trauma presentations in South Australia

HARRIS D, *et al.* (2020)

Airway Management Considerations for Upper Gastrointestinal Endoscopic Procedures in COVID-19 Era

THIRUVENKATARAJAN V, *et al.* (2020)

Surgery triage during the COVID-19 pandemic

BABIDGE W, *et al.* (2020)

Personal protective equipment and evidence-based advice for surgical departments during COVID-19

TAN L, *et al.* (2020)

Evidence, not eminence, in coronavirus disease 2019

MADDERN G, *et al.* (2020)

Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel

IANIRO G, *et al.* (2020)

Safe surgery during the coronavirus disease

PFITZNER J, *et al.* (2020)

An alternative continuous positive airway pressure system for COVID-19 patients

PFITZNER J, *et al.* (2020)

Phacoemulsification and COVID-19 risk

GOGGIN M, *et al.* (2020)

Understanding attitudes, concerns, and health behaviors of patients with inflammatory bowel disease during the coronavirus disease 2019 pandemic

GOODSALL T, *et al.* (2020)

COVID-19 and implications for thiopurine use

Therapy During the COVID-19 E

THIRUVENKATARAJAN V, *et al.* (2020)

Screening and testing f COVID-19 before surge

KOVOOR J, *et al.* (2020)

Challenge of managing pa with COVID-19 and acute behavioural disturbances

LIGHTFOOT J, *et al.* (2020)

Australian and New Zealand consen statement on the management of ly chronic lymphocytic leukaemia and during the COVID-19 pandemic

CIACCI P, *et al.* (2020)

Safe surgery durin the coronavirus disease 2019 crisis

TIVEY D, *et al.* (2020)

Airway Management in the O Room and Interventional Suit Known or Suspected COVID- Patients: A Practical Review

THIRUVENKATARAJAN V, *et al.* (2020)

Uninterrupted Anesthesia Su Technique Adaptations for P Presenting for Electroconvu Therapy During the COVID-

THIRUVENKATARAJAN V, *et al.* (2020)

Consensus stateme the use of clozapine the COVID-19 pand

SISKIND D, *et al.* (2020)

Impact of COVID-19 social re trauma presentations in Soutl

HARRIS D, *et al.* (2020)

Personal protective equipn evidence-based advice for departments during COVI

TAN L, *et al.* (2020)

Screening of faecal microbi donors during the COVID-1 suggestions for urgent upd international expert panel

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Safe surgery during the coro

The Institute

BASIL HETZEL INSTITUTE

RESEARCH REPORT 2020

Translational health research at The Queen Elizabeth Hospital

the hospital research foundation group

TOGETHER. FIGHT.

ON THE COVER

The Basil Hetzel Institute's spectrum of inquiry is broad but is united by a mission to improve clinical care in South Australia through clinical research, therapeutic development and the translation of research outcomes into practice.

It is not surprising that BHI researchers responded promptly and presciently to the COVID-19 pandemic. Since 3 April 2020, less than a month into the South Australian response to the pandemic, BHI researchers published more than 25 journal articles, policy statements and commentaries related to COVID-19. The titles of some of the journal articles comprise the background to the 2020 front cover.

The immediate responses of BHI, TQEH clinicians and researchers grappled with how best to adapt clinical practices, procedures and products to minimise the risk of COVID-19 exposure in patients and staff alike, how to change hospital practices to limit the possibility of COVID-19 contamination, and how to ensure that conditions and drugs that may predispose patients to infections were managed appropriately. These were pressing questions and in many cases BHI researchers joined Australian and international teams to formulate advice, policies and guidelines.

As the pandemic progressed BHI researchers began to interrogate the impact of the pandemic on patient behaviour and on patient responses to the changes in clinical practice bought about by the pandemic. What did patients think about telehealth? Had patients changed how they managed their health? Did the social restrictions change patient presentations at the hospital? There will be more work done as clinicians and researchers further refine practices to accommodate COVID-19, and we can be confident that BHI researchers will continue to be a part of this process in 2021 and beyond.

Photographs: People in photos taken prior to March 2020 are not socially distanced!

BASIL HETZEL INSTITUTE FOR TRANSLATIONAL HEALTH RESEARCH

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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

DIRECTOR'S REPORT 2020

THE OUTPUT FROM THE BHI THIS YEAR HAS BEEN REMARKABLE WITH THE FUNDING BASE HOLDING UP IN SPITE OF THE GREAT DIFFICULTIES THAT HAVE OCCURRED.

Despite a predictable start to 2020 and the first few months seeming manageable and progressing well, the onset of the COVID-19 pandemic in March and the consequent changes in lifestyle, predictability, travel and chaos had, for the Basil Hetzel Institute, the same impact that the rest of the community felt.

Fortunately we started the year with strong grant success which continued during the pandemic and much of the research was able to proceed, albeit somewhat modified, in order to work around the requirements for COVID safety and isolation.

The impact of the pandemic, of course, has been far reaching for all of the Australian population. In particular, the ability to recruit high quality overseas students into the new year has been virtually halted due to the difficulties of travelling in and out of Australia during the pandemic.

Despite having all of the issues associated with COVID-19, it has also been an opportunity for the BHI to demonstrate its extraordinary flexibility, adaptability and innovation in grasping opportunities and providing a service to the community we serve. In particular, the Viral Immunology Group has been successful in attracting substantial funding for research into COVID, the fruits of which may well be realised going forward.

Additionally, there was considerable effort and energy put into researching the data and practical approaches that needed to be applied to delivering healthcare services in a COVID environment. A number of vital publications were generated on appropriate PPE, surgical triaging and the safety of procedures in a COVID environment. Although many of the lessons and approaches have not become particularly relevant in South Australia, the guidance provided for the international surgical community by this research has been widespread and greatly appreciated. This indicates how high quality research that originates in a state and city on the other side of the earth can impact practice around the world.

The year has also seen a significant loss from our administrative staff in the retirement of Gwenda Graves. Gwenda has been with us for more than two decades and has provided wisdom and advice on all facets of The Institute. She has also been a supportive resource for students and researchers alike. We have always been fortunate in having a small but unbelievably dedicated team administering the BHI. Gwenda has been the constant member over the last 20 years, overseeing the move from the old Nurses' Home laboratories to our current state-of-the-art facilities.

2020 also saw the South Australian Productivity Commission calling for submissions on research within South Australia and improvements that could be made. The BHI was active in expressing areas of concern and also highlighting areas of success. We are still waiting for the final report to be made public but at least there is clear indication that the State Government is trying to provide the best possible platform for research to be conducted. Whether the recommendations of the Productivity Commission can and will be implemented remains to be seen.

The output from the BHI this year has been remarkable with the funding base holding up in spite of the great difficulties that have occurred. The research output, as measured by publications, has accelerated and the commitment of the Central Adelaide Local Health Network to foster and improve research within the Local Health Network is being widely articulated. The next twelve months will provide an excellent opportunity to see whether the aspirations can be turned into tangible actions.

2021 will present significant challenges as the world and the Australian community emerge from the COVID pandemic. Hopefully some of the productive lessons learnt, such as remote conferencing and virtual interactions, will be further developed and adopted where appropriate. There is, however, still great value in face-to-face interactions with the opportunity to carry out discussions and explore ideas that were not necessarily formally placed on any agenda. An appropriate blend is what will be required and there is every chance that this is what the next few years will see. It may well be that 2020 will be seen as a challenging but significant year for important changes in how research and the scientific community interact. Once again, the research endeavors within the BHI have been assisted by the generous support of The Hospital Research Foundation Group, without which our efforts would be severely curtailed.

GUY MADDERN
Director of Research

Basil Hetzel Institute for Translational Health Research
THE QUEEN ELIZABETH HOSPITAL
January 2021

SUPPORT STRUCTURES 2020

The translational health research program of the BHI, 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 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:

- **BHI Research Advisory Committee**
- **BHI Management Committee**
- **BHI Scholarship Selection Committee**
- **TQEH Research Expo Organising Committee**

BHI POLICY COMMITTEE REPORT

2020 was a busy year for the BHI Policy Committee. The committee developed and passed an updated version of its Terms of Reference. The new terms reflect better the role of the BHI Policy Committee in the oversight of the clinical and biomedical research activities of the BHI and of the external interactions of BHI with the South Australian health and medical research community.

The committee ratified two key policy documents, the product of an extensive overhaul of a previous policy. The 'Requirements of Groups Occupying TQEH Research Facility' and 'The Assessment of Research Productivity Process' describe two key organising processes of the BHI.

The BHI responded to the South Australian Productivity Commission Health and Medical Research Inquiry, and used in the response material compiled from the Assessment of Research Productivity Process data set, a data set that has tracked measures of research activity at TQEH since 1997. The BHI submission to the commission can be found here.

▸ www.sapc.sa.gov.au/__data/assets/pdf_file/0020/203708/Basil-Hetzel-Institute.pdf

I was pleased that my application for reappointment to the Director of Research, BHI, TQEH position was accepted and I look forward to working with the staff and students of the BHI, TQEH in the future.

Professor Guy Maddern
Chair

BHI RESEARCH ADVISORY COMMITTEE REPORT

This year saw the establishment of a new research advisory committee with a membership that represents the 7 research themes of the BHI and includes members drawn from all levels of seniority.

The BHI Research Advisory Committee functions to ensure that the 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.

BHI Research Advisory Committee activities and initiatives in 2020 resulted in various outcomes. This included for example (1) the creation of novel opportunities for BHI researchers to be involved in teaching at The University of Adelaide, (2) the establishment of more effective frameworks to document translational research outcomes, (3) the restructuring of THRF Group supported BHI scholarships for students, (4) the creation of links to BHI research activities of several research active clinical teams located at TQEH.

Associate Professor Sarah Vreugde
Chair

BHI MANAGEMENT COMMITTEE REPORT

The BHI Management Committee commenced 2020 in a pre-COVID-19 environment with the student representatives organising a well-attended “Off the Clock” session, the fortnightly meditation sessions were happening on Monday lunchtimes, and Kathryn was coordinating the staff, student and external seminar program for the year. We hosted one international guest speaker, Professor John Spertus, from St Luke’s Hospital Kansas City in February, before COVID-19 impacted our activities. Our March speaker, BHI Alumni Associate Professor Rachel Dreyer from Yale University, was required to make an unexpected departure from Adelaide back to the US prior to her seminar, and as South Australia entered lockdown the seminars program ceased. The seminar program recommenced in June in a socially distanced format with additional Zoom streaming.

The committee considered six applications for research equipment, plus the need for replacement equipment and small lab items, with the Committee allocating $205,000 (the sum of the 2020 equipment and travel grant allocations), generously donated by THRF Group, towards key research infrastructure. This year also saw the three-year Chair and Committee positions ending and with a call made for all representative positions, we thanked Dr Lorraine Mackenzie nominating as Deputy Chair and welcomed new committee members – Dr Cher-Rin Chong, Dr Mahnaz Ramezanpour and Roshan Nepal. As for the Chair role, I am delighted that my re-nomination was accepted and I look forward to continuing to support the management of the BHI for our researchers and students.

Associate Professor Rosanna Tavella
Chair

BHI SCHOLARSHIP SELECTION COMMITTEE REPORT

The call for BHI, TQEH, THRF Group Research Scholarship applications went live on THRF Group website in mid-September, and closed at the end of October. The committee considered a total of 22 applications, and awarded support to 4 PhD students, 2 Masters students, 3 Honours students and 3 Vacation scholars. The awards were generously supported by a $125,000 allocation from THRF Group and co-funding support from the Faculty of Health and Medical Sciences, The University of Adelaide and from TQEH research units.

Professor Guy Maddern
Chair

TQEH RESEARCH EXPO ORGANISING COMMITTEE REPORT

After more than 20 years of chairing TQEH Research Expo Organising Committee, Dr Prue Cowled has stepped down and the role of Committee Chair has passed to me.

In what was a difficult year, this experienced committee successfully organised the 29th TQEH Research Expo and initiated me into the ways of the event. A full report of the event can be found on page 27.

▸ See TQEH Research Expo

Associate Professor Joy Rathjen
Chair

RESEARCH SUPPORT SERVICES

Research operations at the BHI, TQEH are supported and enriched by the following services. The on-site, face-to-face service of previous years was interrupted by COVID-19, but support continued throughout the year via 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 with literature and database searches and accessing relevant material from libraries and publishers, and provide training in the use of online resources and bibliographic tools. The librarians also provide the research support team at the BHI with publication lists that document the outputs from TQEH-based researchers and that are used in all our reporting processes.

TQEH Institutional Biosafety Committee

TQEH Institutional Biosafety Committee, chaired by Dr Jennifer Hardingham, ensure that the PC2 laboratory spaces of TQEH 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.
- Mr Richard Bennett, Manager Technical Services, Clinical and Health Sciences, University of South Australia.
- 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.
- Ms Helen Lineage and TQEH Biomedical Engineering team.
- Mr Matthew Smith, Mrs Bronwyn Hutchens and Mrs Michelle Slawinski from TQEH Experimental Surgical Suite.

CALHN Human Research Ethics Committee (HREC) and Research Office Support

The BHI has a dedicated office for use by CALHN Research Services. Research services staff 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 the BHI, and all sites of CALHN. The staff 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 support of BHI staff and students.

L-R: Dr Prue Cowled, Chair of TQEH Research Day/Expo Organising Committee for over 20 years, Professor Guy Maddern, Director of Research BHI, TQEH, and Gwenda Graves, Assistant to the Director, for over 20 years, at the 2016 TQEH Research Day.

CEO REPORT

SCIENTIFIC DIRECTOR REPORT

GROUP RESEARCH STRATEGY AND PROGRAMS REPORT

THRF GROUP GRANTS

BHI RESEARCH EQUIPMENT

THE HOSPITAL RESEARCH FOUNDATION GROUP

IT IS ONLY TOGETHER WITH THE SUPPORT OF THE COMMUNITY, THAT WE CAN HELP YOU PROGRESS LIFESAVING RESEARCH AND IMPROVED PATIENT CARE FOR EVERY SOUTH AUSTRALIAN.

If there is anything the events of 2020 have taught us, it's the importance of medical research to keep our communities safe.

With new threats like COVID-19 adding to our ongoing fights against cancer, heart disease, frailty and more, the work the BHI is doing has never been more critical.

In 2020, The Hospital Research Foundation Group was proud to provide swift funding for the BHI's world-leading Viral Immunology Group, led by Dr Branka Grubor-Bauk, to drive a state- and nation-wide collaboration of COVID-19 research to understand more about the virus and its immunology.

Our **Together.Fight.** campaign is about joining forces to fight the enemy. This team of scientists did just that and should be commended for working together so efficiently with one common goal.

In 2020 we continued to support the position of Scientific Director at the BHI, held by Associate Professor Joy Rathjen who is also a Strategic Medical Research Adviser for our Group.

Since this appointment in 2019, we have been delighted to see Associate Professor Rathjen become such an asset to the institute, driving research excellence and collaboration across the Central Adelaide Local Health Network. I thank her for her commitment to this role and the success of the BHI.

Our highly sought-after Project Grants were announced in early 2020, with Professor Michael Roberts (diabetes), Dr Robert Bryant (ulcerative colitis) and Dr Katharina Richter (mesh implants) successful in receiving funding for their projects.

We were also pleased to once again sponsor TQEH Research Expo, which was an extremely valuable event in October highlighting the research achievements of the BHI, TQEH.

The keynote speaker was Professor Toby Coates who talked about his team's life-changing work in pancreatic islet transplantation. THRF Group is proud to support Prof Coates' research and, excitingly, a new state-of-the-art Biospherix Chamber being installed in Adelaide in 2021 to facilitate these procedures.

We are delighted to support various units within TQEH, many of which are offering procedures which are not available anywhere else in Australia! This includes Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) for hard-to-treat abdominal cancers, using equipment provided through THRF Group.

There are countless examples outlined in this report which demonstrate the incredible impact the BHI is having on patients' lives. Congratulations to all the research groups on such a successful year!

We are proud to help facilitate much of this work through funding equipment, fellowships and other grants. However, none of this is possible without the generous support of our donors, fundraisers, lottery ticket buyers and corporate partners.

It is only together with the support of the community, that we can help you progress lifesaving research and improved patient care for every South Australian.

PAUL FLYNN
CEO

The Hospital Research Foundation Group

2020 WILL NOT BE THE ONLY YEAR THAT OUR LIVES WILL BE IMPACTED BY THE COVID-19 PANDEMIC, BUT IT WAS THE FIRST.

I have a folder in my email archive titled COVID-19 emails. The first email is dated the 4th of March, 2020 and comes with the subject line '*COVID-19 update – be alert, not alarmed*'. It discusses international travel warnings and introduces the need for vigilance, hand washing and self-isolation. The next is from 13th of March. With a subject line of '*COVID Quarantine prepping*' it is clear the situation is escalating.

Two days later social distancing and working from home are mentioned. The following day, the THRF-supported Travel Grant round was cancelled, the seminar series was postponed until further notice and we prepared to divide our activities between TQEH Research Facility and home.

There was an avalanche of questions that needed to be considered, and responses that needed to be made, as our researchers adapted to the reality of March and this very sudden disruption to business as usual.

Rereading the emails of these first weeks I am gratified by the proactive way that we, as an institute, restructured our workplace and work practices to respond to the multiplicity of demands.

What was notable about this time, which now seems like a lifetime ago, is that the BHI responded as a community, working together and focused on the tasks at hand. We should all be incredibly proud of the fact that, apart from three days in November when the whole state shut, the BHI maintained research operations, and research productivity, throughout 2020. The doors of TQEH Research Facility remained open and the labs remained running while complying with SA Health guidelines.

Kathryn, our Facility Manager, kept a watchful eye on the situation and as the state returned to normal so did we, restarting the seminar program from June 9th (to limited audiences and with Zoom options), and holding the 29th TQEH Research Expo as a face-to-face event in October.

2020 will not be the only year that our lives will be impacted by the COVID-19 pandemic, but it was the first. The impact of the pandemic can be seen in this report. There are many fewer references to conferences, community and social events, because for 10 of the 12 months of 2020 such events were few and far between. But what this Research Report really shows is the resilience of BHI staff and students in what has been a very difficult year.

ASSOCIATE PROFESSOR JOY RATHJEN
Scientific Director

Basil Hetzel Institute for Translational Health Research

GROUP RESEARCH STRATEGY AND PROGRAMS REPORT

the hospital research foundation group

TOGETHER. FIGHT.

IN 2020, WE SUPPORTED APPROXIMATELY 40 NEW AND ONGOING GRANTS AND FELLOWSHIPS AT BHI, TQEH.

The Hospital Research Foundation (THRF) Group provides financial support to maintain and grow research activity at the BHI, TQEH through a number of schemes.

THRF Group supports BHI researchers through research grants. In 2020, we supported approximately 40 new and ongoing grants and fellowships at BHI, TQEH. This support has been awarded through our competitive grant process or strategically to projects that support our mission to "together, fight" for better health and wellbeing for our community through life-changing medical research. A description of some of the grants awarded in 2020 can be found on page 14.

▸ See THRF Group Grants

We also support BHI researchers through the core funding we allocate annually to the BHI, which goes towards research training (providing scholarships to PhD, Masters, Honours and Vacation scholars), equipment purchases and travel grants. In 2020, BHI, TQEH researchers had less need for travel funding to attend international conferences, as very few conferences were held. The travel funding allocation was repurposed and spent on much-needed equipment. A summary of the equipment purchased can be found on page 15.

▸ See BHI Research Equipment

In 2020, the amount THRF Group provided for research training support at the BHI was increased by 25%. The institute reviewed their processes around how their scholarship allocation was best used; focussing on balancing the many requests they receive for this funding with the strategic needs of the institute and the importance of this scheme in promoting the BHI as a destination for students of the highest academic standard. The outcomes of the 2020-2021 scholarship round were in line with this vision, and the BHI managed to leverage some of these funds to receive co-funding from the Faculty of Health and Medical Sciences at The University of Adelaide - not an easy task under current circumstances. This was a very good outcome for the BHI and THRF Group.

Our Research Office worked with the BHI throughout the year to improve processes and communication, with a strong working relationship between the Research Office and the BHI Scientific Director helping to facilitate this. Relationships were also strengthened in the first half of 2020 when the BHI hosted me until the new THRF Group offices opened in August. My space at the BHI provided me with a nice (quiet) place to work which I thoroughly enjoyed.

We have also implemented an electronic reporting system that allows us to follow the progress of the research we support and to let THRF Group Communications team know of research stories that we can share with our donors. As THRF Group Research team refines the reporting system, we hope to make it easier for all our grant recipients to share their success with the people of South Australia.

In 2021 the Research Office efforts will be focused on keeping up this momentum, building structures to support researchers and diving into the details of the research programs at the BHI so that we can maximise each project's potential.

DR CAMILLE MORLIERE
Head of Group Research Strategy and Programs

The Hospital Research Foundation Group

GOHAR SHAGHAYEGH
PhD Student
ENT Surgery
THRF Postgraduate Scholarship

COVID-19 SA

Dr Branka Grubor-Bauk
Viral Immunology Group, The University of Adelaide & BHI, TQEH

A group of South Australian virologists, immunologists and clinicians, from the BHI, The University of Adelaide, Royal Adelaide Hospital, South Australian Health and Medical Research Institute, together with colleagues from across Australia, are collaborating to understand patient responses to COVID-19 at the time of infection and during their recovery. The group are following COVID-19 active and convalescent patients in South Australia, and will evaluate virology and short-term and long-term immune responses. This information will inform the development of novel vaccine strategies against SARS CoV-2. This work has been supported by THRF Group and its donor community through a dedicated COVID-19 fundraising campaign, 'Fund the Fight'.

Continuation of work to find new immunotherapeutic approaches for targeting incompletely resected or inoperable tumours

Professor Andreas Evdokiou
Breast Cancer Research Unit, The University of Adelaide & BHI, TQEH

Cancer recurrence is a problem for many patients. This project aims to harness the body's natural defence system to prevent cancer from coming back after it has been surgically removed, or to treat difficult to remove cancers. We have developed a simple, cost effective, safe, and non-invasive injectable gel system of delivering the patient's own cancer fighting T cells directly to the tumour site to kill cancer cells. The use of cancer fighting T cells for localised cancer treatment has not been contemplated before. With this additional funding Professor Evdokiou and his team will investigate new ways to sensitise cancer cells and make them more susceptible to cancer fighting T cells. This work is supported by a generous THRF Group major donor.

Addressing potentially life-threatening ketoacidosis associated with key antidiabetic medicines

Professor Michael Roberts
Therapeutics Research Centre, University of South Australia & BHI, TQEH

Type 2 diabetes (T2D) affects 2 million Australians and over 15% of surgical patients have diabetes. The newest class of antidiabetic drugs, the sodium-glucose cotransporter-2 inhibitors (SGLT2i), has revolutionised management of these patients. Unfortunately, surgical patients taking SGLT2i are at risk of developing life-threatening diabetic ketoacidosis (DKA) peri-operatively. Professor Roberts is collaborating with Dr David Jesudason (Director of Endocrinology and Diabetes, TQEH) to understand why some patients develop DKA. They will use this information to reduce the risk of DKA in diabetic surgical patients through better patient management and guidelines. This work is supported by a THRF Group project grant.

