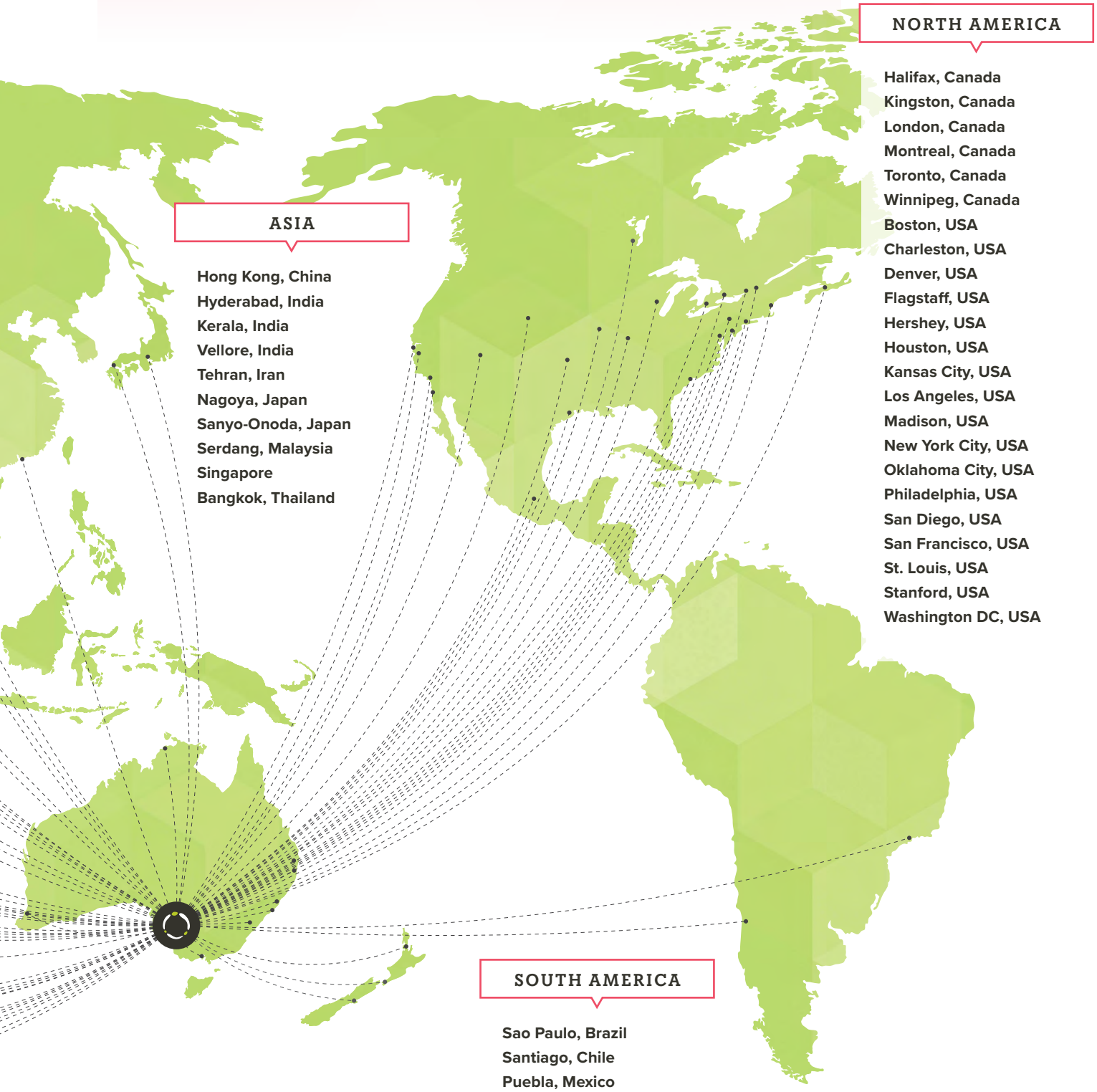
OCEANIA

Adelaide, Australia
Brisbane, Australia
Melbourne, Australia
Newcastle, Australia
Perth, Australia
Gold Coast/Southport, Australia
Sydney, Australia
Auckland, New Zealand
Christchurch, New Zealand
Wellington, New Zealand

25
COUNTRIES

77
CITIES

300+
EXTERNAL COLLABORATORS



NORTH AMERICA

Halifax, Canada
Kingston, Canada
London, Canada
Montreal, Canada
Toronto, Canada
Winnipeg, Canada
Boston, USA
Charleston, USA
Denver, USA
Flagstaff, USA
Hershey, USA
Houston, USA
Kansas City, USA
Los Angeles, USA
Madison, USA
New York City, USA
Oklahoma City, USA
Philadelphia, USA
San Diego, USA
San Francisco, USA
St. Louis, USA
Stanford, USA
Washington DC, USA

ASIA

Hong Kong, China
Hyderabad, India
Kerala, India
Vellore, India
Tehran, Iran
Nagoya, Japan
Sanyo-Onoda, Japan
Serdang, Malaysia
Singapore
Bangkok, Thailand

SOUTH AMERICA

Sao Paulo, Brazil
Santiago, Chile
Puebla, Mexico

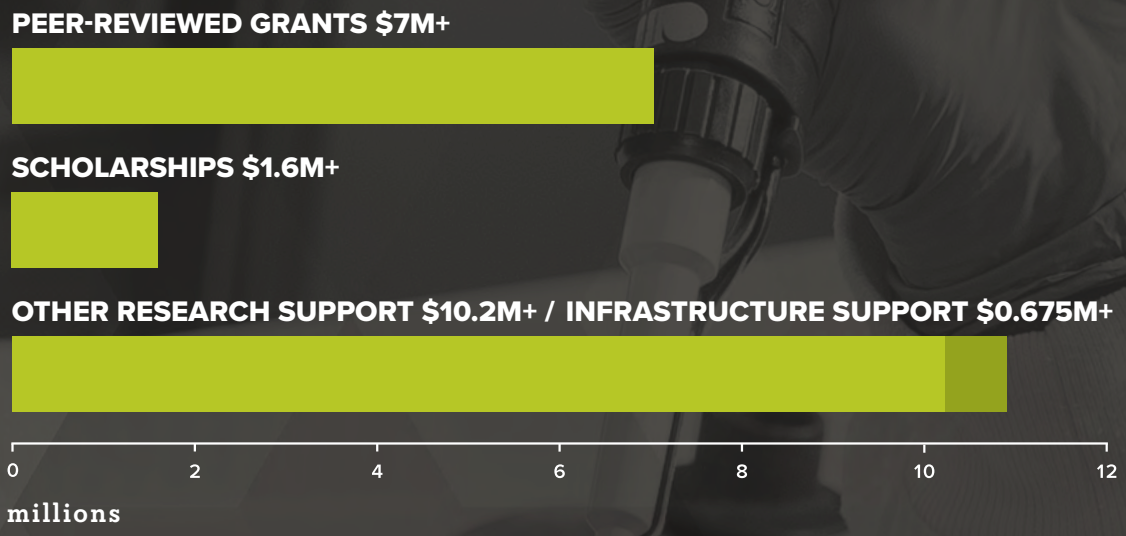
RESEARCH METRICS

FROM THE ANNUAL ASSESSMENT OF RESEARCH PRODUCTIVITY (2020-2021)

At the end of each financial year the Director of Research, BHI, TQEH engages with the research leaders at the precinct to assess productivity and progress. This involves collecting data on research inputs (staff, students and grants) and on the research outputs generated by the institute (including papers, patents, policies, products and graduates). Over the 24 years that this process has been happening TQEH has collected a rich, longitudinal data set of research indicators that track research productivity at the precinct. Below is a summary of the 2020-2021 Annual Assessment of Research Productivity. Detailed information on grants and publications can be found on the BHI website.

▸ www.basilhetzelinstitute.com.au/latest-news/research-reports

FUNDING



$19M+ REVENUE
Grants, clinical academic salaries, contracts, scholarships and infrastructure support

134 GRANTS
New and continuing grants worth $65M+

$1.6M+
Scholarship funding

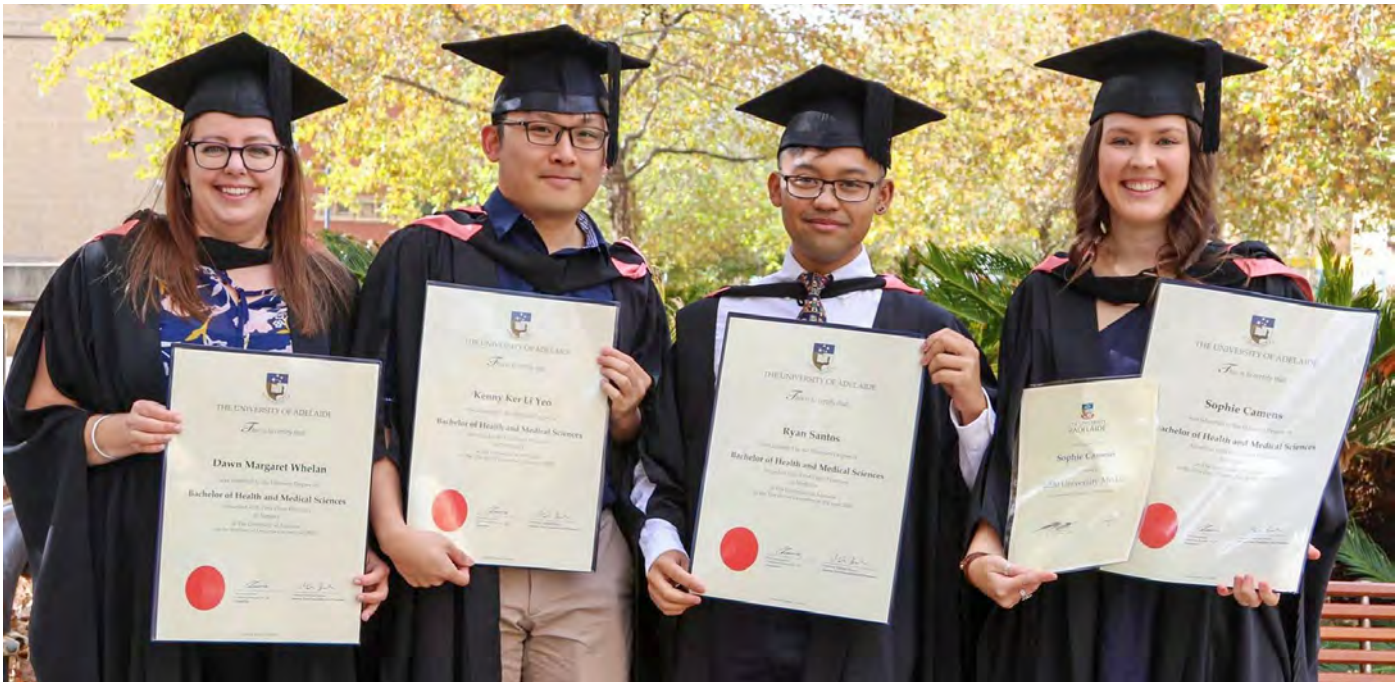
470 PUBLICATIONS
Journal articles, books and abstracts

200+
Researchers

100+
Research students

25+
Research groups

RESEARCH STUDENTS 2021



The Basil Hetzel Institute, TQEH, has provided basic and clinical research training to undergraduate and Higher Degree by Research (HDR) students for more than 50 years through its teaching and research affiliations with the South Australian universities.

In 2021, over 100 research students undertook their Honours, Masters or PhD research projects with BHI, TQEH research supervisors, and over 80% of these students conducted their research within the BHI, TQEH precinct. 2021 saw 14 BHI, TQEH HDR students awarded a PhD or Master's Degree. Four of our graduands from The University of Adelaide received a Dean's Commendation for Thesis Excellence. The number of graduands was down on 2020, but there have been a flurry of completions recently suggesting 2022 will be a big year. All 10 students who completed their Honours degrees with our research groups were awarded First Class Honours. For those students completing their research training with us, we congratulate them on their achievements and wish them well in their future careers.

The BHI plays a central role in Adelaide in training the clinical researchers of the future. Of the total student cohort of 2021, over 60% of our trainees were clinically-trained or allied health practitioners. As you read through the thesis titles of BHI, TQEH students you will be struck by the diversity of the research undertaken and also by the single theme running through them – research for better healthcare outcomes for people around the world. At the BHI, TQEH clinician researchers take an active role in the supervision of clinically-trained and scientifically-trained students, providing valuable insights into unmet needs in healthcare. Through our student training we provide real-life opportunities to make a difference to health and medical outcomes.

BHI, TQEH based research students enrolled through the Faculty of Health and Medical Sciences at The University of Adelaide were expertly assisted by Honours Coordinator Dr Peter Zalewski and Postgraduate Coordinators Dr Prue Cowled, Associate Professor Sarah Vreugde and Professor Betty Sallustio. 2021 marks the end of Dr Prue Cowled's tenure as a Postgraduate Coordinator, a role she has held for over 20 years. Prue was one of the first PGCs to be appointed at The University of Adelaide, joining the PGC team in 1995. Throughout her tenure, Prue has positively impacted the research careers of countless students directly and indirectly through mentoring and providing professional development opportunities with TQEH Research Expo and the student seminar series. She has shared her wealth of experience in postgraduate supervision with supervisors, new and continuing, she has provided support and mentorship to fellow postgraduate coordinators and has initiated new members of staff to the role. This is an extraordinary contribution to the support of University of Adelaide students by a scientist employed by The Queen Elizabeth Hospital. Prue's enthusiastic and thoughtful approach to all matters related to HDR students will be missed.

Work Experience Students

The BHI work experience program continues to be a popular window into medical science for secondary school students. The program was able to continue despite ongoing COVID restrictions in 2021, with 7 secondary school students offered a work experience placement. Six students from Cedar College, Glenunga International High School, Our Lady of the Sacred Heart College, Portside Christian College and Unley High School completed a placement. Each student spent a few days with BHI research groups, observing laboratory and clinical research and contributing to general lab duties.

UniSA Design Students

BHI, TQEH researchers were again fortunate to be partnered with UniSA Creative Bachelor of Design (Communication Design) students. As part of the "Type, Image and Motion" course, 19 students were introduced to BHI researchers across 3 different TQEH research groups. In small groups, students created animations with voice over to simplify 6 medical concepts or studies for the researchers' intended audience. All animations were intended for patient or potential participant use, with some animations doubling as education tools for medical staff.

L-R: Dawn Whelan (Viral Immunology Group), Kenny Yeo (Solid Tumour Group), Ryan Santos (Viral Immunology Group) and Sophie Camens (ENT Surgery) all graduated with First Class Honours in their Bachelor of Health and Medical Sciences (Honours) degree from The University of Adelaide. Photo taken by The University of Adelaide.

COMPLETED COMPLETED HIGHER RESEARCH DEGREES & HONOURS

Listed alphabetically by surname; BHI, TQEH based supervisors are underlined; *indicates students with BHI, TQEH supervisors who undertake their research at other precincts.

THE UNIVERSITY OF ADELAIDE

PhD AWARDED

Micah CEARNS* BPsych

Multimodal machine learning for precision psychiatry

Supervisors: Baune BT (University of Münster, Germany), Clark S

Psychiatry Research Group

The University of Adelaide, PhD awarded 28 February 2021
Dean's Commendation for Doctoral Thesis Excellence

Alice DAY APD (Accredited Practising Dietitian)

Exploring a patient-centered, diet-focused treatment paradigm for Inflammatory Bowel Disease

Supervisors: Andrews J, Bryant R

Inflammatory Bowel Disease Research Group

The University of Adelaide, PhD awarded 17 November 2021

Maria GANCHEVA* BSc(BiomedSci) BHlthSc(Hons)

Investigating Reprogramming Factors and Neural Conditions to Convert Human Dental Pulp Stem Cells into Neural Stem Cells

Supervisors: Koblar S, Kremer K, Gronthos S, Thomas P

Stroke Research Programme

The University of Adelaide, PhD awarded 2 July 2021

Amita GHADGE Integrated BSc MSc

The developmental origins of mammographic density and breast cancer risk

Supervisors: Ingman W, Dasari P, Robker R (Robinson Research Institute, The University of Adelaide)

Breast Biology and Cancer Unit

The University of Adelaide, PhD awarded 8 December 2021

Michael GOUZOS BPhysiotherapy MD

A delicate balance: Modulation of reactive oxygen species after sinus surgery to improve the healing process

Supervisors: Wormald PJ, Psaltis A, Vreugde S

ENT Surgery

The University of Adelaide, PhD awarded 18 March 2021
Dean's Commendation for Doctoral Thesis Excellence

Maryam NAKHJAVANI DPharm

Ginsenoside Rg3 as a Potential Treatment for Metastatic Triple-Negative Breast Cancer

Supervisors: Hardingham J, Townsend A

Solid Tumour Group

The University of Adelaide, PhD awarded 26 May 2021
Dean's Commendation for Doctoral Thesis Excellence

Guilherme PENA MD

Predicting outcomes in patients with diabetic foot ulcers

Supervisors: Fitridge R, Cowled P, Dawson J

Vascular Surgery Research Group

The University of Adelaide, PhD awarded 7 December 2021

Yoko TOMITA MBBS FRACP MSc

Anti-cancer effect of synthetic and plant-based inhibitors of aquaporin 1 in colon cancer

Supervisors: Hardingham J, Yool A, Price T

Solid Tumour Group

The University of Adelaide, PhD awarded 18 October 2021

Rajan Sundaresan VEDIAPPAN MBBS DLO MSurg(ENT) MA(Organisational Leadership)

Modifying post-surgical wound healing

Supervisors: Wormald PJ, Psaltis A, Vreugde S

ENT Surgery

The University of Adelaide, PhD awarded 14 April 2021

THE UNIVERSITY OF ADELAIDE

MASTER OF BIOTECHNOLOGY (BIOMEDICAL) AWARDED

Runhao LI BSc (Biotechnology)

Over-expression of SFRP5 in hepatocytes: a novel treatment strategy for colorectal cancer liver metastases

Supervisors: Smith E, Fenix K, Grubor-Bauk B

Solid Tumour Group

The University of Adelaide, awarded December 2021

THE UNIVERSITY OF ADELAIDE

MASTER OF PHILOSOPHY (SURGERY) AWARDED

Roy (Li Long) ONG MBBS

Factors effecting surgical mortality of oral squamous cell carcinoma resection

Supervisors: Maddern G, Sambrook P

Surgical Science Research Group

The University of Adelaide, MPhil (Surg) 5 February 2021
Dean's Commendation for Master by Research Thesis Excellence

Siang Wei GAN MBBS

Anatomical Factors contributing to Troublesome Dysphagia after Antireflux Surgery

Supervisors: Kiroff G, Meyers J

Oesophageal Physiology Group

The University of Adelaide, MPhil (Surg) awarded 18 May 2021

THE UNIVERSITY OF ADELAIDE

MASTER OF PHILOSOPHY (CLINICAL SCIENCE) AWARDED

Kathryn LAWTON RN

Management of bronchiectasis: a tertiary healthcare perspective

Supervisors: Nottle M, Veale A, Carson-Chahhoud K (University of South Australia)

Respiratory Research Group

The University of Adelaide, MPhil (Clinical Science) awarded 13 October 2021

COMPLETED COMPLETED HIGHER RESEARCH DEGREES & HONOURS

THE UNIVERSITY OF ADELAIDE

BACHELOR OF HEALTH AND MEDICAL SCIENCES (HONOURS) AWARDED

Kelly DANG BHlthMSc
Participant experience in the Flo Kappa clinical trial
Supervisor: Vreugde S
ENT Surgery
The University of Adelaide, First Class Honours awarded November 2021

Shenoi GOONETILLEKE BSc(MedScience)
Development of a bacteriophage cocktail for diabetic foot ulcers
Supervisors: Wormald PJ, Vreugde S, Liu S
ENT Surgery
The University of Adelaide, First Class Honours awarded November 2021

Keirrthana JOTHY BSc(BiomedSci)
The impact of the ovarian cycle on tumour-associated macrophages in MMTV-PyMT mice
Supervisors: Ingram W, Townsend A (Solid Tumour Group)
Breast Biology and Cancer Unit
The University of Adelaide, First Class Honours awarded November 2021

Neha KASTURE MBBS student
The effect of treatment expectancy and social determinants of health on outcomes in the Treatment for Adolescents with Depression Study (TADS)
Supervisors: Schubert KO, Aboustate N, Clark SR
Psychiatry Research Group
The University of Adelaide, First Class Honours awarded November 2021

Jonathan (Chun Yeung) KEI* BMBS student
Beyond ISCHEMIA: Reappraisal of coronary ischemic physiology
Supervisor: Horowitz JD
Cardiovascular Pathophysiology and Therapeutics Group
The University of Adelaide, First Class Honours awarded November 2021

Alek KELEI BSc(BiomedSci)
Developing a novel Zika vaccine
Supervisor: Grubor-Bauk B, Masavuli M
Viral Immunology Group
The University of Adelaide, First Class Honours awarded November 2021

Zuhal NADERI BHlthMSc
Androgen receptor signalling in high mammographic density
Supervisors: Ingman W, Hickey T (Dame Roma Mitchell Cancer Research Laboratories, The University of Adelaide)
Breast Biology and Cancer Unit
The University of Adelaide, First Class Honours awarded November 2021

Armin MUMINOVIC BHlthMSc GradCertPH
Inhibition of Platelet Aggregation by Activators and Stimulators of Soluble Guanylate Cyclase: Potential Mechanism for Overcoming Nitric Oxide Resistance?
Supervisors: Horowitz JD, Chirkov Y
Cardiovascular Pathophysiology and Therapeutics Group
The University of Adelaide, First Class Honours awarded November 2021

UNIVERSITY OF SOUTH AUSTRALIA

PhD AWARDED

Chelsea THORN* BPharm (Hons)
Towards novel delivery strategies for antimicrobial bio-macromolecules
Supervisors: Prestidge C, Thomas N
ENT Surgery (Nanomedicine)
University of South Australia, PhD awarded 27 October 2021

UNIVERSITY OF SOUTH AUSTRALIA

BACHELOR OF BIOMEDICAL RESEARCH (HONOURS) AWARDED

Shi Jie (Kelly) LAW BMedSci
Structure-function relationships of lipid-based delivery systems for the treatment of infections
Supervisors: Prestidge C, Thomas N
ENT Surgery (Nanomedicine)
University of South Australia, First Class Honours awarded December 2021

FLINDERS UNIVERSITY OF SOUTH AUSTRALIA

BACHELOR OF DIETETICS (HONOURS) AWARDED

Tessa BALLARD
Developing a sham diet for ulcerative colitis trials
Supervisors: Day A (The University of Adelaide), Bryant R (The University of Adelaide), Miller M
Inflammatory Bowel Disease Research Group
Flinders University, First Class Honours awarded January 2021

RESEARCH STUDENTS 2021
CONTINUING RESEARCH HIGHER DEGREE & HONOURS STUDENTS

Listed alphabetically by surname; BHI, TQEH based supervisors are underlined; *indicates students with BHI, TQEH supervisors who undertake their research at other precincts; **indicates students based at the BHI, TQEH but who do not have supervisors there.