A new implant to stop infections in hernia surgery

Dr Katharina Richter
Surgical Science Research Group, The University of Adelaide & BHI, TQEH

40,000 hernia repair surgeries are performed every year in Australia. Repair typically involves insertion of a mesh to repair the weakness in the abdominal wall. Up to 40% of meshes become infected with antibiotic-resistant bacteria, causing devastating infections, pain and long-term problems, and putting a significant burden on the healthcare system. Dr Richter is planning to develop a new medical device, specifically designed for hernia repair surgery, which will support the abdominal wall without creating an environment conducive to bacterial infections. If successful, this intervention will improve patient outcomes and reduce the economic burden of these infections on Australia's healthcare system. This work is supported by a THRF Group project grant.

The 4-SURE (4-Sulphide-Reducing) project: pioneering a new diet paradigm in the management of ulcerative colitis

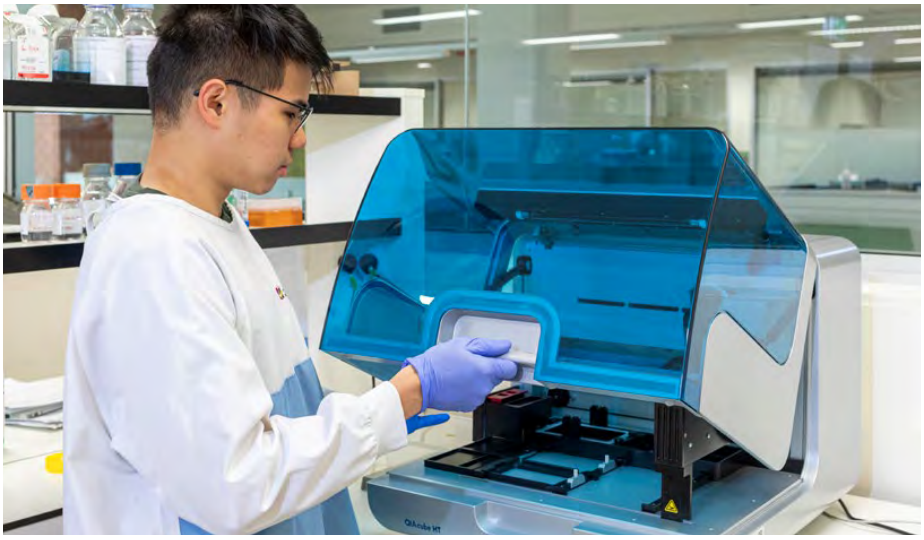
Dr Rob Bryant (pictured)
Inflammatory Bowel Disease Research Group, The University of Adelaide & BHI, TQEH

Existing therapies for ulcerative colitis (UC) are inadequate; only one-third of patients achieve remission, and 20% of patients ultimately require all or part of their colon to be removed. New therapies are needed. Diet is a key factor in the development of UC. Preliminary studies have shown that diets that reduce the production of harmful microbial end-products, like hydrogen sulphide, can reduce mucosal inflammation in UC. Dr Bryant is undertaking a clinical trial to test if the 4-SURE diet, a diet designed to reduce sulphide production, will reduce gut inflammation and gastrointestinal symptoms in UC patients. Success will lead to further testing to see if the 4-SURE diet can be incorporated into treatment plans for UC. This work is supported by a THRF Group project grant.

the hospital research foundation group

TOGETHER. FIGHT.

EACH YEAR, THRF GROUP SUPPORTS THE PURCHASE OF STATE-OF-THE-ART MEDICAL RESEARCH EQUIPMENT TO ASSIST BHI RESEARCHERS IN THEIR WORK. IN 2020, THRF GROUP PROVIDED $205,000 FOR EQUIPMENT. THIS MONEY WAS USED TO BRING NEW TECHNOLOGY TO THE STATE AND TO KEEP BHI TECHNOLOGY AT THE CUTTING EDGE.



QIAcube HT purification system (pictured) and QIAamplifiers

The QIAcube HT purification system is a robot which automates the preparation of DNA and RNA from biological samples. This will be the only QIAcube in an SA research facility.

The QIAcube will allow Dr Branka Grubor-Bauk and the Viral Immunology Group to process their samples for further analysis in-house. Sample processing will be faster and more efficient, and will speed up assessment of the viral load in samples taken during the developing and testing of their novel ZIKA virus vaccine in animal models.

The QIAcube will also be used by cancer researchers in the BHI as they compare gene expression in tumours and adjacent normal tissues, or the impact of menstrual cycle on the diagnosis and treatment of premenopausal breast cancer. The QIAamplifiers that were also purchased will complete the analysis pathway.

Vivid Iq probe

The new Vivid Iq probe complements the Vivid Iq Cardiac Ultrasound system donated by THRF Group in 2018. The probe will let BHI cardiovascular researchers perform echocardiograms on smaller experimental animals. For example, the new probe means that Professors Betty Sallustio, Andreas Evdokiou and John Horowitz can use genetically modified mouse models and cardiac ultrasound to investigate chemotherapy-induced heart damage and disease, and to characterise the role of the TRAIL protein in preventing this damage.

LCMS upgrade

In 2015 THRF Group generously funded a Liquid chromatography mass spectrometer (LCMS) that could be used to detect the type and quantity of chemicals in biological samples. The LCMS is heavily used, and in 2020 the THRF Group supported an LCMS upgrade that will make the machine more sensitive.

One of the challenges in health and medical research is specifically, sensitively and accurately, measuring medicines, hormones, foreign compounds and their metabolites in biological samples. The upgrade will support the work of researchers at the BHI and increase the range of experiments they will be able to perform in-house.

3D Spheroid Module

The Incucyte® Live-Cell Imaging system is a highly specialised and expensive piece of equipment located in the Adelaide Health and Medical School (AHMS) at The University of Adelaide. THRF Group equipment funding contributed to the 3D Spheroid Module software upgrade that expands the applications of the machine, and, specifically for BHI, TQEH, allows researchers to image, in real time, 3-dimensional cellular structures.

With this technology cancer researchers at the BHI can develop high throughput methods for assessing the susceptibility of tumour tissues (cultured as 3-dimensional structures, or tumour organoids) to treatments. Using tumour organoids for pre-clinical treatment testing has been shown to better reflect patient treatment outcomes.

Essential equipment

In addition to these big ticket items, THRF Group funding was used to purchase more mundane, but nonetheless essential, equipment like fridges, freezers, centrifuges and an ice maker. This equipment is used by all at the BHI and without it we would not function.

Arthur Yeow with the QIAcube, Research Assistant, Viral Immunology Group.

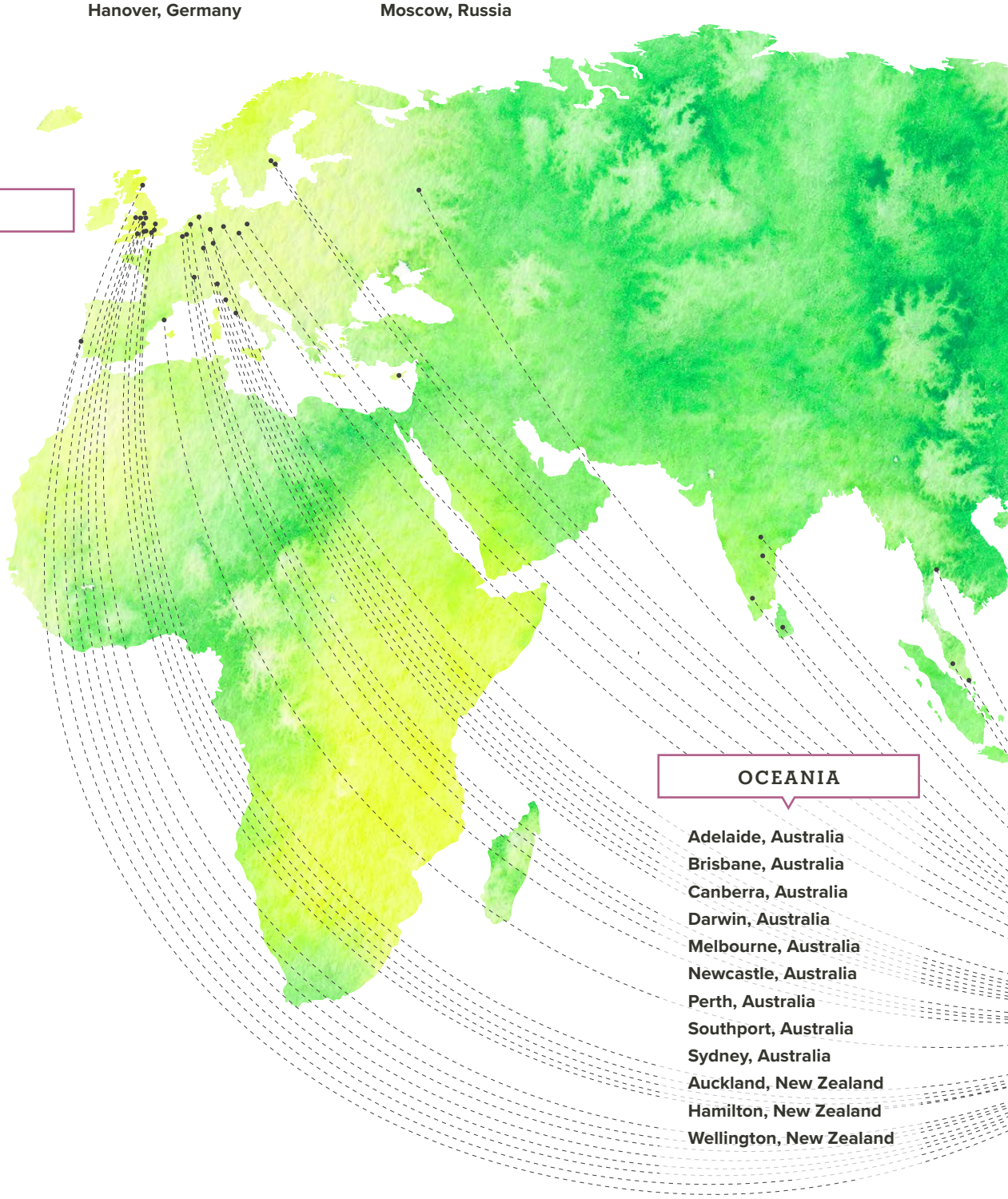
BHI NATIONAL AND INTERNATIONAL COLLABORATORS 2020

EUROPE

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

UK

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



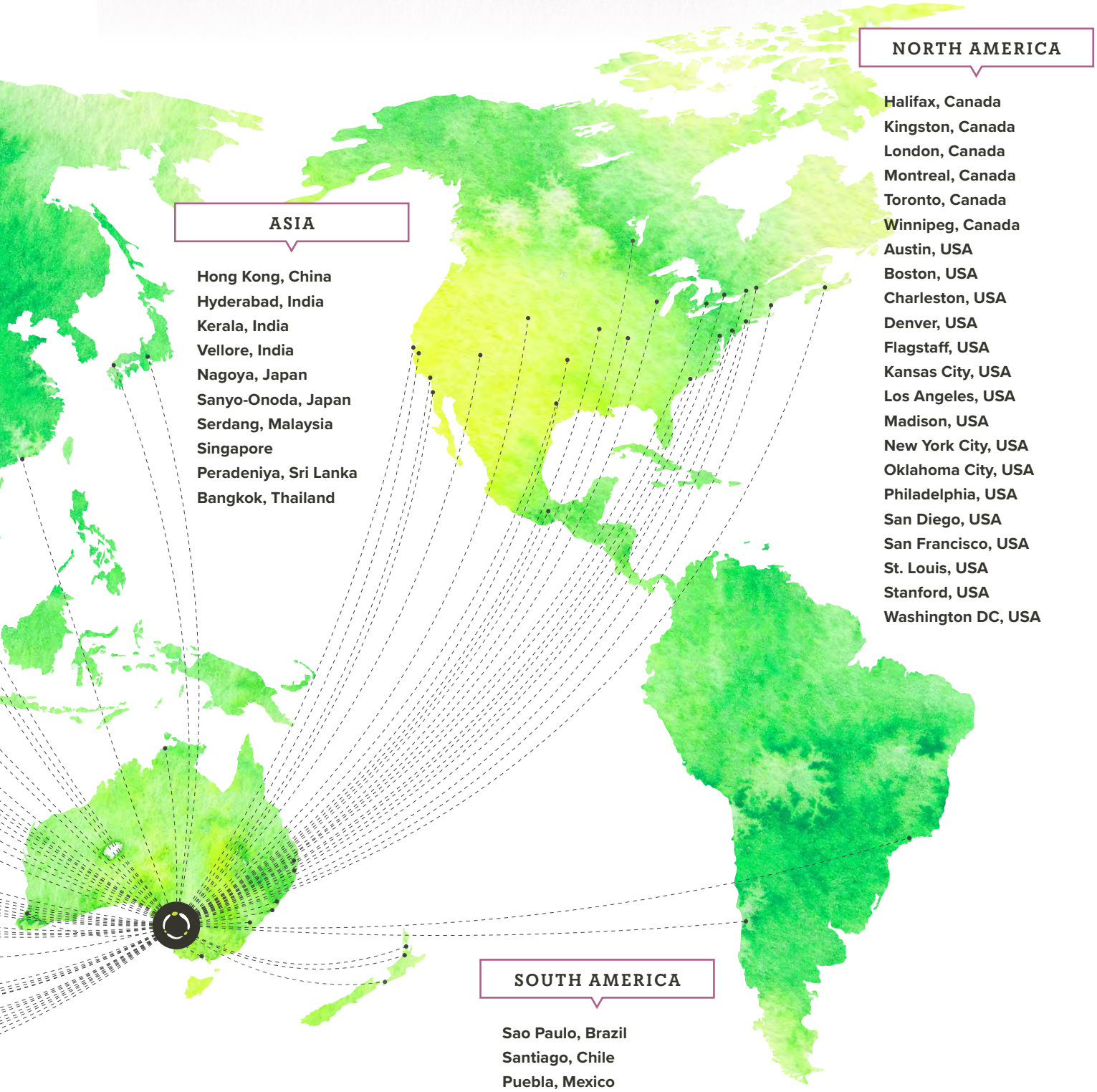
OCEANIA

Adelaide, Australia
Brisbane, Australia
Canberra, Australia
Darwin, Australia
Melbourne, Australia
Newcastle, Australia
Perth, Australia
Southport, Australia
Sydney, Australia
Auckland, New Zealand
Hamilton, New Zealand
Wellington, New Zealand

25
COUNTRIES

75 +
CITIES

300 +
EXTERNAL COLLABORATORS



NORTH AMERICA

Halifax, Canada
Kingston, Canada
London, Canada
Montreal, Canada
Toronto, Canada
Winnipeg, Canada
Austin, USA
Boston, USA
Charleston, USA
Denver, USA
Flagstaff, 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
Nagoya, Japan
Sanyo-Onoda, Japan
Serdang, Malaysia
Singapore
Peradeniya, Sri Lanka
Bangkok, Thailand

SOUTH AMERICA

Sao Paulo, Brazil
Santiago, Chile
Puebla, Mexico

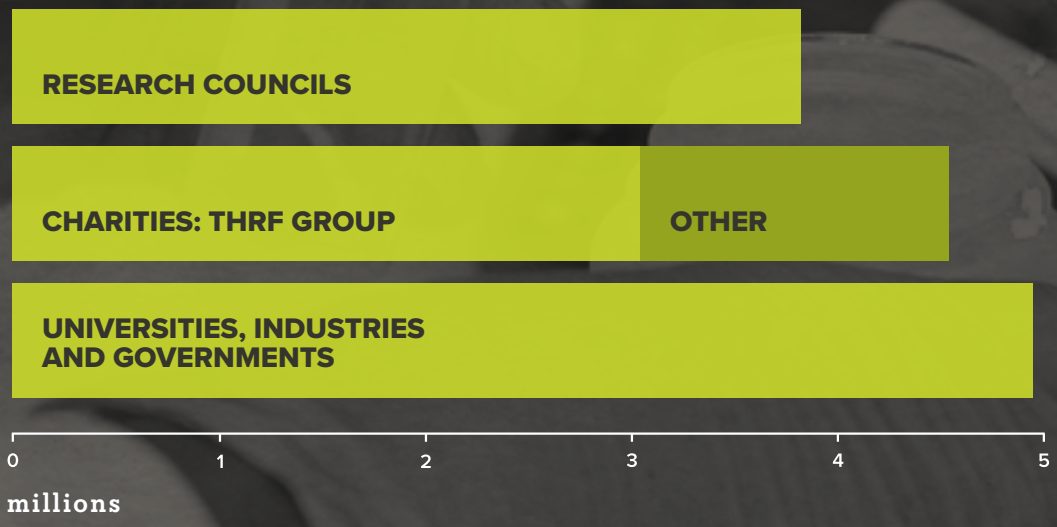
RESEARCH METRICS

FROM THE ANNUAL ASSESSMENT OF RESEARCH PRODUCTIVITY (2019-2020 FY)

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 23 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 2019-2020 Annual Assessment of Research Productivity. Detailed information on grants and publications can be found on our website.

▸ See Basil Hetzel Institute website

GRANTS



$23M+ REVENUE
Grants, clinical academic salaries, scholarships and infrastructure support

126 GRANTS
New and continuing grants

$1.4M+
Scholarship funding

470
Publications

82.74
FTE clinical and research staff

100+
Research students

25+
Research groups

RESEARCH STUDENTS 2020

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 2020, over 100 research students undertook their Honours, Masters or PhD research projects with BHI, TQEH research supervisors. Over 80% of these students conducted their research within the BHI, TQEH precinct. In 2020, 18 students were awarded a PhD or Master's Degree. Half of the students who completed their PhD at The University of Adelaide received a Dean's Commendation for Doctoral Thesis Excellence. In addition, all 12 students who completed their Honours degrees through The University of Adelaide were awarded First Class Honours. For those students completing their research training 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 2020, over 60% of our trainees were clinically-trained or allied health practitioners. TQEH Clinical Researchers take an active role in student supervision of clinically-trained and scientifically-trained students providing valuable insights into practice-based research need. TQEH clinical researchers, clinical academics and research share the training of the MD/PhD and biomedical research workforce of tomorrow. Through our student training we provide real-life opportunities to make a difference to the health and medical outcomes of South Australian, Australian and international patients.

BHI, TQEH based research students enrolled through the Adelaide Medical School 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.

Work Experience Students

As with most activities, secondary school students participating in work experience placements with BHI researchers were affected by COVID-19 restrictions throughout the year. Of the 11 placements planned, nine were able to proceed, some after a short postponement. Students from Brighton High School, Pulteney Grammar School, Henley High School, Urrbrae Agricultural High School, Portside Christian College, Hallett Cove High School and Walford Anglican School for Girls were able to observe bench research, visit clinical areas of the hospital and contribute to general lab duties.

UniSA Design Students

After a successful pilot program in 2019, 10 University of South Australia Bachelor of Design Students studying Visual Communication were partnered with BHI, TQEH researchers to develop short animations as part of their coursework. This real-world experience has students working for clients who brief the students on their topic and target audience. Groups of 2-3 UniSA students created animations for three different BHI Research Groups. Three animations were intended for use in research presentations, to show potential investors, or to share with people directly affected by a condition, while one animation was intended for the general public through websites and social media platforms.

▸ See Breast Biology and Cancer Unit

L-R: Dr Zoe Kopsaftis (completed PhD with the Respiratory Research Group in 2019) and Dr Clementine Labrosciano (completed PhD with the Translational Vascular Function Research Collaborative in 2020) after their graduation ceremony, held at The University of Adelaide in November 2020.

RESEARCH STUDENTS 2020
COMPLETED STUDENTS

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

Maddison ARCHER BSc(Biomed) BHlthSc(Hons)
Immune modulation of mammographic density and breast cancer risk
Supervisors: Ingman W, Dasari P, Evdokiou A
Breast Biology and Cancer Unit
The University of Adelaide, PhD awarded 11 March 2020

Sarah BERNHARDT BSc(Biomed) BHlthSc(Hons)
The effect of menstrual cycling on genomic predictive biomarkers in premenopausal breast cancer
Supervisors: Ingman W, Townsend A, Price T
Breast Biology and Cancer Unit
The University of Adelaide, PhD awarded 18 August 2020

Sunita DESOUSA MBBS
Clinical and Genetic Aspects of Prolactin Hypersecretion
Supervisors: Torpy D, Gagliardi L, Scott H
Endocrinology Unit
The University of Adelaide, PhD awarded 11 April 2020

Stephanie FONG MBBS DipChildHlth
Bacteriophage therapy for chronic rhinosinusitis: Targeting Pseudomonas aeruginosa *biofilms*
Supervisors: Wormald PJ, Vreugde S
ENT Surgery
The University of Adelaide, PhD awarded 8 May 2020
Dean's Commendation for Doctoral Thesis Excellence

Rachel GOGGIN MBBS BMSc(Hons)
The role of viruses in Chronic Rhinosinusitis
Supervisors: Vreugde S, Wormald PJ, Psaltis A
ENT Surgery
The University of Adelaide, PhD awarded 20 July 2020
Dean's Commendation for Doctoral Thesis Excellence

Stephen KAO MBBS
Nasal mucus: friend or foe? The effect of mucus on mucosal barrier dysfunction in chronic rhinosinusitis
Supervisors: Psaltis A, Ramezanpour M, Vreugde S
ENT Surgery
The University of Adelaide, PhD awarded 31 December 2020
Dean's Commendation for Doctoral Thesis Excellence

Clementine LABROSCIANO BSc BHlthSc(Hons)
Readmissions in Australian patients with cardiovascular disease
Supervisors: Beltrame J, Tavella R
Translational Vascular Function Research Collaborative
The University of Adelaide, PhD awarded 9 March 2020
Dean's Commendation for Doctoral Thesis Excellence

Mian Li OOI MBBS
Novel topical anti-biofilm agents in the treatment of recalcitrant chronic rhinosinusitis
Supervisors: Wormald PJ, Psaltis A, Vreugde S
ENT Surgery
The University of Adelaide, PhD awarded 11 May 2020

Beatriz MARTINS BMed (specialisation in Geriatric and Internal Medicine)
Built environment and frailty: understanding the influence of neighbourhood on older people's health
Supervisors: Visvanathan R, Barrie H (University of South Australia)
Adelaide GTRAC Centre
The University of Adelaide / Nagoya University. University of Adelaide, PhD awarded 30 June 2020
Dean's Commendation for Doctoral Thesis Excellence

Beula Subashini PANCHATCHARAM MBBS MD(Microbiology)
Staphylococcus aureus *exoproteins on nasal epithelial barrier in chronic rhinosinusitis*
Supervisors: Wormald PJ, Psaltis A, Vreugde S
ENT Surgery
The University of Adelaide, PhD awarded 21 September 2020

Sathish PARAMASIVAN MBBS BMSc(Hons)
The Host-microbe interface in Chronic Rhinosinusitis
Supervisors: Vreugde S, Wormald PJ, Psaltis A
ENT Surgery
The University of Adelaide, PhD awarded 31 July 2020
Dean's Commendation for Doctoral Thesis Excellence

Mark Q THOMPSON BAppliedScOT MPH
Frailty in older adults: Findings from longitudinal studies
Supervisors: Visvanathan R, Theou O (Dalhousie University, Canada)
Adelaide GTRAC Centre
The University of Adelaide, PhD awarded 6 April 2020

THE UNIVERSITY OF ADELAIDE

MASTER OF CLINICAL SCIENCE AWARDED

Courtney LLOYD MBBS
The effect of advanced recovery room care on postoperative outcomes in medium risk surgical patients
Supervisors: Ludbrook G, Maddern G, Story DA (University of Melbourne)

THE UNIVERSITY OF ADELAIDE

MASTER OF PHILOSOPHY (SURGERY) AWARDED

Bridget HEIJKOOP MBBS
Extended Thromboprophylaxis following Major Open Abdominopelvic surgery for malignancy: a review of efficacy, safety and economic impact
Supervisors: Kiroff G, Spernat D
The University of Adelaide, MPhil (Surg) awarded 10 September 2020

Jacob JERVIS-BARDY MBBS
Comparative microbial genomics of the upper respiratory tract in health and disease
Supervisor: Wormald PJ
ENT Surgery
The University of Adelaide, MPhil (Surg) awarded 23 April 2020

Claire STEVENS MBBS FRACS

An analysis of the trends and variability of hepatic and pancreatic surgery in Australia

Supervisors: Maddern G, Trochsler M

Surgical Science Research Group

The University of Adelaide, MPhil (Surg) awarded 12 May 2020

THE UNIVERSITY OF ADELAIDE

HONOURS AWARDED

Sophie CAMENS BMSc

Preclinical development of a Pseudomonas aeruginosa *bacteriophage cocktail for treating multidrug resistant bacterial infections*

Supervisors: Vreugde S, Psaltis A, Liu S

ENT Surgery

The University of Adelaide, First Class Honours awarded December 2020. Department of Medical Specialties Honours Award.

Vivienne ESSER* BMaSc (Applied Mathematics & Statistics) BHMSc(Adv) Neuroscience

Associations between maternal risk factors, prenatal trajectories of anxiety, depression and health-related quality of life, hypothalamic-pituitary-adrenal (HPA) axis function and maternal and infant outcomes

Supervisors: Clark S, Schubert O (NAHLN), Bednarz J (Adelaide Health Technology Assessment)

Psychiatry Research Group

The University of Adelaide, First Class Honours awarded December 2020

Kitty GERMEIN MBBS student

In vitro *assessment of safety and antibiofilm efficacy of acriflavine dye*

Supervisors: Vreugde S, Psaltis AJ, Wormald PJ

ENT Surgery

The University of Adelaide, First Class Honours awarded December 2020

Olivia GIROLAMO BAppSci

Autacoid signalling in TakoTsubo Syndrome

Supervisors: Horowitz J, Chirkov Y, Nguyen TH

Cardiovascular Pathophysiology and Therapeutics Group

The University of Adelaide, First Class Honours awarded December 2020

Emily KOVACEV BHMedSc

Preliminary study investigating the impact of 3-aminobenzamide on endothelial cell viability and vascular reactivity in a rat model of Type 2 diabetes

Supervisors: Chong CR, Horowitz J, Abdo A

Cardiovascular Pathophysiology and Therapeutics Group

The University of Adelaide, First Class Honours awarded December 2020

Joshua KOVOOR MBBS student

Dilemmas for Surgery during COVID-19: A Global Lesson

Supervisors: Maddern G, Tivey D, Babidge W

Surgical Science Research Group

The University of Adelaide, First Class Honours awarded December 2020. Department of Medical Specialties Honours Award.

Sarena LA BHMedSc (Advanced)

Myocardial Infarction with Non-obstructive Coronary Arteries (MINOCA) Patients Undergoing Cardiac Magnetic Resonance Imaging (CMR)

Supervisors: Tavella R, Pasupathy S

Translational Vascular Function Research Collaborative

The University of Adelaide, First Class Honours awarded July 2020

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, Cobb M (University of Melbourne)

Stroke Research Programme

The University of Adelaide, First Class Honours awarded December 2020

Ryan SANTOS BHlthSc

Evaluating novel Zika virus DNA vaccines

Supervisors: Grubor-Bauk B, Masavuli M, Mekonnen Z

Viral Immunology Group

The University of Adelaide, First Class Honours awarded December 2020

Michelle SIMS BHMedSc

The Role of TRAIL-Signalling in Doxorubicin-Induced Cardiotoxicity

Supervisors: Sallustio B, Evdokiou A, Licari J

Clinical Pharmacology Research Group

The University of Adelaide, First Class Honours awarded December 2020

Dawn WHELAN BHlthSc

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, First Class Honours awarded December 2020

Kenny Ker Li YEO BSc(Biomedical Science)

Elucidating the mechanism of cell death by bacopaside II in triple-negative breast cancer

Supervisors: Hardingham J, Smith E

Solid Tumour Group

The University of Adelaide, First Class Honours awarded December 2020

UNIVERSITY OF SOUTH AUSTRALIA

PhD AWARDED

Lemlem GEBREMICHAEL MSc(Clinical Pharmacology)

Assessing patterns and appropriateness of prescriptions in elderly patients admitted to South Australian hospitals

Supervisors: Roberts MS, Mackenzie L, Wiese M, Russell P (RAH), Warner M (TQEH), Gilbert A (RAH), Williams D, Phillips C

Therapeutics Research Centre

University of South Australia, PhD awarded 22 August 2020

TORRENS UNIVERSITY, ADELAIDE

PhD AWARDED

Rachel AMBAGTSHEER* BA(Hons) MInformationStudies(Librarianship)

Assessing the Appropriateness of Frailty Screening in the Australian General Practice Context: Ethics, Accuracy, Feasibility and Acceptability

Supervisors: Beilby J, Yu S (The University of Adelaide), Dent E (Baker Heart and Diabetes Institute & Torrens University)

Adelaide GTRAC Centre

Torrens University, Australia, PhD awarded 21 February 2020

RESEARCH STUDENTS 2020
CONTINUING STUDENTS

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 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

Mirabel ALONGE BHMedSc(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

Micah CEARNS* BPsych
Personalised Psychiatry: A Machine Learning Approach
Supervisors: Baune B (University of Munster, Germany), Clark S
Psychiatry Research Group

Anupam DATTA GUPTA MBBS MD ClinDipPallMed GradDipMuscMed FAFRM(RACP)
Lower limb spasticity and dystonia
Supervisors: Visvanathan R, Koblar S, Cameron I (University of Sydney)
Adelaide GTRAC Centre

Alice DAY APD (Accredited Practising Dietitian)
Diet and Inflammatory Bowel Disease
Supervisors: Andrews J, Bryant R
Inflammatory Bowel Disease Research Group
The University of Adelaide Research Training Program Stipend; The Hospital Research Foundation Clinical Project Grant

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

Christopher DIFELICE BSc(Hons)
Fibrosis, cancer and the pre-metastatic niche: implications for peroxidases
Supervisors: Evdokiou A, De Nichilo M (University of South Australia), Zinonos I
Breast Cancer Research Unit
The University of Adelaide Research Training Program Stipend

Zenab DUDHWALA BHlthSc(Hons)
Promotion of Crypt Fission by The Wnt Beta Catenin Signalling Pathway
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 – A Cohort Study
Supervisors: Kiroff G, Myers J, Shenfine J (FMC)
Oesophageal Physiology Group
RP Jepson 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

Maria GANCHEVA* BSc(BiomedSci) (Hons)
Induction of Neural Stem Cells from a Human Neural Crest-derived Stem Cell Population
Supervisors: Koblar S, Kremer K
Stroke Research Programme
The University of Adelaide Research Training Program Stipend

Amita GHADGE Integrated BSc MSc
The impact of pubertal adiposity on mammographic density and breast cancer
Supervisors: Ingman W, Dasari P, Robker R
Breast Biology and Cancer Unit
The University of Adelaide International Wildcard Scholarship

Michael GOUZOS BPhysiotherapy MD
Effect of antibiotic reagents on Nitrogen reactive species and postoperative adhesions
Supervisors: Wormald PJ, Psaltis A, Vreugde S
ENT Surgery
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

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 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

THE UNIVERSITY OF ADELAIDE CONT.

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)

Adeel Akbar KHOJA* MBBS MSc(Epidemiology & Biostatistics)
Assessing the Influence of Pregnancy and its Complications on Cardiovascular Disease Risk
Supervisors: Arstall M, Tavella R, Andraweera P
Translational Vascular Function Research Collaborative (& Northern Cardiovascular Research Group)
The University of Adelaide International Scholarship

Kareeann Sok Fun KHOW MBChB FRACP
Frailty, falls, hip fractures and clinical outcomes in older people
Supervisors: Visvanathan R, Yu S, Shibu P
Adelaide GTRAC Centre
NHMRC Postgraduate Research Scholarship

Tanya 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

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
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 BHMSc(Advanced)(Hons)
Clinical insights into patients with chest pain and NOCA (non-obstructive coronary arteries) syndromes
Supervisors: Tavella R, Beltrame J, Pasupathy S
Translational Vascular Function Research Collaborative
The University of Adelaide Research Training Program Stipend

Celine Man Ying LI BSc BHMSc(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

Anna MEGOW MBBS
New treatments for Chronic Rhinosinusitis: exploring the role of viruses
Supervisors: Wormald PJ, Vreugde S
ENT Surgery
The University of Adelaide Faculty of Health and Medical Sciences Divisional Scholarship

Martha MENBERU MSc
Microbial interactions in chronic rhinosinusitis
Supervisors: Vreugde S, Wormald PJ, Psaltis A
ENT Surgery
The University of Adelaide International Scholarship

Reger MIKAEEL MSc
Factors Underlying Colorectal and Appendiceal Cancer 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

Maryam NAKHJAVANI DPharm
Investigation of the Mechanism of Action of a Ginsenoside Compound on Tumour Growth and Angiogenesis in Advanced Breast Cancer
Supervisors: Hardingham J, Townsend A
Solid Tumour Group
The University of Adelaide International Wildcard Scholarship; The Doctor Chun Chung Wong and Madam So Sau Lam Memorial Postgraduate Cancer Research Top-Up Scholarship 2019

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

Linh Thi Hai NGO DMed - transferred to University of Queensland in April 2020
Outcomes of catheter ablation for treatment of Atrial Fibrillation in Australia: a population-wide study
Supervisors: Adams R (Flinders University), Ganesan A (Flinders University), Ranasinghe I
The Hospital Research Foundation Postgraduate Research Scholarship 2018

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

Andrew OLAGUNJU* MBBS Psych
Predictors of functional outcome in individuals with Psychosis
Supervisors: Baune B (University of Munster, Germany), Clark SR
Psychiatry Research Group
The University of Adelaide International Scholarship

Gao ONG MBChB FRACP
The natural history and treatment of TakoTsubo Cardiomyopathy
Supervisors: Horowitz JD, Chirkov Y
Cardivascular Pathophysiology and Therapeutics Group

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

RESEARCH STUDENTS 2020
CONTINUING STUDENTS

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 CONT.

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

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 Research Training Program Stipend 2018

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

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

James SMYTH MB BCh BAO FACEM FRCEM FRCSI FFSEM DCH BA(Mod)
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 BHSc
Exploring the Relationship between Electroencephalography Aperiodic Slope, Neuroinflammation, Cognition and Function in Posttraumatic Stress Disorder
Supervisors: Schubert O, Clark S, 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

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 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

Rajan Sundaresan VEDIAPPAN MBBS DLO MSurg(ENT) MA(Organisational Leadership)
Chitosandetran (Chitodex) gel with and without Deferiprone and Gallium Protoporphryrin: wound healing and postoperative outcomes in Chronic Rhinosinusitis
Supervisors: Wormald PJ, Psaltis A, Vreugde S
ENT Surgery
The Hospital Research Foundation Postgraduate Scholarship

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

MASTER OF BIOTECHNOLOGY (BIOMEDICAL) STUDENT

Zahraa AL-DELFI BSc
Development of novel DNA-based COVID-19 vaccines
Supervisor: Grubor-Bauk B
Viral Immunology Group

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

THE UNIVERSITY OF ADELAIDE CONT.

MASTER OF PHILOSOPHY (CLINICAL SCIENCE) STUDENTS

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

Usman MUSHTAQ MBBS FRACP
Pathophysiology and management of changes in calcium homeostasis and regulation of bone mineral density following bariatric surgery
Supervisors: Wittert G, Jesudason D
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, Bryant R
Inflammatory Bowel Disease Research Group
Gastroenterology Network of Intestinal Ultrasound (GENIUS) Fellowship Grant

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

MASTER OF PHILOSOPHY (SURGERY) STUDENTS

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

Siang Wei GAN MBBS
Anatomical Factors contributing to Troublesome Dysphagia after Antireflux Surgery
Supervisors: Kiroff G, Myers J
Oesophageal Physiology Group

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

Suchitra KRISHNAN PILLAI MBBS
The efficacy of ergonomic interventions on musculoskeletal disorders in surgeons
Supervisors: Maddern G, Tiong L
Surgical Science Research Group

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

Roy (Li Long) ONG MBBS
Factors effecting surgical mortality of oral squamous cell carcinoma resection
Supervisors: Maddern G, Sambrook P
Surgical Science Research Group

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

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

HONOURS STUDENT

Kelly DANG BHMSc
Participant experience in the Flo Kappa clinical trial
Supervisor: Vreugde S
ENT Surgery
The Hospital Research Foundation Honours Scholarship

UNIVERSITY OF SOUTH AUSTRALIA

PhD STUDENTS

Sadikalmahdi ABDELLA MSc(ClinPharmacy)
Development of novel topical products for treatment of skin and musculoskeletal disorders
Supervisors: Roberts M, Mackenzie L, Williams D
Therapeutics Research Centre
The Hospital Research Foundation Postgraduate Scholarship; University of South Australia President's Fee Scholarship

Tadesse ABEGAZ MSc(ClinPharmacy)
Toxicokinetics and Adverse Health Outcomes of Common Exogenous Substances
Supervisors: Roberts M, Mackenzie L, Williams D, Suppiah V
Therapeutics Research Centre
University of South Australia President's Scholarship (UPS)

UNIVERSITY OF SOUTH AUSTRALIA CONT.

Victor KRAWCZYK* BSocSc(Hum Serv) BA(Hons) GDipArtHist
Human-animal relations in organizations: Identifying discourses for compassionate engagements with animals.

Supervisors: Caluya G (Deakin University), Hamilton-Bruce MA (The University of Adelaide), Walton S

Stroke Research Programme

Sean MANGION BBiomedRes(Hons)
Exploring the hair follicles as targets to improve the effectiveness of antidandruff therapies

Supervisors: Roberts M, Holmes A, Grice J (University of Queensland), Mackenzie L, 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: Roberts M, Hayball J, Mackenzie L, 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: Roberts M, Mackenzie L, 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)

Chelsea THORN* BPharm(Hons)
Towards novel delivery strategies for antimicrobial bio-macromolecules

Supervisors: Thomas N, Prestidge C, Boyd B

ENT Surgery

Endeavour Leadership Program Scholarship

Vicky VISVANATHAN* BN
TakoTsubo Syndrome in an Intensive Care Unit setting

Supervisors: Kucia A (NALHN), Reddi B (CALHN), Horowitz JD (The University of Adelaide)

Cardiovascular Pathophysiology and Therapeutics Group

FLINDERS UNIVERSITY

PhD STUDENTS

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

Reuben WHEELER BSc(Hons)
Developing a microbial therapy for ulcerative colitis

Supervisors: Mitchell J, Costello S (The University of Adelaide), Dann L

Inflammatory Bowel Disease Research Group

Australian Government Research Training Program Stipend

HONOURS STUDENT

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

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 (University of South Australia), Mackenzie L (University of South Australia), Lui X, Grice J

Therapeutics Research Centre

University of Queensland Postgraduate Research Scholarship

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

Dr Rachel Black (completed her PhD with the Rheumatology Research Group in 2019) with her daughters after her graduation ceremony at The University of Adelaide in November 2020.

TQEH RESEARCH EXPO 2020

WE WERE JOINED AT THE EXPO BY SUPPORTERS, STAKEHOLDERS AND FRIENDS, AND EVEN THOUGH THERE WERE CHANGES, THE EVENT WAS EVERYTHING WE HOPED IT WOULD BE.

TQEH Research Expo, held in the third week of October every year, provides researchers in training an opportunity to explain their research and talk about their findings in front of a broad audience. TQEH Research Expo is now part of a larger event, CALHN Research Week and the Expo follows the Royal Adelaide Hospital Research celebration known as RAHsearch.

In 2020, planning for TQEH Research Expo was a little touch and go. How do you make decisions about an event when society is disrupted by a pandemic and no one knows what October will be like? How do you hold a conference and remain physically distant? Will we need to use Zoom? The Organising Committee of TQEH Research Expo held their collective nerve and delivered a face-to-face conference experience for students and staff over two days, the 15th and 16th of October, 2020, with pandemic appropriate distancing and catering and augmented by Zoom live-streaming. The event achieved its goal of providing a forum for 34 TQEH-based research students to present their work at a conference. This goal was especially important during the pandemic as most conferences were cancelled and students had almost no opportunities to practice their presentation skills. Prizes were awarded, photos were taken and our community came together to celebrate research.

Professor Toby Coates gave a wonderful plenary lecture on his team's ground-breaking surgeries for South Australians suffering from chronic pancreatitis, and how additional support from The Hospital Research Foundation Group will revolutionise the service they are able to provide. It was inspirational, and if you missed it is available on the BHI website.

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

In the final session of the Expo our five University of Adelaide 2020 three minute thesis (3MT®) presenters were given the opportunity to deliver their talks to a live audience. It was a great way to finish what was a very good two days.

We were joined at the Expo by supporters, stakeholders and friends, and even though there were changes, the event was everything we hoped it would be. TQEH Research Expo works because so many people give of their time and resources to support us, and so there are many to say thank you to:

- The sponsors without whom we would not be able to hold the Expo: The Hospital Research Foundation Group, The University of Adelaide (Faculty of Health and Medical Sciences), University of South Australia (Clinical and Health Sciences), plus industry sponsors Southern Cross Science, Bio-Strategy, the Australian Genome Research Facility (AGRF), Eppendorf, Chem-Supply, Lonza and Beckmann Coulter.
- Our plenary speaker, Professor Toby Coates.
- The Hon. Stephen Wade MLC for awarding the prizes and congratulating the winners.
- Invited speakers Paul Flynn, CEO THRF Group and Raymond Spencer, Chair, CALHN.
- Colleagues who chaired the sessions.
- The committee and TQEH research community who organise the event and give of their time to assess the student performance.
- The CALHN Research Week committee and team for their support.

The 30th TQEH Research Expo will be held on Thursday 14th and Friday 15th of October 2021. We look forward to marking this important anniversary.

ASSOCIATE PROFESSOR JOY RATHJEN
Chair

TQEH Research Expo Organising Committee
BASIL HETZEL INSTITUTE

TQEH RESEARCH EXPO 2020
AWARD WINNERS

AWARD CATEGORY	VALUE AWARD SPONSOR	WINNER	BHI RESEARCH GROUP
Best Lay Description	**$350** The Hospital Research Foundation Group	**Sean Mangion**	Therapeutics Research Centre, University of South Australia
Best Mini-Oral Presentation: Undergraduate Students	**$500** The University of Adelaide	**Dawn Whelan**	Viral Immunology Group, The University of Adelaide
Best Mini-Oral Presentation: PhD Students	**$500** University of South Australia	**Muhammed Awad**	ENT Surgery, University of South Australia
Best Oral Presentation: Honours Students	**$1,000** Lonza and The Hospital Research Foundation Group	**Michelle Sims**	Clinical Pharmacology Research Group, The University of Adelaide
Best Oral Presentation: Junior Laboratory PhD students	**$1,000** Southern Cross Science and The Hospital Research Foundation Group	**Gohar Shaghayegh**	ENT Surgery, The University of Adelaide
Best Oral Presentation: Senior Laboratory PhD Students	**$1,000** University of South Australia	**Dr Michael Gouzos**	ENT Surgery, The University of Adelaide
Best Oral Presentation: Clinical Research Group 1	**$1,000** The University of Adelaide	**Dr Alannah Quinlivan**	Rheumatology Research Group, The University of Adelaide
Best Oral Presentation: Clinical Research Group 2	**$1,000** The Hospital Research Foundation Group	**Dr Giri Krishnan**	ENT Surgery, The University of Adelaide

L-R: Dr Giri Krishnan, Dr Alannah Quinlivan, Dawn Whelan, Gohar Shaghayegh, Muhammed Awad, Michelle Sims.

RESEARCH GROUPS

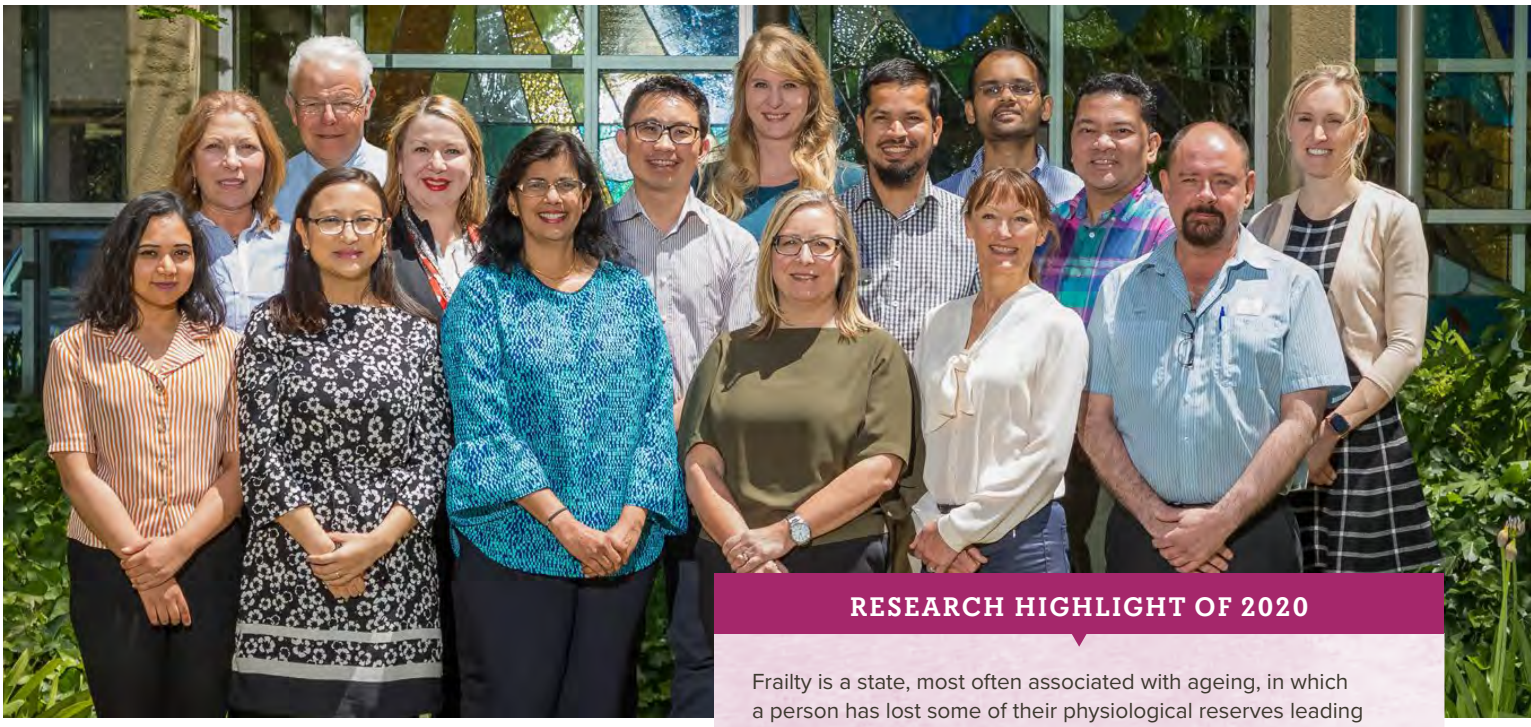
Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre

Rehabilitation Medicine

AGEING

Photo provided by Adelaide GTRAC Centre

ADELAIDE GERIATRICS TRAINING AND RESEARCH WITH AGED CARE (GTRAC) CENTRE



Linked to The University of Adelaide and the Aged and Extended Care Services (Geriatric Medicine) at The Queen Elizabeth Hospital, the GTRAC Centre is part of a global network that shares the vision of improving health outcomes of older people through high-quality geriatric medicine, excellence in gerontology training and innovative translational research. Our research focus covers gerontechnology, nutritional frailty and sarcopenia, falls prevention, genetic epidemiology, dementia 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.