THE UNIVERSITY OF ADELAIDE

PhD STUDENTS

Sally Suriani AHIP* MMed MBBS Doctor of Family Medicine
The Malaysian Pictorial Fit-Frail Scale (M-PFFS): Development and testing of feasibility, validity and reliability in Malaysia
Supervisors: Visvanathan R, Theou O (Dalhousie University, Canada), Shariff S (Universiti Putra Malaysia)
Adelaide GTRAC Centre
Government of Malaysia Scholarship

Zahraa AL-DELFI BSc
Development of novel DNA-based COVID-19 vaccines
Supervisor: Grubor-Bauk B, Makutiro M, Mekonnen Z
Viral Immunology Group
THRF Group BHI TQEH Research Scholarship

Mirabel ALONGE BHlthMSc(Hons)
Using pharmacokinetic principles to improve the safety of tacrolimus in kidney transplant recipients
Supervisors: Sallustio B, Coller J, Jesudason S (CALHN), Reuter-Lange S (University of South Australia)
Clinical Pharmacology Research Group
The University of Adelaide Faculty of Health & Medical Sciences Divisional Scholarship; The Hospital Research Foundation Top-Up Scholarship

Stephen BACCHI* MBBS
Deep learning in the prediction of clinically significant outcomes in Stroke and General Medicine patients
Supervisors: Koblar S, Kleinig T, Jannes J
Stroke Research Programme

Avisak BHATTACHARJEE MBBS FCPS FMAS MPH
Breast density: Optimising communication and clinical care
Supervisors: Ingman W, Dasari P, White S (Macquarie University)
Breast Cancer and Biology Unit

Anupam DATTA GUPTA MBBS, MD, Clin Dip Pall Med, Grad Dip Musc Med, FAFRM (RACP)
Use of botulinum toxin A in improving health outcomes in neurological patients with spasticity and dystonia
Supervisors: Visvanathan R, Wilson D, Koblar S (SAHMRI), Cameron I (University of Sydney)
Adelaide GTRAC Centre

Bimala DHAKAL BSc MSc
Porous silicon nanoparticles as drug delivery system for anti-metastatic therapy
Supervisors: Maddern G, Hauben E, Voelcker N (Monash University)
Surgical Science Research Group
Schlumberger Foundation Faculty for the Future Fellowship

Zenab Mustansir DUDHWALA BHlthSc(Hons)
Wnt beta catenin signalling pathway increases crypt fission in the small intestine in humans and rats
Supervisors: Cummins A, Howarth G
Growth and Repair of the Small Intestine
The University of Adelaide Research Training Program Stipend

Tom ELDREDGE* MBBS
Bile Reflux Post Bariatric Surgery
Supervisors: Kiroff G, Shenfine J (FMC), Myers J
Oesophageal Physiology Group
RP Jepson Research Scholarship, Royal Australasian College of Surgeons

Sholeh FEIZI MSc
Green synthesis of silver nanoparticles and their biomedical applications
Supervisors: Wormald PJ, Vreugde S, Psaltis AJ
ENT Surgery
The Hospital Research Foundation Postgraduate Research Scholarship

Olivia GIROLAMO BAppSci BHlthMSc(Hons)
Pathogenesis of TakoTsubo Syndrome: Role of vascular and platelet reactivity
Supervisors: Chirkov Y, Horowitz JD, Nguyen TH, Chong C-R
Cardiovascular Pathophysiology and Therapeutics Group
The University of Adelaide Research Training Program Stipend

Chelsea GRAHAM* BSc (Animal Sc)(Hons)
Developing a Schwann cell line from Tasmanian devil (Sarcophilus harrisii) dental pulp stem cells
Supervisors: Hamilton-Bruce MA, Pyecroft SB, Kremer KL
Stroke Research Programme

Aashray GUPTA BMBS MS (Cardiothoracic Surgery) GDipSurgAnat GDipClinUS
Evidence supporting strategies for coronary artery revascularisation
Supervisors: Maddern G, Bennetts J (FMC, Flinders University)
Surgical Science Research Group

Mitchell HERRICK* BSc(Hons)
Comparison of Novel Volumetric Imaging Systems for Adaptive Proton Therapy
Supervisors: Penfold S, Santos A, Hickson K (TQEH)
Molecular Imaging and Therapy Unit
The University of Adelaide Research Training Program Stipend

Ghais HOUTAK BMed, MNeuroscience(Research) MMed
Development of a personalised therapeutic protocol for S. aureus recalcitrant CRS
Supervisors: Vreugde S, Wormald PJ
ENT Surgery
The University of Adelaide Faculty of Health and Medical Sciences Divisional Scholarship; The Hospital Research Foundation Postgraduate Research Top-Up Scholarship

Unyime JASPER BMR(PT) MSc
Sedentary behaviour and physical activity in hospitalised older people
Supervisors: Visvanathan R, Yu S, Jadczak A, Dollard J
Adelaide GTRAC Centre
The University of Adelaide International Wildcard Scholarship; CRE Frailty in Healthy Ageing Top-up Scholarship

Laurine KAUL* MPharm & PharmSc
Novel treatments with antibacterial and wound-healing properties
Supervisors: Richter K, Zannettino A, Suess R (Freiburg University, Germany)
Surgical Science Research Group
Joint Postgraduate Research Scholarship (The University of Adelaide & Freiburg University, Germany)

THE UNIVERSITY OF ADELAIDE CONT.

Adeel Akbar KHOJA MBBS MSc(Epidemiology & Biostatistics)
Assessing the Influence of Pregnancy and its Complications on Cardiovascular Disease Risk

Supervisors: Arstall M (NAHLN), Tavella R, Andraweera P

Translational Vascular Function Research Collaborative

Northern Cardiovascular Research Group/Translational Vascular Function Research Collaborative; Adelaide Scholarship International, The University of Adelaide

Kareeann Sok Fun KHOW MBChB
Frailty, falls, hip fractures and clinical outcomes in older people OR Lower limb spasticity and dystonia

Supervisors: Visvanathan R, Yu S, Shibu P

Adelaide GTRAC Centre

NHMRC Postgraduate Research Scholarship

Tanja KLOTZ BOccTherapy MClinSci
Hypertrophic scar measures relationship to transepidermal water loss, and the effect of generic moisturisers on transepidermal water loss model

Supervisors: Maddern G, Wagstaff M

Surgical Science Research Group

Joshua KOVOOR BHlthMSc(Hons) MBBS
Characterisation of Gastrointestinal Recovery After General Surgery

Supervisors: Maddern G, Jones K

Surgical Science Research Group

The Hospital Research Foundation/Basil Hetzel Institute/The Queen Elizabeth Hospital Postgraduate Research Scholarship

Giri KRISHNAN MBBS MClinSc
Evaluating the accuracy of lymphotropic iron tracers for sentinel lymph node mapping in an orthotopic VX2 rabbit head and neck cancer model

Supervisors: Wormald PJ, Foreman A (RAH)

ENT Surgery

The University of Adelaide Faculty of Health and Medical Sciences Divisional Scholarship; Avant Doctors in Training Advancement of Medicine Scholarship; The Garnett Passe and Rodney Williams Memorial Foundation Academic Surgeon-Scientist Research Scholarship (2018); Fulbright Scholarship (2018-2019)

Sarena LA BHlthMSc(Advanced) (Hons)
Clinical insights into patients with chest pain and NOCA (non-obstructive coronary arteries) syndromes

Supervisors: Tavella R, Pasupathy S, Beltrame J

Translational Vascular Function Research Collaborative

The University of Adelaide Research Training Program Stipend

Celine Man Ying LI BSc BHlthMSc(Hons)
Investigation on the cytokine induced killer cells (CIK) in the treatment of colorectal cancer liver metastasis

Supervisors: Maddern G, Fenix K

Surgical Science Research Group

The University of Adelaide Divisional Scholarship

Suellen LYNE* MBBS
Epidemiology, Clinical Phenotype and Treatment Implications of Giant Cell Arteritis in Australia and New Zealand

Supervisors: Hill C, Ruediger C, Shanahan M (Flinders University)

Rheumatology Research Group

The University of Adelaide Research Training Program Stipend

Sonya McDOWELL* BVetTechnol
A quantitative study to evaluate the current standards and guidelines of Therapy and Service dogs within Australia

Supervisors: Hazel S, Hamilton-Bruce MA

Stroke Research Programme

Annika MASCARENHAS MBBS
An endoscopic ovine model of small vessel intracranial arterial haemorrhage control

Supervisors: Wormald PJ, Psaltis A, Vreugde S

ENT Surgery

The University of Adelaide, Faculty of Health & Medical Sciences Scholarship; The Neurosurgical Research Foundation (NRF)

Anna MEGOW MBBS
Improving management of recalcitrant chronic rhinosinusitis by enhancing currently available topical treatments and improving delivery of topical medication

Supervisors: Wormald PJ, Vreugde S

ENT Surgery

The University of Adelaide Faculty of Health and Medical Sciences Divisional Scholarship

Martha MENBERU MSc
Investigating Microbiome - Targeted Treatments for Chronic Rhinosinusitis: A novel approach to combat dysbiosis in the nasal microbiome

Supervisors: Vreugde S, Wormald PJ, Psaltis A

ENT Surgery

The University of Adelaide International Scholarship

Reger MIKAEEL MSc
Towards an Understanding of the Growing Incidence of Colorectal Cancer and Appendiceal Neoplasms in Young Adults

Supervisors: Price T, Young J, Smith E, Wollnick B (University of Göttingen, Germany)

Solid Tumour Group

The University of Adelaide International Wildcard Scholarship and a Hans-Jürgen & Marianne Ohff Research Grant

Alex Tony MINOPOULOS BHlthSc BHlthMSc(Hons)
The role of endothelial dysfunction and the expression of rho-kinase in coronary artery spasm

Supervisors: Beltrame J, Tavella R, Sallustio B

Translational Vascular Function Research Collaborative

THRF Group BHI TQEH Research Scholarship

Roshan NEPAL BSc MScience(Biotechnology)
Synthetic phage and phage lysins as potential antibacterial agents against multi-drug resistant pathogens

Supervisors: Vreugde S, Wormald PJ

ENT Surgery

The Hospital Research Foundation Postgraduate Research Scholarship; The University of Adelaide Fee scholarship

Jem NINAN MBBS MD FRACP FACP CCPU
Giant Cell Arteritis - understanding mechanisms of disease, improving the diagnostic certainty, and optimising management through Fast Track Clinics

Supervisors: Hill C, McNeil J

Rheumatology Research Group

Modbury Hospital Foundation Research Grant

RESEARCH STUDENTS 2021
CONTINUING RESEARCH HIGHER DEGREE & HONOURS STUDENTS

Listed alphabetically by surname; BHI, TQEH based supervisors are underlined; *indicates students with BHI, TQEH supervisors who undertake their research at other precincts; **indicates students based at the BHI, TQEH but who do not have supervisors there.

THE UNIVERSITY OF ADELAIDE CONT.

Andrew Toyin OLAGUNJU* MBBS MSc FWACP FMCPsych
Cognitive deficits, functioning and quality of life in individuals with schizophrenia and major depression
Supervisors: Baune BT (University of Münster, Germany), Clark SR
Psychiatry Research Group
The University of Adelaide International Scholarship

Gao-Jing ONG MBChB FRACP
TakoTsubo Syndrome: Investigations related to pathogenesis and impact
Supervisors: Horowitz JD, Chirkov Y
Cardivascular Pathophysiology and Therapeutics Group
The University of Adelaide Faculty of Health & Medical Sciences Divisional Scholarship

Eng Lee OOI* MBBS
Coronary and Peripheral Haemodynamic Studies in Obstructive Sleep Apnoea Population with Angina
Supervisors: Arstall M, Mahadevan G, Beltrame J, Rajendran S
Translational Vascular Function Research Collaborative
The University of Adelaide Research Training Program Stipend

Namfon (Bee) PANTARAT BSc(Biology) MSc(Biotech)
Hydrogel-based delivery of cancer fighting T cells for the localised treatment of completely resected or inoperable tumours
Supervisors: Evdokiou A, Zinonos I, Hauben E
Breast Cancer Research Unit
The University of Adelaide Discipline of Surgery Scholarship

Huai Leng (Jessica) PISANIELLO MBBS FRACP
The role of mobile health application in real-time capture of self-reported pain symptoms, and the use of intensive longitudinal data analysis in examining day-to-day pain variability in rheumatic and musculoskeletal disorders
Supervisors: Hill C, Beltrame J, Dixon W (University of Manchester), Whittle S
Rheumatology Research Group
Arthritis Australia Ken Muirden Travelling Scholarship 2018; The University of Adelaide Faculty of Health and Medical Sciences Divisional Scholarship

Karen ROYALS RN
Outreach respiratory nursing in the management of Chronic Obstructive Pulmonary Disease (COPD)
Supervisors: Nottle M, Veale A, Carson-Chahhoud K (University of South Australia)
Respiratory Research Group

Tomomichi SAKAI* MD
The validation Study of FRAIL-NH in Japanese Nursing Homes and the Comparison Study with Australia
Supervisors: Visvanathan R, Masafumi K (Nagoya University), Jadczak A
Adelaide GTRAC Centre
Adelaide Nagoya Scholarship, University of Adelaide

Jonathon SCHUBERT BSc BEng(Hons) MD
Patterns of Helicobacter pylori resistance
Supervisors: Rayner C (RAH), Roberts-Thompson I, Bryant R
Inflammatory Bowel Disease Research Group

Gohar SHAGHAYEGH BSc MDSc
Investigating the relationship between exoprotein production and inflammation in Chronic Rhinosinusitis
Supervisors: Vreugde S, Cooksley C, Psaltis A
ENT Surgery
The Hospital Research Foundation Postgraduate Research Scholarship; The University of Adelaide Fee scholarship

Deeksha SHARMA* BHlthMSc(Hons)
Find A Simple Test for TIA (FAST-IT)
Supervisors: Hamilton-Bruce MA, Koblar SA
Stroke Research Programme

Michelle SIMS BHlthMSc(Hons)
Preventing Heart Damage During Chemotherapy in Cancer Patients
Supervisors: Evdokiou A, Sallustio B, Licari J
Breast Cancer Research Unit
The University of Adelaide Research Training Program Stipend

James SMYTH BA(Mod), MB, BCh, BAO, DCH, FRCSI, FACEM, FRCEM, FFSEM
Roles of assessment activities of daily living (ADL's) and frailty for transfers of nursing home (NH) residents to the emergency department
Supervisors: Visvanathan R, Arendts G (The University of Western Australia), Grantham H (Curtin University/Flinders Medical Centre)
Adelaide GTRAC Centre

Tim SURMAN* MBBS
The structural apparatus of the aortic valve and patient outcomes for transapical and open aortic valve surgery
Supervisors: Beltrame J, Worthington M
Translational Vascular Function Research Collaborative
The Hospital Research Foundation Postgraduate Research Scholarship

Kai Tit TAN BHlthSc
Exploring the relationship between electroencephalography aperiodic slope, neuroinflammation, cognition and function in posttraumatic stress disorder
Supervisors: Schubert KO, Clark SR, Goldsworthy M
Psychiatry Research Group
The University of Adelaide International Scholarship; The Hospital Research Foundation Top Up Scholarship

Karmen TELFER BPharm BMBS
The development, maintenance and changes of the gastrointestinal microbiome, and their relationship to Ulcerative Colitis
Supervisors: Weinstein P, Costello S, Breed M (Flinders University)
Inflammatory Bowel Disease Research Group
NHMRC Postgraduate Scholarship

Joanna TIEU MBBS BMedSc FRACP
Optimising therapy in ANCA-associated Vasculitis
Supervisors: Hill C, Proudman S, Jayne D (University of Cambridge)
Rheumatology Research Group
NHMRC Postgraduate Research Scholarship

THE UNIVERSITY OF ADELAIDE CONT.

Stephen TRONCHIN* BSc(Hons) MPhil
Dosimetry analysis for 225-Ac: Modelling the biodistribution and dose of 225-Ac including individual daughter biokinetics, combined with a micro dosimetry component
Supervisors: Bezak E (University of South Australia), Forster J (TQEH), Hickson K (TQEH)
Molecular Imaging and Therapy Unit
The University of Adelaide Research Training Program Stipend

Jannatul Ferdoush TULI BSc MSc
Effect of bacterial exotoxin on mucosal barrier in Chronic Rhinosinusitis
Supervisors: Wormald PJ, Ramezanpour M
ENT Surgery
The University of Adelaide Research Training Program Stipend

Dawn WHELAN BHlthMSc(Hons)
Maternal immunisation with a novel Zika vaccine to protect offspring from congenital Zika syndrome
Supervisors: Grubor-Bauk B, Masavuli M, Mekonnen Z
Viral Immunology Group
The University of Adelaide Research Training Program Stipend

Joe WRIN BSc
Development of an anti-human C1q monoclonal antibody as a novel breast cancer therapeutic
Supervisors: Ingman W, Evdokiou A (Breast Cancer Research Unit)
Breast Biology and Cancer Unit
The University of Adelaide Australian Postgraduate Award

Kenny Ker Li YEO BSc(Hons) BSc (Biomedical Science)
The role of local microbiota and tumour microenvironment in head and neck cancer
Supervisors: Vreugde S, Fenix K, Valentine R, Ghaemmaghami A (University of Nottingham)
ENT Surgery
The University of Adelaide and the University of Nottingham, UK joint scholarship

Nikki YEO MB ChB FCICM
Optimising end-of-life care during critical illness
Supervisors: Deane A (Royal Melbourne Hospital), Reddi B (RAH)
Intensive Care Medicine Research Group

MASTER OF BIOTECHNOLOGY (BIOMEDICAL) STUDENT

Hashan DILENDRA BBiomedSc
Association between mucosal barrier disruption by Staphylococcus lugdunensis exoproteins in patients with chronic rhinosinusitis
Supervisors: Ramezanpour M, Vreugde S
ENT Surgery

MASTER OF CLINICAL SCIENCE STUDENT

Oscar RUSSELL MBBS
The impact of socioeconomic factors on medication use in Australian rheumatoid arthritis patients
Supervisors: Hill C, Gill T
Rheumatology Research Group
The University of Adelaide Research Training Program Stipend

MASTER OF PHILOSOPHY (CLINICAL SCIENCE) STUDENTS

Madeleine BRYANT MBBS
Patient Reported Experience Measures in Australian outpatient rheumatology care
Supervisors: Hill C, Black R
Rheumatology Research Group
The University of Adelaide Research Training Program Stipend

Usman MUSHTAQ MBBS FRACP
Pathophysiology and management of changes in calcium homeostasis and regulation of bone mineral density following bariatric surgery
Supervisors: Jesudason D, Kiroff G, Wittert G
Endocrinology Unit
Freemason's Centre for Men's Health Scholarship

MASTER OF PHILOSOPHY (MEDICAL SCIENCE) STUDENTS

Tom GOODSALL BSc MBBS(Hons) MClinEpid FRACP
The use of gastrointestinal ultrasound in the diagnosis and monitoring of inflammatory bowel disease
Supervisors: Andrews J (RAH), Bryant R
Inflammatory Bowel Disease Research Group
Gastroenterology Network of Intestinal Ultrasound (GENIUS) Fellowship Grant

Shridhar Ram KRISHNAN MBBS BDS
Evaluating a novel magnetic approach to sentinel lymph node biopsy for improved minimally invasive staging of head and neck cancer
Supervisors: Wormald PJ, Foreman A (Royal Adelaide Hospital)
ENT Surgery

William MURPHY BHlthSc MD
Use of mesalazine in chronic rhinosinusitis
Supervisors: Psaltis A, Wormald PJ, Vreugde S
ENT Surgery

Sreecanth RAJA BSc(Hons) MBBS
Faecal Microbiota Transplant (FMT) as a safe and efficacious therapeutic alternative for refractory proctitis: a pilot study
Supervisors: Rayner C (RAH), Costello S, Bryant R
Inflammatory Bowel Disease Research Group

MASTER OF PHILOSOPHY (SURGERY) STUDENTS

Victor AGUIRRE GUTIERREZ MBBS
Novel video recording systems in surgery: a new era in surgical education, safety and medico legal documentation
Supervisors: Fitridge R, Maddern G
Surgical Science Research Group

Harrison BOLT MD
Understanding the immunoepigenetic function of mucosal epithelial cell FOXP3 expression in chronic inflammatory sinonasal disease
Supervisors: Psaltis A, Wormald PJ, Vreugde S, Ramezanpour M
ENT Surgery

Sean BRIEN* MBBS AFRACMA
Surgical perioperative mortality for urological oncological procedures performed in Australia 2001-2015
Supervisor: Maddern G, Catterwell R
Surgical Science Research Group

THE UNIVERSITY OF ADELAIDE CONT.