2020 research

- Dr Danielle Taylor was awarded the 2020 Institute of Australian Geographers (IAG) Presidents' Leadership Award for Contribution by an Early Career Scholar to the discipline of Geography for her work on the **Frailty Web Map**. The map estimates the geographic distribution of, and predicts changes in, Australia's frail and pre-frail populations.
  ▶ **View Frailty Web Map**
- Mr Unyime Jasper, Dr Joanne Dollard and an external collaborator, Associate Professor Mellick Chehade, were awarded a grant by the RM Gibson Research Fund of the Australian Association of Gerontology to further their research aimed at reducing sedentary behaviour in older hospitalised Australians. Sedentary behaviour in hospital has been associated with delayed recovery from illness and injuries, longer hospitalisations and increased adverse outcomes.
- Professor Renuka Visvanathan was part of an international collaboration reporting on consensus principles to guide clinical practice, research and education for frail older people. This report was endorsed by Australian and International Frailty Societies.
  ▶ **www.jamda.com/article/S1525-8610(20)30371-6/fulltext**

RESEARCH HIGHLIGHT OF 2020

Frailty is a state, most often associated with ageing, in which a person has lost some of their physiological reserves leading to a loss of resilience and a greater risk of adverse outcomes like disability, institutionalisation and death. We have estimated that by 2027, 600,000 older Australians will be living with frailty in our community. Previously, we have shown the importance of identifying those living with frailty, identified appropriate screening tools that can be used in Australian general practise to measure frailty within the patient cohort, and shown that regularly reviewing older adults for frailty status is needed if we are to accurately predict survival. General practitioners (GPs) are open to the concept of screening for frailty, but as yet there has not been a frailty intervention trial in Australian general practice.

In 2020 we published preliminary evidence that showed that a comprehensive geriatric assessment, undertaken in general practice, has beneficial effects on health.[1] This research highlighted that many older Australians assessed for aged care services, some of whom are frail, are missing out on services such as health assessment, chronic disease management plans and home medication review. The timely provision of these services in general practice has the potential to improve health in this population cohort, and will become increasingly important as the proportion of Australians living with frailty within the population increases. This important research was published in *Age Ageing*, a journal ranked 6th (out of 51) in geriatrics and gerontology journals.

1. Visvanathan R, Amare A et al. Utilisation of general practice health assessments around an aged care assessment is associated with lower mortality risk in older Australians. *Age Ageing*. 2020 Jul 2:aafa091. Online ahead of print.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32614940/**

- Professor Renuka Visvanathan's submission to the SA Health Awards scheme relating to the Registry of Senior Australians was shortlisted as a finalist in the Ministers Research and Innovating Category.
- Professor Renuka Visvanathan was an invited expert at two World Health Organisation meetings: Learning From COVID19 To Strengthen Care For Older People (Oct 20) and the Clinical Consortium for Healthy Ageing (Nov 20).

THE TEAM IS COMMITTED TO BUILDING THE NEXT GENERATION OF CLINICIAN AND RESEARCH LEADERS IN THE FIELD OF GERIATRIC MEDICINE AND GERONTOLOGY.

GROUP MEMBERS

Professor and Head of Department
Renuka Visvanathan

Clinical Associate Professor and Deputy Head of Department
Solomon Yu

Professor
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 Assistants - Casual
Anna Ali
Jane Edwards
Jayanthi Selvam

CRE Manager
Leonie Baker

Postgraduate Students
Sally Suriani Ahip
Rachel Ambagtsheer
Anupam Datta Gupta
Unyime Jasper
Kareeann Khow
Beatriz Martins
James Smyth
Mark Thompson

BHI COLLABORATOR

Guy Maddern
Surgical Science Research Group

EXTERNAL COLLABORATORS

Mellick Chehade
David Gonzalez-Chicca
Kylie Lange
Damith Ranasinghe
Veronica Soebarto
Nigel Stocks
Lalit Yadav
The University of Adelaide, Adelaide, Australia

Ian Chapman
Michael Horowitz
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Mandy Archibald
University of Manitoba, The Children's Hospital Research Institute of Manitoba (CHRIM), Manitoba, Canada

Jon Karnon
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John Muscedere
Canadian Frailty Network, Kingston, Canada

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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

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Sarah Bray
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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

Natalie Luscombe-Marsh
CSIRO, Adelaide, Australia

Sazlina Shariff
University Putra, Malaysia, Serdang, Malaysia

Jean Woo
The Chinese University of Hong Kong, Hong Kong, China

Steve Manjalay
Jubilee Mission Medical College, Kerala, India

Prasad Matthews
Christian Medical College, Vellore, India

Roberto Hernandez Zermeño
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Beatriz Martins
Austin Hospital, Melbourne, Australia

Robin Daly
David Scott
Deakin University, Melbourne, Australia,

Andrea Maier
Kate Fetterplace
Royal Melbourne Hospital, Melbourne, Australia

GROUP MEMBERS

Research Leader
Anupam Datta Gupta

Registrar
Jessica Smith

Intern
John Snow

BHI COLLABORATORS

Renuka Visvanathan
David Wilson
Graeme Tucker
Adelaide GTRAC Centre

Suzanne Edwards
Statistician,
The University of Adelaide

Associate Professor Anupam Datta Gupta leads the Rehabilitation Medicine research group of the Central Adelaide Local Health Network (CALHN). The group's research focusses on the rehabilitation of neurologically impaired individuals, such as those suffering from stroke and Parkinson's disease, with the aim of improving functions like walking (gait) and balance, and preserving patient quality of life.

2020 research

- We have finished recruiting into our Randomised Control Trial (RCT) that will assess the efficacy of Botulinum Toxin A as a treatment for modifying lower limb spasticity after a stroke. We will be measuring if the treatment can improve walking functions and the quality of life of these patients. We aim to publish the results in 2021.
- We completed a comprehensive systematic review and meta-analysis of the use of Botulinum Toxin A in neuropathic pain and found that it offers some promise in certain types of neuropathic pain. This paves the way for robust RCT design on this topic.
- In 2020 we completed a retrospective review of the effects of exercise on Cancer Related Fatigue (CRF), functioning, and quality of life. In this study, we analysed effects of a supervised exercise program on CRF amongst 203 patients participating in the day rehabilitation unit of a private rehabilitation hospital. We found a significant benefit of a supervised exercise program on CRF, wellbeing and improvement in activities of daily living amongst cancer survivors.

RESEARCH HIGHLIGHT OF 2020

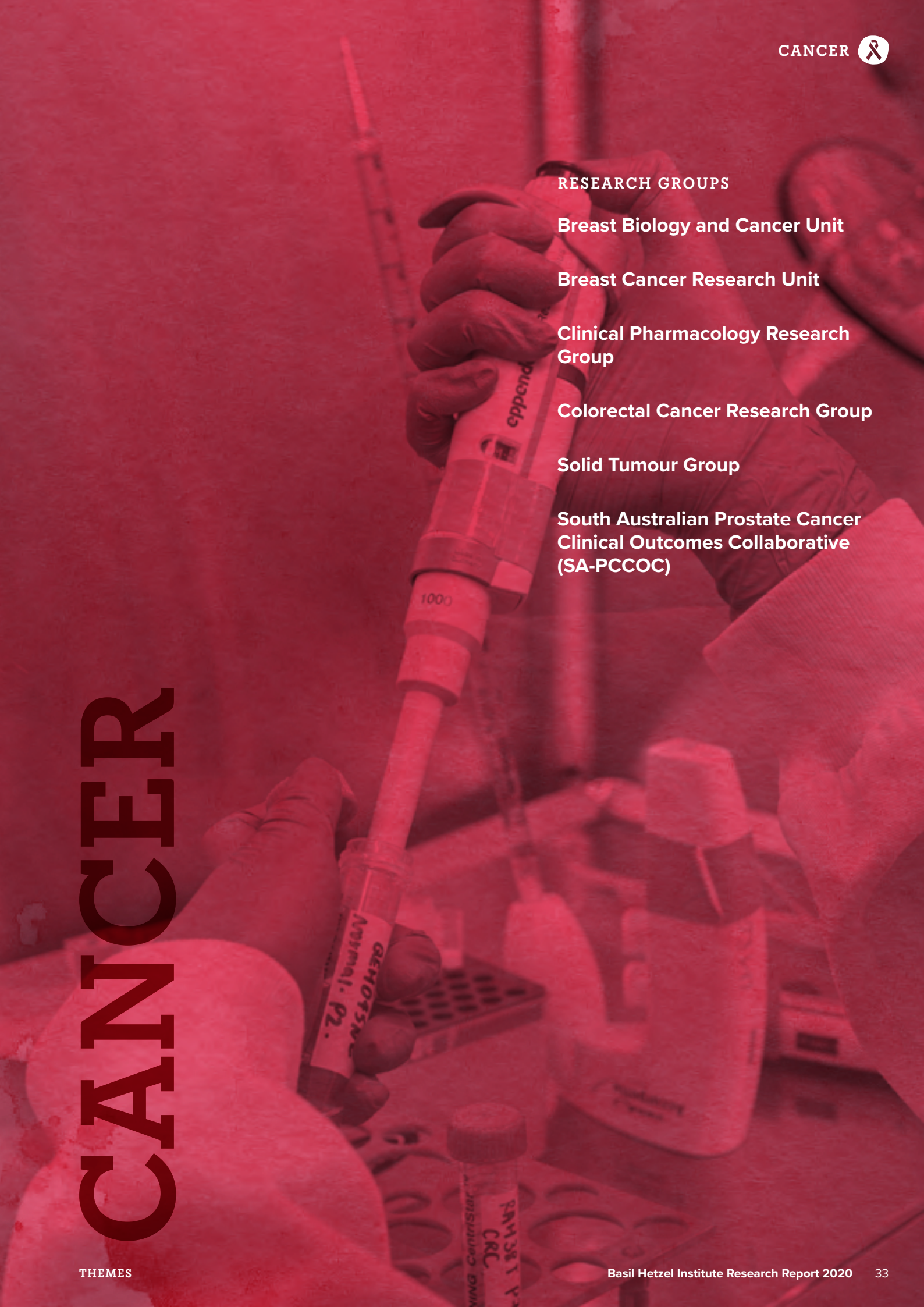
In 2020 we focussed on healing long-standing, treatment-resistant hand ulcerations caused by focal spasticity in a group of patients following stroke. These patients constitute a vulnerable group who had been moved to residential care as a result of their significant physical and cognitive impairments. Ulcers arise in their hands when spastic fingers, a consequence of the stroke, press hard into the palm.

In our study, we have shown that a method of treatment involving Botulinum toxin A, splinting and hand therapy resulted in complete healing of these distressing hand ulcerations. We have also shown that the treatment improved passive functions, such as maintenance of hand hygiene, and significantly lessened carer burden. This study was published in *International Wound Journal*[1] and *The Medical Journal of Australia*.[2]

1. Gupta AD, Addison S. Healing hand ulcers caused by focal spasticity. *Int Wound J.* 2020; 17(3):774-780.
▶ **https://pubmed.ncbi.nlm.nih.gov/32135027/**

2. Datta Gupta A, Wilson DH. Use of botulinum toxin to heal atypical pressure ulcers in the palm. *Med J Aust.* 2020; 212(2):65-66.
▶ **https://pubmed.ncbi.nlm.nih.gov/31834632/**

WE WILL BE MEASURING IF THE TREATMENT CAN IMPROVE WALKING FUNCTIONS AND THE QUALITY OF LIFE OF THESE PATIENTS.



CANCER

RESEARCH GROUPS

Breast Biology and Cancer Unit

Breast Cancer Research Unit

Clinical Pharmacology Research Group

Colorectal Cancer Research Group

Solid Tumour Group

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

The research of the Breast Biology and Cancer Unit integrates the basic biology of breast development and function with clinical and public health research to understand the drivers of breast health across the life course and investigate how disease states occur.

We research breast cancer risk factors, including breast density and menstrual cycling, to understand better the underlying biology of disease, with the view to developing new ways to prevent breast cancer.

We also investigate the causes of mastitis, a common lactation condition, and ask 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, pathologists and lactation consultants.

2020 research

- Our publication "Atashgaran V, Dasari P, Hodson LJ, Evdokiou A, Barry SC, Ingman WV. Foxp3 heterozygosity does not overtly affect mammary gland development during puberty or the estrous cycle in mice. *Reproduction Fertility and Development.* 2020; 32(8):774-782" won SRB-RFD Publication of the Year Award. Mice with a mutation in one copy of the *Foxp3* gene spontaneously develop breast cancers. In this paper we were unable to find any changes in breast development, structure or function in pre- or post-puberty mice that might account for the predisposition to develop breast cancer, highlighting that more work is needed to uncover the role of Foxp3 in the breast and breast disease.
- PhD student Amita Ghadge won the ASMR Robinson Research Institute Prize for her presentation titled "Deposition of adipose tissue during puberty alters mammary cancer risk in adulthood".
- Associate Professor Wendy Ingman gave a plenary lecture titled "The biology of lactation: Challenging old paradigms to improve breastfeeding outcomes" at the Turning the Tide for Birth and Breastfeeding international conference in Warrnambool, Victoria.
- We developed an animation to educate the community about breast density and launched a social media campaign to raise awareness.
  ▶ **www.youtube.com/watch?v=EZHjEFGEtaA**

RESEARCH HIGHLIGHT OF 2020

Breast cancer is one of the most commonly diagnosed cancers in women worldwide. What is rarely appreciated is that approximately 25% of cases occur in young, premenopausal women. These women are more likely to present with aggressive breast cancer subtypes and advanced disease, and often exhibit worse clinical outcomes, when compared to older women. This year the Breast Biology and Cancer Unit made ground-breaking progress in improving our understanding of how the menstrual cycle affects breast cancer diagnosis and treatment in premenopausal women.

Diagnosis and treatment decisions are often informed by the presence or level of specific indicators (biomarkers) of the cancer or cancer subtype. We found patient age can significantly affect the presence or level of the breast cancer biomarkers.[1] We also found that there is potential for the menstrual cycle to impact surgical and adjuvant treatments for breast cancer.[2] Despite evidence that menstrual cycling can affect diagnosis and treatment of breast cancer in younger women this is not considered during routine management.

Premenopausal women are an under-represented subpopulation in clinical research and our ability to understand better the impact of the menstrual cycle is impeded by the lack of large datasets that include information on menstrual cycle history.[3] As we engage in a new era of precision medicine, there is an ongoing effort to improve prediction of treatment response and outcomes. For premenopausal breast cancer, this must include incorporation of menstrual cycle data into treatment recommendations. We are now advocating that menstrual cycle phase at the time of diagnosis and treatment is routinely recorded. This will enable establishment of robust datasets to support research on how best to incorporate menstrual cycle-associated changes in breast cancer biology into breast cancer care.

The significance of this research was recognised by the Australian Society of Medical Research, who awarded the Ross Wishart Award to early career researcher, Dr Sarah Bernhardt, for her presentation at their annual conference titled “The impact of menstrual cycling on precision medicine for premenopausal breast cancer patients.”

1. Bernhardt SM, Dasari P, Wrin J, Raymond W, Edwards S, Walsh D, Townsend AR, Price TJ, Ingman WV. Discordance in 21-gene recurrence scores between paired breast cancer samples is inversely associated with patient age. *Breast Cancer Res.* 2020; 22(1):90.
▶ **https://pubmed.ncbi.nlm.nih.gov/32811558/**

2. Bernhardt SM, Dasari P, Walsh D, Townsend AR, Price TJ, Ingman WV. Timing of breast cancer surgery during the menstrual cycle – is there an optimal time of the month? *Oncol Lett.* 2020; 20(3):2045-2057.
▶ **https://pubmed.ncbi.nlm.nih.gov/32782523/**

3. Bernhardt SM, Dasari P, Walsh D, Raymond W, Hull ML, Townsend AR, Price TJ, Ingman WV. The menstrual cycle is an under-appreciated factor in premenopausal breast cancer diagnosis and treatment. *Curr Opin Endocr Metab Res.* 2020; 15:37-42.
▶ **www.sciencedirect.com/science/article/pii/S2451965020301095**

WE ARE NOW ADVOCATING THAT MENSTRUAL CYCLE PHASE AT THE TIME OF DIAGNOSIS AND TREATMENT IS ROUTINELY RECORDED.

GROUP MEMBERS

Research Leader
Wendy Ingman

Postdoctoral Researchers
Sarah Bernhardt
Pallave Dasari

Research Assistant
Leigh Hodson

Research Nurse
Michelle Warnes

Postgraduate Students
Maddison Archer
Sarah Bernhardt
Amita Ghadge
Joseph Wrin

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BREAST CANCER RESEARCH UNIT

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Our research aims to provide robust preclinical data that facilitates the translation of novel therapeutics to clinical trials for breast cancer and its spread.

We know that many medicines used to treat cancer can have severe side-effects. We are working towards the development of new medications that selectively target cancer cells and new ways of delivering anticancer medications to target them to cancer tissue. These approaches should limit toxicity and damage to normal tissues and organs while maintaining anticancer efficacy.

Our work has the potential to increase the patients' ability to receive a full course of cancer therapy, thereby also increasing cancer cure rates.

RESEARCH HIGHLIGHT OF 2020

Improved adoptive gamma delta T cell immunotherapy using HER-2 affibody-targeted liposomes loaded with the synthetic phosphoantigen HMBPP

In Australia, around 20,000 women will be diagnosed with breast cancer in 2021, and of these 20% will be characterized as HER-2 positive. HER-2 is a protein found on the surface of breast cancer cells that helps them grow and divide abnormally. HER-2-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 HER-2 positive breast cancers by packaging them into small membrane carriers known as liposomes. These drug-loaded carriers accumulate only in HER-2 positive tumours where they release their contents killing cancer cells while leaving normal cells unharmed.

2020 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. We are now developing new drugs to stop TRAIL's function during chemotherapy with the aim of preventing heart failure while maintaining or enhancing anticancer efficacy.

OUR WORK HAS THE POTENTIAL TO INCREASE THE PATIENTS' ABILITY TO RECEIVE A FULL COURSE OF CANCER THERAPY, THEREBY ALSO INCREASING CANCER CURE RATES.

CLINICAL PHARMACOLOGY RESEARCH GROUP

The Clinical Pharmacology Research Group aims to improve the effectiveness and safety of medicines by better understanding how they work within the body.

Recently we have focussed on an important side effect of many cancer chemotherapies, heart damage, with the aim of developing new therapies to prevent this occurring and treating the damage.

We are also working to develop better monitoring of cancer patients to allow individually tailored chemotherapy doses that improve cancer cure and reduce the risk of unwanted adverse effects, such as heart disease. We are working towards becoming a centre for individualised patient cancer therapy.

2020 research

- We have shown previously that anthracyclines require a protein called TRAIL to cause damage. This work was done in a test tube with isolated heart cells. We have now shown TRAIL is necessary for anthracyclines to cause heart damage within the body. These findings may help develop completely new therapies for heart disease in cancer and other patients.
- In collaboration with the Flinders Centre for Innovation in Cancer, we are investigating whether monitoring blood levels of cancer chemotherapies in patients can improve treatment outcomes. We have completed the development of methods to detect and measure four different chemotherapy drugs in blood and will commence patient testing in 2021.

▸ See also Clinical Pharmacology Research Group - Chronic Disease

RESEARCH HIGHLIGHT OF 2020

The use of precision-dosing of chemotherapy drugs, that is optimising the dose for each patient to achieve cancer treatment while minimising side-effects, is hindered by a lack of knowledge of the factors that impact how these drugs act within the body. The optimal dose for one patient may well be highly damaging in another.

In our research we are developing tests and models to guide initial dosing strategies and ongoing monitoring to adjust for pharmacokinetic variability (that is, variability in drug metabolism and clearance that results in higher or lower blood drug levels). To show that this approach can work we have focussed on developing precision-dosing regimens for the anthracycline group of chemotherapies. These drugs are vital for the treatment of blood and breast cancers, but can cause serious side effects, including blood disorders and a propensity to cause heart damage in patients. These can limit the quality and length of life in cancer survivors.

As a result of her research in this area, Professor Betty Sallustio was invited to contribute to a special issue of the *British Journal of Clinical Pharmacology* devoted entirely to advancing individualised cancer chemotherapy treatments.[1] This publication, written in collaboration with Professor Alan Boddy (University of South Australia), reviews the current clinical evidence for using mathematical models to predict personalised patient doses for the anthracyclines.

There are currently mathematical models that could be applied clinically for individualised dosage selection in children but Professors Sallustio and Boddy advocated for more work to be done to develop similar models for adults. This, together with other clinical information, could result in personalised and optimised dosing strategies to achieve cancer cure without adverse side effects.

1. Sallustio BC and Boddy AV. Is there scope for better individualisation of anthracycline cancer chemotherapy? *Br J Clin Pharmacol* (invited review). 2020; DOI:10.1111/bcp.14628.
   ▸ **https://pubmed.ncbi.nlm.nih.gov/33118175/**

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COLORECTAL CANCER RESEARCH GROUP

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Our primary research focus continues to be on peritoneal malignancy. Cancer that involves the lining of the abdomen (the peritoneum) is common and can spread from a number of different organs. It can be difficult to treat because chemotherapy given into the veins may not effectively penetrate into the cancer to treat it.

Pressurised intraperitoneal chemotherapy (PIPAC) delivers the chemotherapy directly to the surface of the cancer under pressure. 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.

2020 research

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. It is expected the current study will finish in 2021.

RESEARCH HIGHLIGHT OF 2020

New treatment options for patients with peritoneal malignancy

The clinical safety and efficacy trial using PIPAC started recruiting patients in 2019. To date 6 patients have had PIPAC treatments with one patient undergoing 4 treatments.

This study is designed to confirm PIPAC as a new treatment option for patients with peritoneal malignancy.

THIS STUDY IS DESIGNED TO CONFIRM PIPAC AS A NEW TREATMENT OPTION FOR PATIENTS WITH PERITONEAL MALIGNANCY.

The Solid Tumour Group is a large, multidisciplinary group, led by Professor Tim Price, which 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, 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**
- **Molecular Oncology Group**
- **Clinical Trials Group**

YOUNG ONSET COLORECTAL AND APPENDIX CANCER GROUP

Young onset colorectal cancer incidence is rising in Australia, and elsewhere in the developed world, at a time when incidence of this condition in older adults is declining. 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.

2020 research

- We have confirmed that cancer of the appendix is on the rise using national figures from the Australian Institute of Health and Welfare. The cause of this observation is currently unknown.
- This year we have begun trialling a new blood test (BibCon Trial) for the detection of early recurrences in colorectal cancer patients. Early detection of these events allows for more timely and effective treatments to be provided for affected patients increasing the odds for longer survival.