James CONNELL MBBS
Ecological interactions between fungal and bacterial elements in chronic rhinosinusitis
Supervisors: Psaltis A, Wormald PJ, Vreugde S
ENT Surgery

Nelson GRANCHI* MBBS
Surgical coaching in the outpatient environment - a video-based intervention
Supervisor: Maddern G
Surgical Science Research Group
The University of Adelaide Research Training Program Stipend

Li Lian KUAN MBChB FRACS
Studies on benign pancreatic and hepatic pathology
Supervisors: Maddern G, Trochsler M
Surgical Science Research Group

Beatrice KUANG MBBS
Technological developments in the assessment and management of diabetic foot ulcers
Supervisors: Fitridge R, Cowled P, Dawson J
Vascular Surgery Research Group
The University of Adelaide Research Training Program Stipend

Paul PATINIOTT* MBBS
Developing a Hernia Mesh Tissue Integration Index
Supervisors: Maddern G, Karatassas A, Anthony A
Surgical Science Research Group
The Hospital Research Foundation Postgraduate Scholarship

Richard SMITH FRACS
Optimising post-operative radiotherapy for retroperitoneal sarcoma
Supervisors: Maddern G, Neuhaus S
Surgical Science Research Group

Ying Yang TING MBBS
Coaching in surgical ward rounds
Supervisors: Maddern G, Bruening M
Surgical Science Research Group
THRF Group BHI TQEH Research Scholarship

Edward YOUNG MBBS
Factors influencing the clinical outcomes of emergency general surgery in Australia
Supervisors: Maddern G, Trochsler M
Surgical Science Research Group

UNIVERSITY OF SOUTH AUSTRALIA

PhD STUDENTS

Muhammed AWAD MSc Pharmaceutical Sciences
Antimicrobial photodynamic therapy against chronic infectious diseases
Supervisors: Prestidge C, Barnes T, Thomas N
ENT Surgery (Nanomedicine)
University of South Australia Research Training Program International (RTPi) Stipend

Victor KRAWCZYK* BSocSc(Hum Serv) BA(Hons) GDipArtHist
Compassion for Animals in Culture and Organizational Life: Exploring and Actualizing Compassion for Suffering Animals
Supervisors: Walton S, Higgins-Desbiolles F, Hamilton-Bruce MA (The University of Adelaide), Caluya G (Deakin University)
Stroke Research Programme

Sean MANGION* BHlthSc(Adv) BBiomed Research(Hons) GradCert(Innov&Enterp)
Exploring the hair follicles as targets to improve the effectiveness of antidandruff therapies
Supervisors: Mackenzie L, Roberts M, Holmes A, Grice J (University of Queensland), Kempson I, Alinaghi A, Weightman W (TQEH)
Therapeutics Research Centre
University of South Australia Research Training Program Stipend

Antti Tapani MIKKONEN* BSc
Investigation of the pharmacokinetics pharmacodynamics of per- and polyfluoroalkyl substances (PFAS) in food production animals and development of models to predict biological loading and potential
Supervisors: Mackenzie L, Roberts M, Hayball J, Burzynski F (University of Manitoba, Canada), Martin J (Environmental Protection Authority, Victoria), Liu X (University of Queensland), Upton R
Therapeutics Research Centre
University of South Australia Research Training Program Stipend

Shuping QIANG BSc MSc
Quantification, pharmacokinetics and efficacy of drug poisoning treatment
Supervisors: Mackenzie L, Roberts M, Liu X (University of Queensland), Isbister G (University of Newcastle), Buckley N (University of Sydney)
Therapeutics Research Centre
University of South Australia Research Training Program Stipend; University of South Australia President's Scholarship (UPS); UniSA Postgraduate Research Award (USAPA)

Vicky VISVANATHAN* MN GradDipN(CC
TakoTsubo Syndrome in an Intensive Care Unit setting
Supervisors: Kucia A (NALHN), Horowitz JD (The University of Adelaide), Reddi B (CALHN),
Cardiovascular Pathophysiology and Therapeutics Group

MASTER OF SCIENCE STUDENT

Shalee BIRAJDAR BSc
Development of fibre optic dosimetry system for medical applications
Supervisors: Afshar S, Hickson K (TQEH), Zhang WQ, Santos S (The University of Adelaide)
Molecular Imaging and Therapy Unit

UNIVERSITY OF SOUTH AUSTRALIA CONT.

HONOURS STUDENT (MID-YEAR INTAKE)

Lana MATTEUCCI
Vaginal Mucosa Infections; an unmet clinical challenge

Supervisors: Holmes A, MacKenzie L, Roberts M
Therapeutics Research Centre
THRF Group BHI TQEH Research Scholarship (Honours)

FLINDERS UNIVERSITY OF SOUTH AUSTRALIA

PhD STUDENT

Louise HEUZENROEDER BNurs MBA MPH MHealthSci
Developing and testing the reliability and validity of a questionnaire to measure Dignity in Care for older people (and their carer) in the hospital setting

Supervisors: Kitson A, Woodman R, Ibrahim F (The University of Adelaide, TQEH)
Adelaide GTRAC Centre
Dementia Australia Consumer Priority PhD Scholarship

UNIVERSITY OF QUEENSLAND

PhD STUDENT

Mohammad Suleman KHAN PharmD MSc MPhil
Pharmacotherapy consideration in older people with cardiovascular diseases and diabetes- focus on prescribing complication and pharmacokinetics

Supervisors: Roberts M, Mackenzie L, Lui X (University of Queensland), Grice J (University of Queensland)
Therapeutics Research Centre
University of South Australia Research Training Program Stipend

CHARLES STURT UNIVERSITY, NSW

MASTER OF MEDICAL SCIENCE STUDENT

Donna KEATLEY BSc(Biomed) (Hons) GradCertRespSci
Comparison of a step test to the 6MWT (6 minute walk test) in patients with exercise induced dyspnoea: a preliminary validation trial

Supervisors: Micalos P, Pak S, Jurisevic M (TQEH), Kopsaftis Z (TQEH)
Respiratory Research Group

30TH TQEH RESEARCH EXPO 2021

In October 2021 TQEH Research Expo was held for the 30th consecutive year. This milestone prompted an evaluation of the history of research at the hospital and of TQEH Research Day. In 1994, the third year of TQEH Research Day, "[the] committee resolved to maintain the established philosophy of promoting the day for student researchers and those in training from either medical or scientific backgrounds, to enhance their scientific communication skills under conditions which are typical of most professional society congresses.

...it is hoped that medical research of TQEH will be further enhanced when these folk move on to deliver their research work to such congresses..."

This statement is as true for the 30th TQEH Research Expo as it was for the third.

We received 35 abstracts from student researchers and those in training working in laboratory-based and clinical projects. We enjoyed 4 hours and 19 minutes of student talks and 2 hours and 8 minutes of questions over a day and half. We gave out $6350 in prizes. The talks were universally excellent, and the students made the job of the abstract and presentation judging panels very difficult. It was a wonderful research expo. Congratulations to all the students who presented.

Our Plenary Lecturer, Dr Michael Cusack, Chief Medical Officer of South Australia, gave an inspiring presentation on the critical role data plays in ensuring the quality and safety of health services and in minimizing the risk to patients. Drawing on the experience of health service failures in the United Kingdom, and particularly what happened in the Bristol Royal Infirmary in the early 1990s, Dr Cusack developed a compelling case for using performance data to inform health service improvement initiatives. Dr Cusack was our 30th plenary lecturer; a full list of BHI Plenary Lecturers can be found in the program, which can be downloaded from the BHI website.

▸ **www.basilhetzelinstitute.com.au/research/information-for-researchers/bhi-activities/research-expo/**

The 30th TQEH Research Expo concluded with prize-giving, and we were pleased to welcome back the Honorable Steven Wade MLC, SA Minister for Health and Wellbeing, to congratulate the winners and present the prizes. Minister Wade showed himself to be a fan of the 3-minute thesis (3MT®) competition, as again we asked our 3MT® presenter to revisit their presentation in the final session - thank you to Muhammed Awad, PhD student with the University of South Australia.

This event does not happen without the contribution of a great many people. Thank you to:

- the judges who shoulder the difficult burden of deciding the winners, with particular note of 3 judges – Dr Yuliy Chirkov, Emeritus Professor John Horowitz and Dr Prue Cowled who acted as judges in 1994 and 2021, and no doubt for most of the years in between;
- the chairs, who find the time in their diaries to join us, encourage the students and add to the experience;
- the Plenary Lecturer, Dr Michael Cusack, SA Chief Medical Officer;
- the Hon. Stephen Wade MLC, Minister for Health and Wellbeing;
- the sponsors, with particular note of TQEH Research Foundation (now THRF Group) who sponsored TQEH Research Day in 1994 and who have continued to sponsor this event to this day.
- the audiences – colleagues and friends without whom we would not achieve conditions "typical of most professional societies."
- And, finally, to TQEH Research Expo Organising Committee. I extend my sincere gratitude to colleagues on the organising committee for the work they have done planning for and running the expo.

ASSOCIATE PROFESSOR JOY RATHJEN
Chair

TQEH Research Expo Organising Committee
BASIL HETZEL INSTITUTE

30TH TQEH RESEARCH EXPO 2021
AWARD WINNERS

AWARD CATEGORY	VALUE AWARD SPONSOR	WINNER INSTITUTION	BHI RESEARCH GROUP
Best Lay Description	**$350** The University of Adelaide, Faculty of Health & Medical Sciences	**Amita Ghadge** The University of Adelaide	Breast Biology and Cancer Unit, The University of Adelaide
Best Mini-Oral Presentation	**$500** Southern Cross Science	**Dr Madeleine Bryant** The University of Adelaide	Rheumatology Research Group, The University of Adelaide
Best Mini-Oral Presentation	**$500** University of South Australia, Clinical & Health Sciences	**Dr Sheree Cross** CALHN	Solid Tumour Group, The University of Adelaide
Best Oral Presentation: Honours & Summer Students	**$1,000** The Hospital Research Foundation Group	**Lana Matteucci** University of South Australia	Therapeutics Research Centre, University of South Australia
Best Oral Presentation: Junior Laboratory Research	**$1,000** The University of Adelaide, Faculty of Health & Medical Sciences	**Man Ying (Celine) Li** The University of Adelaide	Surgical Science Research Group, The University of Adelaide
Best Oral Presentation: Senior Laboratory Research	**$1,000** University of South Australia, Clinical & Health Sciences	**Muhammed Awad** University of South Australia	ENT Surgery, University of South Australia
Best Oral Presentation: Junior Clinical Research	**$1,000** The Hospital Research Foundation Group	**Joshua Kovoor** The University of Adelaide	Surgical Science Research Group, The University of Adelaide
Best Oral Presentation: Senior Clinical Research	**$1,000** AusHealth	**Dr Anna Megow** The University of Adelaide	ENT Surgery, The University of Adelaide

30th TQEH Research Expo Award Winners with leaders and invited guests. L-R: Professor Andrew Zannettino, CALHN/The University of Adelaide, Man Ying Li, Minister Stephen Wade MLC, Joshua Kovoor, Lana Matteucci, Matt Cowdry MP, Dr Anna Megow, Professor Guy Maddern, Director of Research BHI, TQEH, Muhammed Awad and Paul Flynn, CEO THRF Group.

60 YEARS OF TQEH RESEARCH

A gala dinner celebrating 60 years of life-changing research at The Queen Elizabeth Hospital (TQEH) and the 30th anniversary of TQEH Research Expo was held at the National Wine Centre on Wednesday 13 October 2021. The dinner's host, Director of Research at the BHI, TQEH, Professor Guy Maddern, summed up the night "The 60/30 dinner and celebration was a great success, bringing together the old, the new and the future leaders in medical science. I have always been very proud of what the BHI has achieved, and after last night's event I have no doubt about its future."

Guests were welcomed by MCs Dr Giri Krishnan and Dr Jessica Reid. Giri recently submitted his PhD thesis, which he completed with the ENT Surgery group, while Jess is a research officer with the Surgical Science Research Group. Jess and Giri invited Professor Maddern to introduce the guest speakers, Young Australian of the Year Isobel Marshall and her business partner Eloise Hall, who spoke about how their business, Taboo Period Products, came to be and how everyone can help end period poverty.
▸ **tabooau.co**

Invited guests, including colleagues and supporters from CALHN, the three major South Australian Universities, The Hospital Research Foundation Group, current and former researchers at TQEH, and students working at the BHI, TQEH enjoyed a meal together, and, as evidenced by the noise levels in the room, partook in lively conversation. Conversations were prompted by the place mats – BHI Research Reports from the previous 2 decades – and a revolving slide show of old and new photos and clippings documenting TQEH's history of research.

A video [▸ **www.youtube.com/watch?v=2kPzLDBoDEk**] celebrating 60 years of research at TQEH was screened, before Professor Maddern announced that three inaugural Basil Hetzel Institute Awards were to be presented by the very recently sworn in Governor of South Australia, Her Excellency the Honourable Frances Adamson AC. He did not realise that a fourth award was to follow these! The biographies read out for each recipient are included below. Recipients received a Tom Dixon designed salt grinder, a momento that references Basil Hetzel's pioneering campaign to iodize salt and prevent the impact of iodine deficiency on the brain development of unborn children. This campaign continues today through the Iodine Global Network.
▸ **www.ign.org**

To a standing ovation Professor Maddern was presented with the inaugural BHI award for Excellence in Research Leadership by the Director of Research at CALHN, Professor John Beltrame AM, and the Chair of CALHN, Mr Raymond Spencer. Professor Maddern was presented with a 'Taste of Australia' decanter created by local artist Emma Klau, and with a stopper filled with salt. When asked a few days afterwards about the night, fellow awardee Professor Dick Ruffin said "...while the dinner contained many highlights for me – memories rekindled, meeting colleagues and hearing about the brilliant young innovators and researchers, the major highlight for me was to see the public recognition of Guy Maddern for his endeavours at TQEH, and to be able to participate in the standing ovation that occurred in recognition of his work for research and the BHI, TQEH. Over the past 30 years Guy has shown leadership, persistence, advocacy, innovation and a personal publication record that have been translated into producing a stream of researchers, a new building and an annual record of BHI research as some of the markers of his success. A truly remarkable feat."

Following the awards, Professor Caroline McMillen AO, Chief Scientist of South Australia, closed the formal proceedings with some thoughtful remarks about the importance of health and medical research and research training to South Australia.

The BHI, TQEH thanks the Faculty of Health and Medical Sciences at The University of Adelaide for their assistance with audiovisual support, CALHN for the leadership award, and our major sponsor - The Hospital Research Foundation Group [▸ **www.hospitalresearch.org.au**] for joining with us to hold a dinner celebrating 60 years of health and medical research at TQEH.

L-R: Mr Paul Flynn CEO THRF Group, Professor John Beltrame AM, Director of Research CALHN, Professor Richard Ruffin AM, Her Excellency the Honourable Frances Adamson AC, Mr Raymond Spencer, Chair CALHN, Dr Prue Cowled and Professor Guy Maddern, Director of Research BHI, TQEH.

PROFESSOR RICHARD RUFFIN AM

Professor Richard Ruffin AM: "Richard Ruffin (Dick) joined The Queen Elizabeth Hospital as the senior director of the Thoracic Medicine Unit on the 13th of August 1990. He was recruited from the Flinders Medical Centre where he had spent 12 years as a senior consultant.

In 1998 Dick was appointed as the Michell Professor of Medicine at The University of Adelaide, based at The Queen Elizabeth Hospital, a position he held until 2010.

Dick's research focused on the epidemiology of asthma and chronic obstructive pulmonary disease, defining the incidence, prevalence, severity and burden of disease. He was instrumental in establishing the North West Adelaide Health Study, a longitudinal study of South Australians that has run from 1999 and continues today. He has an impressive publication record, a current h-index of 61 and has continued to publish with colleagues at the BHI, his most recent publication being in 2017. Dick also continued his involvement in research as Chair of the Human Research Ethics Committee at TQEH from 2014 until late 2017.

Dick has received many other awards for his outstanding contributions to research in respiratory medicine, including a Member of the Order of Australia in 2005 and a SA Great Award in 2008.

Tonight, we honour Emeritus Professor Richard Ruffin with an inaugural Basil Hetzel Institute Award in recognition of his exceptional contribution to research at the BHI, TQEH."

DR PRUE COWLED

"The first paper Prue Cowled published, in July 1978, was three years after commencing with the Department of Medicine at The Queen Elizabeth Hospital. There was a time when her affiliations also included the Department of Obstetrics and Gynaecology. It was all settled, however, when she defected to Surgery in November 1994, being appointed the RP Jepson Research Fellow, a role she holds to this day. Prue's career at The Queen Elizabeth Hospital has been long and influential.

Prue has shown exceptional leadership and made lasting contributions to the research programs of staff and students at the BHI, TQEH. She has acted as a post-graduate coordinator for The University of Adelaide from 1994 to the present. For over 21 years she developed and ran TQEH Research Day (now TQEH Research Expo). TQEH Research Expo is a postgraduate conference for students studying on TQEH precinct and is currently in its 30th year, a milestone we are celebrating tonight. TQEH Research Expo's success is in a large part due to Prue's long and passionate stewardship.

Prue is threatening to retire after some 47 years of service to research at The Queen Elizabeth Hospital and our community will be impoverished for this, if it happens!

Tonight, we honour Dr Prue Cowled with an inaugural Basil Hetzel Institute Award in recognition of her exceptional contribution to research at the BHI, TQEH."

After receiving the award Prue said of her time at TQEH "I recall being at a meeting of TQEH researchers in the late 1980's where I became aware of the concept of a research institute. After this, research at TQEH ramped up and I continue to be amazed at how far we have come!"

THRF GROUP AND MR PAUL FLYNN

"Research at The Queen Elizabeth Hospital has always been promoted and funded by The Queen Elizabeth Hospital Research Foundation. TQEH Research Foundation was the first of its kind in the state. Approved in principle in 1960, the foundation was incorporated on the 21st of September 1965. The history of research and the history of the foundation have been entwined ever since. We would not all be in this room tonight celebrating the long and illustrious history of research at The Queen Elizabeth Hospital without what is now known as The Hospital Research Foundation Group.

Mr Paul Flynn joined The Hospital Research Foundation Group in 2009 as the Chief Executive Officer after a multifaceted career in the Finance and Not-for-profit sectors.

Paul is an innovative and entrepreneurial leader who enjoys working with health networks, universities and other stakeholders to fulfil THRF Group's vision to deliver world-leading medical research and patient care initiatives across South Australia. He is passionate about giving medical and scientific researchers the opportunity to progress their lifesaving work for the benefit of all Australians. THRF Group continues to support that mission of the BHI, TQEH.

Tonight, we honour the role of The Hospital Research Foundation Group, and their inspirational CEO, Mr Paul Flynn, with an inaugural Basil Hetzel Institute Award in recognition of exceptional contribution to supporting research at the BHI, TQEH."

Paul writes of this award "On behalf of my colleagues at The Hospital Research Foundation Group we congratulate TQEH on their 60 years of life saving medical research and we are very humbled to be acknowledged with an inaugural Basil Hetzel Institute Award."

THE BHI, TQEH HAS BEEN MOST FORTUNATE TO HAVE GUY'S LEADERSHIP OVER THE PAST 28 YEARS, AND WE EXPECT THAT HE WILL CONTINUE THESE ROLES FOR MANY YEARS TO COME.

PROFESSOR GUY MADDERN

"It is with great pleasure and an honour to be able to say a few words about Professor Guy Maddern, who would be known to most people here tonight. Guy exemplifies a passionate clinical academic, with relentless drive, energy and commitment as reflected in his multiple current roles, which include:

- The RP Jepson Professor of Surgery & the Surgical Discipline Lead at The University of Adelaide
- Director of Research, Basil Hetzel Institute for Translational Health Research, TQEH
- Coordinator of Rural Surgical Services for The University of Adelaide, and
- Surgical Director of Research & Evaluation at the Royal Australasian College of Surgeons

Guy undertook his undergraduate medical training, PhD, Master of Surgery and MD at The University of Adelaide, receiving multiple awards including the RP Jepson medal, and Nimmo Prize on two occasions (since one wasn't enough). His postdoctoral studies were undertaken at multiple institutions, including in Switzerland, France, Germany, England and the United States; thereby providing a vast international experience, which would serve him well in his clinical academic career.

In 1993, he literally returned to his place of birth, The Queen Elizabeth Hospital; to a dual appointment as The University of Adelaide RP Jepson Professor of Surgery and the Director for the Division of Surgery at the hospital. Thus, *his name has been synonymous with TQEH surgery & research for more than 28 years.*

In 1996, he was appointed as the Director of the Clinical Development Research Centre at The Queen Elizabeth Hospital, a role that he has developed and still holds today at what is now called the BHI. Under his visionary leadership, research at TQEH has evolved with major infrastructure innovations including:

- Establishment of the Basil Hetzel Institute for Translational Health Research
- Formal review of research performance of the BHI groups
- A comprehensive and creative Annual BHI Research Report
- Developing a close relationship with TQEH Research Foundation, which has now evolved to The Hospital Research Foundation Group
- Maintaining basic research facilities and support at TQEH, and
- Attracting outstanding research groups to the Basil Hetzel Institute

In addition to these research achievements, Guy has been a leader and advocate for improved health service delivery and health technology assessment with innovations such as:

- SAPACT – South Australian Policy Advisory Committee on Technology, which he chairs
- ASERNIP-S – Australian Safety & Efficacy Register of New Interventional Procedures – Surgical
- and the development of surgical skills simulation laboratories

Indeed, he has an exemplary research track record with over 570 publications and reports, and more than $65 million in research funding.

With all these outstanding achievements, he does have some flaws! Firstly, he is a surgeon, and we physicians are weary of these folk and secondly, he is a crazed Port Power fan.

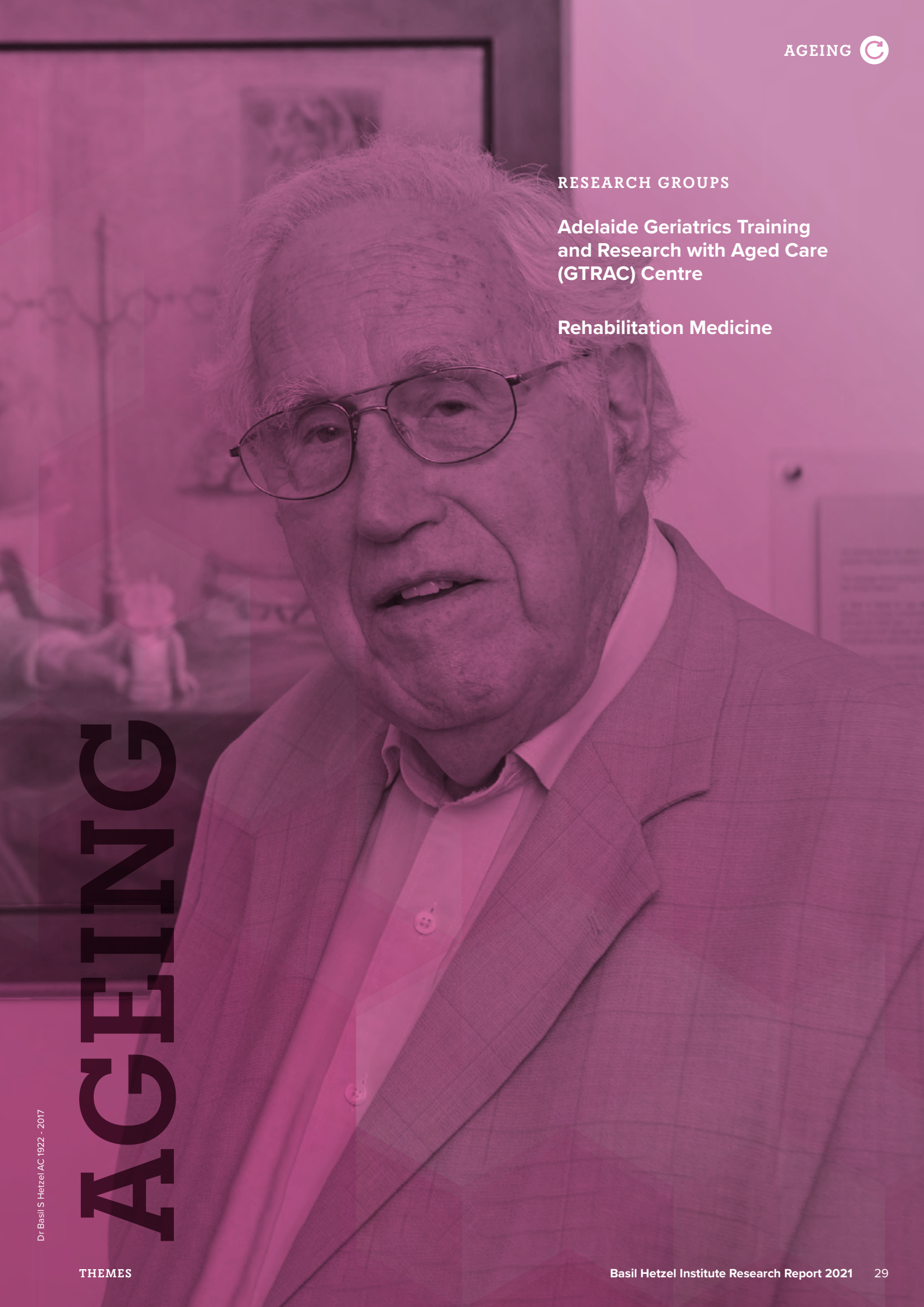
Joking aside, the BHI, TQEH has been most fortunate to have Guy's leadership over the past 28 years, and we expect that he will continue these roles for many years to come; particularly as *he is a giant on whose shoulders future generations will stand upon to carry on TQEH motto of Petimus, Docemus, Curamus* – We Seek, We Teach, We Heal.

Thus tonight, we honour the achievements of the RP Jepson Professor of Surgery, Professor Guy Maddern, with the inaugural Basil Hetzel Institute Award In recognition of his Excellence in Research Leadership at the BHI, TQEH.

Thank you Guy."

PROFESSSOR JOHN BELTRAME AM
Director of Research
CALHN

L-R: Professor Guy Maddern receives the inaugural BHI award for Excellence in Research Leadership from Mr Raymond Spencer, Chair CALHN.



RESEARCH GROUPS

Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre

Rehabilitation Medicine

AGEING

Dr Basil S Hetzel AC 1922 - 2017

Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre

Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre is associated with The University of Adelaide and the Aged and Extended Care Services (Geriatric Medicine) at The Queen Elizabeth Hospital. Our research focus includes nutritional frailty and sarcopenia, falls prevention, dementia assessment and management, gerontechnology, genetic epidemiology and precision geography. The team is committed to building the next generation of clinician and research leaders in the field of geriatric medicine and gerontology.

As part of a global network, GTRAC shares with other world-leading research and teaching groups the vision of improving the health outcomes of older people through high-quality geriatric medicine, excellence in clinical and research training and innovative translational research.

RESEARCH HIGHLIGHT OF 2021

An important aspect of our research program is providing research training to international students, and through this helping neighbouring countries improve health care delivery for vulnerable older populations. Facilitating knowledge exchange is another strength of our research program.

A visit of Dr Sally Ahip (photo, inset), a family physician from Kuching, Sarawak, Malaysia, to Adelaide in 2015 coincided with a visit of Dr Olga Theou, a colleague of GTRAC from Dalhouise University, Canada. Dr Theou had just developed a new frailty tool called the Pictorial Fit Frail Scale, and we believed the pictorial tool would be beneficial in areas with low health literacy.

With our support and collaboration, Dr Ahip secured research funding from the Malaysian Ministry of Health to fund the translation and testing of this tool in Malaysia. Together, we found the tool was suitable for use with older people with lower health literacy, and, importantly, that the tool could be administered by healthcare assistants, healthcare workers with secondary school qualifications. Sally is completing her PhD studies in GTRAC, supervised by Renuka Visvanathan, Olga Theou and Sazlini Shariff (Universiti Putra, Malaysia) and supported by the Malaysian Government, on the implementation of the pictorial Fit Frail Scale. Sally published this work in 2021.

While studying with us Dr Ahip has established Malaysia's first community geriatric clinic within the public health primary care system, incorporating knowledge gained from her research and clinical experience with GTRAC and has improved the management of frailty at the clinic. Her clinical service was visited by the Prime Minister of Malaysia in 2021. Dr Ahip is regularly invited to present on her experience in establishing this clinical service and the service is translating to other primary healthcare centres within her state.

Indicating a growing research and clinical profile in Malaysia, Dr Ahip was recently invited to the National Joint Learning Network Core Group and within that network has been appointed as working group leader tasked with developing a patient pathway for COVID-19.

Our ongoing support and collaboration with Sally, which extends beyond her area of study, highlights the importance of our program to improving health outcomes of older people through high-quality geriatric medicine in not only in Australia but also in the health systems of our neighbours.

Ahip S et al. Translation, adaptation and pilot testing of the Pictorial Fit Frail Scale for use in Malaysia - the PFFS Malay Version. *Malays Fam Physician* 2021, **16**(2):27-36.

▶ https://pubmed.ncbi.nlm.nih.gov/34386161/

OUR ONGOING SUPPORT AND COLLABORATION WITH SALLY, WHICH EXTENDS BEYOND HER AREA OF STUDY, HIGHLIGHTS THE IMPORTANCE OF OUR PROGRAM.

2021 research

- Professor Visvanathan was a co-investigator in a project funded by the Australian Research Council, "Improving thermal conditions in housing to support ageing in place" (DPP 180102019). From this research the first thermal comfort guidelines for older people living in South Australia have been developed: "Thermal Comfort at Home: A Guide for Older South Australians". The development of the guidelines included co-design with older consumers.
  ▸ **https://adelaide.figshare.com/articles/online_resource/_/17073578**
- Professor Visvanathan and Dr Mark Thompson authored the Frailty Health Pathway for Health Pathways SA. Health Pathways SA is an online portal providing general practitioners and other health practitioners easy access to comprehensive, evidence-based assessment and management and referral resources for specific health conditions.
- The FRAIL-NH screening tool for use in residential aged care, proposed by our research team in 2015, has been adapted, investigated and put into clinical use. It has been applied in 20 countries and adapted into three languages. The FRAIL-NH has been incorporated into frailty care guidelines developed by the New Zealand Health Quality and Safety Commission.
- In collaboration with Professor Bell from Monash University, we published international consensus principles for medication management in frail older people. These principles were endorsed by the European Geriatric Medicine Society, International Conference for Sarcopenia and Frailty Research and the Australian and New Zealand Sarcopenia and Frailty Research Society.
- Dr Azmeraw Amare, a post-doctoral fellow and genetic epidemiologist, was awarded a 2022 Discovery Early Career Researcher Award (DECRA) from the Australian Research Council and a 2022 NHMRC Investigator Grant for Emerging Leadership. He accepted the NHMRC award that will support him to develop genetic testing tools for optimising pharmacotherapy and enabling a precision mental health care.
- PhD student Mr Unyime Jasper was awarded the 'Office for Ageing Well Tackling Ageism Award' in 2021. Jasper was nominated for his research work aimed at reducing prolonged periods of sitting and lying (sedentary behaviour) and promoting physical activity among hospitalised older people.

GROUP MEMBERS

Professor and Head of Department
Renuka Visvanathan

Clinical Associate Professor and Deputy Head of Department
Solomon Yu

Professor of Epidemiology
David Wilson

Senior Lecturers
Bavand Bikdelli
Kareeann Khow
Neha Mahajan
Graeme Tucker

Clinical Senior Lecturers
Faizal Ibrahim
Pazhvoor Shibu

Clinical Lecturers
Fin Cai
Zanatt Fatema
Shailajar Nair
Jason Ng
Shasti Smith
Khai Tam

Manager Aged Care Alternatives Regional Assessment Service
Grant Edwards

General Practitioners
Barbara Allan
Sorayya Martin

Geriatric Evaluation & Management Liaison Team
Kathy Bray

Postdoctoral Research Fellows
Azmeraw Amare
Joanne Dollard
Agathe Jadczak
Danielle Taylor
Mark Thompson

Research Officer
Lalit Yadav

Research Assistant - Casual
Jane Edwards

CRE Manager
Leonie Baker

Postgraduate Students
Sally Suriani Ahip
Anupam Datta Gupta
Unyime Jasper
Kareeann Khow
Tomomichi Sakai
James Smyth

BHI COLLABORATOR

Guy Maddern
Surgical Science Research Group

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Kylie Lange
Damith Ranasinghe
Veronica Soebarto
Nigel Stocks
The University of Adelaide, Australia

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Michael Horowitz
The University of Adelaide & RAH, Australia

Jon Karnon
Alison Kitson
Michael Lawless
Shin Liau
Aubyn Pincombe
Alejandro Pinero De Plaza
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Rachel Ambagtsheer
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Vasi Naganathan
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University of Milan, Milan, Italy

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Olga Theou
Dalhousie University, Halifax, Canada

John Muscedere
Canadian Frailty Network, Kingston, Canada

Jothee Swaran Thiyagarajan
WHO, Geneva, Switzerland

John Beard
University of NSW, Sydney, Australia

John Morley
St Louis University, St Louis, USA

Isuru Ranasinghe
The Prince Charles Hospital & The University Queensland, Brisbane, Australia

Olivia Wright
The University Queensland, Brisbane, Australia

Tina Cooper
Sue McKechnie
Leonie Robson
Resthaven Inc., Adelaide, Australia

Michael Headland
Meera Verma
Adelaide University Judo Club Inc, Adelaide, Australia

Maria Inacio
Jyoti Khadka
Steve Wesselingh
SAHMRI & SA Academic Science and Health Translation Centre, Adelaide, Australia

Karen Jones
CRE Translating Nutritional Science To Good Health, The University of Adelaide, Adelaide, Australia

Masafumi Kuzuya
Nagoya University, Nagoya, Japan

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Rehabilitation Medicine

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PEOPLE SUFFERING FROM CANCER IN AUSTRALIA HAVE ACCESS TO WORLD CLASS CANCER CARE AND EXPERIENCE SOME OF THE HIGHEST CANCER SURVIVAL RATES IN THE WORLD.

Associate Professor Anupam Datta Gupta leads the Rehabilitation Medicine research group in Central Adelaide Local Health Network, with areas of interest in Stroke Rehabilitation and Cancer Rehabilitation. The focus for 2021 was to improve functioning, such as walking (gait) and hand function, and to preserve the quality of life in individuals affected by stroke. In 2021 we also focussed on the improving Cancer Related Fatigue (CRF) amongst cancer survivors.

2021 research

- We completed the pilot trial on the use of Brain Computer Interface for improving hand functions following Stroke in collaboration with Dr Sam Darvishi, RehabSwift (ThincLab, University of Adelaide) and Prof Derek Abbott (University of Adelaide). This safe and non-invasive intervention is another armamentarium for improving hand function following stroke and has recently been approved by the TGA. The next step is to take this technology for routine clinical use in appropriate cases through further trials. We aim to publish the results from the pilot study in 2022.
- We have completed a retrospective study, conducted over five years, on the effects of a supervised exercise program on Cancer Related Fatigue (CRF) amongst 268 patients participating in the day rehabilitation unit from 2015-2020. Australia ranks third globally in the incidence of cancer. People suffering from cancer in Australia have access to world class cancer care and experience some of the highest cancer survival rates in the world. Survival is often tainted by extraordinary fatigue, with a prevalence estimated to be between 45% and 99%. We analysed the effects of a supervised exercise program on CRF amongst 268 patients, assessing impact on physical, social, emotional, and functional well-being, 6 Min Walk test, and the instrumental activities of daily living by LAWTON's scale. We have noted significant improvement of CRF with supervised rehabilitation. This will be published soon.
- We completed the Randomised Control Trial on Efficacy of Botulinum Toxin A in Modifying Spasticity to Improve Walking and Quality of Life in Post-Stroke Lower Limb Spasticity - a Randomized Double-blind Placebo Controlled Study.

RESEARCH HIGHLIGHT OF 2021

We have just published a comprehensive systematic review and meta-analysis of the efficacy of botulinum toxin A in neuropathic pain. Neuropathic pain is common, affecting 7-10% in general population. The currently available pharmacological therapy is inadequate. Botulinum toxin A has demonstrated a positive effect on neuropathic pain. This systematic review with meta-analysis has called for the design of a randomised controlled trial (RCT) investigating botulinum toxin A and its use as a first line agent. Dr Jessica Smith, Rehabilitation Medicine registrar and Dr John Snow, a resident medical officer participated in this research.

Datta Gupta A, Edwards S, Smith J, Snow J, Visvanathan R, Tucker G, Wilson D. A Systematic Review and Meta-Analysis of Efficacy of Botulinum Toxin A for Neuropathic Pain. *Toxins* 2022, **14**(1):36. [accepted 29 December 2021]

▶ **https://pubmed.ncbi.nlm.nih.gov/35051013/**

CANCER

RESEARCH GROUPS

Breast Biology and Cancer Unit

Breast Cancer Research Unit

Clinical Pharmacology Research Group

Colorectal Cancer Research Group

Molecular Imaging and Therapy Unit

Solid Tumour Group

South Australian Prostate Cancer Clinical Outcomes Collaborative (SA-PCCOC)

Breast Biology and Cancer Unit

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The Breast Biology and Cancer Unit investigates development and function of the breast across puberty, lactation and ageing to understand how disease states occur. Our research integrates basic biology model systems together with clinical and public health research to improve breast health across the life course.

We research breast cancer risk factors, including breast density and menstrual cycling, to understand better the underlying biology of the disease and with a view to developing new ways to prevent the disease. We also research a common lactation condition known as mastitis, investigating why some women are more susceptible than others.

With a focus on community-driven outcomes, we work alongside clinicians within the Breast-Endocrine Surgical Unit and the Oncology Unit at TQEH, with pathologists at SA Pathology and with lactation consultants.

RESEARCH HIGHLIGHT OF 2021

Girls who gain weight during puberty develop fatty breasts and this lowers their chance of developing breast cancer as an adult, compared to their peers who develop dense breasts. Dense breasts matter because they are linked to one-third of breast cancers.

Our research in mice has suggested that adequate weight gain during puberty is a healthy part of development that protects against breast cancer later in life. Overall, our research supports a new paradigm that the chance of getting breast cancer as an adult is already established by the type of breasts women develop as teenagers. Some of this work was published in the journal *Seminars in Cell and Developmental Biology* in 2021, with another important research publication currently in preparation.

The significance of this research was recognised by the Australian Society of Medical Research (ASMR), who awarded the Ross Wishart Award to early career researcher Dr Amita Ghadge for her presentation at their annual conference titled "Developmental origins of mammographic density and breast cancer risk". Amita also won The Hospital Research Foundation Group's "Best Lay Abstract" award at the 2021 TQEH Research Expo.

Ghadge AG, Dasari P, Stone J, Thompson EW, Robker RL, Ingman WV. Pubertal mammary gland development is a key determinant of adult mammographic density. *Semin Cell Dev Biol* 2021, **114**: 143-158.
▶ **https://pubmed.ncbi.nlm.nih.gov/33309487/**

2021 research

- PhD student Avisak Bhattacharjee won Best Clinical Oral Presentation at the South Australian Breast Cancer Study Group Symposium for his presentation titled "Breast density: Optimising communication and clinical care".
- PhD graduate Dr Sarah Bernhardt was a finalist in the South Australian Young Achiever Awards (nominated by Associate Professor Wendy Ingman)
- Associate Professor Wendy Ingman conducted a national speaking tour for the Australian Breastfeeding Association as part of their Healthcare Professional Seminar Series. She presented two talks in Sydney, Melbourne, Brisbane and Perth in the space of 1 week. The talks were titled "Mastitis: are we just like cows?" and "Breast cancer risk and the modern woman".

Breast Cancer Research Unit

The aim of the Breast Cancer Research Unit is to find novel treatments for breast cancer. We are focusing on using the patient's own immune system and instructing it to recognize, attack and eliminate primary and metastatic breast cancer.

We have developed a world first approach of delivering therapies directly into cancer cells. We have packaged chemical sensitizers, known as phosphoantigens, in lipid carriers for transportation into the cancer cells. The patient's own circulating cancer fighting T-cells recognize the chemical sensors and bind to and eliminate cancer cells selectively, leaving normal cells unharmed.

This research provides robust preclinical data that will facilitate the translation of novel therapeutic drugs and approaches to clinical trials for breast cancer and its spread.

RESEARCH HIGHLIGHT OF 2021

HER2 is a protein found on the surface of cells in normal breast tissue, where it functions to regulate tissue growth and repair. HER2 can be found at higher than normal levels on the surface of breast cancer cells (HER2-positive breast cancer), and when this happens it promotes abnormal growth. HER2-positive breast cancer is a more aggressive form of breast cancer and is more likely to come back after treatment. We have developed an innovative approach of delivering anticancer drugs directly to HER2-positive breast cancers by packaging them into small membrane carriers known as liposomes. These drug-loaded carriers accumulate only in HER2-positive tumours where they release their contents killing cancer cells while leaving normal cells unharmed. This technology has now been patented and IP protected.

Evdokiou A, Licari G, Prestidge C. (2021), Method and composition for novel cancer immunotherapy, APSZ-2110508379

2021 research

Protecting the heart from chemotherapy induced cytotoxicity

Chemotherapy has many unwanted side effects particularly causing heart damage. We have recently shown that mice genetically deficient in a protein known as TRAIL (TNF-related apoptosis inducing ligand) are protected from the toxic effects of chemotherapy, demonstrating for the first time that TRAIL is a major protein responsible for causing heart failure in cancer patients. As a prelude to therapeutic development, we showed that intravenous administration of the TRAIL blocking drug, sDR5-Fc, in mice protected the heart from dox-induced damage and consequently improved cardiac function. We are continuing our drug development program and in collaboration with Dr Matt Sykes, from Pharmaceutical Sciences, University of SA, we used molecular modelling approaches to successfully identify existing drugs used for other purposes that may be re-purposed in this setting.

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Clinical Pharmacology Research Group

CANCER

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...WE HAVE FOUND THAT AN OLDER MEDICINE USED TO TREAT HEART DISEASE KILLS CANCER CELLS WITHOUT DAMAGING HEALTHY LIVER CELLS.

The Clinical Pharmacology Research Group aims to improve the effectiveness and safety of medicines by better understanding how they work within the body. This is particularly important for the medicines used to treat cancer, as individual patients can have very different responses to the same dose of chemotherapy drugs.

We are seeking to develop better monitoring of cancer patients that allows individually tailored chemotherapy doses to improve cancer cure and reduce the risk of adverse effects.

RESEARCH HIGHLIGHT OF 2021

Individualisation of cancer chemotherapy currently focusses on choosing the most effective drugs based on correctly identifying the genetic origin of a patient's tumour. Whilst this allows the choice of the best drug combinations, it is not sufficient to determine the best dose of each chemotherapy drug.

Precision-dosing of chemotherapy drugs requires tailoring doses based on pharmacokinetic differences between patients. Achieving the right amount of drug at the site of the cancer depends on the patients' ability to absorb the drug into the blood stream, to distribute the drug to the cancer and to eliminate the drug from the body. The optimal dose for one person may be highly damaging or ineffective for another. Understanding these processes for each patient allows optimisation of the dose to achieve cancer cure whilst minimising side effects.

In partnership with the Flinders Centre for Innovation in Cancer we have established the first clinical service in South Australia to monitor blood levels of a group of chemotherapy drugs called kinase inhibitors. In 2021 the Clinical Pharmacology Laboratory began providing tests for imatinib, erlotinib, gefitinib and everolimus, used to treat leukaemia, gastrointestinal, lung and breast cancers. The service has obtained media attention as well as interest from interstate oncologists.

Our research suggests that a significant number of patients whose cancers do not respond to standard doses have low blood levels of kinase inhibitors. This simple knowledge provides oncologists with the confidence to increase dosage rather than discontinue therapy or change to second-line chemotherapy combinations. With ongoing research, we aim to expand our clinical service to include other chemotherapy drugs for which precision-dosing is shown to be effective at improving clinical outcomes.

2021 research

- In collaboration with the Breast Cancer Research Unit we are developing new therapies to prevent a serious side effect of many cancer chemotherapies, heart damage. Following our discovery that, TRAIL, a protein present in the cells of the heart, plays an important role in chemotherapy-induced heart damage, we have moved forward to pre-clinical studies of new compounds that inhibit TRAIL. We are investigating the ability of these compounds to protect the heart during chemotherapy without diminishing the cancer killing effects. The work was partly funded by the National Health and Medical Research Council (NHMRC) and is being conducted by our PhD student Ms Michelle Sims. Michelle was awarded the Florey Medical Research Foundation Award for best basic science presentation at the 2021 Florey Postgraduate Research Conference.
- Clinical Pharmacology is collaborating with researchers from the Department of Surgery in a project discovering new uses for old drugs, focussing on potential new treatments for advanced colorectal cancer that has spread to the liver. These advanced cancers have very poor prognoses and few effective treatments. Using cancer cells isolated from the livers of patients with advanced colorectal cancer, we have found that an older medicine used to treat heart disease kills cancer cells without damaging healthy liver cells.