RESEARCH HIGHLIGHT OF 2020

This year we confirmed our pilot study findings that a personal history of type 2 diabetes is associated with developing young onset colorectal cancer.

We analysed information from ninety young onset colorectal cancer patients and from another two hundred and forty patients in the same age group who had undergone colonoscopy and returned a clear colon result. We found that patients developing colorectal cancer under 55 years of age were four times more likely to have a personal history of type 2 diabetes than those with clear colons. In addition, 75% of the young adults with colorectal cancer AND type 2 diabetes reported at least one close relative with type 2 diabetes. In those young adults with colorectal cancer but no evidence of type 2 diabetes, only 28% reported having close relatives diagnosed with type 2 diabetes.

Colorectal cancer develops within pre-cancerous polyps in the bowel and these are of two different types (adenomas and serrated polyps). Polyps can take up to 10 years to transform into a cancer, and most of them will remain benign. Having polyps in the bowel increases an individual's risk of developing colorectal cancer, and these can be removed at colonoscopy.

We therefore performed a colonoscopy series audit of 1400 procedures to find out whether diabetes was associated with a particular type of polyp. From this we identified the adenoma (the most common polyp type and the polyps which are responsible for the majority of colorectal cancers) as being highly associated with having type 2 diabetes, including in young adults.

The impact of these findings is that we can now identify one of the factors that puts young adults in the population at increased risk for colorectal cancer. Those who are diagnosed at a young age with type 2 diabetes may require regular bowel screening to facilitate diagnosis of cancers at an early stage or prevention of cancers by removal of pre-cancerous adenomas.

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 developing novel drugs for the treatment of breast or colorectal cancer, and in deciphering the mechanisms of action of the drugs on cell signalling and cell death

2020 research

- We have commenced a new project in collaboration with Professor Shudong Wang and Dr Susan Woods. We plan to use tissues grown in culture from patient cancer cells (known as tumour organoids) to test the safety and efficacy of new drugs targeted against gastrointestinal cancers. Generous funding from the BHI/THRF Group helped us buy a multiuser IncuCyte software module that we will use in this new project.
- PhD student Dr Maryam Nakhjavani has shown anti-cancer activities in purified compounds from the herbal plant ginseng.[1] Maryam presented this work at the San Antonio Breast Cancer Symposium, 2020 (due to COVID-19 she gave her talk on-line) and was awarded the Innovation and Commercial Partners Prize for this work at the 2020 Florey Postgraduate Research Conference, The University of Adelaide. We also lodged a patent application, protecting specific ratios of the compounds Maryam has identified.

1. Nakhjavani M, Smith E, Townsend AR, Price TJ, Hardingham JE. Anti-Angiogenic Properties of Ginsenoside Rg3. *Molecules*. 2020; 25(21):4905.
▶ **https://pubmed.ncbi.nlm.nih.gov/33113992/**

RESEARCH HIGHLIGHT OF 2020

Breast cancer comes in many different forms, or subtypes. Amongst these subtypes, triple negative breast cancer has a worse prognosis than other subtypes, largely due to a lack of targeted therapies.

Immunotherapy is a relatively new biological therapy that primes the body's own immune system to fight cancer. To date, strategies to prime the body's immune system to fight triple negative breast cancer have shown disappointing results. One reason for this is that these strategies result in cancer cell death through a process called apoptosis, and apoptosis induces immune tolerance.

Cell death through an alternative process, called necroptosis, leads to the release of immunogenic antigens and inflammatory cytokines that prime the body's immune response by activating the body's immune cells. If we could find a medicine that induces necroptosis, and use it in conjunction with immunotherapy in triple negative breast cancer patients, then we would expect improved responses to therapy.

Our group has been investigating the anti-cancer activities of compounds purified from the plant *Bacopa monnieri* (Brahmi), a commonly used traditional medicine. We have shown that one of these compounds induces necroptosis in cancer cells. The compound was effective in inducing immunogenic cell death in breast cancer cells, and could overcome the chemotherapy resistance of these cells. This work may lead to a combinatorial therapeutic strategy that will improve the efficacy of immunotherapies in triple negative breast cancer and provide a promising new therapy option for these patients.

L-R: Dr Jenny Hardingham and Dr Maryam Nakhjavani, Molecular Oncology Group.

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 2020

Randomised trials looking at the new, solid cancer, molecular targets have seen us move beyond purely tumour streams (like breast cancer, or bowel cancer) to targets that are common to cancers that occur within a number of tumour streams. The select group of cancers that carry the KRAS(G12C) mutation, for example, can be found within a large range of cancers including bowel, uterus, lung and even appendix.

The successful trial of AMG 510, a drug that targets the KRAS(G12C) mutation, was published in 2019 [Canon J, Rex K, Saiki A. ...Price TJ.....*et al*. The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity. *Nature* 2019; 575:217–223]. In 2020 we were again part of the international team that is testing AMG 510, and have been involved in exploring the activity of AMG 510 beyond the Phase I patient population.

The results of this trial confirmed significant activity in key cancer subgroups, including non-small cell lung cancer, bowel cancer and other cancers of the gastrointestinal tract. These results were published in *The New England Journal of Medicine*[1] and our group were asked to present the data from the gastrointestinal subgroup at the 2020 ESMO Asia meeting[2] (European Society of Medical Oncology). We are planning to start additional expansion trials of AMG 510 in select subgroups with new combinations to see if we can further improve patient outcomes.

1. Hong DS, Fakih MG, Strickler JH, Desai J, Durm GA, Shapiro GI, Falchook GS, Price TJ et al. KRASG12C Inhibition with Sotorasib in Advanced Solid Tumors. *N Engl J Med*. 2020;383(13):1207-1217.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32955176/**
2. Strickler JH, Fakih M, Price TJ et al. AMG 510, a novel small molecule inhibitor of KRAS (G12C), for patients (pts) with advanced gastrointestinal (GI) cancers: Results from the CodeBreaK100 phase I trial. *Annals of Oncology.* 2020; (31) S1274-S1275.
   ▶ **www.annalsofoncology.org/article/S0923-7534(20)42594-3/fulltext**

2020 research

- We have recently started new first in human trials looking at the p53 mutation as a target with the novel agent AMG 650.
- In 2020 we enrolled the final patient in the intrahepatic Rose Bengal study for patients with advanced neuroendocrine tumours. The results from the first patient cohort have confirmed safety and activity of Rose Bengal. With the final patients enrolled we will be able to complete the analysis of the trial and will be in a position to develop new combination protocols which will benefit patients with neuroendocrine tumours.

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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 with 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.

2020 research

- SA-PCCOC published work describing clinical outcomes for men with a family history of prostate cancer.[1] Using a sample of 9459 men from the registry we showed that 658 (7%) had a recorded family history of prostate cancer. Men with a positive family history of prostate cancer appear to have better overall survival outcomes. This better survival may represent lead time bias and early initiation of PSA screening. Family history of prostate cancer was not associated with different survival outcomes in men who were treated with either radical prostatectomy or radiotherapy.
- SA-PCCOC is now hosting four higher degree by research students.
- Crossing a milestone of 17,000 men in the registry.

1. Ang, M., Borg, M., O'Callaghan, M.E. et al. Survival outcomes in men with a positive family history of prostate cancer: a registry based study. *BMC Cancer* 20, 894 (2020).
▶ https://doi.org/10.1186/s12885-020-07174-9

RESEARCH HIGHLIGHT OF 2020

In 2020, SA-PCCOC contributed to the PCOR-ANZ Annual report [▶ https://prostatecancerregistry-org.s3.amazonaws.com/pcor_cms/media/filer_public/eb/e2/ebe2352f-ff5f-4aeb-88fb-fbf623da0e90/pcor-anz_2019_annual_report.pdf]. This report brings together information on prostate cancer diagnosis, treatment and outcomes from multiple registries to generate a comprehensive picture of prostate cancer in Australia and New Zealand. The report describes quality indicator reporting across the region with high level bench marks for 12 key outcome domains.

The benchmarks include process metrics (such as documentation of PSA levels and clinical T stage), treatment metrics (appropriate treatment selection by patient risk category), clinical outcomes (mortality and surgical margins) and patient reported outcomes (urinary, sexual and bowel bother). This allows the national registry to assess performance of prostate cancer treatment across the country and provide feedback to institutions and clinicians about their work.

MEN WITH A POSITIVE FAMILY HISTORY OF PROSTATE CANCER APPEAR TO HAVE BETTER OVERALL SURVIVAL OUTCOMES.

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 and shortage of breath, predominantly in older women**
- **The frequent problem of spasm of the coronary arteries**
- **The detrimental impact that some cancer treatments have on heart health**
- **The cardiovascular damage that frequently occurs with diabetes**
- **The serious heart diseases that can be triggered by environmental challenge or COVID-19 infection.**

RESEARCH HIGHLIGHT OF 2020

The importance of nitric oxide (NO) for the health of the heart and blood vessels is well understood, and our interest in the effects of NO on protecting the ageing heart goes back 8 years. We have shown that as people age they become resistant to the beneficial effects of NO in the body; with diminished effects of NO, blood vessels tend to constrict, and clots form readily, increasing risk of coronary disease and stroke. We suggest that this explains why many forms of heart disease and strokes increase with age, irrespective of whether patients smoke, have high cholesterol levels, high blood pressure or even diabetes.

We recently showed it is not only NO that is affected by normal ageing. The effect of another major protective chemical within blood vessels, prostacyclin (PGI_2), is also diminished with age. These findings demonstrate that protective therapies aimed at maintaining blood vessel health and reducing heart disease and stroke risk in ageing individuals need to restore the beneficial effects of PGI_2 *and* NO.

PGI_2 and NO are only part of the story of heart health and ageing. In our ongoing studies of TTS we have shown that NO and PGI_2 effects are preserved during ageing, and indeed attacks of TTS are not initiated by clotting. With surges of the stress hormone adrenaline, however, TTS patients develop acute and debilitating inflammation within their hearts.

TTS patients have similar risks of dying as those experiencing "conventional" heart attacks, even though very few heart cells are permanently damaged. One unusual feature of TTS patients is that they develop shock, with very low blood pressure readings, within 24 hours of the onset of attacks. Studies by Dr Gao-Jing Ong and Olivia Girolamo suggest that the falls in blood pressure reflect a combination of inappropriate dilatation of blood vessels and vessel leakiness. This finding provides a target for treatments to prevent TTS patients from developing shock.

THIS FINDING PROVIDES A TARGET FOR TREATMENTS TO PREVENT TTS PATIENTS FROM DEVELOPING SHOCK.

2020 research

- Dr Cher-Rin Chong, working with Emily Kovacev, started experiments to test if the activation of PARP-1, an enzyme activated in response to DNA damage, might contribute to cardiovascular damage in diabetes. These first experiments looked at the impact of evaluating PARP-1 in isolated heart cells and in blood vessels, as a prelude to looking at the impact of activating PARP-1 in models of diabetes. Emily was awarded a First Class Honours degree for her work on this project.
- Dr Vivek Nooney, an alumnus of the group, published his PhD work[1] showing that it is possible to assess adequacy (or otherwise) of inhibition of platelet aggregation in patients after coronary artery stenting, without using multiple blood samples. This facilitates individualization of therapy, currently a major problem.
- Hydrogen Sulfide (H_2S) interacts with NO to prevent clotting and blood vessel spasm. We have observed that Coronary Artery Spasm (CAS), a commonly occurring, debilitating, but rarely diagnosed condition, results from problems in H_2S generation. We are now focussed on how best to incorporate this understanding into new treatments for CAS, and into treatments to limit the size of heart attacks and strokes. An article related to this work has just been accepted for publication in the *British Journal of Pharmacology*.
- Summer 2019-2020 was characterised by extreme heat, bushfires close to Adelaide and increases in air pollution. Dr Gao-Jing Ong and others are attempting to determine the individual and combined influences of each of these factors on the risk of heart attacks, the risk of TTS and the incidence of cardiac chest pain. The results will help shape public health priorities in the era of climate change.
- In 2020, members of our group published 20 papers in leading cardiology journals. Our interest in TTS accounts for half of these publications.

  ▶ **www.basilhetzelinstitute.com.au/research/research-theme/cardiovascular-disease/cardio-vascular-disease-pathogenesis-therapeutics/#key-publications**

1. Nooney VB, Hurst NL, deCaterina R, Chirkov YY, Horowitz JD. Does high on-treatment platelet aggregability reflect poor individual response to clopidogrel? *Thromb Res.* 2020; 196:510-515.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/33091705/**

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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 basic, clinical and epidemiological studies 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 TVFRC comprises 3 subgroups:

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

TRANSLATIONAL VASCULAR MOLECULAR PHYSIOLOGY

The Molecular Physiology group focuses on providing a mechanistic understanding of vascular disorders, including coronary artery spasm, coronary microvascular disorders, peripheral vascular disorders and reperfusion injury. The approach used seeks to underpin to the development of evidence-based improvements to treatment regimens.

RESEARCH HIGHLIGHT OF 2020

We use a unique endothelial biopsy technique to isolate endothelial cells from the linings of human coronary arteries during coronary angiography with no harm to the patient. This technique has allowed us to study the molecular and genetic basis of vascular dysfunction and cardiovascular disease and to establish an endothelial cell biobank of over 250 patient samples.

The biobank has been used to improve our understanding of the role zinc plays in vascular disease. In 2020, a collaborative study with Dr Peter Zalewski, an expert in zinc biology, has demonstrated, for the first time, that zinc levels in the blood may have an important role in vascular health. This research has provided the rationale for the development of zinc interventional clinical trials whereby zinc supplementation will be assessed for its role in improving cardiovascular disease symptoms.

The role of zinc was elucidated by analysing patient-derived samples and data. This points to the potential for using an individual's biological data, in this case blood zinc levels, to inform personalised treatments.

▸ See also Zinc and Cardiovascular Research Group

TRANSLATIONAL VASCULAR CLINICAL PHYSIOLOGY

The Clinical Physiology research team use 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).

THIS GROUP IS DEVELOPING GLOBAL STANDARDS IN THE DIAGNOSIS OF CARDIAC CONDITIONS REFERRED TO AS CORONARY VASOMOTOR DISORDERS.

RESEARCH HIGHLIGHT OF 2020

About one half of patients with chest pain do not have obstructive coronary artery disease and cannot be treated by traditional approaches, such as stents, balloons and heart surgery. For these patients, coronary vasomotor disorders may explain their symptoms. Coronary vasomotor disorders involve the spasm of the large vessels, or the coronary microvessels, within the heart. These disorders cause the restriction of blood flow to the heart muscle, inducing myocardial ischemia that can be transient or chronic. Many patients with these conditions suffer from ongoing chest pain, impaired quality of life and adverse prognosis.

Specialised tests performed during invasive coronary angiography can assess coronary vasomotion function and help to exclude, diagnose, and treat these conditions. These tests, however, are not performed often, leaving many patients without a diagnosis for their chest pain. The COVADIS (COronary VAsomotor Disorders International Study) group, an international committee of cardiologists co-chaired by Prof John Beltrame [▶ **https://covadis.online**], is developing global standards for the diagnosis of coronary vasomotor disorders. In 2020, the COVADIS group published a comprehensive review of why, how, and when coronary vascular dysfunction should be assessed invasively.[1]

The COVADIS group proposed a consensus approach to how these interventional diagnostic procedures should be performed with a focus on the practical aspects of the procedures. They discussed the clinical scenarios for which measurement of coronary vascular function may be helpful for clinical care for patients with varying presentations of chest pain. Lastly, the group highlighted that stratifying treatment based on tests of coronary vasomotion can transform the management and well-being of these patients.

This publication is a significant contribution towards improving the care of patients with coronary vasomotor disorders.

1. Ford TJ, Ong P, Sechtem U, Beltrame J, Camici PG, Crea F, Kaski JC, Bairey Merz CN, Pepine CJ, Shimokawa H, Berry C, COVADIS Study Group. Assessment of Vascular Dysfunction in Patients Without Obstructive Coronary Artery Disease: Why, How, and When. *JACC Cardiovasc Interv*.2020;13(16):1847-1864.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32819476/**

TRANSLATIONAL VASCULAR CLINICAL PHYSIOLOGY

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SOUTH AUSTRALIAN CARDIOVASCULAR OUTCOMES REGISTRY (SACOR)

The SACOR group is focused on 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.

RESEARCH HIGHLIGHT OF 2020

In 2020, Clementine Labrosciano graduated with a Dean's Commendation for Doctoral Thesis Excellence following completion of her PhD in the SACOR research group. Dr Labrosciano's research analysed large registry and hospital databases to improve our understanding of patient care and outcomes following hospitalisation for a cardiac condition. Her research specifically focused on understanding hospital readmissions better, since this outcome is related to high costs for the health care system and poor quality of life for patients

Her study[2] investigated sleep quality and quantity as a potential contributor to readmissions in the cardiac disease setting in South Australian hospitals. Participants were asked to wear a digital health watch during their hospital stay and for two weeks post discharge. The watch tracked the amount of sleep, the number of awakenings, and the time between sleep and awake periods experienced by the participants.

The study showed that cardiac patients who report poor sleep quality (these patients took longer to fall sleep after waking up during the night and woke up more times during their hospitalisation) were more likely to be readmitted within 30 days compared to patients whose sleep was not as disturbed, and highlighted the importance of improving sleep, both in and out of the hospital, to improve the readmission outcomes of cardiology inpatients.

2. Labrosciano C, Tavella R, Reynolds A, Air T, Beltrame JF, Ranasinghe I, Adams RJT. The Association between Sleep Duration and Quality with Readmissions: An Exploratory Pilot-Study among Cardiology Inpatients. *Clocks & Sleep.* 2020; 2(2), 120-142.
▶ **www.mdpi.com/2624-5175/2/2/11**

VASCULAR SURGERY RESEARCH GROUP

The Vascular Surgery Research Group is affiliated with the CALHN Vascular Surgery Unit and operates across both The Queen Elizabeth Hospital and Royal Adelaide Hospital precincts.

We are studying the outcomes of diabetic foot ulceration and wound healing in the diabetic foot to examine which factors are critical in determining which patients with diabetic foot ulcers will need major amputation, and which factors are associated with wound healing. We also have an emphasis on diabetic foot disease in Aboriginal populations where the burden of disease is particularly high.

2020 research

- Professor Rob Fitridge was the Editor of a textbook, "Mechanisms of Vascular Disease: A Textbook for Vascular Specialists" (Springer Nature), which was published in August 2020 (doi.org/10.1007/978-3-030-43683-4). Dr Prue Cowled played a major role in completion of the textbook and Drs Cowled, Dawson and Pena contributed chapters to the book. This textbook will form an integral part of the curriculum for advanced vascular trainees at the Royal Australasian College of Surgeons and will be an ideal resource for trainee and practicing vascular surgeons seeking an up-to-date resource on the topics.
- We have initiated new collaborations to improve the treatment of diabetes-related foot ulcers in Aboriginal populations. Our group has collaborated with Cathy Loughry and Sonja Rogasch (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.
- We have commenced a multi-centre collaboration of major centres with an interest in Diabetes-related Foot Disease (DRFD) (Perth and Hamilton, NZ) to assess factors influencing outcomes of DRFD and to validate the role of the new arterial classification system developed as part of the Global Guidelines for Chronic Limb-threatening Ischaemia.

RESEARCH HIGHLIGHT OF 2020

Professor Rob Fitridge is a member of the International Working Group for the Diabetic Foot which, in 2019, published five updated guidelines for the prevention, assessment and treatment of the diabetic foot [▶ **https://iwgdfguidelines.org/guidelines/**]. This high-profile international position has resulted in his contribution to the new guidelines to inform best evidence-based practice for the treatment of the diabetic foot. In 2020 these guidelines[1], along with three Systematic Reviews on the topic[2], were published in *Diabetes and Metabolism Research Reviews*. The updated guidelines will have major impacts on improving patient care in affected patients, and are translated into over 20 languages as part of ensuring their value internationally. Rob is also leading the development of Australian diabetic foot practice guidelines and pathways, which will be published in 2021.

1. Hinchliffe RJ, Forsythe RO, Apelqvist J, Boyko EJ, Fitridge R, et al. Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev.* 2020; 36 Suppl 1:e3276.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/31958217/**
2. Three consecutive systematic reviews by Forsythe RO, Apelqvist J, Boyko EJ, Fitridge R, et al. in *Diabetes Metab Res Rev.* 2020; 36 Suppl 1:e3277, e3278 and e3279.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32176448/**
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32176442/**
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32176439/**

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ZINC AND CARDIOVASCULAR DISEASE RESEARCH GROUP

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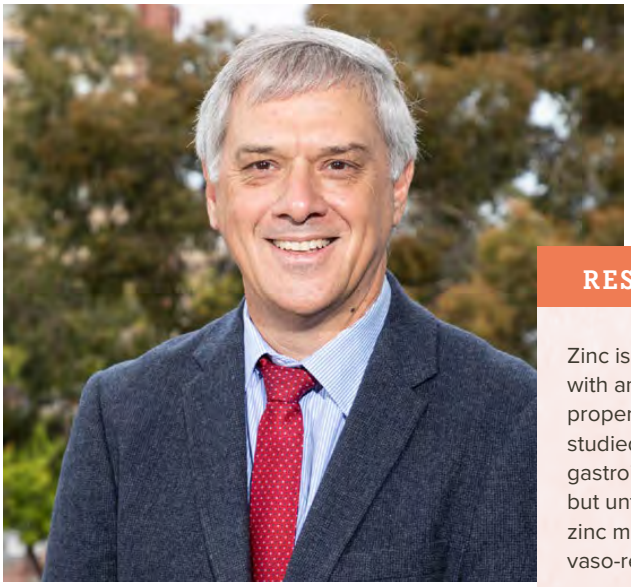

The Zinc and Cardiovascular Disease Research Group investigate the role of the major dietary metal, zinc, in the blood vessels and in vascular diseases. Our work will enable us to directly relate endothelial zinc levels and zinc transporter expression with endothelial dysfunction, vasoconstriction, cigarette smoking and small and large vessel disease in humans. It will provide the rationale for zinc interventional clinical trials.

2020 research

In 2020 the group completed the first Australian study of zinc levels in the blood of 200 patients who underwent a coronary angiogram or coronary stenting procedure. We showed that 41 of the patients (20.5%) had plasma zinc concentrations below the recognized lower cut-off for normal zinc levels, suggesting an underlying zinc deficiency or altered zinc metabolic state.

THE RESULTS OF THIS IMPORTANT STUDY SHOW THAT SPECIFIC MEMBERS OF THE ZINC KINETIC SYSTEM ARE SENSITIVE TO THE LEVELS OF ZINC IN THE BLOOD...

RESEARCH HIGHLIGHT OF 2020

Zinc is an important and essential micronutrient, with anti-oxidative and anti-inflammatory properties in humans. Zinc signalling has been studied widely in the nervous system, endocrine, gastrointestinal, renal and reproductive systems but until now we have known little of the roles zinc may play, if any, in vascular health and vaso-relaxation.