▸ **See also Clinical Pharmacology Research Group - Chronic Disease**

Colorectal Cancer Research Group

The research focus of the Colorectal Surgical Unit at TQEH continues to be on peritoneal cancers. There are a variety of cancers that can spread to the lining of the abdomen (the peritoneum). They can be difficult to treat because they grow into the cavity (the peritoneal cavity) surrounding the abdominal organs and chemotherapy given into the blood stream may not effectively penetrate the peritoneum and the cavity to treat peritoneal cancers.

Pressurised intraperitoneal chemotherapy (PIPAC) delivers chemotherapy, under pressure, into the cavity and directly to the surface of the cancer. This is done using keyhole surgery to lessen any discomfort. It is hoped that this new treatment will be another effective treatment to improve quality of life and increase life expectancy for these incurable cancers.

RESEARCH HIGHLIGHT OF 2021

New treatment options for patients with peritoneal malignancy

To date 11 patients have been enrolled into a safety and efficacy trial with full recruitment to be completed shortly. Our program of debulking abdominal tumours and treating them with Heated Intraperitoneal Chemotherapy (HIPEC) has now treated over 150 patients.

Implementing PIPAC in South Australia has improved knowledge around the technical requirements for success. Less is known about the optimal chemotherapeutics to combine with PIPAC as limited testing for tumour sensitivity to chemotherapy agents has been performed.

2021 research

- In 2020 we established a collaboration with Dr Susan Woods from SAHMRI to grow organoids from peritoneal cancers to find the best chemotherapy regime for individual patients.
- Dr Dilshn Udayasiri is currently investigating the implications of further surgical procedures on overall survival and disease-free survival following an index operation for colorectal cancer.

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EXTERNAL COLLABORATOR

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Molecular Imaging and Therapy Unit

The Queen Elizabeth Hospital Nuclear Medicine department provides diagnostic and therapy services to South Australian (SA) and Northern Territory (NT) patients. With a strong collaborative focus across the disciplines of Oncology, Cardiology, Endocrinology and Surgery we have been involved in clinician-led research for many years.

We are the sole SA centre providing Peptide Receptor Radionuclide Therapy (PRRT) for patients with metastatic neuroendocrine tumours (NETs), we coordinate the state-wide NET multi-disciplinary meeting and provide individualised management plans for NET patients. We have developed strong collaborations with other National PRRT centres. We continue to play an active role in the management of a range of other tumours, especially thyroid and liver cancer, and are working towards Theranostic services for prostate cancer.

2021 research

- We continue to refine and implement written Personalised Patient Schedules for patients. Created by our NET nurse Jessica, these are an invaluable guide to help patients track tests and appointments and is a testament to our commitment to patient-centred care. We are also committed to ensuring equitable access for rural and remote patients by using SA Telehealth.
- At a National level, we contributed to many NET centred projects in 2021, including the Optimal Care Pathway for NET and revision of the COSA guidelines for the management of NET; National Action Plan for NET, launched on World NET day 10th November; and the development of local and national guidelines for the identification and management of potentially life-threatening carcinoid crisis management.
- We continue to educate other health care professionals by presenting at Educational grand rounds, World NET day seminars and various Education forums to highlight the latest advances in the management of patients with neuroendocrine tumours.
- In collaboration with Professor Bezak and Dr Koh, we have published a meta-analysis on targeted alpha therapy in NET.[1]

1. Koh TT, Bezak E, Chan D, Cehic G. Targeted alpha-particle therapy in neuroendocrine neoplasms: A systematic review. *World J Nucl Med* 2021, **20**:329-35.
▶ **https://pubmed.ncbi.nlm.nih.gov/35018146/**

RESEARCH HIGHLIGHT OF 2021

Neuroendocrine tumours (NETs) occur in many different organs of the body with no common set of symptoms, often leading to delayed diagnosis. NETs affect men, women and children of all ages. PRRT is a form of systemic targeted radiotherapy that can stabilise the disease, often improving quality of life by reducing the impact of hormones and controlling patients' symptoms. TQEH is the only SA site to provide this service to SA/NT patients with metastatic NET. We are leading an international study to understand how PRRT affects quality of life.

In 2021 we established a NET registry that captures clinical data from all SA and NT patients who have received PRRT. This venture has been supported by The Hospital Research Foundation Group who fund the NET research Fellow, Dr Liesl Altus, and NET Nurse, Jessica Mercurio. This online data registry is supported by CALHN and will enable long-term follow-up of treatment related toxicity, quality of life and overall survival. Analysis of the data will identify key performance indicators that can be used to inform patient care and outcomes.

The SA NET registry will contribute to the Australian registry for NET cancers (PLANET). This robust database aims to deliver impacts for patients by ensuring access to best practice and clinical trials.

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Director of Peptide Receptor Radionuclide Therapy (PRRT) Service, Chair SA Gastroenteropancreatic Neuroendocrine Tumours (GEPNET) Multidisciplanary Meeting
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The Solid Tumour Group is a large, multidisciplinary group, led by Professor Tim Price, that brings together researchers and clinicians from the BHI, TQEH and collaborators from across the state.

The group has a comprehensive research program that works towards improved prevention strategies, better diagnostics and new therapeutics for colorectal, appendix, neuroendocrine and breast cancers. The group links directly with the clinical services at TQEH, a link which facilitates the clinical trials program and enables an opportunity to translate pre-clinical findings into improved patient care.

The group comprises three parts:

- **Young Onset Colorectal and Appendix Cancer Group**
- **Clinical Trials Group**
- **Molecular Oncology Group**

YOUNG ONSET COLORECTAL AND APPENDIX CANCER GROUP

Population screening for colorectal (bowel) cancer has been successful in decreasing the incidence and mortality from this malignancy in adults 50 years and over. However, the incidence in younger adults is rising in Australia, and elsewhere in the developed world. The South Australian Young Onset Colorectal Polyp and Cancer Study (SAYO) is a multidisciplinary state-wide consortium which seeks to identify the risk factors and warning signs for colorectal cancer in young adults, in order to provide screening and prevention to those most at risk. In 2020 we extended SAYO to understand why appendiceal cancers are also on the rise in our population, including in young adults.

RESEARCH HIGHLIGHT OF 2021

In 2021 we have demonstrated that diagnosis of type 2 diabetes at an early age is associated with an increased risk of colorectal cancer in younger adults of approximately four-fold over that of the general population. We have also observed that precancerous polyps of the bowel are more frequently observed in younger adults with type 2 diabetes.

Taken together, these findings suggest that routine bowel cancer screening in young adults with type 2 diabetes has the potential to prevent or detect at an early stage a proportion of young onset colorectal cancers. In 2022 we hope to implement a pilot study to determine the feasibility of including young diabetics in the national bowel cancer screening program (NBCSP).

2021 research

- We observed, in two families with multiple cases of bowel cancer, inherited mutations in the gene RNF43, suggesting that this mutation could be the causative event. Previously such mutations have only been seen in rare families with numerous bowel polyps.
- Inherited mutations in young onset bowel cancer patients was not strongly predicted by either family history of bowel cancers or a high bowel polyp burden.
- The breast cancer gene BRCA2 is mutated in a proportion of young onset bowel cancer patients, which supports the observation that mutations in this gene can give rise to other cancer types besides breast cancer.

CLINICAL TRIALS GROUP

The Medical Oncology and Haematology group undertakes clinical trials of emerging cancer therapies, ranging from first in human and Phase I trials to larger, randomised trials. The group continues to prioritise early phase trials of drugs directed at new therapeutic targets. We are linked into cooperative groups within Australia and internationally, and to major pharmaceutical companies. Our aims are to provide access to new therapies for our patients, to provide evidence that will lead to new therapies being adopted into practice, and to explore personalised cancer therapy through better targeting of the therapeutic approach to the patient.

RESEARCH HIGHLIGHT OF 2021

The Solid Cancer group is part of a global clinical trial initiative investigating the anti-cancer potential of a new cancer therapy, Sotorasib (AMG510). Sotorasib targets a specific mutation of the KRAS gene, known as KRAS G12C. KRAS G12C is a potent driver of cancer, and until recently this version of KRAS was thought to be 'undruggable'. KRAS G12C is seen in a number of cancers, including, importantly, a high percentage of non-small cell lung cancers and in colorectal cancer.

In 2020 we reported the results of the phase 1 study demonstrating that Sotorasib showed anticancer activity in patients with KRAS G12C-containing advanced solid tumors, including in non-small cell lung cancer tumours. Based on this evidence the trial was expanded to explore the activity of Sotorasib specifically in non-small cell lung cancer. In 2021, we reported the results of the Phase II study in the highly prestigious New England Journal of Medicine.[1] We showed that when patients who had failed normal therapy were treated with Sotorasib, 37% of patients responded with reduction in cancer volume, and overall all patients had disease stabilisation. These data led to the availability of this new treatment firstly to US populations through an FDA approval and subsequently to an access program in Australia.

We continue to explore additional combinations of Sotorasib with other agents to increase the impact on disease control, and the application of the drug to other cancers beyond lung cancer.

1. Skoulidis F, Li BT, Dy GK, Price TJ, et al. Sotorasib for Lung Cancers with KRAS p.G12C Mutation. *N Engl J Med* 2021, **384**(25):2371-2381.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34096690/**

2021 research

In keeping with our focus on novel treatments the group has a broad range of clinical trials looking at new therapies for most cancer types. We continue an active program of early phase trials with agents targeting p53 (AMG650) and a new immunotherapy agent AMG404.

MOLECULAR ONCOLOGY GROUP

The Molecular Oncology team form part of the Solid Tumour Group headed by Professor Tim Price and Dr Amanda Townsend, Medical Oncology Unit, TQEH. Research is focused on identification of biomarkers, drug repurposing, and development of novel therapeutics for the treatment of solid tumours including colorectal and breast cancer.

RESEARCH HIGHLIGHT OF 2021

Colorectal (bowel) cancer is the third most common cancer in the world and a leading cause of cancer related deaths. Deaths from colorectal cancer are frequently the result of metastases to distant organs including the liver. We recently reported the novel finding that the levels of a protein known as secreted frizzled related protein 5 (SFRP5) are elevated in the blood of patients with colorectal cancer. We have also shown that within a group of colorectal cancer patients, a comparatively lower level of SFRP5 in the blood appeared to be associated with an increased risk of developing liver metastasis.

These findings raise the possibility that a blood test measuring SFRP5 may be a useful diagnostic tool. The potential clinical uses of SFRP5 have been patented (AU2020903281) and funding from AusHealth has been secured to validate circulating SFRP5 as a biomarker for early detection and prognosis of progression of colorectal cancer in a cohort of more than 1000 patients and healthy donors. Ongoing research in the group is evaluating the role of SFRP5 in modifying the tumour microenvironment and its potential as a therapeutic.

2021 research

- Dr Maryam Nakhjavani was awarded a Dean's Commendation for Doctoral Thesis Excellence for her PhD thesis entitled "Ginsenoside Rg3 as a Potential Treatment for Metastatic Triple-Negative Breast Cancer" and an Alfred Deakin Postdoctoral Research Fellowship from Deakin University, Victoria, Australia.
- Runhao Li was awarded a Master of Biotechnology (Biomedical), with a GPA of 6.8/7, for his thesis entitled *"Over-expression of SFRP5 in hepatocytes: a novel treatment strategy for colorectal cancer liver metastases"* and received an International Wildcard PhD Scholarship from The University of Adelaide which will commence in 2022.

SA-PCCOC (South Australian Prostate Cancer Clinical Outcomes Collaborative)

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The South Australian Prostate Cancer Clinical Outcomes Collaborative (SA-PCOCC) was established in 1998 as an ongoing venture of Flinders University, Royal Adelaide Hospital (RAH), The Queen Elizabeth Hospital (TQEH), The University of Adelaide and the University of South Australia.

The flagship of this collaborative is a database which tracks men with prostate cancer in major metropolitan South Australian public hospitals, as well as collaborating private institutions and clinicians. As part of a bi-national collaboration the SA-PCCOC contributes to the Prostate Cancer Outcomes Registry – Australia and New Zealand (PCOR-ANZ), which is funded by the Movember Foundation.

2021 research

- SA-PCCOC is currently hosting four HDR students
- We have crossed another milestone, with 19,000 men now in the registry.

RESEARCH HIGHLIGHT OF 2021

SA-PCCOC contributes to the Prostate Cancer Registry of Australia and New Zealand, and in 2021 this gave the group the opportunity to assess radiation treatment of prostate cancer in collaboration with other centres.

Across Australia and New Zealand there has been rapid uptake of radiation therapy delivered by hypofractionation. This delivery method involves treating patients with fewer doses of radiation therapy (meaning they need to visit the radiation therapy centre fewer times), but with each dose delivering a higher amount of radiation. This change in treatment has been achieved without any increases in adverse effects that patients might experience from the radiation treatment.[1]

1. Pryor DI, Martin JM, Millar JL, Day H, Ong WL, Skala M, FitzGerald LM, Hindson B, Higgs B, O'Callaghan ME, Syed F, Hayden AJ, Turner SL, Papa N. Evaluation of Hypofractionated Radiation Therapy Use and Patient-Reported Outcomes in Men With Nonmetastatic Prostate Cancer in Australia and New Zealand. *JAMA Netw Open* 2021, **4**(11): e2129647.
▶ **https://pubmed.ncbi.nlm.nih.gov/34724555/**

CARDIOVASCULAR DISEASE

RESEARCH GROUPS

Cardiovascular Pathophysiology and Therapeutics Group

Translational Vascular Function Research Collaborative (TVFRC)

Vascular Surgery Research Group

Zinc and Cardiovascular Disease Research Group

Cardiovascular Pathophysiology and Therapeutics Group

Heart disease is highly complex, and the causes and forms of the disease are ever-changing in our society. The Cardiovascular Pathophysiology and Therapeutics Group seeks to unravel this disease complexity, identifying new causes and forms of disease and developing new therapeutic approaches for disease management.

The group focusses on:

- **TakoTsubo Syndrome (TTS; "Broken Heart Syndrome") that causes chest pain, shortage of breath, and increased risk of death, predominantly in older women**
- **The frequent problem of spasm of the coronary arteries**
- **Preventing the detrimental impact of some cancer treatments on heart health**
- **The cardiovascular damage that frequently occurs with diabetes**
- **Serious heart diseases that can be triggered by environmental challenge or COVID-19 infection.**

RESEARCH HIGHLIGHT OF 2021

Unlocking the function and dysfunction of small coronary arteries

It has always been thought that angina pectoris (chest pain or discomfort resulting from too little blood flowing to the heart) and heart attacks are caused by partial or total blockage of large coronary arteries due to lipid (fat) deposition. Two recent clinical trials have shown that "unblocking" coronary arteries in patients with angina made little difference to their symptoms or outcomes, suggesting that the partial blockage of the arteries cannot fully explain angina. Our group has focused on finding out the role played by the small coronary arteries in the development of angina and its outcomes.

Honours student Jonathan Kei summarised evidence that small coronary arteries are susceptible to structural and functional changes that impair blood flow and predispose them towards constriction and thrombus (clot) formation.

We have extended this concept by examining physiological changes in the common but under-diagnosed condition of coronary artery spasm (CAS). We found that CAS patients have crises because of loss of nitric-oxide mediated artery dilatation and inhibition of clotting, predisposing arteries to constriction and thrombus formation. Further, we have found that the ultimate cause of these crises is lack of hydrogen sulphide (H_2S). We have demonstrated that replacing H_2S relieves symptoms and normalises coronary physiology in CAS patients. This means that CAS is like "cardiac migraine" and we now have a pathway for better treatments that replace H_2S and improve arterial responses to nitric oxide.

Honours student Armin Muminovic showed that it should be possible to improve arterial response to nitric oxide by using soluble guanylate cyclase stimulators. These drugs have not previously been used for angina. Specifically, he showed that soluble guanylate cyclase stimulators, which act to potentiate nitric oxide interaction with its receptor, normalise the effect of nitric oxide, preventing clot formation in blood from CAS patients. All that really remains is to improve efficiency of diagnosis of CAS!

OUR GROUP HAS FOCUSED ON FINDING OUT THE ROLE PLAYED BY THE SMALL CORONARY ARTERIES IN THE DEVELOPMENT OF ANGINA AND ITS OUTCOMES.

2021 research

- A longstanding interest of our group has been Takotsubo Syndrome (TTS), a disorder that occurs mainly in ageing women and which mimics heart attacks. TTS is often precipitated by severe physical or emotional stress and carries similar mortality risks to those after heart attacks. We have developed an integrative pathophysiological model for TTS that incorporates the early occurrence of damage to blood vessels causing low blood pressure and shock, followed by the progressive appearance of inflammatory changes within the heart (rather similar to changes described after COVID). Our studies suggest that over-production or increased effects of nitric oxide throughout the body may play a major part in the development of shock. We are currently running a clinical trial (NACRAM) to try and prevent shock and the subsequent inflammatory changes in the heart. Dr Gao-Jing Ong, who has played a leading part in this work, has just completed the research for his PhD and is close to submitting his thesis.
- Signalling defects of prostacyclin, a vasodilator and antiaggregant, which functions alongside nitric oxide, have been poorly investigated in CAS patients. Kate Spuler (Vacation Student) is exploring this area as well as the relationship between decreased prostacyclin signalling and ageing.
- In 2021, members of our group published 15 papers in leading Cardiology journals, with a total of 7 publications on TTS.
  ▸ See Publications

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Translational Vascular Function Research Collaborative (TVFRC)

TRANSLATIONAL VASCULAR MOLECULAR PHYSIOLOGY

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Vascular diseases remain a major cause of death and poor health in Australia. Vascular diseases can be largely attributed to abnormalities within blood vessels and compromised blood supply to the organs, including the heart. The Translational Vascular Function Research Collaborative (TVFRC) undertakes interdisciplinary discovery, clinical and epidemiological research into vascular diseases aimed at improving our understanding of these disorders, optimising healthcare management and developing new and effective therapies.

The TVFRC comprises clinicians and medical scientists working at the BHI, The University of Adelaide, the Cardiology Departments of the Heart and Lung Unit, Central Adelaide Local Health Network and the Cardiology Department of Northern Adelaide Local Health Network, who together form a large, multidisciplinary collaborative group that prioritises interdisciplinary input to the development of clinically relevant solutions for the treatment of vascular disease.

The group is arranged around 3 themes:

- **Translational Vascular Molecular Physiology**
- **Translational Vascular Clinical Physiology**
- **South Australian Cardiovascular Outcomes Registry (SACOR)**

TRANSLATIONAL VASCULAR MOLECULAR PHYSIOLOGY

The Molecular Physiology group focuses on the pathophysiology and molecular signalling of vascular disorders including coronary artery spasm, coronary microvascular disorders and reperfusion injury. Laboratory studies include the assessment of isolated human vessel function using myography, followed by a series of biomolecular assays aimed to provide a mechanistic understanding of the disorders and thus direct the translation to improvements in medical therapy.

RESEARCH HIGHLIGHT OF 2021

We have pioneered an endothelial biopsy technique which isolates endothelial cells from the linings of human arteries during routine coronary angiography with no harm to the patient. This technique has enabled us to study the molecular and genetic basis of vascular dysfunction and cardiovascular disease and to establish an endothelial cell biobank from over 300 patients. This research infrastructure has demonstrated that there is a real potential for capture of biological data for personalised medicine. In particular, this biobank has been used to improve our understanding of zinc and its role in vascular disease, as detailed in the report from the [▶ **Zinc and Cardiovascular Disease Research Group**] The details of this biobank were published in June 2021 in the high impact factor *Journal of American College of Cardiology*.

Zalewski PD, Tvorogova Z, Abdo A, Wawer AA, Hodge S, Murgia C, Tavella R, Psaltis P, Zeitz CJ, Beltrame JF. Harvesting Endothelial Cells During Routine Invasive Coronary Procedures. *JACC* 2021, **77**(24): 3136-3138.
▶ **https://pubmed.ncbi.nlm.nih.gov/34140112/**

TRANSLATIONAL VASCULAR CLINICAL PHYSIOLOGY

The Clinical Physiology research team uses invasive and non-invasive techniques to identify the presence of vascular dysfunction in patients with vascular symptoms including angina (chest pain due to insufficient blood supply to the heart) and intermittent claudication (pain and/or cramping in the lower leg due to inadequate blood flow to the muscles). Techniques include the assessment of coronary artery spasm, coronary blood flow, cardiac magnetic resonance imaging, subcutaneous blood flow and endothelial function.

THIS COMPREHENSIVE ANALYSIS SHOWED THAT MINOCA PATIENTS HAVE A MUCH HIGHER RISK OF MORTALITY AND RE-INFARCTION...

RESEARCH HIGHLIGHT OF 2021

Myocardial infarction (MI) or heart attack is typically associated with 'cholesterol blockages' in coronary artery disease (CAD) that can be treated with stents or surgery. One in 10 heart attack presentations, however, do not show CAD, causing confusion for clinicians and patients, as the cause of the heart attack is not clear. In these patients, coronary vasomotion disorders may explain their heart attack. Coronary vasomotor disorders involve the spasm of the large vessels or dysfunction in the coronary microvessels within the heart that in turn leads to restricted blood flow and heart muscle damage. Our pioneering work has coined the term MINOCA (Myocardial Infarction with Non-Obstructive Coronary Arteries) to bring attention to these patients, who have previously been ignored or mis-diagnosed.

Although patients with MINOCA are considered to experience better outcomes than patients who present with a 'traditional' heart attack (MI with CAD or MI-CAD), it is not clear if MINOCA patients have similar outcomes to a normal, healthy population. With the growth of recent literature in MINOCA prognosis, we performed an in-depth analysis of MINOCA prognosis, in relation to 1-year all-cause mortality and 1-year re-infarction compared with MI-CAD patients and a healthy cohort. This comprehensive analysis showed that MINOCA patients have a much higher risk of mortality and re-infarction over time compared to a healthy population, but the risk is lower than for MI-CAD patients.

This global data collaboration based at the BHI and led by post-doctoral researcher Dr Sivabaskari Pausapthy, pooled data from multiple countries including Sweden, Denmark, Canada, New Zealand, Italy, USA and Australia and generated the largest MINOCA database to date. In 2021, this work was published in Circulation: Cardiovascular Quality and Outcomes, a journal of American Heart Association[1] and built on previous work undertaken by Dr Pasupathy during her PhD studies at the BHI.

1. Pasupathy S, Lindahl B, Litwin P, Tavella R, Williams MJA, Air T, Zeitz C, Smilowitz NR, Reynolds HR, Eggers KM, Nordenskjöld AM, Barr B, Jernberg T, Marfella R, Bainey K, Alzuhairi KS, Johnston N, Kerr A, Beltrame JF. Survival in Patients With Suspected Myocardial Infarction With Nonobstructive Coronary Arteries: A Comprehensive Systematic Review and Meta-Analysis From the MINOCA Global Collaboration. *Circ Cardiovasc Qual Outcomes* 2021, **14**(11): e007880.
▶ **https://pubmed.ncbi.nlm.nih.gov/34784229/**

TRANSLATIONAL VASCULAR CLINICAL PHYSIOLOGY

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SOUTH AUSTRALIAN CARDIOVASCULAR OUTCOMES REGISTRY (SACOR)

The SACOR group is focused on health service delivery and patient health outcome improvement through healthcare quality assessment and evaluation of the health status of patients including symptoms, physical limitations and quality of life. Consistent with the changing environment in medicine, this group adopts a 'patient-orientated' approach to the delivery of health care by evaluating patient health status and quality of care delivered.

The group has developed large databases and clinical quality registries from patients with coronary artery disease, microvascular disease, coronary spasm and peripheral artery disease. Most of these databases have international links thereby providing collaborative opportunities.

DID THE FACT OF THE PANDEMIC, SOCIAL ISOLATION AND PHYSICAL DISTANCING IMPACT ACCESS AND USE OF HEALTH CARE SERVICES?

RESEARCH HIGHLIGHT OF 2021

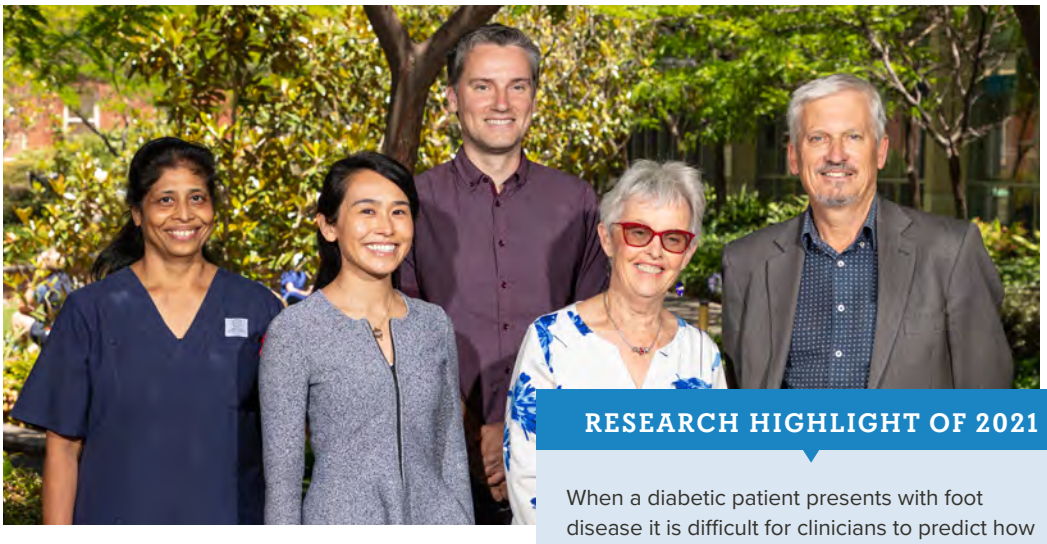
Data and analytics to monitor health services and health outcomes during the COVID-19 pandemic has become a major focus worldwide. The question raised is 'Did the fact of the pandemic, social isolation and physical distancing impact access and use of health care services?' International data has demonstrated that there was a fall in heart attack presentations during the onset of the pandemic, raising concern as to whether patients were afraid to present to hospital with their heart attack symptoms. To understand the impact of COVID-19 in SA, we performed analyses using various data sources in South Australia, including the CADOSA Registry (a large database of patients undergoing coronary angiography in SA), the SA Pathology database (including all public hospital pathology testing), and the SA Emergency Department Presentations database.

Our analyses focused on the 2020 period when we were faced with border closures and lockdowns (late January to April) and compared it to health services activity during the same period in 2019. Our data showed that the incidence of heart attack presentations in SA was essentially unchanged during COVID-19, despite a 10% fall in chest presentations following the onset of the pandemic. To understand this further, the SA Pathology data showed a decrease in the total number of troponin pathology tests (troponin is a specific protein found in the heart muscles and during a heart attack troponin is sent into the bloodstream), and in particular, fewer troponin tests conducted in the older population. The pathology data analysis also showed that troponin test results (the percentage positive or negative for heart attack) did not differ between the 2020 and 2019 time periods.

This data suggests the COVID-19 restrictions had an impact on the use of pathology testing, although the incidence of heart diagnosis remained stable. Further analyses are needed to investigate the long term of effect on patient health outcomes as a result of the COVID-19 restrictions. Some data from these analyses was published in the Internal Medical Journal in August 2021,[1] bringing attention to Australia's response during the COVID-19 pandemic.

1. Gillam MH, Roughead E, Tavella R, Dodd T, Beltrame JF, Ryan R, O'Loughlin P. Impact of COVID-19 restrictions on pathology service utilisation. *Intern Med J*. 2022, **52**(1):44-48. [ePub Aug 2021]
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34432345/**

Vascular Surgery Research Group



The Vascular Surgery Research Group is affiliated with CALHN Vascular and Endovascular Services and operates across The Queen Elizabeth Hospital and Royal Adelaide Hospital precincts.

We are studying outcomes of diabetic foot ulcers to identify factors critical in determining the need for amputation and factors associated with wound healing, leading to better treatment decisions and outcomes. We study diabetes-related foot disease (DFD) in Aboriginal populations where the burden of disease is particularly high. New initiatives in telehealth and virtual reality are being developed to improve the treatment and outcomes of DFD in rural and remote communities.

2021 research

- Our group has collaborated with Cathy Loughry (Podiatry, RAH) and the SAHMRI Aboriginal Chronic Disease Consortium to develop the South Australian Diabetic Foot Telehealth service, which aims to provide best practice advice and care to affected patients in rural and remote locations, particularly Aboriginal patients.
- A multi-centre collaboration, between this group and two other major centres with an interest in DFD (Perth, Australia and Hamilton, NZ), continues to assess factors influencing outcomes of DFD and to validate the ability of a new arterial classification system, developed as part of the Global Guidelines for Chronic Limb-threatening Ischaemia, to predict success of endovascular revascularisation and limb preservation at 12 and 24 months. Patient recruitment and follow up will continue in 2022.
- In collaboration with researchers at SAHMRI and the University of South Australia, we have begun to collect and store diabetic foot wound data and biopsies, as well as patient blood samples, creating a diabetic foot wound biobank. One future use of this material will be to identify characteristics of these wounds (biomarkers) that predict wound healing.
- Professor Fitridge was Principal Investigator on a successful grant from the Commonwealth of Australia, with development now underway for a Virtual Reality training program for community health workers to assess, manage, and triage diabetes-related foot disease in Aboriginal people living in rural and remote communities.

RESEARCH HIGHLIGHT OF 2021

When a diabetic patient presents with foot disease it is difficult for clinicians to predict how the disease will progress and the treatment options that should be considered. In 2021 we published a significant paper, in the European Journal of Vascular and Endovascular Surgery, a prestigious vascular surgery journal, that addressed this issue.[1]

The study, led by PhD student and Vascular Surgical Trainee Dr Guilherme Pena, followed 153 patients with Diabetes-related Foot Disease (DFD) for 12 months, documenting clinical indicators and outcomes. This prospective study showed that the WIfI classification system, a classification system used to assess the severity of disease, predicted one-year key clinical outcomes in a diabetic population with foot ulcers.

Patients with WIfI stage 4 disease had a disproportionally higher risk of major amputation compared with other stages. Our study also found that diabetic patients with foot ulcers *and* low grip strength, as measured by the Fried phenotype criteria, were 50% less likely to have their wounds heal within one year compared with those with adequate grip strength. This link between frailty and poor outcomes has not previously been reported. Defining important prognostic factors associated with diabetic foot disease might help to identify targets for more aggressive intervention.

1. Pena G, Kuang B, Edwards S, Cowled P, Dawson J, Fitridge R. Factors Associated with Key Outcomes in Diabetes Related Foot Disease: A Prospective Observational Study. *Eur J Vasc Endovasc Surg* 2021, **62**(2):233-240.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34024706/**

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Zinc and Cardiovascular Disease Research Group

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The Zinc and Cardiovascular Disease Research Group investigate the role of the major dietary metal, zinc, in the blood vessels and in vascular diseases.

Our work will enable us to directly relate blood vessel zinc levels and zinc transporter expression with blood vessel dysfunction, inflammation, vasoconstriction, cigarette smoking and small and large artery disease in humans. It will provide the rationale for zinc interventional clinical trials.

2021 research

Our Zinc and Cardiovascular studies were presented by Dr Zalewski at the Oceania and Asia Regional Meeting of the International Society for Zinc Biology (ISZB) in July 2021 and the Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand (CSANZ) in August 2021. In addition, our NHMRC Ideas Grant Application based on these studies fell just short of funding in the recent funding round.

OUR ANALYSIS HAS SHOWN THAT WHEN LEVELS OF Zn IN THE BLOOD VESSEL LININGS ARE LOW, AS OCCURS IN MULTIPLE CARDIAC DISEASE RISK FACTORS, THERE IS INCREASED INFLAMMATION.

RESEARCH HIGHLIGHT OF 2021

In 2021, we completed the first Australian study of zinc biomarkers in 400 South Australian cardiac patients. In this study we used samples from a unique endothelial biobank we have created that stores tissue taken from the lining of the blood vessels (the endothelium) of over 300 patients. The techniques used to gain these samples was published in the Journal of American College of Cardiology.[1]

We know that as many as one in every two patients with chronic chest pain have recurrences that are not amenable to standard therapies, such as stenting and bypass surgery. Novel therapies are being trialled that target other aspects of the coronary (heart) circulation that may be responsible for the chest pain such as spasm and inflammation of coronary blood vessels. The lining of these blood vessels (the endothelium), produces substances that influence the development of spasm and inflammation. Nitric oxide is released by the endothelium and has long been recognised to influence the occurrence of vascular spasm via the production of cGMP. Novel therapies that target this pathway may provide incremental benefits and improve clinical outcomes.

Our analysis of zinc biomarkers in the endothelium of blood vessels has led us to propose a new way of thinking about nitric oxide signalling in cardiovascular disease, mediated through dynamic pools of zinc. The nitric oxide pathway triggers a second signalling pathway that results in a rise in labile zinc, a pathway that our preliminary data suggests protects against vascular inflammation.

Our analysis has shown that when levels of Zn in the blood vessel linings are low, as occurs in multiple cardiac disease risk factors, there is increased inflammation. Future strategies in treatment will target components of this zinc-mediated pathway and help maintain healthy vascular levels of zinc. The new data we have generated, and the new way of thinking it has provoked, provides the rationale for zinc interventional clinical trials whereby zinc supplementation will be assessed for its role in improving cardiovascular disease symptoms.

1. Zalewski PD, Tvorogova Z, Abdo A, Wawer AA, Hodge S, Murgia C, Tavella R, Psaltis P, Zeitz CJ, Beltrame JF. Harvesting Endothelial Cells During Routine Invasive Coronary Procedures. *JACC* 2021, **77**(24): 3136-3138.
▶ **https://pubmed.ncbi.nlm.nih.gov/34140112**

CHRONIC DISEASE

RESEARCH GROUPS

Clinical Pharmacology Research Group

Endocrinology Unit

Stroke Research Programme

Clinical Pharmacology Research Group

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The Clinical Pharmacology Research Group aims to improve the effectiveness and safety of medicines used to prevent rejection following kidney transplantation. These immunosuppressant medicines must be used with careful monitoring as too much immunosuppression can cause adverse side effects, whilst too little can lead to rejection of the new kidney. Monitoring immunosuppressant blood levels allows transplant physicians to tailor doses for each transplant patient to minimise both the risk of rejection and adverse effects.

2021 research

- Most of the tacrolimus in blood is inside the red cells and is not available to enter the immune cells (to stop rejection) or the kidneys (where it can cause damage). Only tacrolimus that is free in plasma (collected after centrifuging the blood to remove the red cells) is considered pharmacologically active. Our clinical studies in kidney transplantation suggest that large changes in red blood cell numbers occur following transplantation, and that using blood tacrolimus levels (levels in the cells and plasma combined) may not reliably predict pharmacologically active tacrolimus.
- Our PhD student, Ms Mirabel Alonge, has been investigating ways to monitor tacrolimus dosage more effectively from blood samples by determining if monitoring tacrolimus in plasma can improve individual dosage regimes and better prevent rejection and tacrolimus toxicity. She has shown there is a poor relationship between tacrolimus levels measured in the blood and the plasma. A comparison of patients with similar plasma tacrolimus levels detected differences in whole tacrolimus levels and showed that blood measurements reflected red cell number rather than plasma levels. Adjusting doses based on blood tacrolimus levels may result in tacrolimus in the plasma above or below the therapeutic range. In her study Mirabel identified transplant patients with low blood levels of tacrolimus but high plasma levels of tacrolimus in whom a dosage increase could potentially increase the risk of toxicity without being necessary to prevent rejection. Ms Alonge was awarded the Adelaide Medical School – Department of Medical Sciences Prize at the 2021 Florey Postgraduate Research Conference and was also a finalist for the Percy Prize for best PhD poster presentation at the 2021 Scientific Meeting of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists.

▸ See also Clinical Pharmacology Research Group - Cancer

RESEARCH HIGHLIGHT OF 2021

Even with careful monitoring of patients after kidney transplantation rejection and immunosuppressant toxicity can occur. Our laboratory is investigating new monitoring methods to better predict organ rejection and adverse effects, and tailor the doses of immunosuppressant medicines given to improve the health of the patient and their transplanted kidney.

In 2021 we completed the last of a series of clinical studies, funded by the National Health and Medical Research Council (NHMRC), investigating whether differences in the genes that determine the distribution and elimination of immunosuppressants in the body can affect immunosuppressant levels in the blood and transplanted kidney. We focussed on the immunosuppressant tacrolimus which, although essential for preventing rejection, can also damage the newly transplanted kidney.

Using highly sensitive mass spectrometry we measured tacrolimus levels in tiny pieces of kidney biopsy tissue taken during routine clinical care of transplant recipients. We showed there was only a modest correlation between tacrolimus levels in blood and tacrolimus levels in the transplanted kidney. This is important as the dose of tacrolimus given is currently based on levels of the drug in the blood, meaning that many patients may have too much drug within the transplanted kidney, leading to poor outcomes. Our data also revealed that the relationship between kidney and blood tacrolimus levels appeared to be different in patients with kidney damage caused by tacrolimus. Comparison of data from patients with the same blood tacrolimus levels showed that patients with kidney damage had higher tacrolimus levels within the transplanted kidney.

Finally, whilst genetic variability explained differences in blood tacrolimus levels between patients, it did not explain the difference in tacrolimus exposure of the transplanted kidneys. With future research, it may be possible to use early biopsy samples to measure tacrolimus within the transplanted kidney to better identify patients at greatest risk of developing kidney damage. We published the results from this study, the first to describe the relationship between blood and kidney concentrations of tacrolimus, in 2021.

Sallustio BC, Noll BD, Hu R, Barratt DT, Tuke J, Coller JK, Russ GR and Somogyi AA. Clinical factors, but not CYP3A5/ABCB1 genetics, are determinants of the relationship between blood and allograft tacrolimus concentrations in renal transplant recipients. *Br J Clin Pharmacol* 2021, **87**(10):3901-3909.
▸ **https://pubmed.ncbi.nlm.nih.gov/33646566/**

Endocrinology Unit

The Endocrinology Unit at TQEH, CALHN, focuses research in areas relating to diabetes treatment and care in all members of the Australian population, including Aboriginal populations, and people with osteoporosis. The aim is to gain clinical endocrine knowledge through clinical studies and other research. We conduct translational research and patient quality improvement studies to improve patient care.

2021 research

- Dr Lucy Gagliardi continued working with her international collaborations to elucidate the molecular mechanisms by which mutations in armadillo repeat containing 5 (ARMC5) drive adrenal tumorigenesis, and to identify new ARMC5 mutations.

THE AIM OF THIS RESEARCH IS TO DEVELOP PATIENT CARE GUIDELINES AND DRUG MANAGEMENT PROTOCOLS THAT MINIMISE THE RISK OF DKA IN DIABETIC SURGERY PATIENTS TAKING SGLT2i.

RESEARCH HIGHLIGHT OF 2021

The Endocrinology Unit has been shown previously that drugs used to control diabetes, the sodium-glucose co-transporter-2 inhibitors (SGLT2i), can cause life-threatening euglycaemic diabetic ketoacidosis (eDKA; diabetic ketoacidiosis without changes in blood sugar levels) in patients around the time of surgery. This world-leading research has changed Australian guidelines on the safe use of SGLT2i and led to further research to understand the mechanisms behind the development of eDKA in diabetic surgical patients.

Drs David Jesudason and Emily Meyer have expanded this focus of their study to quantify the small but critical risk of diabetic ketoacidosis (DKA; with changes to blood sugar levels) for peri-operative patients. A research group has been formed to explore why some patients develop DKA around the time of surgery, and measuring the relationships between DKA, the choice of SGLT2i, plasma drug levels, patient factors and other precipitating factors. We will use this data to develop a model that predicts the development of DKA in patients. The aim of this research is to develop patient care guidelines and drug management protocols that minimise the risk of DKA in diabetic surgery patients taking SGLT2i. This work is supported by a research grant from The Hospital Research Foundation Group and Diabetes SA.

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Stroke Research Programme

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Our research group investigates genetic, protein and lipid factors that affect the risk of stroke and Transient Ischaemic Attack (TIA), an early marker of stroke that impacts the progress of stroke.

Through TQEH and RAH, our Stroke Research Programme links internationally for stroke-related research on genetic investigations via collaborations with the International Stroke Genetics Collaborative and the Australian Stroke Genetics Collaborative. This includes investigating cellular and molecular therapeutic applications of adult stem cells to repair the brain after stroke. We are also investigating the effect of dog-visiting to the Stroke Unit at the RAH, to see if there is a change in the mood of patients, formal and informal supports, as well as monitoring the effect on the dog, in an Action Research project 'DOgSS' – Dogs Offering Support after Stroke.

2021 research

- TIA may be a warning sign for stroke but is difficult to diagnose without expensive and time-consuming imaging tests. We have an ongoing program, the FAST-IT study ('Find A Simple Test – In Transient Ischaemic Attack' (TIA)), to identify a panel of biomarkers that diagnose TIA and differentiates it from minor stroke and other TIA mimics such as migraine and seizures. The FAST-IT study will analyse the composition of the blood plasma of TIA patients, seeking to identify consistent changes in composition that correlate with TIA. The study will include the analysis of plasma proteins, lipids and oxidative stress markers as potential biomarkers. Our new doctoral student, Deeksha Sharma, is undertaking this potentially impactful research.
- Associate Professor Anne Hamilton-Bruce is leading the 'DOgSS' study – Dogs Offering Support after Stroke. DOgSS is designed to determine if dog visits make a difference to the expressed mood of stroke patients. The project will also monitor the dog's wellbeing. To be undertaken in the Royal Adelaide Hospital (RAH) Stroke Unit, this study will involve a multi-disciplinary research team that includes medical scientists, medical, nursing and allied health clinicians, academics from The University of Adelaide and University of South Australia, and the RAH volunteers. Dog-visits will be initiated early in 2022.
- In January 2021 Associate Professor Hamilton-Bruce became Director of the Stroke Research Programme on Professor Simon Koblar's retirement from The University of Adelaide. Professor Koblar remains an active member of the SRP in his capacity as an Emeritus Professor at Adelaide Medical School, The University of Adelaide.
- Dr Maria Gancheva was awarded a PhD for her research on investigating reprogramming factors and neural conditions to convert human dental pulp stem cells into neural stem cells.

RESEARCH HIGHLIGHT OF 2021

Stroke remains one of the leading causes of disease burden in Australia and across the globe, despite many clinical advances that have improved mortality and morbidity outcomes. Cell therapies (CTs) have long been proposed as potential therapeutics for stroke, and in preclinical stroke models and exploratory clinical studies CTs have been shown to improve neurovascular repair and reduce neuroinflammation. Despite promise, CTs are yet to be translated into clinical use in stroke. Instead, there is a long history of expensive translational failure of CTs for stroke. In part, this can be attributed to researchers in academia and industry not fully understanding the clinical development pathways that lead to clinical implementation of promising research.

To address this issue, we have undertaken a program of research identifying the key characteristics of the clinical development pathway for CTs and formulating a practical framework that will help accelerate research into viable cell therapeutic products. We used a mixed methodology approach to evaluate the impact of study design, regulatory policy, ethical and health economic considerations for efficient implementation of early phase CTs studies. This work culminated, in 2021, in the publication of the Clinical Translation of Cell Therapies in Stroke (CT2S) checklist.[1]

The checklist incorporates key parameters that can impact on the quality of execution of early-phase clinical CTs studies in stroke. The proposed checklist organises key considerations of clinical trial design into four domains critical to efficient operationalisation: study design, regulatory and economic considerations and patient involvement. Working through the checklist we believe will help research teams undertake state of the art clinical trials by guiding decision-making in the design phase of the trial, highlighting gaps in expertise and prompting the appropriate allocation resources to the different areas of the project.