Proteins that transport zinc (the zinc kinetic system) are important to protect the function of zinc. There are three families of proteins potentially involved in the cellular handling of zinc in endothelial and smooth muscle cells in the blood vessels. With funding from NHMRC, Drs Zalewski and Abdo and Professor Beltrame, completed the first comprehensive assessment of the expression of all members of the zinc kinetics system in vascular endothelial and smooth muscle cells and their response to zinc status.[1]

The results of this important study show that specific members of the zinc kinetic system are sensitive to the levels of zinc in the blood and thus could be involved in the mechanisms and management of vascular disease. Specifically, we showed that expression of two of these proteins, ZIP2 and ZIP12, were strongly upregulated in zinc-deprived endothelial cells suggesting critical roles for these transporters in maintaining healthy levels of endothelial zinc. Interestingly, genetic polymorphism studies have linked alterations in ZIP2 to carotid artery stenosis in the elderly. We are now exploring the role of ZIP2 in other types of cardiovascular disease.

This study used primary human coronary artery endothelial and smooth muscle cells obtained from a commercial source. Future research will repeat these experiments in vascular endothelial cells harvested from the peripheral and coronary arteries of patients via our unique endothelial biopsy technique. This will allow us to correlate gene and protein expression of ZIP2 and ZIP12 with circulating levels of zinc, genetic polymorphisms and clinical disease parameters in these patients.

1. Abdo AI, Tran HB, Hodge S, Beltrame JF, Zalewski PD. Zinc Homeostasis Alters Zinc Transporter Protein Expression in Vascular Endothelial and Smooth Muscle Cells. *Biol Trace Elem Res*. 2020; doi.org/10.1007/s12011-020-02328-z.
▶ https://pubmed.ncbi.nlm.nih.gov/32776265/

CHRONIC DISEASE

RESEARCH GROUPS

Clinical Pharmacology Research Group

Endocrinology Unit

Stroke Research Programme

CLINICAL PHARMACOLOGY RESEARCH GROUP

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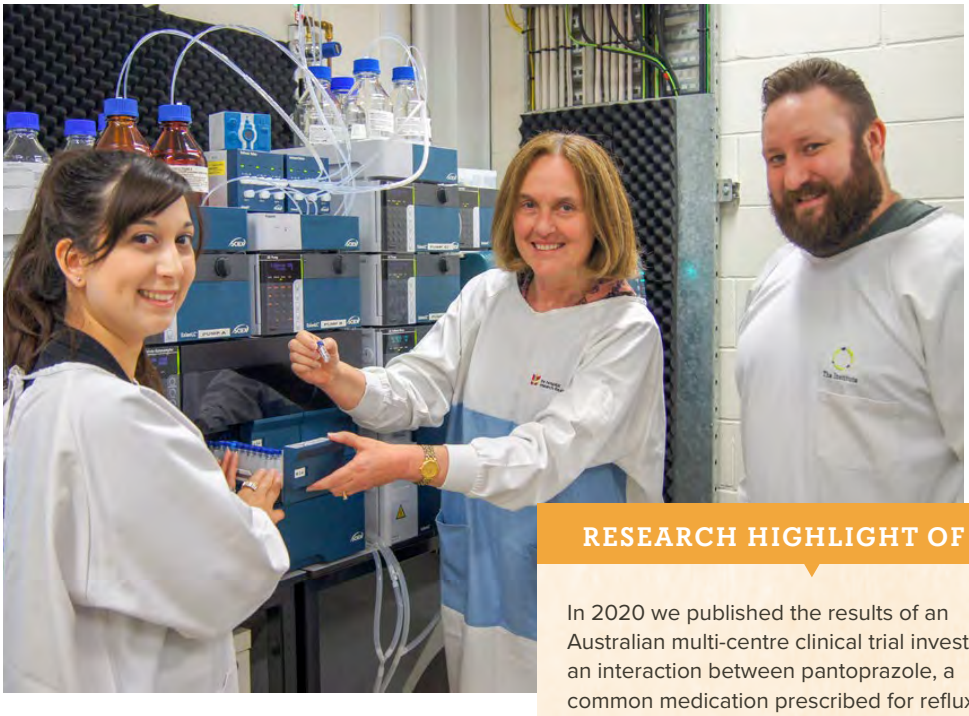

The Clinical Pharmacology Research Group aims to improve the effectiveness and safety of medicines used to prevent rejection following kidney transplantation. These immunosuppressant medicines must be used with careful monitoring as too much immunosuppression can cause adverse side effects, whilst too little can lead to rejection of the new kidney.

We are investigating new monitoring methods to better predict each individual transplant patient's risk of rejection or adverse side effects, and thereby specifically tailor doses to improve patient health and the long-term health of the transplanted kidney.

2020 research

- In kidney transplant patients we investigated mutations in genes that control the innate immune system. We studied 17 mutations in 12 genes and found none affected the risk of early rejection. However, further research is required to confirm whether a mutation of the interleukin-6 gene may significantly increase rejection.
- The immunosuppressant tacrolimus can cause kidney damage. Our work suggests that early signs of damage may be related to high tacrolimus concentrations within the transplanted kidney, which are poorly predicted by the transplant patient's tacrolimus dose and current monitoring of blood tacrolimus concentrations.

▸ See also Clinical Pharmacology Research Group - Cancer

RESEARCH HIGHLIGHT OF 2020

In 2020 we published the results of an Australian multi-centre clinical trial investigating an interaction between pantoprazole, a common medication prescribed for reflux in transplant patients, and the immunosuppressant mycophenolic acid.[1]

Mycophenolic acid is administered to nearly all kidney transplant patients to prevent rejection. It is available in two different forms, MMF and EC-MPA, made by two different pharmaceutical companies.

This study demonstrated that the amount of mycophenolic acid available in the blood of transplant patients was significantly affected if they were also taking pantoprazole. Importantly the effect of pantoprazole was different, depending on whether patients were prescribed MMF or EC-MPA. Pantoprazole reduced the blood levels of mycophenolic acid if patients were taking MMF, but the blood levels were increased in patients taking the EC-MPA form.

Therefore, it is possible that, without careful monitoring, commencing or stopping pantoprazole in transplant patients can increase their risk of rejection or their risk of adverse effects, depending on which formulation of mycophenolic acid they take.

1. Sunderland A, Russ G, Sallustio B, Cervelli M, Joyce D, Ooi E, Jeffrey G, Boudville N, Chakera A, Dogra G, Chan D, Wong G, Lim WH. Effect of the proton-pump Inhibitor pantoprazole on MycoPhenolic ACid exposure in kidney and liver transplant recipienTs (IMPACT study): a randomized trial. *Nephrol Dial Transplant*. 2020; 35:1060–1070.
▸ https://pubmed.ncbi.nlm.nih.gov/32516810/

ENDOCRINOLOGY UNIT

The Endocrinology Unit in TQEH, CALHN conducts research in a number of areas relating to endocrinology and diabetes including diabetes drug safety, diabetes in Aboriginal patients, adrenal genetics and osteoporosis.

We aim to gain knowledge through clinical trials and other research. We also conduct translational research and patient quality improvement studies to improve patient care. As an example of our work we have completed and analysed results from the NHMRC sponsored multicentre trial "Testosterone therapy to prevent type 2 diabetes in at-risk men" and expect the results to be published in 2021.

2020 research

- Dr Lucy Gagliardi formed international collaborations to understand the molecular mechanisms by which mutations in the gene armadillo repeat containing 5 (ARMC5) drive adrenal tumorigenesis, and to identify new ARMC5 mutations.
- Dr Gagliardi has worked with the Australian Diabetes Society to develop evidence-based guidelines for the management of type 2 diabetes.
- Dr Emily Meyer has continued her research on corticosteroid binding globulin (CBG) and cortisol delivery in sepsis. This work has been published in *Protein Science* and presented at the US Endocrine Society Meeting (ENDO) 2020.
- Dr David Jesudason is a co-investigator on the successful grant awarded by the Medical Research Future Fund titled "Translation of culturally informed diabetes training for Aboriginal Health Practitioners on Aboriginal patient outcomes: a cluster randomised trial of effectiveness". This work will commence in 2021.

RESEARCH HIGHLIGHT OF 2020

Our research has shown that sodium-glucose co-transporter-2 inhibitors (SGLT2i), although an important therapy for diabetes, can cause euglycaemic diabetic ketoacidosis (DKA) in situations of medical or surgical stress, and particularly around the time of surgical procedures.

Our research in this area, led by Drs David Jesudason and Emily Meyer, has resulted in the publication of several papers. The most recent of these was published in *Diabetes Care*[1] on SGLT2i DKA risk in the setting of bowel preparation, in collaboration with Drs Edward Mignone, Venkatesan Thiruvenkatarajan (Anaesthesia Research Group) and Robert Bryant (Inflammatory Bowel Disease Research Group). The work was the subject of a Diabetes Society of Australia alert issued to all its members and changed Australian guidelines on the safe use of SGLT2i [▶ **https://diabetessociety.com.au/downloads/20201015%20ADS_DKA_SGLT2i_Alert_update_Sept_2020.pdf**]. This work was presented at the Australian Diabetes Congress in November 2020.

A research collaboration has been formed between Drs Jesudason, Meyer, Thiruvenkatarajan and Professor Michael Roberts (Therapeutics Research Centre) to explore the mechanisms behind SGLT2i-dependent peri-operative DKA to understand why it develops in some patients and to explore the relationship between DKA and the choice of SGLT2i, plasma drug levels, patient factors and other precipitating factors. This work will enable us to develop a model to predict the risk of developing of DKA. This work has attracted significant research grants from both The Hospital Research Foundation and Diabetes SA.

1. Meyer EJ, Mignone E, Hade A, Thiruvenkatarajan V, Bryant RV, Jesudason D. Periprocedural Euglycemic Diabetic Ketoacidosis Associated With Sodium-Glucose Cotransporter 2 Inhibitor Therapy During Colonoscopy. *Diabetes Care.* 2020; 43(11):e181-e184. ▶ **https://pubmed.ncbi.nlm.nih.gov/32943440/**

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

Through TQEH and RAH we link internationally in our 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 and the role of the *Npas4* gene to repair the brain after stroke.

RESEARCH HIGHLIGHT OF 2020

Our group participates in the 'Targeting Optimal Thrombolysis Outcomes (TOTO) multicentre cohort study' – an Australia-wide study seeking to optimise the use of thrombolytic, or 'clot-busting', therapies for stroke. This study is one of a portfolio of studies being conducted by the International Stroke Genetics Consortium [▶ **www.strokegenetics.org**] aimed at deciphering the biological mechanisms that drive early brain injury after a patient suffers an acute stroke and that can be used therapeutically to predict acute ischaemic stroke outcome. The protocol (or operating procedure) for this study was published in 2020.[1] The results of this work will impact patients globally.

1. Holliday E, Lillicrap T, Kleinig T.... Hamilton-Bruce MA,.... Koblar S, et al. Developing a multivariable prediction model for functional outcome after reperfusion therapy for acute ischaemic stroke: study protocol for the Targeting Optimal Thrombolysis Outcomes (TOTO) multicentre cohort study. *BMJ Open.* 2020; 10(4):e038180.
▶ **https://pubmed.ncbi.nlm.nih.gov/32265253/**

2020 research

- We collected patient blood samples (a process that was then suspended because of Covid-19) for our 'FAST-IT' – TIA Biomarker Study ('Find A Simple Test – In Transient Ischaemic Attack or TIA). This study aims to find diagnostic markers that will differentiate TIA from minor stroke and TIA mimics like migraine and seizures. TIA may be a warning sign of stroke and is difficult to diagnose without expensive and time-consuming imaging tests.
- Dr Anjali Nagpal, an alumnus of the SRP, published the Clinical Translation of Cell Therapies in Stroke (CT2S).[1] The Checklist is a tool, based on Anjali's PhD research, designed to help researchers accelerate development of human cell therapy products.
- Olga Pandos, another alumnus of the SRP, partnered with the group to publish a Letter to the Editor in the *International Journal of Stroke* calling for stroke law reform in countries where legislation is lacking to facilitate consistent and uniform standards of care globally.[2]
- Maria Gancheva was awarded a travel grant from Boehringer Ingelheim Fonds to support her attendance at the EMBL Conference: *Advances in Stem Cells and Regenerative Medicine*.
- Associate Professor Anne Hamilton-Bruce and Mr Austin Milton were each awarded Honorary Faculty Research Fellow appointments at SAHMRI's Lifelong Health Theme for making a significant contribution to their research culture and productivity.
- Professor Simon Koblar was awarded an Honorary Research Senior Fellowship with SAHMRI.

1. Nagpal A, Milton AG, Koblar SA, Hamilton-Bruce MA. Clinical Translation of Cell Therapies in Stroke (CT2S) Checklist – a pragmatic tool to accelerate development of cell therapy products. *Stem Cell Res Ther.* 2020. Accepted for publication December 7.
▶ **https://pubmed.ncbi.nlm.nih.gov/33514411/**
2. Pandos OC, Milton AG, Nagpal A, Kleinig TJ, Jannes J, Koblar SA, Hamilton-Bruce MA. Stroke unit legislation – Mandating a uniform standard of care? *Int J Stroke.* 2020;15(2):NP6-NP7.
▶ **https://pubmed.ncbi.nlm.nih.gov/31996103/**

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

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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:

- **Improving the outcome of type 2 diabetic patients coming for surgery, especially those who are taking a new class of medications called Gliflozins;**
- **Efficacy and cost-effectiveness of ultrasound guided blocks for postoperative pain relief;**
- **Applications of high flow nasal oxygen in high risk patients undergoing sedation or anaesthesia;**
- **Applications and complications of supraglottic airway devices; these are devices that sit above the vocal cords and assist breathing during anaesthesia; *and***
- **New applications of drugs as co-analgesics or co-anaesthetics in anaesthesia to reduce opioid use during and after surgery.**

2020 research

- Our group reviewed our own experience of the application of a novel airway device, called LMA Gastro, and found that the device was successful in improving outcomes during advanced endoscopic procedures. These procedures are often performed in sick patients outside the operating room. For airway management for complex patients undergoing advanced endoscopic interventions procedures under deep sedation, our research showed the use of LMA Gastro and a high-flow nasal cannula was a viable alternative technique.
- One of the complications of diabetes can be an increase in acidity in the blood combined with high glucose levels. Some newer anti-diabetes medications called gliflozins, when stopped before surgery, can increase the acid load in the body without an increase in glucose levels (EDKA). We reviewed this complication from the events reported to the Therapeutic Goods Administration Australia, and found that EDKA is likely to be under-recognised and this may delay the diagnosis. Understanding this clinical entity and vigilance towards monitoring plasma/capillary ketones helps in early identification. Our work has been referenced in some of the national and international guidelines in the management of patients who take these medications and present for surgical and other procedural interventions.
- Dr Venkatesan Thiruvenkatarajan received an award from The University of Adelaide in the category “A connected and enriched community” as a titleholder making an exception contribution.

RESEARCH HIGHLIGHT OF 2020

With the emergence of COVID-19 during early 2020 there was a need to address the knowledge gap in our understanding and management of these cases. Anaesthetists and intensive care and emergency medicine physicians are at a higher risk of catching COVID-19 than other healthcare workers as they are likely to be involved in placing breathing tubes or masks into the patient’s airway to assist their breathing.

Dr Venkatesan Thiruvenkatarajan reviewed airway management techniques in detail, including the layout of the operating rooms, procedural suites, application of personal protective equipment, ways to mitigate the infection spread during bag mask ventilation, inserting and removing breathing tube, and during bronchoscopy, cardiopulmonary resuscitation and in pregnant patients.[1] This work was one of the most comprehensive reviews covering a myriad of clinical scenarios.

We highlighted the importance of risk mitigation in contracting the virus during airway interventions applicable across the globe. We emphasised that the locally-derived protocols should be a valuable resource and reiterated that further waves of infection were likely and airway invention practices should be constantly reviewed and updated. This work was undertaken in collaboration with experts from Canada, US, and Singapore.

Our group also reviewed the importance of risk mitigation in the COVID-19 pandemic during endoscopy procedures and electroconvulsive therapy (ECT).[2,3] These reports were prepared in collaboration with gastroenterologists from Australia and anaesthetists from Italy, and with psychiatrists who are experts in ECT, respectively.

1. Thiruvenkatarajan V, Wong DT, Kothandan H, Sekhar V, Das Adhikary S, Currie J, Van Wijk R. Airway Management in the Operating Room and Interventional Suites in Known or Suspected Coronavirus Disease 2019 Adult Patients: A Practical Review. *Anesth Analg.* 2020; 131(3):677-689.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32502132/**
2. Thiruvenkatarajan V, Lorenzetti M, Chung A, Wong CK, Currie J, Wahba M, Van Wijk RM, Skinner MW, Sorbello M. Airway Management Considerations for Upper Gastrointestinal Endoscopic Procedures in COVID-19 Era. *Dig Dis Sci.* 2020; 65(9):2739-2742.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32712781/**
3. Thiruvenkatarajan V, Dharmalingam A, Armstrong-Brown A, Weiss A, Waite S, Van Wijk R. Uninterrupted Anesthesia Support and Technique Adaptations for Patients Presenting for Electroconvulsive Therapy During the COVID-19 Era. *J ECT.* 2020; 36(3):156-157.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32511113/**

INTENSIVE CARE MEDICINE RESEARCH GROUP

The Queen Elizabeth Hospital, Department of Intensive Care Medicine participates in, and conducts, research aimed at improving patient outcomes, answering pragmatic, relevant clinical questions that are of importance to the clinicians who provide patient care, and also at delivering more efficient and effective treatments that will not only benefit critically ill patients but also decrease costs, preserve resources and increase access to scarce critical care beds.

2020 research

- In 2020 Professor Sandra Peake (CIA), Patricia Williams (AI) and colleagues were awarded an NHMRC MRFF Research Grant (APP1200084) to support the Australasian Resuscitation In Sepsis Evaluation: Fluid or Vasopressors in Emergency Department Sepsis (ARISE: Fluids) Trial. ($2,335,540 over 5 years). Planning is underway to commence the ARISE: Fluids Trial in 2021. This grant application was successful, in part, because of the completion and publication of the Australasian Resuscitation in Sepsis Evaluation multi-centre randomised controlled trial (ARISE RCT) in *The New England Journal of Medicine* in 2014 and three 2020 publications.[1, 2, 3]

1. Delaney A, Finnis M, Bellomo R, Udy A, Jones D, Keijzers G, MacDonald S, Peake S. Initiation of vasopressor infusions via peripheral versus central access in patients with early septic shock: A retrospective cohort study. *Emerg Med Australas*. 2020; 32(2):210-219.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/31599084/**
2. Tian DH, Smyth C, Keijzers G, Macdonald SP, Peake S, Udy A, Delaney A. Safety of peripheral administration of vasopressor medications: A systematic review. *Emerg Med Australas*. 2020; 32(2):220-227.
   ▶ **https://pubmed.ncbi.nlm.nih.gov/31698544/**
3. Keijzers G, Macdonald SP, Udy AA, ... Peake S, Taylor D, Williams P; the ARISE FLUIDS Observational Study Group. The Australasian Resuscitation In Sepsis Evaluation: Fluids or vasopressors in emergency department sepsis (ARISE FLUIDS), a multi-centre observational study describing current practice in Australia and New Zealand. *Emerg Med Australas*. 2020; 32(4):586-598.
   ▶ **https://onlinelibrary.wiley.com/doi/full/10.1111/1742-6723.13469**

RESEARCH HIGHLIGHT OF 2020

Acute kidney injury (AKI) is a common complication of critical illness and patients receiving acute renal replacement therapy (RRT) have a high mortality. Sepsis and septic shock are a common cause of AKI and timely, appropriate antimicrobial therapy is a key therapeutic strategy. Nonetheless, optimal antimicrobial prescription to achieve therapeutic concentrations is unknown in the presence of RRT.

The SMARRT study[1] was a large, prospective, observational, multinational, pharmacokinetic study conducted in 29 intensive care units across 14 countries. In this study the trough concentration (that is, the lowest blood concentrations of a drug observed before the next dose is administered) of the antimicrobials meropenem, piperacillin-tazobactam, vancomycin or linezolid was observed in 384 critically ill patients undergoing continuous or extended intermittent RRT. The study was led by the NHMRC-funded REDUCE Centre for Research Excellence, of which Professor Sandy Peake is a Chief Investigator.

The key findings were that renal prescription and clearance varied widely, as did antimicrobial dosing (up to 8-fold differences). Increasing clearance was also associated with decreasing trough concentrations. Importantly, recommended trough concentrations did not meet therapeutic targets in up to 72% of patients (depending on the antimicrobial).

The results of this study have important implications for antimicrobial dosing and have informed ongoing work on therapeutic drug monitoring and individualised dosing algorithms in critically ill patients with sepsis and AKI receiving RRT.

1. Roberts JA, Joynt G, Lee A, Choi G, Bellomo R, Kanji S, Mudaliar MY, Peake SL, ... Williams T ... et al. The effect of renal replacement therapy and antibiotic dose on antibiotic concentrations in critically ill patients: Data from the multinational SMARRT Study. *Clin Infect Dis*. 2020 Mar 9; [online ahead of print].
   ▶ **https://pubmed.ncbi.nlm.nih.gov/32150603/**

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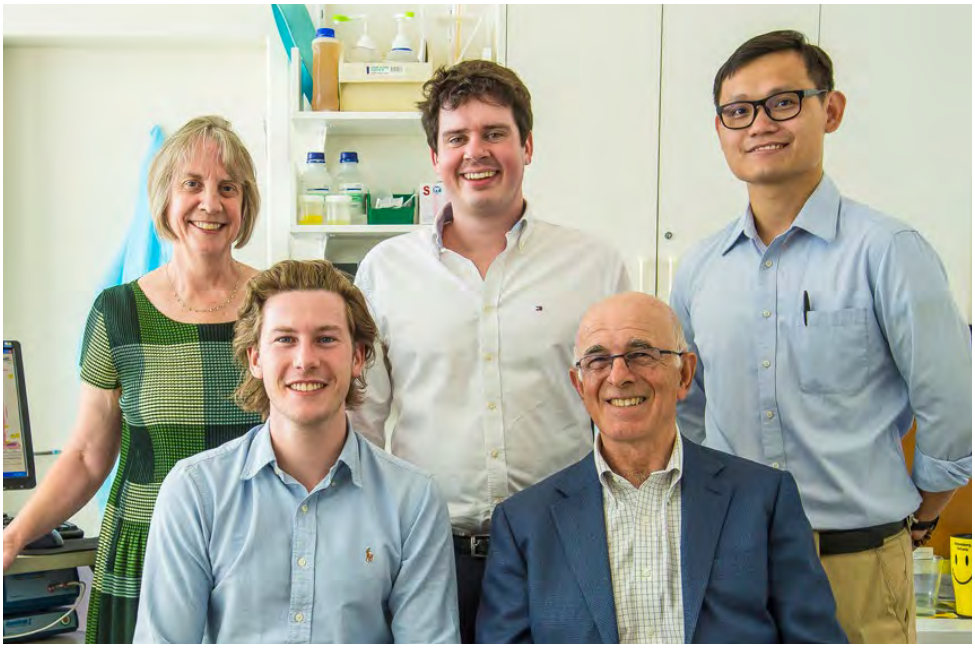

The Oesophageal Physiology Group explores abnormalities of swallowing function (known as oesophageal motility) that impact eating and drinking; and stomach reflux, that is often associated with heartburn and regurgitation.

Understanding oesophageal function and dysfunction through the use of technology and measurements is complex, and yet subtle but informative variations are being identified that can be used clinically, such as swallow muscle strength or patterns of reflux from the stomach. These findings are expanding current knowledge and improving understanding of abnormal physiology in patients struggling with eating and drinking.

This clinical research aids formal medical diagnosis and guides treatment and symptom management options for patients, which may include anti-reflux surgery, a myotomy for stomach flap-valve surgery or obesity surgery.

2020 research

Bile reflux after obesity surgery: An increasingly overweight population are undergoing weight loss operations (bariatric surgery) and are at risk of bile reflux. Dr Tom Eldredge, a PhD student, is evaluating patients after bariatric surgery (a gastric bypass, a gastric sleeve or a single anastomosis bypass). By using nuclear medicine imaging he can detect small amounts of bile reflux with high accuracy and reproducibility. This finding will lead to improved bile reflux assessment of patients after weight loss surgery and will influence surgical approaches to reduce the risk of this happening.

RESEARCH HIGHLIGHT OF 2020

Swallowing difficulty after reflux surgery linked to altered anatomy of the upper gullet

For over 30 years keyhole surgery has been offered to patients to stop reflux and provide relief from debilitating heartburn and regurgitation. A concern for surgeons is how to avoid the difficulty in swallowing that is experienced by some patients after this surgery. A unique exploratory study was conceived: to understand how reflux surgery changes the shape (or anatomy) of the distal oesophagus nearest the stomach and the valve at the top of the stomach, and the way substances flow through.

During 2018-2020, our team devised new measurements to record anatomical features of the oesophagus that can be seen on barium swallows in radiology. Our collaborative efforts reveal, for the first time, that patients who experience a sluggish passage of food or drink after surgery for reflux have different oesophageal anatomy. Specifically, we have shown that there is an abnormal angle of the distal oesophagus and the region is pushed forward (displaced anteriorly). This is a key finding of the Thesis submitted for Master of Philosophy (Surgery) by Dr Siang Wei Gan, and will lead to an evaluation of the technical steps of reflux surgery with a view to reducing the distortion and displacement of the oesophagus and potentially reduce swallowing problems.

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.**

2020 research

- The group will be the South Australian node of PRE-EMPT (Prediction of Early Mental Disorder and Preventive Treatment), an NHMRC Centre of Research Excellence that will commence in 2021 and will be supported by $2,500,000 of NHMRC funding. The aim of PRE-EMPT is to better understand how psychosis and other mental illnesses develop and progress, to identify risk factors that will exacerbate or protect against disease progression, and to generate tools for use in clinical practice that will better predict the onset of serious mental disease.
- Other collaborative grants awarded to the group and that will recruit through the BHI, TQEH include:
  - 'Impact of Relapse in Schizophrenia Study' and 'Real World Functional and Quality of Life status of Patients Treated with Paliperidone Palmitate 3 Monthly (PP3M) for More than Two Years: An Australian Experience', both funded through Janssen-Cilag; and
  - 'Saliva Monitoring in Patients Taking Lithium', in collaboration with researchers at University of California, Irvine and funded by the Prentiss Foundation.

RESEARCH HIGHLIGHT OF 2020

The COVID-19 pandemic has created a pressing need for researchers and clinicians to formulate advice, policies and guidelines to address the potential and real threats to existing patients from infection and also from disruption to normal clinical services.

Associate Professor Clark was part of an international team that developed recommendations for minimising COVID-19 transmission in patients with schizophrenia by safely increasing the duration of mandatory routine physical health monitoring of antipsychotic treatment with the drug clozapine, while acknowledging the risks posed by infection itself.[1] This statement has been adopted internationally in centres across the US, Europe and New Zealand and has received over 40 citations in only 9 months.

1. Siskind D, Honer WG, Clark SR, et al. Consensus statement on the use of clozapine during the COVID-19 pandemic. *J Psychiatry Neurosci.* 2020; 45(4):200061.
▶ **https://pubmed.ncbi.nlm.nih.gov/32242646/**

ASSOCIATE PROFESSOR CLARK WAS PART OF AN INTERNATIONAL TEAM THAT DEVELOPED RECOMMENDATIONS FOR MINIMISING COVID-19 TRANSMISSION IN PATIENTS WITH SCHIZOPHRENIA...

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The Respiratory Research Group is the research arm of The Queen Elizabeth Hospital's Respiratory Medicine Unit (Head of Unit, Dr Jonathan Polasek) and is involved in running a number of sponsored Clinical Trials and Investigator-led projects.

The unit has a number of 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.

2020 research

- We found that a modified step test protocol may be an acceptable alternative to the gold standard six minute walk test in detecting exercise-induced hypoxia in dyspnoeic patients with respiratory disease. The shorter step test protocol duration was sufficient to reveal exercise-induced hypoxia while offering a practical alternative in space-limited clinics.
- We have surveyed patients referred to the Respiratory Medicine Unit about their experiences during the pandemic. Patients reported that the onset of COVID-19 restrictions affected their anxiety, depression and/or stress levels, which in turn led to a change in their smoking status. Sixty-three percent of these individuals reported a mild to severe fear of COVID-19. We continue to gather data.

RESEARCH HIGHLIGHT OF 2020

Data indicates that South Australia leads the nation for asthma-related hospitalisations. This presents a challenge to the health system and importantly indicates that people with asthma may not be receiving a high level of care and education about managing their disease. We have been working with our partner, Asthma Australia, over the last few years on a multiphase, multisite research project that endeavours to uncover reasons why this may be happening in South Australia.

In 2020 we finalised a qualitative exploration of the current asthma care landscape in South Australia, taking into account the perspectives of health professionals and people with asthma. Our results indicate that health professionals feel demotivated by an inability to optimise care, perceived to be a result of the combination of reduced patient knowledge and capability, and insufficient resources. They believed this stemmed largely from asthma being a low ranking health priority with a lack of current socio-political awareness surrounding it.

People with asthma believed that there is a need to redefine inaccurate perceptions of asthma amongst health professionals and the general population. Additionally, they reported that they currently lack effective information and resources to feel empowered to lead their own health journey.

In 2020 we also took significant strides to further our quantitative evaluation of asthma care in hospital and community settings across South Australia and Queensland. The outcomes of this work are expected in 2021 and, together with the qualitative findings, will support the future research and advocacy strategy of our partners Asthma Australia in South Australia.

PATIENTS REPORTED THAT THE ONSET OF COVID-19 RESTRICTIONS AFFECTED THEIR ANXIETY, DEPRESSION AND/OR STRESS LEVELS, WHICH IN TURN LED TO A CHANGE IN THEIR SMOKING STATUS.


finding cures improving
WILL NOT


bio-strategy
delivering technology
Instrumentation
Consumables
Chemicals
Reagents & Assays
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Cleanroom Products
Fume Extraction
Plasticware
Glassware
SCIENCE
Central Adelaide
Local Health Network


Teaching Room 3

RHEUMATOLOGY RESEARCH GROUP

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

The group has expertise in population epidemiology, randomised clinical trials (RCTs), qualitative research, statistics, 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 Sjögren's Syndrome (SApSS) Research Clinic and Database and the South Australian Giant Cell Arteritis Registry.

2020 research

- Dr Samuel Whittle has led the development of the Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis [▸ **www.mskguidelines.org**], the world's first rheumatology clinical guideline to use 'living evidence' methodology in which recommendations are updated in near real time as new evidence emerges.
- Dr Huai Leng (Jessica) Pisaniello was:
  - awarded the Australian Rheumatology Association's New Investigator Award at the virtual 60th Annual Scientific Meeting in August. Jess presented part of her PhD research.
  - a faculty finalist in The University of Adelaide's Three Minute Thesis competition.
  - awarded the best clinical presentation at the SA Rheumatology Association 2020 meeting for her work on increased mortality in anti-neutrophil cytoplasm antibody associated vasculitis.
- Dr Joanna Tieu was awarded an unrestricted educational grant ($188,370) from Vifor to support a postdoctoral study (to commence in 2021 when her PhD is completed) entitled "Epidemiology of anti-neutrophil cytoplasm antibody (ANCA) associated vasculitis (AAV) in South Australia".

RESEARCH HIGHLIGHT OF 2020

In October 2020, Professor Catherine Hill led two international, virtual OMERACT (Outcome Measures in Rheumatology) workshops, which obtained consensus on core domain sets to be used in all rheumatology RCTs that include glucocorticoids. The core domain set will be published in *Seminars Arthritis and Rheumatism* and will determine outcomes measured in all rheumatology clinical trials including glucocorticoids. OMERACT workshops include clinicians, researchers, patients, industry and regulators (including the Food and Drug Administration, FDA).

Reaching consensus in these workshops is the culmination of 6 years of work by Professor Hill and her international collaborators Professor Susan Goodman and Associate Professor Sarah Mackie. Professor Hill has been assisted in this work by Dr Joanna Tieu (OMERACT fellow) and Dr Rachel Black (previous OMERACT fellow). This has been a data-driven program of research which has encompassed extensive qualitative research over 3 continents, systematic literature reviews of qualitative and quantitative work and Delphi surveys.

- Sue Lester was a finalist in the 2020 Unsung Hero of South Australian Science Awards.
  ▸ **See article on page 64**
- The Rheumatology Unit published 48 peer reviewed reports in 2020, including reports in highly prestigious journals like *Cell* and *The New England Journal of Medicine*.
  ▸ **www.basilhetzelinstitute.com.au/research/research-theme/inflammatory-disease-clinical-sciences-health-services-population-health/rheumatology-research-group/**

SOUTH AUSTRALIAN PRIMARY SJÖGREN'S SYNDROME (SApSS) RESEARCH CLINIC AND DATABASE

Primary Sjögren's Syndrome (pSS) is a common autoimmune disease manifesting with dry eyes and mouth, often resulting in serious damage to other organs. The SApSS Database, which incorporates a Registry and Repository, was established in 1991 by Professor Maureen Rischmueller and based at the BHI, TQEH. This database was recognised in 2020 to be in the top 10% of disease registries worldwide with respect to high quality publication output. It is unique with respect to placement in clinical practice, strong academic focus, longitudinal data, and translational research collaborations. In 2020 TQEH Rheumatology Clinical Trials Unit was appointed as the national lead site for industry-sponsored clinical trials into pSS, further enabling novel investigator-led sub-studies.

RESEARCH HIGHLIGHT OF 2020

A major contribution from the SApSS Research Clinic and Database was published in 2020 in the leading international scientific journal *Cell*.[1] This study, undertaken in collaboration with Dr Joanne Reed from the Garvan Institute of Medical Research and others, identified a number "rogue" clones (B lymphocytes) from the immune system of pSS patients that produced destructive autoantibodies. These antibodies, which recognise the patient's own cells and tissues, cause damage to the patient's blood vessels, kidneys and other organs. The rogue clones accumulated mutations in genes regulating growth and antibody production; several of these are already known to be associated with B cell malignancies such as lymphoma and leukaemia.

As patients with pSS are known to have a twenty-fold increased risk of developing lymphoma compared with the general population, the findings of this study shed light on mechanisms involved in this process. Our ability to isolate and examine rogue clones individually, using state of the art technology, enabled identification of specific markers on these cells, which in theory will enable them to be targeted by genetically engineered drugs - some of which are already available for the treatment of rheumatoid arthritis and lymphoma, and might in the future be effectively repurposed for individuals with SS using precision medicine.

This work was incorporated into a review and opinion piece on the role of B cells in Sjögren's Syndrome "When B cells break bad", published in the annual Sjögren's Syndrome supplement of the international journal *Clinical and Experimental Rheumatology*.[2]

1. Singh M, Jackson KJL, Wang JJ, ... Rischmueller M et al. Lymphoma Driver Mutations in the Pathogenic Evolution of an Iconic Human Autoantibody. *Cell*. 2020; 180(5):878-894.
▶ **https://pubmed.ncbi.nlm.nih.gov/32059783/**

2. Reed J, Verstappen G, Rischmueller M, Bryant V. When B cells break bad: Development of pathogenic B cells I Sjögren's syndrome. *Clin Exp Rheumatol.* 2020;38 Suppl 126(4):271-282.
▶ **https://pubmed.ncbi.nlm.nih.gov/33025890/**

2020 research

- The Clinical Trials Unit participated in the execution, analysis and publication of a number of studies of transformative agents for the treatment of rheumatoid and psoriatic arthritis, including one published in the prestigious *The New England Journal of Medicine*.[1]
- Collaborations continued with international researchers in Europe and USA on the genetics, clinical outcomes, and treatment guidelines for Sjögren's Syndrome.
- Exploration of the type of cells present in the diseased salivary glands of patients with Sjögren's Syndrome is underway in collaboration with researchers at the University of Queensland.
- Work is progressing on expansion of the SApSS Registry to become a National Registry and Repository, based at the BHI.

1. Rubbert-Roth A, Enejosa J, Pangan AL, Haraoui B, Rischmueller M, . . . Xavier RM. Trial of Upadacitinib or Abatacept in Rheumatoid Arthritis. *N Engl J Med.* 2020; 383(16):1511-1521.
▶ **https://pubmed.ncbi.nlm.nih.gov/33053283/**

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OMERACT Remission in RA-patient perspective Working Group

OMERACT Glucocorticoid Adverse Events Working Group

OMERACT Sjögren's Disease Working Group

Australian Scleroderma Interest Group (ASIG)

Australian Arthritis & Autoimmune Biobank Collaborative (A3BC)

Finalist, Unsung Hero of South Australian Science, 2020 SA Science Excellence and Innovation Awards

SUE LESTER
Rheumatology Research Group

I HAVE BEEN VERY PRIVILEGED TO HAVE HAD THE OPPORTUNITY TO DO VARIED AND INTERESTING WORK...

Sue Lester, Chief Medical Scientist with the Rheumatology Research Group at the Basil Hetzel Institute, TQEH, was selected as a finalist in the Unsung Hero of South Australian Science Awards [▸ **https://inspiringsa.org.au/unsung-hero-award-finalists-2020**], as announced as part of National Science Week in August 2020. The Unsung Hero Awards of South Australian Science are a joint initiative of National Science Week SA and the Australian Science Communicators. The award is intended to recognise those whose contribution has been significant over a long period of time but who have not yet received formal public recognition.

Sue moved to Adelaide soon after graduating with a Bachelor of Science Honours degree in Genetics from the University of Melbourne. She spent the first 20 years of her career working in various roles with the Australian Red Cross Blood Transfusion Service (ARCBTS). She joined as a research assistant under the guidance of Professor Jim McCluskey in 1979 but was quickly promoted to be the inaugural scientist in charge of the Quality Control Laboratory within the ARCBTS. Here she worked on improving the quality of the production of blood and blood components, thereby safeguarding countless lives. In 1991 an Immunogenetics Laboratory was established, and Sue was promoted to Senior Scientist. According to McCluskey she was “instrumental in guiding the establishment of DNA-based testing to determine patient tissue types for transplant matching... Sue’s contribution to these technologies was enormous and critical to establishing the testing carried out for the SA node of the Australian Bone Marrow Donor Registry.”

Since 1999 Sue has worked with the Rheumatology Department at TQEH. She has therefore worked under the directorship of Professor Kevin Pile, Associate Professor Maureen Rischmueller and Professor Catherine Hill. During her more than 20 years in Rheumatology Research Sue has established databases and sample repositories for many rheumatic diseases including Sjögren's Syndrome, Giant Cell Arteritis, Myositis and Scleroderma.

She has been an invaluable collaborator across multiple projects, most recently as an investigator with the newly formed Australian Arthritis and Autoimmune Biobank Consortium (A3BC). Sue’s expertise in advanced statistical analysis of data has contributed immensely to the department’s research output. These skills combined with her contributions to research design, grant applications, sample management, and the collation, analysis and interpretation of large population health data-sets has been instrumental to the department’s successes.

Sue has also been directly involved in supervising and mentoring Honours, Masters and PhD students within the Rheumatology Department. One former student wrote in support of her nomination “Sue taught me like no other, the core qualities of scientific writing and oral presentations, and before this the importance of how to become a skeptical and objective investigator. Her support and instruction was a requisite for the completion of my PhD, and she remains my most influential mentor.” In addition to Sue’s research contributions at the Basil Hetzel Institute, TQEH, she has been a key member of the TQEH Research Expo Organising Committee for many years, in particular with assistance in the judging of student abstracts and presentations.

Sue’s Rheumatology colleagues summarised Sue’s suitability for this award with the closing paragraph of their nomination stating “Sue is the epitome of an unsung hero. She has had a profound impact on the quality of science produced in South Australia, has mentored countless emerging physician-scientists and continues to generate world-class scientific research, with a singular focus on the quality of the science rather than any personal or extraneous considerations.”

After being told of her nomination Sue said “I have been very privileged to have had the opportunity to do varied and interesting work throughout the course of my career, and to work with some truly great people. I have learnt a lot."

https://youtu.be/lEcNtCnmkI0

Sue Lester
Chief Medical Scientist

Rheumatology Research Group
Basil Hetzel Institute, TQEH

L-R: Dr Carlee Ruediger, Sue Lester and Dr Rachel Black.


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The Surgical Science Research Group is primarily interested in clinical research and translational benchtop to bedside medicine in the surgical setting.

2020 research

- Drs Katharina Richter and Marcus Trochsler were awarded an NHMRC Ideas Grant for the project titled "Improving clinical outcomes of antimicrobial resistant infections with a drug-free intervention".
- Dr Kevin Fenix and senior researchers from the University of South Australia organised a symposium titled "Patient-derived *in vitro* models: advances & challenges" to bring together scientists and clinicians who use patient-derived samples in their programs, and fostered collaboration and the sharing of ideas. Held on 30 October 2020, in person and online, the symposium attracted approximately 100 attendees.
- In collaboration with the Viral Immunology Group and Dr Zlatko Kopecki (University of South Australia), Dr Kevin Fenix identified a novel immune cell population that may be involved in psoriatic re-flares.[1] This work was co-funded by THRF Group.
- Dr Kevin Fenix received funding from Tour de Cure to develop hepatic cellular immunotherapy for colorectal metastatic disease, a project titled "Pre-clinical assessment of a patient-derived cellular immunotherapy for metastatic colorectal cancer."

WE BELIEVE THAT OUR APPROACHES TO THE PROBLEM AND OUR RESEARCH EXPERIENCES WILL PROVIDE VALUABLE INSIGHTS FOR FUTURE RESPONSES TO THIS PANDEMIC AS WELL AS PANDEMICS TO COME.

1. Fenix K, Wijesundara DK, Cowin AJ, Grubor-Bauk B, Kopecki Z. Immunological Memory in Imiquimod-Induced Murine Model of Psoriasiform Dermatitis. *Int J Mol Sci*. 2020; 21:7228.

RESEARCH HIGHLIGHT OF 2020

The sudden arrival of COVID-19 presented surgical services globally with numerous dilemmas: Was it safe to perform procedures, such as laparoscopy, that might generate virus-containing aerosol? What personal protective equipment (PPE) should surgical staff wear? How should patients be prioritised for surgery during the pandemic? How should surgical patients be screened and tested for COVID-19?

To find solutions for these dilemmas, we sought evidence. We conducted rapid reviews of the literature and combined these with the advice of a working group of experts to produce evidence-based guidance for surgical services adapting to COVID-19 across Australia and New Zealand, specifically addressing the concerns around intraoperative safety, PPE use, surgical triage, and preoperative screening. This advice was published immediately on the Royal Australasian College of Surgeons website.

▶ **www.surgeons.org/media-centre/covid-19-information-hub#RACS%20guidelines%20on%20COVID-19%20safe%20practice**

COVID-19-related articles pertaining to surgical services were being produced at rapid rate from centres across the world. We adopted a novel approach to literature review to ensure our recommendations remained up-to-date. We conducted weekly rapid reviews, targeting literature addressing intraoperative safety, PPE, and surgical triage. We believe this generated the most comprehensive review of the COVID-19 surgical literature to date. The initial recommendations that we developed in April 2020 required no further modifications in response to the findings of subsequent literature. This work was published in the ANZ Journal of Surgery.[1, 2, 3, 4, 5]

The COVID-19 pandemic is likely to be the most significant health crisis of our lifetime. In what were unprecedented circumstances, we strove to maintain an evidence-based philosophy to facilitate the adaptation of surgical services across Australia and New Zealand with maximal reliability. We believe that our approaches to the problem and our research experiences will provide valuable insights for future responses to this pandemic as well as pandemics to come.

1. Maddern G. Evidence, not eminence, in coronavirus disease 2019. *ANZ J Surg*. 2020; 90(9):1537-1537.
▶ **https://pubmed.ncbi.nlm.nih.gov/32924298/**

2. Tivey DR, Davis SS, Kovoor JG, Babidge WJ, Tan L, Hugh TJ, Collinson TG, Hewett PJ, Padbury RTA, Maddern GJ. Safe surgery during the coronavirus disease 2019 crisis. *ANZ J Surg*. 2020; 90(9):1553-1557.
▶ **https://pubmed.ncbi.nlm.nih.gov/32594617/**

3. Babidge WJ, Tivey DR, Kovoor JG, Weidenbach K, Collinson TG, Hewett PJ, Hugh TJ, Padbury RTA, Hill NM, Maddern GJ. Surgery triage during the COVID-19 pandemic. *ANZ J Surg*. 2020; 90(9):1558-1565.
▶ **https://pubmed.ncbi.nlm.nih.gov/32687241/**

4. Tan L, Kovoor JG, Williamson P, Tivey DR, Babidge WJ, Collinson TG, Hewett PJ, Hugh TJ, Padbury RTA, Langley SJ, Maddern GJ, Personal protective equipment and evidence-based advice for surgical departments during COVID-19. *ANZ J Surg*. 2020; 90(9): 1566-1572.
▶ **https://pubmed.ncbi.nlm.nih.gov/32671968/**

5. Kovoor JG, Tivey DR, Williamson P, Tan L, Kopunic HS, Babidge WJ, Collinson TG, Hewett PJ, Hugh TJ, Padbury RTA, Frydenberg M, Douglas RG, Kok J, Maddern GJ. Screening and testing for COVID-19 before surgery. *ANZ J Surg*. 2020; 90(10):1845-1856.
▶ **https://pubmed.ncbi.nlm.nih.gov/32770653/**

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DRUG AND VACCINE DEVELOPMENT

RESEARCH GROUPS

Therapeutics Research Centre

Viral Immunology Group

In the Therapeutics Research Centre (University of South Australia) we study the variability in how patients respond to their various medicines and especially the impact of ageing, disease and multiple medications on their responses. 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.

A key focus is what happens when the body, especially the skin, is exposed to materials and products and when drugs, small molecules, nanoscale materials (tiny molecules 1-100nm in size used in commercial products) and cells enter the body. Our findings are then used to improve patient outcomes and to assist regulators in guiding future product development.

RESEARCH HIGHLIGHT OF 2020

Professor Roberts gave the 2020 Tom Watson Memorial Oration at the School of Pharmacy, University of Sydney.[1] Mike, a world leader in his field, used this talk to reflect on his career as a pharmaceutical researcher, highlighting key achievements and the impact of his and his Centre's work on the regulation of therapeutic agents across the world.

He spoke about how drugs interact with, and are changed by, the body. This included insights he has gained on how molecules are absorbed into the body, distributed throughout the body, broken down by the various body systems (metabolism), eliminated from the body and what toxic effects they may have had during this whole process, and critically, how this information can be used to develop evidence-based guidelines for the regulation of use.

1. Roberts MS. "Reflecting back on my journey as a pharmaceutical researcher", Tom Watson Memorial Oration 16 December 2020; School of Pharmacy, University of Sydney.