1. Nagpal A, Milton AG, Koblar SA et al. Clinical Translation of Cell Therapies in Stroke (CT2S) Checklist—a pragmatic tool to accelerate development of cell therapy products. *Stem Cell Res Ther* 2021, **12**(1):93.
▶ **https://pubmed.ncbi.nlm.nih.gov/33514411/**

CLINICAL SCIENCES, HEALTH SERVICES AND POPULATION HEALTH

RESEARCH GROUPS

- Anaesthesia Research Group
- Intensive Care Medicine Research Group
- Oesophageal Physiology Group
- Psychiatry Research Group
- Respiratory Research Group
- Rheumatology Research Group
- Surgical Science Research Group

Anaesthesia Research Group

GROUP MEMBERS

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The Anaesthesia Research Group is linked to Critical Care & Perioperative Services: Anaesthesia at TQEH. The primary research interests of our group are:

- **To enhance the surgical outcome of patients with type 2 diabetes, especially those who are prescribed a new class of medications called Gliflozins**
- **To implement a strategy to minimise preoperative opioid use and long-term opioid use after surgery**
- **To explore the application of ultrasound guided nerve blocks for postoperative pain relief and reduction in opioid use;**
- **Applications of high flow nasal oxygen for airway management and procedural sedation**
- **To assess the pattern and diagnostic utility of various tests for severe hypersensitivity reactions/anaphylaxis during anaesthesia**
- **To validate the diagnostic tools to screen sleep apnoea in patients presenting for surgery.**

2021 research

- Our group was successful in conducting a randomised control trial exploring pain management of a newly introduced regional nerve block technique, termed erector spinae block. The trial assessed acute pain outcomes in patients who presented for laparoscopic colorectal surgeries. It involved comparing the new block versus local anaesthetic infiltration into the laparoscopic ports and muscle layers.[1]

1. Rao Kadam V, Ludbrook G, van Wijk RM, Hewett P, Thiruvenkatarajan V, Edwards S, Williams P, Adhikary S. A comparison of ultrasound guided bilateral single injection shot Erector Spinae Plane blocks versus wound infiltration for post-operative analgesia in laparoscopic assisted colonic surgery- a prospective randomised study. *BMC Anesthesiol* 2021, **21**(1):255.
▶ https://pubmed.ncbi.nlm.nih.gov/34702183/

RESEARCH HIGHLIGHT OF 2021

Patients who present for an advanced endoscopy procedure such as endoscopic retrograde cholangiopancreatography (ERCP) are usually elderly with plenty of other health problems (comorbid conditions). ERCP is a complex procedure that requires patients to be positioned in prone position (lying face down), and it is usually done outside the main operating room. ERCPs are commonly performed under deep sedation and due to the high prevalence of comorbid conditions and the prone position, the risk of oxygen desaturation (low blood oxygen) is increased in the elderly patient group.

Using a multicentre trial, our group showed that if a specific technique is used for administering sedation, along with combined nasal and oral oxygen administration, the risk of oxygen desaturation would be reduced. This trial was performed across 2 centres in Adelaide and a single centre at New South Wales. Despite limited assistance and restrictions in using certain oxygen delivery devices during the early COVID-19 pandemic, we were successful in completing this trial. This was published in one of our high impact journals *Anaesthesia*.[1]

1. Thiruvenkatarajan V, Dharmalingam A, Arenas G, Wahba M, Liu WM, Zaw Y, Steiner R, Tran A, Currie J, collaborators. Effect of high-flow vs. low-flow nasal plus mouthguard oxygen therapy on hypoxaemia during sedation: a multicentre randomised controlled trial. *Anaesthesia* 2022, **77**(1):46-53. [Epub Jun 2021]
▶ https://pubmed.ncbi.nlm.nih.gov/34182603/

THE TRIAL ASSESSED ACUTE PAIN OUTCOMES IN PATIENTS WHO PRESENTED FOR LAPAROSCOPIC COLORECTAL SURGERIES.


CELEBRATING 60 YEARS OF TQEH RESEARCH
60 YEARS
TQEH RESEARCH
30 YEARS
TQEH RESEARCH EXPO

Intensive Care Medicine Research Group

The Queen Elizabeth Hospital Department of Intensive Care Medicine participates in, and conducts, research aimed at improving patient outcomes, particularly in the areas of sepsis and nutrition.

We seek to answer pragmatic, relevant clinical questions that are of importance to the ICU clinicians who provide patient care, and deliver more efficient and effective treatments; treatments that will not only benefit critically ill patients but also decrease costs, preserve resources and increase access to scarce critical care beds. We are also dedicated to ensuring timely and appropriate interventions for ward-based patients whose health is deteriorating, promoting safety and preventing escalation of their care and increased use of hospital resources.

SINCE THE START OF THE COVID-19 PANDEMIC, THE REMAP-CAP TRIAL HAS BEEN PIVOTAL IN THE INTERNATIONAL RESPONSE...

RESEARCH HIGHLIGHT OF 2021

The Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia is a global trial that evaluates multiple treatment options simultaneously and efficiently to ensure patients receive treatments that are most likely to be effective for them (The REMAP-CAP Study. Rationale and Design: ▸ https://pubmed.ncbi.nlm.nih.gov/32267771/). Professor Sandra Peake is a member of the REMAP-CAP Australian Regional Management Committee and TQEH ICU is South Australia's only participating site. Following the 2009 "Swine Flu" pandemic, the study investigators modified the trial to include the ability to adapt to evaluate the most relevant treatment options and generate time-critical clinical evidence to improve patient outcomes during a global pandemic, such as the world is presently experiencing.

Since the start of the COVID-19 pandemic, the REMAP-CAP trial has been pivotal in the international response, generating quality evidence relating to the most effective treatment options for critically ill patients and contributing to changes in international practices. To date nearly 9,000 patients have been randomised into the COVID-19 REMAP-CAP platform in 340 sites globally. The results of the REMAP-CAP trials complement Professor Peake's participation in the National COVID-19 Clinical Evidence Taskforce, which provides a living systematic review with weekly updated guidelines for the treatment of patients with COVID.

▸ https://covid19evidence.net.au/

The following were published in 2021 in high quality peer reviewed journals by REMAP-CAP in response to the COVID-19 pandemic:

Arabi YM et al. Lopinavir-ritonavir and hydroxychloroquine for critically ill patients with COVID-19: REMAP-CAP randomized controlled trial. *Intensive Care Med.* 2021 Aug;47(8):867-886.

ATTACC Investigators; ACTIV-4a Investigators; REMAP-CAP Investigators, Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. *N Engl J Med.* 2021 Aug 26;385(9):790-802.

REMAP-CAP Investigators; ACTIV-4a Investigators; ATTACC Investigators, Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19. *N Engl J Med.* 2021 Aug 26;385(9):777-789.

Writing Committee for the REMAP-CAP Investigators, Effect of Convalescent Plasma on Organ Support-Free Days in Critically Ill Patients With COVID-19: A Randomized Clinical Trial. *JAMA*. 2021 Nov 2;326(17):1690-1702.

REMAP-CAP Investigators, Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. *N Engl J Med.* 2021 Apr 22;384(16):1491-1502.

Tleyjeh IM, et al. Efficacy and safety of tocilizumab in COVID-19 patients: a living systematic review and meta-analysis, first update. *Clin Microbiol Infect.* 2021 Aug;27(8):1076-1082.

2021 research

- In 2021 the Australasian Resuscitation In Sepsis Evaluation: Fluid or Vasopressors in Emergency Department Sepsis (ARISE: Fluids) Trial commenced recruitment. This multicentre, randomised controlled trial will enrol 1000 patients presenting with septic shock to the emergency department (ED) of 56 participating hospitals in Australia and New Zealand. The trial is funded by an MRFF Research Grant (APP1200084, $2,335,540 over 5 years) held by Professor Sandra Peake (CIA) and colleagues, including Patricia Williams (AI).
- A crossover, cluster randomised controlled trial of Selective Decontamination of the Digestive Tract in Intensive Care Unit patients (SuDDICU) completed recruitment in Australia in 2021. The trial is one of the largest SDD trials ever conducted with more than 14,300 patients in the final database. Results of this trial will be published in 2022.
- Professor Sandra Peake and colleagues were awarded the following NHMRC funding in 2021:

  A Centre for Research Excellence to Transform Outcomes of Critically Ill Patients in ICU (CRE-ICU) C Hodgson, D Cooper, J Fraser, S Peake (CID), R Bellomo, P Macdonald, S Bernard, M Bailey, D McGiffin, A Higgins. (APP2006514) $2,500,000.

  Centre of Research Excellence - REduce the burden of antimicrobial reSistance through oPtimal, persONalised Dosing (RESPOND). J Roberts, M Slavin, D Paterson, T Comans, J Lipman, C Landersdorfer, G Joynt, R Bellomo, J Clark, S Parker, S Peake (AI). (APP2007007) $2,772,570.

  Low OxyGen Intervention for Cardiac Arrest injury Limitation trial (LOGICAL) C Hodgson CIA, R Bellomo, P Young, S Peake (CID), M Bailey, C McDonald, A Higgins, A Nichol, A Udy, A Deane (APP 2001237) $2,314,403.

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Jeff Lipman (BLING III study)
Bala Venkatesh (Vascular responsiveness in Septic Shock)
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Oesophageal Physiology Group

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The Oesophageal Physiology Group explores abnormalities of swallowing function (known as oesophageal motility) that impact the enjoyment of meals with swallowing discomfort; and gastric reflux, often associated with heartburn and regurgitation.

Studies of swallow pressures and bolus flow are complex, yet reveal subtle variations, like the interplay between swallow muscle vigour and impaired food passage in those struggling to eat or drink. This clinical research will help us better manage patients undergoing surgery at TQEH Upper GI & Bariatric Surgery Unit for reflux disease, swallowing disorders or obesity.

2021 research

- Difficulty swallowing (dysphagia) is an unwanted adverse effect of anti-reflux surgery. In unique exploratory research, Dr Siang Wei Gan assessed anatomical features after surgery using barium swallows (radiological images of swallowing). He found that of 11 measures, 2 showed anatomical features, specifically the anterior displacement of stomach entry point (pushed forward) and the angulation of the oesophagus-stomach junction, that correlated with swallowing difficulty.
- The 4th international guideline for oesophageal motility disorders (Chicago classification 4.0), evaluates swallowing function of liquids and solids, while lying and sitting. In April 2021, invited chair and presenter, Dr Jennifer Myers, in conjunction with international colleagues from Zürich & St Louis, provided (via video link) a live demonstration of clinical acquisition and education on data interpretation.

RESEARCH HIGHLIGHT OF 2021

Detecting bile reflux after surgery for obesity

Bile, made in the liver and stored in the gallbladder, is essentially the body's 'detergent' and is released to aid the breakdown and digestion of food. After obesity surgery, altered anatomy to promote weight loss may inadvertently lead to bile reflux, with possible damage to the tissue lining the remaining stomach, gastric pouch or oesophagus.

In Australia and across the world, an increasingly overweight population are undergoing weight loss operations (bariatric surgery) and are at risk of bile reflux. The incidence of bile reflux, however, is unknown as it is difficult to measure after surgery. Dr Tom Eldredge, a PhD student, is taking up the challenge by evaluating patients after bariatric surgery (a gastric bypass, a gastric sleeve or a single anastomosis bypass) to find out the prevalence and impact of bile reflux.

In his research, Dr Eldredge used nuclear medicine imaging techniques tailored for these patients. He modified the procedure in 3 ways: first, by using biliary scanning along with 3D CT scan, to ensure the remaining anatomy could be seen clearly; next, by stimulating gallbladder emptying, by administering a fatty meal, and last, by lengthening the scan duration, to allow for slower bowel motility. Using the modified protocol, he was able to detect small amounts of bile reflux with a high degree of accuracy and reproducibility. He showed that low-volume bile reflux to the gastric pouch frequently occurred after single anastomosis bypass and gastric sleeve surgery, and sometimes occurred in the gastric remnant after gastric bypass surgery. Pre- and post-operative endoscopy was undertaken to examine any inflammation or tissue damage present before or after surgery. Importantly, Dr Eldredge showed that bile reflux was not associated with an increase in tissue damage or reflux symptoms, indicating that at 6 months after surgery, low level bile reflux is not a clinical problem.

This work was presented at the 2021 annual conference of the Australian & New Zealand Metabolic and Obesity Surgery Society. Dr Eldredge, who delivered an engaging presentation, was awarded the Young Investigator Award for best oral presentation.

Psychiatry Research Group

The Discipline of Psychiatry's research follows 6 main themes:

- **Personalised psychiatry and genomics of psychiatric disorders**
- **Psychiatric neuroscience and neuroimmunology of psychiatric disorders**
- **Neuropsychiatry and psychiatric and medical comorbidities**
- **Clinical phenotype research into the cognitive, emotional and behavioural underpinnings of psychiatric disorders**
- **The identification of electrophysiological markers of cognition and function in psychiatric disorders**
- **The conduct of clinical trials, including pharmacological, psychological and neurostimulation interventions. The conduct of clinical trials, including pharmacological, psychological and neurostimulation interventions.**

2021 research

- 4 publications in high impact journals linking genes to lithium response
- Leading a national study of the impact of long-acting injectable antipsychotic medication on daily function in schizophrenia.
- The translation of research on the side effects of the antipsychotic drug clozapine into policy to prevent adverse outcomes, focussing on increased risks with COVID-19 infection.

RESEARCH HIGHLIGHT OF 2021

Research is often most effectively achieved in collaboration, with multiple groups working together and bringing a diverse range of knowledge, approaches and technologies to a single problem. This year has seen the establishment of two large collaborative ventures that include our team.

The NHMRC Centre for Research Excellence (CRE) - PREdiction of Early Mental Disorder and Preventive Treatment (PRE-EMPT) was initiated in 2021. Led by Orygen and the University of Melbourne, PRE-EMPT brings together an international team of researchers and large multimodal datasets to focus on the development of more accurate models of psychosis prediction. These models will drive strategies for early intervention aimed at prevention and improved management of psychotic illness. The work of the CRE will build on prior work by our group in novel Bayesian, longitudinal and machine learning analyses.

Also in 2021, the local implementation of the National Institute of Mental Health (USA) - funded Prescient study (a project of AMP-Schizophrenia) was initiated. In partnership with Adelaide headspace, the Prescient trial will provide detailed clinical and biological assessments (imaging, electrophysiology, genomics and blood-based biomarkers, digital assessments of speech, facial expression, daily activity and symptoms) for youth at high risk of psychotic illness, following them for two years to observe outcomes.

Our role will build on our existing expertise and support us to collect a diverse set of novel multi-modal biomarkers in schizophrenia. As collaborators in these two, linked initiatives, the discipline is placed firmly at the forefront of efforts to understand the biological basis of psychotic illness.

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Respiratory Research Group

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The Respiratory Research Group is the research arm of The Queen Elizabeth Hospital's Respiratory Medicine Unit and is involved in running several sponsored Clinical Trials and Investigator-led projects.

The unit has research studies underway addressing knowledge and practice gaps for prevalent respiratory conditions, including chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, sleep apnoea and non-invasive ventilation, pneumonia, respiratory failure, intervention pulmonology, smoking and Indigenous Health.

2021 research

Karen Royals, Registered Nurse and Midwife, from Respiratory Nursing, was the winner 2020/21 South Australian Nursing and Midwifery Award- Excellence in Research and Knowledge Translation.

▸ https://bit.ly/3tXfQj5

PRELIMINARY ANALYSIS SHOWS THERE IS A LINK BETWEEN ANXIETY CHANGES AND SMOKING CHANGES DURING RESTRICTIONS.

RESEARCH HIGHLIGHT OF 2021

- Karen Royals, as part of her PhD, undertook two investigations:
  - A feasibility collaboration between SA Ambulance Service and CALHN respiratory nurses to reduce COPD-related ED presentations. Recruitment has ceased and outcomes will be reported in 2022.
  - COPD outreach nursing to deliver home-based disease management: A systematic review. Preliminary analysis indicates that outreach nursing services had no effect on the number of hospitalisations, however, a positive impact is noted on quality of life. These outcomes were based on predominantly outdated studies which may not accurately reflect the current outreach nursing model.
- Karen Royals and Kathy Lawton, Respiratory Nursing, conducted an assessment on the efficiency of Telehealth in supporting existing clients with chronic respiratory disease. Telehealth was found to be a suitable tool to support and educate clients in their management of exacerbations and hospital avoidance.
- As of December 2021, Karen Royals is the acting member of TSANZ representation for the Lung Health Framework (National Strategy).
- Pamela Kidd, Pulmonary Function Laboratory, conducted a survey during the COVID-19 pandemic to gain a snapshot of how patients were coping with the pandemic restrictions and whether their smoking habits were impacted. Preliminary analysis shows there is a link between anxiety changes and smoking changes during restrictions. Full outcomes will be reported in 2022.
- Xiao-Hui Liu, Pulmonary Function Laboratory, is currently performing a study that aims to investigate the 6-minute Walk Distance (6MWD) reference range in COPD patients from local population, by following latest 2014 European Respiratory Society guidelines. The study will aid in updates of TQEH Pulmonary Function Laboratory 6-Minute Walk Test protocol and improve the quality of clinical interpretation. Data collection is due to be completed in 2022.

CELEBRATING 60 YEARS OF TQEH RESEARCH

60 YEARS TQEH RESEARCH

30 YEARS TQEH RESEARCH EXPO

Rheumatology Research Group

The Rheumatology Unit research program use clinical data and biological samples from clinical cohorts with autoimmune and chronic inflammatory diseases to investigate the epidemiology, causation, clinical outcomes, to develop new treatments, and new models of disease monitoring that incorporate patient reported outcome measures.

The group has expertise in population epidemiology, randomised clinical trials, qualitative research, biobanking, laboratory science and quality improvement. It is the South Australian hub of Australian Arthritis and Autoimmune Biobank (A3BC) and incorporates the South Australian Primary Sjogren's Syndrome Research Clinic and Database and South Australian Giant Cell Arteritis Registry.

RESEARCH HIGHLIGHT OF 2021

During 2021, the Rheumatology Unit has led a range of research to determine the impact of COVID-19 on people with rheumatic diseases. This has included leading collaborative research with the RAH Rheumatology Unit to determine impact of telehealth on rheumatology outpatients, as well as the impact of COVID-19 in a national sample of patients with inflammatory rheumatic diseases using the Australian Rheumatology Association Database. This work has provided unique insights into barriers to vaccination as we had data regarding vaccine hesitancy which was collected in January 2020 (prior to the pandemic) as well as in April 2021.

Catherine Hill has contributed to three publications emanating from the COVID-19 Global Rheumatology Alliance which highlighted the impact of COVID-19 on patient experience,[1] early vaccine experience[2] and effect of COVID-19 on systemic vasculitis.[3] Sam Whittle led the development of Australian Guidelines for COVID-19 vaccination for people with autoimmune inflammatory rheumatic diseases on immunomodulatory therapies.[4]

1. Hausmann JS, Kennedy K, Simard JF, ... Hill CL et al. Immediate effect of the COVID-19 pandemic on patient health, health-care use, and behaviours: results from an international survey of people with rheumatic diseases. *Lancet Rheumatol* 2021, 3(10):e707-e714.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34316727/**
2. Sattui SE, Liew JW, Kennedy K, Sirotich E, Putman M, Moni TT, Akpabio A, Alpízar-Rodríguez D, Berenbaum F, Bulina I, Conway R, Singh AD, Duff E, Durrant KL, Gheita TA, Hill CL, et al. Early experience of COVID-19 vaccination in adults with systemic rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey. *RMD Open* 2021, 7(3):e001814.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34493645/**
3. Sattui SE, Conway R, Putman MS, Seet AM, Gianfrancesco MA, Beins K, Hill C, et al. Outcomes of COVID-19 in patients with primary systemic vasculitis or polymyalgia rheumatica from the COVID-19 Global Rheumatology Alliance physician registry: a retrospective cohort study. *Lancet Rheumatol* 2021, 3(12):e855-e864.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/34778843/**
4. Australian Rheumatology Association. Advice for GPs and other Health Professionals caring for patients with autoimmune inflammatory rheumatic diseases (AIRD) in the COVID-19 (Coronavirus) pandemic. 03 November 2021.
   ▶ **https://bit.ly/3HVPkwe**

THIS WORK HAS PROVIDED UNIQUE INSIGHTS INTO BARRIERS TO VACCINATION AS WE HAD DATA REGARDING VACCINE HESITANCY WHICH WAS COLLECTED IN JANUARY 2020.

2021 research

Publications:

- 41 peer reviewed publications in 2021

▸ See Publications

Grants awarded in 2021:

- NHMRC-NIHR Collaborative Research Grants: "Steroid-Reducing Options for ReLapsING PMR (STERLING-PMR): a pragmatic, randomised trial to compare the clinical and cost-effectiveness of adding immunosuppression to steroid-tapering treatment for patients with relapsing PMR" APP 2006408 $823,322. Catherine Hill Chief Investigator CIA.
- NHMRC Centres of Research Excellence "CRE for Better Outcomes in Inflammatory Arthritis (IA)" APP2006579 $2,500,000. Catherine Hill Chief Investigator.
- MRFF Preventive and Public Health Research Initiative Healthy Choices: "Co-designed community programs to enhance healthy lifestyle choices for people with chronic conditions". MRF1200276. $780,670. Catherine Hill Chief Investigator.
- MRFF 2020 Efficient Use of Existing Medicines: Cost-Utility Comparison of Down-Titration Strategies for Safer and More Efficient Use of Biologics in Adults with Rheumatoid Arthritis and Psoriatic Arthritis. $2,720,942.80. Sam Whittle Chief Investigator. Catherine Hill Associate Investigator.

Awards:

- Dr Madeleine Bryant: Best mini-oral presentation at TQEH Research Expo, October 2021.
- Dr Oscar Russell: Best clinical presentation at the South Australian Rheumatology Association conference, October 2021.

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OMERACT Polymyalgia Rheumatica (PMR) Working Group

OMERACT Remission in RA-patient perspective Working Group

OMERACT Glucocorticoid Adverse Events Working Group

OMERACT Sjogren's Disease Working Group

Australian Scleroderma Interest Group (ASIG)

Australian Arthritis & Autoimmune Biobank Collaborative (A3BC)

Surgical Science Research Group

The Surgical Science Research Group is a large, multidisciplinary group focussed on clinical research, health service innovation and translational benchtop to bedside medicine in the surgical setting.