2020 research

- Professor Roberts was invited to present at the 17th Advanced Imaging Methods Workshop (January 2020) at University of California, Berkeley, USA and also at Photonics West SF, the world's largest biomedical optics conference, in San Francisco, in February 2020. Professor Roberts presented our new work using Fluorescent Lifetime Imaging (FLIM) and an advanced phasor technique to study retinoids in the liver.
- Professor Roberts presented at the Food and Drug Administration (FDA) meeting in Washington DC, February 2020 on the safety of sunscreens for topical use. This presentation has led to an invited publication describing all of our work to date on the fate of sunscreens in the body when they are applied to human skin. This work demonstrated that the sunscreen zinc oxide did not pass through the skin and hence did not pose a safety risk. This was not the case for other sunscreens we tested, which we showed were able to permeate the skin. This work has been important for the development of FDA guidelines and policies on the safety of sunscreen products.
- Professor Robert's NHMRC Senior Principal Research Fellowship (SPRF) was renewed for an additional year (2021) and the Food and Drug Administration (FDA) extended both of our grants for the next year of award.

THIS WORK HAS BEEN IMPORTANT FOR THE DEVELOPMENT OF FDA GUIDELINES AND POLICIES ON THE SAFETY OF SUNSCREEN PRODUCTS.

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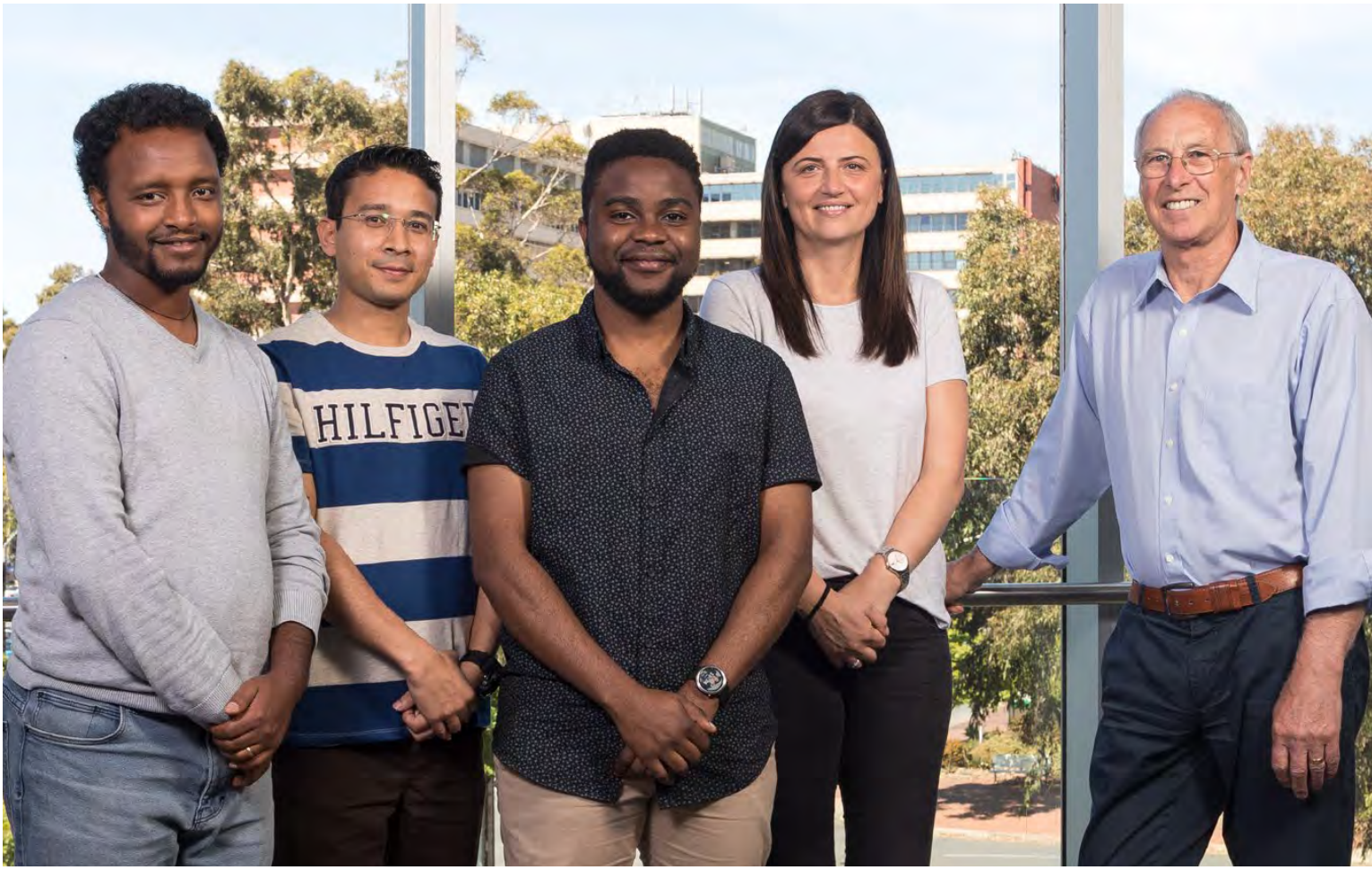
VIRAL IMMUNOLOGY GROUP



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

In 2020, 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 control pandemics we have.

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 2020 we incorporated the SARS-CoV-2 virus into our approach and are working towards a novel and effective vaccine for COVID-19 disease.

RESEARCH HIGHLIGHT OF 2020

In 2020 we were awarded a Medical Research Future Fund MTP Connect Biomedical Translation Bridge Program award.[1] This grant will support the development of our Zika virus vaccine into a commercial product.

Key to the work is our partnership with our commercial partner, Enesi Pharma, UK. The vaccine we are developing together will be in a solid-dose form that can be given without a needle, and will be stable at room temperature. These properties mean that the vaccine can be easily moved around the globe without the need to maintain cold or ultracold storage conditions. This vaccine not only has the potential to protect millions of individuals at risk of Zika virus infection, but has the potential to transform global vaccination logistics and become an exemplar for future vaccine development.

Now more than ever, we are reminded that fast, equitable, and logistically simple vaccine development and distribution is absolutely necessary to curb viral outbreaks, eliminate infections and keep the human population safe.

1. $1.35M for world-first needle free Zika virus vaccine, Newsroom, University of Adelaide, September 3, 2020.
▶ **www.adelaide.edu.au/newsroom/news/list/2020/09/03/135m-for-world-first-needle-free-zika-virus-vaccine**

2020 research

- In 2020 we initiated a 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 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 Women's and Children's Hospital Research Foundation and private philanthropy, is providing as yet unappreciated insights into the impact of the virus on patients.
- Dr Branka Grubor-Bauk participated in the Rapid Research Information Forum (RRIF), a forum convened by Australia's Chief Scientist and led by the Australian Academy of Science, to provide a mechanism to gather relevant multidisciplinary research expertise to address pressing questions about Australia's response to COVID-19 as they emerge. Outcomes of the forum are presented to the Chief Scientist of Australia, the Federal Health Minister and the Prime Minister of Australia, and inform Australia's pandemic response.
- Dr Branka Grubor-Bauk was invited to a virtual roundtable meeting with Hon Minister Payne, Minister for Foreign Affairs, to discuss COVID-19 vaccine development and progress, and the impact of the COVID-19 pandemic on women in the medical research sector.
- Dr Branka Grubor-Bauk was elected Vice-President of the Australian Centre for Hepatitis Virology (ACHV).
- Dr Makutiro Masavuli won an ACHV Early Career Researcher Project Award.

WE ARE REMINDED THAT FAST, EQUITABLE, AND LOGISTICALLY SIMPLE VACCINE DEVELOPMENT AND DISTRIBUTION IS ABSOLUTELY NECESSARY TO CURB VIRAL OUTBREAKS, ELIMINATE INFECTIONS AND KEEP THE HUMAN POPULATION SAFE.

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INFLAMMATORY DISEASE

RESEARCH GROUPS

ENT Surgery

Growth and Repair of the Small Intestine

Inflammatory Bowel Disease Research Group

UNDERSTANDING AND TREATING CHRONIC RHINOSINUSITIS

Our research team 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 bench to bedside approach where novel therapeutic candidates that are discovered in our laboratories undergo extensive testing before being used as treatments for 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.

RESEARCH HIGHLIGHT OF 2020

A bacteriophage (phage) is a virus that can infect and kill a bacterium, including a bacterium that is resistant to all therapeutic antibiotics, a so-called superbug. Interest in using phage as antibacterial therapies has been rekindled in the last 10 years due to the emergent superbug epidemic.

Professor Wormald and his team have been interested in phage therapy for over 5 years and have previously conducted a world first clinical trial testing the safety and effectiveness of phage treatments for therapy refractory chronic rhinosinusitis patients. Phages can be isolated from the environment, but extensive testing is needed to ensure the selection of phages that are effective as antibacterials and safe to be used in patients.

Supported by a strong interest and investments by Aushealth and patient organisations (e.g. CFSA and Cure4CF), the ENT department has established the “Adelaide Phage Therapy and Research Centre” within the premises of the Basil Hetzel Institute, TQEH. The Centre will source therapeutic phages for use in the treatment of patients infected with antibiotic resistant bacteria where all other therapies fail. The Centre will also conduct research activities aimed at developing effective phage-based therapeutics. The purpose of the Centre is to make phage treatments available for patients in Australia and beyond.

2020 research

- In an international multi-centre study of more than 500 patients from 14 centres, the ENT department has identified the core sinonasal microbiome in CRS patients versus non-CRS patients.[1] Based on these findings, we are now better positioned to develop novel approaches to manipulate a diseased microbiome into a healthy one.
- We have established a unique mouse model of chronic rhinosinusitis. This model can be used to test novel therapeutic compounds prior to translation into human clinical trials.
- We have found that various antibiotics can affect wound healing to a different extent.[2] This information is important in clinical practice and may help with the selection of antibiotics in the peri-operative period that could enhance wound healing and help prevent scar formation.
- We are conducting several human clinical trials of novel therapeutic agents aimed at biofilm eradication in patients with CRS. The development of such therapies may help combat the growing world-wide pandemic of antibiotic resistance.

1. Paramasivan S, et al. The international sinonasal microbiome study (ISMS): a multi-centre, international characterization of sinonasal bacterial ecology. *Allergy*. 2020; 75(8):2037-2049.
▶ **https://pubmed.ncbi.nlm.nih.gov/32167574/**

2. Gouzos M, Ramezanpour M, Bassiouni A, Psaltis AJ, Wormald PJ Vreugde S. Antibiotics Affect ROS Production and Fibroblast Migration in an *In-vitro* Model of Sinonasal Wound Healing. *Front Cell Infect Microbiol.* 2020; 10:110.
▶ **https://pubmed.ncbi.nlm.nih.gov/32266162/**

WE ARE NOW BETTER POSITIONED TO DEVELOP NOVEL APPROACHES TO MANIPULATE A DISEASED MICROBIOME INTO A HEALTHY ONE.

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NANOMEDICINE AND INFECTIOUS DISEASE

As part of the inflammatory disease theme (ENT surgery) the Nanomedicine Group, University of South Australia explores how the efficacy of critically needed medicines can be improved while reducing side effects. Specifically, the group investigates the interaction of microscopic drug carriers with bacteria that are surrounded by a slime (biofilms). Biofilms are associated with devastating and difficult to treat chronic infections of the sinuses, lungs and wounds.

The team translates developments in material sciences, biology and pharmaceutics into medicines that are more effective compared to currently available treatments.

2020 research

- Muhammed Awad's presentation on the healing power of light was awarded best Mini-Oral Presentation at the 29th TQEH Research Expo.
- Chelsea Thorn received an award for best presentation (runner-up) at the Australian Controlled Release Society Annual Meeting (held online due to COVID-19).

RESEARCH HIGHLIGHT OF 2020

Infectious diseases are a major threat to global communities. In 2019 the United Nations/WHO sounded the alarm, predicting that drug-resistant infections are on track to cause 10 million deaths every year by 2050 unless the world acts.

The Nanomedicine Group has identified a novel way to upcycle existing, but fading antibiotics, and making them up to 10,000-fold more effective. We achieve this by incorporating the existing antibiotic into a new delivery system, encapsulating the drug into microscopic capsules, too small to be seen by the eye, that are made from food-grade lipids.

Over the last 2 years these formulations have been intensively characterised in collaboration with leading researchers from Australia (Professor Ben Boyd, Monash University) and Germany (Professor Claus-Michael Lehr, Helmholtz Institute for Pharmaceutical Research Saarland).

Upcycling antibiotics will cut down the time to approval for use by regulatory bodies by several years - valuable time in the fight against infections. Our group has recently patented this discovery and are looking to partner with investors to translate this exciting result into the market.

Muhammed Awad
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GROWTH AND REPAIR OF THE SMALL INTESTINE

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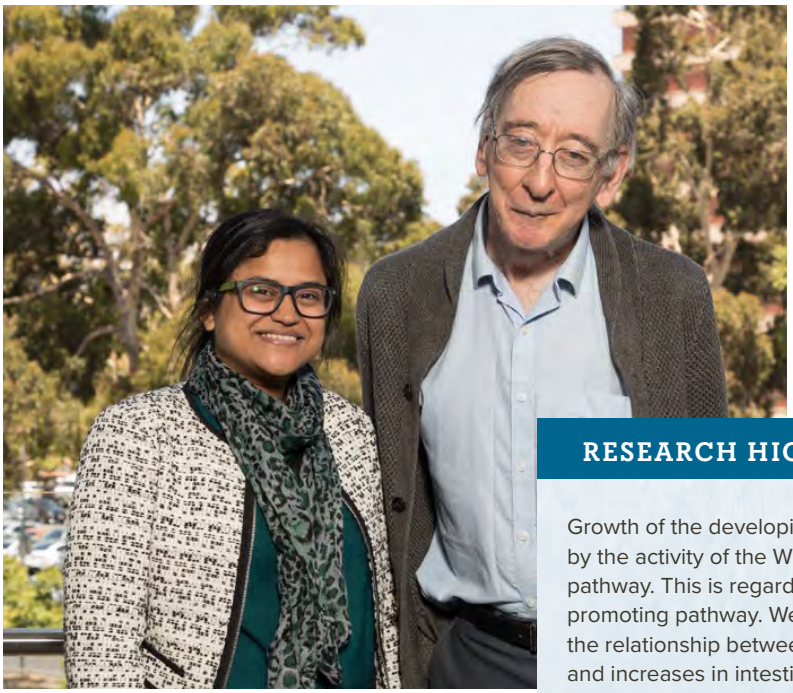

The Growth and Repair of the Small Intestine Group studies the basic mechanisms of growth of the small intestine. Growth of any cell population occurs by an increase in birth of new cells or by preventing cell loss from the population.

Our work suggests that postnatal intestinal growth is driven by preventing cell loss, through the suppression of intestinal stem cells death (or apoptosis). We hypothesise that signalling pathways, active in the developing small intestine, promote nurseries for intestinal stem cells, called crypts. Crypts protect stem cells from dying and foster increasing stem cells numbers with little increase in stem cell division.

We have had support and assistance of the Department of Gastroenterology and Hepatology at The Queen Elizabeth Hospital and the Department of Gastroenterology, Women's and Children's Hospital.

2020 research

- Our work has applications in agriculture such as in pork production.
- We are waiting to see success of funding or otherwise on a project examining whether too many intestinal stem cells cause obesity.

RESEARCH HIGHLIGHT OF 2020

Growth of the developing small intestine is driven by the activity of the Wnt/β-catenin signalling pathway. This is regarded as the principal growth promoting pathway. We have been investigating the relationship between Wnt/β-catenin signalling and increases in intestinal crypts (a process called crypt fission).

We demonstrated that growth factors that activate the Wnt/β-catenin signalling pathway (Wnt3 and R-spondin-1) are present in the small intestines of rats and humans, as others have shown in mice, and that Wnt3 and R-spondin-1 are active and peak during infancy. Our work showed that crypt fission also peaked during infancy in humans and in rats. More importantly, we showed that if we block the Wnt/β-catenin signalling pathway in infant rats fewer crypts were formed and there were fewer stem cells per crypt. These studies lead to a basic understanding of how the small intestine grows, and support a model that growth occurs through crypt proliferation and enhanced intestinal stem cell survival.

Furthermore, our work has shown that intestinal stem cells are surviving because their death by apoptosis is being actively suppressed by the Wnt/β-catenin signalling pathway. This work was conducted by Zenab Dudhwala in her studies towards a PhD, and has resulted in one publication in 2020[1] and another that has been submitted for publication.

These findings open up many avenues of investigation for the future, including investigating if some nutrients, found in foods, are able to protect the lining of the small intestine. Of particularly interest is investigating if natural polyphenols, like those found in turmeric, strawberries, pears, apples, coffee and tea, modulate and augment growth of the small intestine by increasing the survival of intestinal stem cells and preventing cell death.

1. Dudhwala ZM, Hammond PD, Howarth GS, Cummins AG. Intestinal stem cells promote crypt fission during postnatal growth of the small intestine. *BMJ Open Gastro*. 2020; 7:e000388
▶ **https://pubmed.ncbi.nlm.nih.gov/32586946/**

Our research focuses on the role of the gut microbiome and diet in inflammatory bowel disease (IBD) and other gut disorders, and on manipulating the microbiome and diet for therapeutic effect. In addition, we undertake clinical research in the area of IBD, with a particular focus on gastrointestinal ultrasound, with the overarching aim of improving patient outcomes and quality of life.

2020 research

- Our research group has undertaken studies to evaluate the use of gastrointestinal ultrasound (GIUS) in routine IBD care. We have led a large international collaborative project validating the accuracy of GIUS in IBD, with the goal of developing a GIUS score which could be used in clinical trials and in practice. In addition, we explored the role of GIUS as a non-invasive tool for assessing IBD in the setting of the COVID-19 pandemic.
- We have contributed to national and international guidelines on the use of FMT therapy, and toward the Australian regulation of FMT therapy through engagement with the Therapeutic Goods Administration.
- We have undertaken a large multi-disciplinary project evaluating *Helicobacter pylori* antibiotic-resistance patterns in Australia and locally at TQEH. This work has generated a systematic review of the literature,[1] and a large dataset which may inform local antibiotic prescribing guidelines for *H. pylori*.
- We are investigating patient and physician perceptions of FMT as a therapy for *C. difficile* infection.

1. Schubert JP, Gehlert J, Raynor CK, Roberts-Thomson IC, Costello S, Mangoni AA, Bryant RV. Antibiotic resistance of *Helicobacter pylori* in Australia and New Zealand: A systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2020 Nov 20; [online ahead of print].
▶ **https://pubmed.ncbi.nlm.nih.gov/33217029/**

RESEARCH HIGHLIGHT OF 2020

Our research group has made a number of contributions towards developing new therapies, understandings and monitoring tools for patients with inflammatory bowel disease in 2020.

We have undertaken clinical trials of dietary therapy and faecal microbiota transplantation (FMT) for the treatment of ulcerative colitis. These therapies have individually demonstrated promise as treatments for ulcerative colitis, and we have reported on the potential of combining these new therapies into a single treatment regimen.[1]

These studies are yielding data that give us a greater understanding of how microbes and dietary factors contribute to the disease. This is important because the current therapies for ulcerative colitis are hampered by incomplete efficacy, and many act to suppress the immune system and therefore have potential side effects of infection or cancer. New therapies that do not target the immune system are required. The insights we are gaining from dietary and FMT studies in ulcerative colitis are being used to identify candidate microbes and prebiotic dietary fibres that may be developed for use separately and together as new, effective and safe therapies for ulcerative colitis.

1. Costello SP, Day A, Yao CK, Bryant RV. Faecal microbiota transplantation (FMT) with dietary therapy for acute severe ulcerative colitis. *BMJ Case Reports C*. 2020; 13:e233135.
▶ **https://pubmed.ncbi.nlm.nih.gov/32843418/**

THESE THERAPIES HAVE INDIVIDUALLY DEMONSTRATED PROMISE AS TREATMENTS FOR ULCERATIVE COLITIS...

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Finalist, PhD Research Excellence, 2020 SA Science Excellence and Innovation Awards

DR SAM COSTELLO
Inflammatory Bowel Disease Research Group

ULCERATIVE COLITIS IS AN INCURABLE, RELAPSING AND REMITTING INFLAMMATORY BOWEL DISEASE...

Dr Sam Costello is a gastroenterologist based at The Queen Elizabeth Hospital and a research leader of the Inflammatory Bowel Disease Research Group at the BHI, who completed his PhD at The University of Adelaide in 2019. Sam's PhD research investigated faecal microbiota transplantation (FMT) as a novel therapy for ulcerative colitis (UC). Sam was a finalist in the 2020 SA Science Excellence and Innovation awards in the category of *PhD Research Excellence* in recognition of the importance and quality of his research work.

Ulcerative colitis is an incurable, relapsing and remitting inflammatory bowel disease characterised by inflammation of the colonic mucosa (the lining of the bowel) that affects approximately 40,000 Australians. The disease significantly impacts the lives of patients, with an unacceptably high rate of persistent or relapsing symptoms including bloody diarrhoea, anaemia, weight loss and abdominal pain. UC is associated with a risk of surgical colectomy (removal of ulcerated bowel tissue) and there is an increased risk of colorectal cancer relative to the general population. Current treatments can have unacceptable side effects including allergy, intolerance, serious infection and malignancy due to long-term immunosuppression. When Sam began his PhD studies there was a pressing need for new therapies for UC.

FMT involves the transfer of faecal material (stool) from a healthy individual to a person with disease with the aim of treating that disease. The aims of Sam's PhD were to provide rigorous evidence of efficacy and safety of FMT as a treatment for UC and understand how FMT therapy might work by analysing changes to the gut microbiome, bacterial metabolic activity and the mucosal immune system in patients. During his PhD Sam demonstrated that FMT was an effective therapy for UC and uncovered the mechanisms that underpinned its success. This led to the development of a defined microbial therapy that will enter further clinical trials soon. The trial was awarded best clinical trial at the world's largest Crohn's and Colitis meeting ECCO in Barcelona in 2017.

Sam's was the first study to assess bacterial metabolites and mucosal immune cell populations following FMT in UC. He concluded that the treatment effect of FMT may have resulted from changes to the metabolic functional capacity of the gut bacteria, and that this change was contributed by donor microorganisms from the FMT.

To run a clinical trial of FMT a source of donor stool prepared as a therapeutic was needed. This required the creation of a stool bank and methods for the preparation, screening, storage and transport of donor stool. The stool bank created during Sam's PhD not only supported the clinical trial, but provided a reliable supply of treatments for *C. difficile* infections for South Australian patients. Prior to his work, these patients could not access potentially life-saving FMT therapy locally. 70 patients were treated for *C. difficile* infection with FMT in South Australia, with an overall cure rate of 97%.

Following his PhD, Sam has been instrumental in establishing a stool bank, BiomeBank, in collaboration with The Hospital Research Foundation Group and co-founder Dr Rob Bryant. BiomeBank [▸ **www.biomebank.com**] aims to reliably and safely supply patients in Australia and Asia with life-saving FMT therapy and develop second generation defined microbial therapies. BiomeBank is TGA accredited and supplies hospitals Australia wide with FMT to treat recurrent and refractory *C. difficile* infection.

https://youtu.be/j6q9_LNwZ38

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TQEH RESEARCH EXPO 2020

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