...WITH SUPPORT FROM EXPERIENCED RESEARCHERS, MEDICAL SCHOOL STUDENTS CAN ESTABLISH A BASE OF CORE RESEARCH SKILLS, UNDERTAKE RELEVANT AND NEEDED RESEARCH, AND PUBLISH WIDELY IN CRITICALLY ACCLAIMED JOURNALS.

RESEARCH HIGHLIGHT OF 2021

The BHI plays a central role in Adelaide in training the clinical researchers of the future, and over half of the institute's research trainees are clinically-trained/in clinical training or allied health professionals.

Dr Joshua Kovoor MBBS joined the Surgical Science Research Group in 2020 as an Honours student while in his fifth year of the University of Adelaide medical degree. In 2021 Dr Kovoor continued his research education with the group, and successfully completed his final year of medicine, concurrently commenced his PhD studies (part-time), published sixteen peer-reviewed manuscripts (thirteen as first author), and a further 4 published abstracts. From his research studies Joshua has 27 publications, with over 90 citations (an indication of research impact). His increasingly wide range of expertise is reflected in the topics of his publications – he has contributed to work on COVID-19 and evidence-based practice, patient education, emergency neurosurgery, pancreatoduodenectomy, gastrointestinal recovery after surgery, telehealth, smart technology, and early career researchers. These manuscripts have been published in high-quality surgical journals such as *British Journal of Surgery, Surgery*, *World Journal of Surgery* and *ANZ Journal of Surgery*. In addition to this, Dr Kovoor won Best Oral Presentation in the Junior Clinical Research category at the 30th TQEH Research Expo.

Dr Kovoor is a wonderful example of an emerging surgeon-scientist. His record shows that with support from experienced researchers, medical school students can establish a base of core research skills, undertake relevant and needed research, and publish widely in critically acclaimed journals.

2021 research

- PhD students Celine Li and Bimala Dhakal presented at the 30th TQEH Research Expo and at the Australian and New Zealand Society for Immunology 2021 Adelaide Immunology Retreat. Celine was awarded the Best Oral Presentation in the Junior Laboratory Research at TQEH Research Expo.
- Bimala Dhakal was selected to present her PhD research at the Adelaide Pharmacology Group Annual Meeting.
- Dr Markus Trochsler designed and wrote a protocol to allow patients with curative gastric cancer to be administered one dose of intraperitoneal chemotherapy with the aim of preventing metastatic disease.[1] We are the first centre in the Southern Hemisphere to offer this procedure.
- In 2021 Professor Guy Maddern was made an Honorary Fellow of the American College of Surgeons (the second SA recipient in the award's 108-year history) and was awarded the inaugural BHI Excellence in Research Leadership award in recognition of his visionary research leadership of the BHI, TQEH.

1. Reid J, Kanhere H, Hewett P, Price T, Maddern G, Trochsler M. Can pressurised intraperitoneal aerosol chemotherapy with oxaliplatin (PIPAC-O+) be added to standard treatment for resectable high-risk gastric cancer patients? A study protocol. *Pleura Peritoneum* 2021, **17**(6):151-154.
▶ **https://pubmed.ncbi.nlm.nih.gov/35071735/**

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CELEBRATING THE 30TH TQEH RESEARCH EXPO

60 YEARS TQEH RESEARCH

30 YEARS TQEH RESEARCH EXPO

RESEARCH GROUPS

Therapeutics Research Centre

Viral Immunology Group

DRUG AND VACCINE DEVELOPMENT

Therapeutics Research Centre

In the Therapeutics Research Centre (University of South Australia) we study ways in which drugs and medicines interact with the body, particularly when applied to the skin. We investigate what the fate of drugs and medicines are after they are applied to skin, determining if they transverse the skin and enter the body, where they go and how the body breaks them down for elimination.

We also help in the management of adverse effects associated with medicines and other poisons using state-of-the art analytical, product characterisation, imaging and mathematical modelling approaches. Our findings are then used to improve patient outcomes and assist regulators in guiding future product development requirements.

RESEARCH HIGHLIGHT OF 2021

The Therapeutics Research Centre Director, Professor Michael Roberts (Mike) was recognised by the Web of Science as a highly cited researcher in his field of Pharmacology/Toxicology, ie. in the top 1% in the world for his discipline in 2021. This was an extremely prestigious recognition of Mike's scientific contributions throughout his career with > 803 articles, 31,309 citations and an H-Index of 90 (Google Scholar), including 10 research books, 1 textbook, 571 papers, 75 book chapters, 12 major reports and 10 patents/patent applications as of 2021. We look forward to continued productivity in 2022.

2021 research

- There are concerns raised about the safety of zinc oxide nanoparticle sunscreens applied to the skin in various products. Using a naturally occurring zinc isotope, ^{67}Zn we provided strong evidence that the nanoparticular form of zinc oxide sunscreens is safe after topical application to intact human skin. This work was showcased on the front cover of *International Journal of Molecular Science*[1] and supports the recent FDA proposal for sunscreen marketing that only two of the 16 currently marketed sunscreens, zinc oxide and titanium dioxide, can generally be regarded as safe and effective.
- Our review on topical drug delivery covering the history, the localised transport across the skin and the clearance to other sites within the body was published in the prestigious journal *Advanced Drug Delivery Reviews*[2] (ranked 4th of 275 Journals in Pharmacology & Pharmacy). This review is particularly relevant as there is increasing regulatory interest in understanding topical product delivery behaviour under 'in use' conditions and being able to predict *in vivo* responses that account for population variations in skin barrier function. This review was well-received and resulted in an invitation to submit a further manuscript.
- Our FDA funding (administered through the University of South Australia) that supports our analysis of topical drug delivery systems (FDA Award U01FD006700: Sensorial and Functional Characteristics of Topical Formulations and FDA Award 1U01FD006496: Bioequivalence of Topical Products: Elucidating the Thermodynamic and Functional Characteristics of Compositionally Different Topical Formulations) was renewed.
- Gearing up for the future, our analytical capabilities were further enhanced to next generation with an upgrade to the LC-MSMS to top of the range, Shimadzu 8060 courtesy of an equipment grant from The Hospital Research Foundation Group, and a complete revamp of our analytical team strengthening our capabilities.

1. Khabir Z, Holmes AM, Lai Y-J, Liang L, Deva A, Polikarpov MA, Roberts MS, Zvyagin AV. Human Epidermal Zinc Concentrations after Topical Application of ZnO Nanoparticles in Sunscreens. *Int J Mol Sci* 2021, **22**(22):12372.
▶ https://pubmed.ncbi.nlm.nih.gov/34830253/

2. Roberts MS, Cheruvu HS, Mangion SE, Alinaghi A, Benson HAE, Mohammed Y, Holmes A, van der Hoek J, Pastore M, Grice JE. Topical drug delivery: History, percutaneous absorption, and product development. *Adv Drug Deliv Rev* 2021, **177**:113929.
▶ https://pubmed.ncbi.nlm.nih.gov/34403750/

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Viral Immunology Group

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Viruses pose significant challenges to human health. Our history is replete with references to plagues, pestilence, and contagions, and until 2019 we relegated these events to history and down-played the threat that pandemics pose.

In 2020-2021, the enormous human and economic toll of the rapidly spreading COVID-19 pandemic demonstrated that infectious disease pandemics remain one of the greatest existential threats to humanity. We are again reminded that harnessing the body's defence system through immunisation is the most effective approach to end pandemics.

Our group is focussed on developing novel vaccines for viruses for which no effective immunisation regimens exist, including Zika virus and hepatitis C virus. In 2021 we incorporated the SARS-CoV-2 virus into our approach and are excited to start a Phase I Human Clinical Trial (HCT) of our novel vaccine in 2022.

2021 research

- In 2021 we continued and expanded our state-wide clinical study, COVID-19 SA, in partnership with collaborators at The University of Adelaide, Royal Adelaide Hospital, South Australian Health and Medical Research Institute (SAHMRI) and colleagues nationally, to evaluate immunity and host-virus interplay in COVID-19 active and convalescent patients in South Australia. This work, funded by THRF Group, the WCH Research Foundation and private philanthropy, is providing as yet unappreciated insights into the impact of the virus on patients.
- Dr Branka Grubor-Bauk was invited to participate in The Bridge Program, a program funded by MTP Connect and delivered by the Queensland University of Technology to equip researchers with the knowledge, skills and networks they need as they commercialise their new medicines and medical technologies.
- Dr Branka Grubor-Bauk was re-elected Vice-President of the Australian Centre for Hepatitis Virology
- Drs Makutiro Masavuli and Branka Grubor-Bauk received Emerging Leader Awards from the Faculty of Health and Medical Sciences at The University of Adelaide.

RESEARCH HIGHLIGHT OF 2021

In 2016 we received a grant from the National Foundation for Medical Research and Innovation (NFMRI, a not-for-profit organisation) that led to the development of a novel Zika virus vaccine. NFMRI supports medical research in three key gap areas, one of them often referred to as the "valley of death". This is the area where research is required to attract and compete for potential investors and collaborators. In 2020, we received a second grant in this category from NFMRI and in 2021 commenced studies with collaborators in the USA to complete critical experiments for our Zika virus vaccine, to enable a Phase I HCT.

With the award of funding from the Medical Research Future Fund (MRFF) MTP Connect Biomedical Translation Bridge Program and partnership with Enesi Pharma in the UK, we have developed a solid dose thermally stable formulation of our Zika vaccine delivered with Enesi's needle-free delivery technology. We have shown that this solid dose Zika vaccine is stable at a range of temperatures, including room temperature and above 37°C.

The last couple of years of the COVID pandemic has shown that cold chain logistics remain a challenge for vaccine rollout, with specialist transport and storage equipment needed to keep doses of the vaccine at temperatures close to -80°C before use. The ability to create heat-stable, syringe-free vaccines such as our Zika virus vaccine, could minimise cold chain requirements for global deployment and mass vaccination programmes, especially in resource poor countries.

INFLAMMATORY DISEASE

RESEARCH GROUPS

ENT Surgery

Growth and Repair of the Small Intestine

Inflammatory Bowel Disease Research Group

ENT Surgery

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Amber Luong
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Our research team of clinical academic surgeons, research scientists, bio-informaticians and engineers is focused on improving treatment outcomes for patients suffering from chronic relapsing infections of the nose and sinuses (Chronic Rhinosinusitis, CRS) and wound-healing after surgery.

We have a translational medicine approach where novel therapeutic candidates discovered in our laboratory undergo extensive testing before being used in the treatment of patients. In addition, we implement a surgical training program aimed at educating the next generation of surgeons and surgeon scientists in advanced surgical techniques of the sinuses and skull base.

2021 research

- Silver is known to have antimicrobial properties. To enable the use of silver as a clinical antimicrobial in the sinuses we are formulating silver into very small particles, nanoparticles, that we can deliver to the sinuses. We have developed a novel method to synthesise silver nanoparticles. In contrast to available methods that are extremely labour-intensive and use harmful chemicals, our method uses only natural products and can manufacture silver nanoparticles in a fast and efficient way. These nanoparticles will be used in a clinical trial to test their antimicrobial properties in the coming year.
- Currently, there are no devices that effectively deliver medications into the sinuses. We are developing a novel device that uses sound

RESEARCH HIGHLIGHT OF 2021

This year our team has made substantial progress towards developing bacteriophage treatments for patients. Bacteriophage (phage) is a virus that infects and kills bacteria, including bacteria that are resistant to all antibiotics (“superbugs”). The use of phage as a therapy for infections has regained interest in the last 10 years due to the emergent superbug epidemic. Phages can be isolated from the environment, but extensive testing is needed to select those phages that are effective at killing bacteria and safe to be used in patients.

Supported by a strong interest and investments by Aushealth, the MRFF and patient organisations (e.g. CFSA and Cure4CF), we have established the “Adelaide Phage Therapy and Research Centre-APTC” within the premises of the Basil Hetzel Institute. The Centre has successfully sourced therapeutic phages targeting various bacterial pathogens. We are developing these phages as treatments for patients infected with antibiotic resistant bacteria where all other therapies have failed.

The APTC is testing the use of the phages they have developed and conducting the first randomised controlled trial in patients. In this trial APTC will evaluate phage safety and effectiveness, and the time required to achieve eradication of infection in therapy refractory chronic rhinosinusitis patients. The long-term objective of the APTC is to make phage treatments available for patients in Australia and beyond.

waves to produce fine drug particles to enhance the penetration of drugs into the sinuses. The technique has the potential to revolutionize drug delivery to the sinuses.

- No two bacteria are the same. Our research has found that patients with severe chronic rhinosinusitis are often infected with bacteria that contain specific bacterial viruses. These viruses carry proteins that help the bacteria survive the immune response of the patient.
- *Pseudomonas aeruginosa* is a nasty bug. Our research has found that these bacteria can destroy the mucosal lining or "mucosal barrier" of the nose and sinuses. Pseudomonas aeruginosa strains that have a strong effect on the barrier are found in patients that have not only chronic rhinosinusitis but also asthma.

NANOMEDICINE

As part of the inflammatory disease theme, ENT Surgery, the nanomedicine group investigates the interaction of microscopic drug carriers with bacteria embedded in a slime. These slimy structures, known as biofilms, are associated with recurring and difficult to treat chronic infections of the nose, lungs, and wounds. Through a combination of nanotechnology and pharmaceutics the team develops novel medicines that are more effective compared to currently available treatments.

2021 research

We further explored the combination of nanotechnology and the healing power of light (photodynamic therapy) as a powerful alternative to existing antimicrobials. PhD student Muhammed Awad was awarded best oral presentation at the BHI Research Expo for his impressive work on this topic.

In collaboration with Monash University we have shown how the incorporation of antimicrobial compounds in synthetic carriers can dramatically enhance the antimicrobial efficacy of established compounds. Moreover, we identified a novel mode of action by some of these carriers.

RESEARCH HIGHLIGHT OF 2021

Cystic fibrosis (CF) is an inherited disorder affecting 1 in 2500 babies in Australia. The lives of CF patients are shortened due to repeated, severe lung infections which permanently damage the lungs. Despite multiple daily administrations, currently available medicines fail to eradicate the infection and can have serious side effects including damage to the ear and kidneys.

Over the last 3 years our team has been developing and preclinically evaluating a nano-formulation for a critically important antibiotic that is used against CF lung infections, tobramycin. In collaboration with the Helmholtz Institute for Infectious Diseases (Professor Claus-Michael Lehr, Saarland, Germany) we have developed an infection model with close resemblance to CF lungs infected with biofilms.

In 2021 we demonstrated up to a 100,000-fold increase in antimicrobial activity when tobramycin is presented in this new way, as a nano-antibiotic, when compared to the currently used formulation. Importantly, after only 2 applications of our nano-antibiotic, we were able to completely eradicate a stubborn lung infection in the laboratory. In contrast, the currently available antibiotic formulation caused infection relapse with subsequent decay of the lung tissue.

We reported these findings in the top multidisciplinary journal *Small*.[1] Our findings were broadcast on national and international media platforms including 7News [▶ **bit.ly/3lYTfbH**]. We are now looking to partner with investors to translate this exciting result into the market.

1. Thorn CR, de Souza Carvalho-Wodarz C, Horstmann JC, Lehr CM, Prestidge CA, Thomas N, Tobramycin Liquid Crystal Nanoparticles Eradicate Cystic Fibrosis-Related Pseudomonas aeruginosa Biofilms. *Small* 2021, 17, 2100531.
▶ **https://pubmed.ncbi.nlm.nih.gov/33978317/**

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Growth and Repair of the Small Intestine

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Women's and Children's Hospital, Adelaide, Australia

WE ARE INVESTIGATING IF PERTURBATION OF STEM CELL SURVIVAL, AND STEM CELL NUMBERS, PLAYS A ROLE IN THE ENTEROPATHY OF OBESITY.

The Growth and Repair of the Small Intestine Group has continued to make progress in understanding the basic mechanism of growth of the small intestine and we are now extending this to understanding the enteropathy of obesity. We see many similarities of control of the small intestine between infancy and obesity, but with loss of regulation of the intestinal surface in obesity because of excessive inflammation.

We have had the assistance of the Department of Gastroenterology and Hepatology at The Queen Elizabeth Hospital, the Department of Gastroenterology, Women's and Children's Hospital, and the School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy. We have begun to cooperate with the Intestinal Nutrient Sensing Group of the South Australian Health and Medical Research Institute (SAHMRI).

RESEARCH HIGHLIGHT OF 2021

We have been studying how the lining of the small intestine grows and matures, tracking development in babies, children and adults. This was the work of PhD student, Zenab Dudhwala, who finishes soon and is about to submit her thesis. We are collaborating with Dr Paul Hammond at WCH to get small intestine biopsies (from the duodenum) from infants, children and adults.

Zenab has found that a molecular signalling pathway, called the Wnt beta catenin pathway, promotes intestinal growth by actively inhibiting the death of intestinal stem cells leading to their increased survival. Although the stem cells proliferate slowly, they underpin the growth of villi in the small intestine and ensuring appropriate stem cell numbers, through stem cell survival, is necessary to develop and maintain normal villi numbers. This mechanism of growth through increased survival of stem cells may occur elsewhere in normal development and disease.

We are investigating if perturbation of stem cell survival, and stem cell numbers, plays a role in the enteropathy of obesity. We suspect that there is increased survival of intestinal stem cells in obesity through protection from death in response to a false 'danger' signal. We will analyse intestinal biopsies taken from lean and obese adults for stem cell numbers, villi numbers and molecular characteristics to test this hypothesis.

These samples will be sourced from an existing BioBank of intestinal tissue taken at endoscopy and located at SAHMRI under the care of Associate Professor Richard Young. We hope to continue the collaboration with Dr Paul Hammond to analyse intestinal tissue taken from obese teenagers.

TQEH Gala Dinner Guest Speakers were co-founders of Taboo Period Products Eloise Hall and 2021 Young Australian of the Year Isobel Marshall.

▶ tabooau.co

Inflammatory Bowel Disease Research Group

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Our research focuses on the role of the gut microbiome and diet in inflammatory bowel disease (IBD) and other gut disorders with the overarching aim of improving patient outcomes and quality of life. We are investigating interventional approaches to manipulate the gut microbiome for therapeutic effect, in particular using dietary therapies and faecal microbiota transplantation (FMT); and undertaking clinical research in the area of IBD and gastrointestinal ultrasound.

2021 research

- Intestinal ultrasound (IUS) is a valuable tool for assessment of Crohn's disease (CD) but use is limited by the lack of a standard way of interpreting the results. Our research group has led an international consensus panel tasked with describing the optimal component items that will be used for standardisation of the scoring of IUS for clinical trials in IBD.[1] The outcomes are essential as they will enable the comparison of clinical trials conducted globally. We have been involved in key international consensus statements on defining IUS treatment response and remission in IBD, as well as optimal reporting methodology in IUS.
- We have undertaken a large multi-disciplinary project evaluating *Helicobacter pylori* antibiotic-resistance patterns at The Queen Elizabeth Hospital over 20 years, revealing a significant rise in resistance. This will likely inform local antibiotic prescribing guidelines for *H. pylori*.[2]
- We have undertaken a prospective interventional study exploring the use of FMT for remission induction of resistant ulcerative proctitis. The pilot study will evaluate feasibility and tolerability of FMT for this novel indication and is expected to inform a larger randomised controlled trial.

1. Goodsall TM, Jairath V, Faegan BG et al. Standardisation of intestinal ultrasound scoring in clinical trials for luminal Crohn's disease. *Aliment Pharmacol Ther* 2021, **53**(8):873-886.
▶ **https://pubmed.ncbi.nlm.nih.gov/33641221/**
2. Schubert JP, Warner MS, Rayner CK et al. Increasing Helicobacter clarithromycin resistance in Australia over 20 years. *Intern Med J* 2021. Online ahead of print.
▶ **https://pubmed.ncbi.nlm.nih.gov/34865299/**

RESEARCH HIGHLIGHT OF 2021

Our research group has made several contributions towards a deeper understanding of habitual dietary intake and food-related quality of life (FRQoL) in patients with IBD in 2021.

Systematic review data revealed a paucity of studies exploring dietary intake in patients with IBD.[1] In response, we have undertaken a multicentre cross-sectional evaluation of habitual fibre intake in patients with IBD, revealing inadequate consumption of dietary fibre, in particular prebiotic fibre and resistant starch.[2] The finding is important given the potential deleterious impact of low prebiotic intake on the gut microbiota, which has the propensity to perpetuate dysbiosis. Further research is required to determine the influence of low fibre intake on clinical outcomes in IBD.

Many patients with IBD are reported to restrict their diets to alleviate their symptoms or for perceived benefit. The impact of restrictive eating patterns has been poorly explored. We undertook a prospective multicentre evaluation of FRQoL in patients with IBD using a novel tool, revealing poorer FRQoL in patients with active disease and restrictive eating patterns.[3] Further research is underway to determine strategies for prevention or management of impaired FRQoL in IBD.

1. Day AS, Davis R, Costello SP, Yao CK, Andrews JM, Bryant RV. The adequacy of habitual dietary fibre intake in individuals with inflammatory bowel disease: a systematic review. *J Acad Nutr Diet* 2021, **121**(4):688-708.
▶ **https://pubmed.ncbi.nlm.nih.gov/33485803/**
2. Davis R, Day AS, Barrett J, Vanlint A, Andrews JM, Costello SP, Bryant RV. Habitual dietary fibre and prebiotic intake is inadequate in patients with inflammatory bowel disease: findings from a multicentre cross-sectional study. *J Hum Nur Diet* 2021, **34**(2):420-428.
▶ **https://pubmed.ncbi.nlm.nih.gov/32954608/**
3. Day AS, Yao CK, Costello SP, Day A, Andrew JM, Bryant RV. Food-related quality of life in adults with inflammatory bowel disease is associated with restrictive eating behaviour, disease activity and surgery: a prospective multi-centre observational study. *J Hum Nutr Diet* 2022, **35**(1):234-244. [Epub 2021 June 11]
▶ **https://pubmed.ncbi.nlm.nih.gov/34008222/**

The Institute

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