RAH RESEARCHER

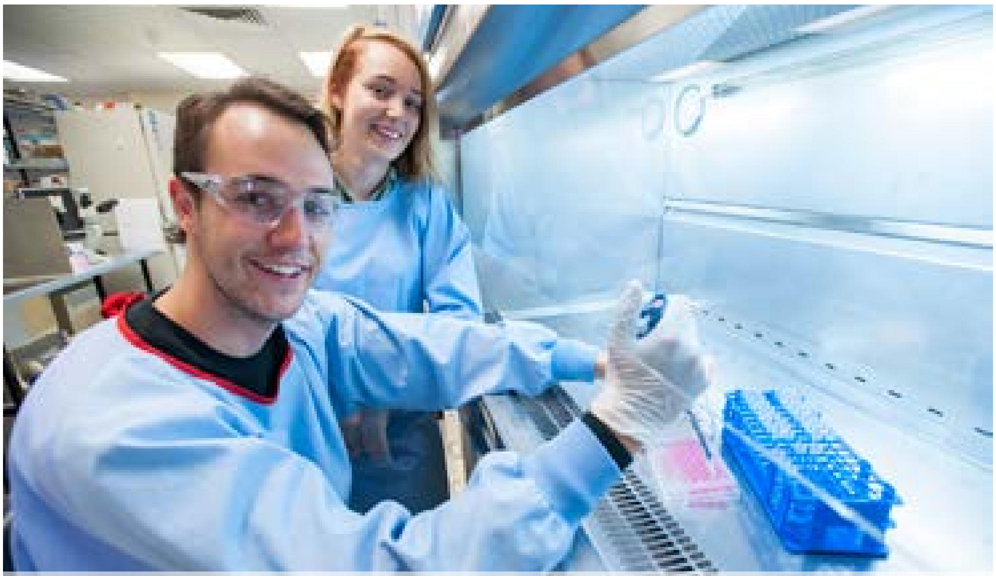
RAH RESEARCH FUND

Fundraising for medical research at the Royal Adelaide Hospital and with our research partners – the Hanson Institute, SA Pathology and the Centre for Cancer Biology.

Edition 2
2016

A promising protein to enhance blood cancer therapies

PhD students Alexander Lewis and Melissa Bennett may be researching differing blood cancers, but their goal is the same – to enhance current treatments in the hope of improving survival outcomes for patients.



Alexander Lewis and Melissa Bennett are two young and fresh minds passionate about improving survival rates for patients with blood cancer.

Both researchers are investigating sphingosine kinase, a protein that plays an all important role in promoting the growth of cancer cells.

Both students are under the supervision of Professor Stuart Pitson from the Centre for Cancer Biology at the Royal Adelaide Hospital (RAH) who with his team has discovered the important role this protein plays in cancer growth.

“It’s very hard to kill cancer cells because they increase a lot of survival pathways to keep themselves alive,” Professor Pitson said.

“One of these pathways comes from the sphingosine kinase proteins and that’s why we have pushed targeting those in the hope of enhancing existing therapies to kill all the cancer cells. This is the foundation for Alexander and Melissa’s research as they apply our findings to blood cancer.”

In the early stages of their PhDs, Alexander’s research focuses on Acute Myeloid Leukaemia (AML) and Melissa’s on Multiple Myeloma. These are both common blood cancers in Australia with unfortunately low survival rates.

“AML is a particularly aggressive blood cancer that is commonly found in the elderly population,” Alexander said.

“Based on past research we have found that sphingosine kinase plays an important role in keeping AML patient’s cancer cells alive even after chemotherapy treatment.”

Melissa came to the same conclusion through her honours project looking at multiple myeloma and has now achieved a Dawes Scholarship through the RAH Research Fund to pursue her findings through a PhD.

“Multiple myeloma is an incurable disease and whilst current treatment is very good at prolonging life expectancy nearly every patient will eventually develop a resistance and sadly their cancer will come back,” Melissa said.

“Also multiple myeloma is a disease that grows and multiplies meaning that patients will generally have different variations of it and the likelihood that every single cell in that population will be killed by one drug is unlikely.

“In my honours project I was looking at targeting another pathway in combination with the current treatment to enhance it and try to make it more effective. The pathway I was looking at targeting was this sphingosine kinase protein.

Now both Melissa and Alexander are investigating different inhibitors that could be used in combination with current treatments to improve outcomes for patients.

“In my project I am now trying to work out how the sphingosine kinase protein is helping to promote the survival

cont’d on page 2

Giving Back in Memory of a Family Man

Brian Dobie was a loving husband, father and grandfather whose life was cut short when he sadly passed away from pancreatic cancer in 2011 at the young age of 64.

Whilst dealing with the heartbreak that comes with losing her husband and the father of her four children, Jean Dobie with the support of her family, decided to give back to research into pancreatic cancer in memory of her beloved Brian.

"Brian went through so much with pancreatic cancer, he survived 18 months. He was a wonderful man, very kind, loving and supportive," Jean said.

"I wanted to feel as if he didn't go through it for nothing, that something good has come out of it to give us hope that other people won't have to go through what our family did in the future. There is not much known about pancreatic cancer and you don't hear about it very often even though it is terminal most of the time."

To continue Brian's legacy Jean and her children set up their own cause '*For Brian*' and on the last Sunday of November 2011 hosted their first fun day, a family friendly event for the local community.

"After talking with my children we decided we would raise money ourselves, and that's how our charity came to life.

"Our son suggested we do a family fun day, Brian always loved going across to the park near our house to play bocce and cricket. He loved playing with our children and grandchildren."

Jean's son Wayne speaking for a cause very close to his heart at one of the '*For Brian*' fundraising days.

Jean and her beloved late husband, Brian Dobie, who will forever remain in her heart.

With help from family and friends along with amazing community support from local shops and government, Jean and her family were blown away by the fun day's success. The event then became an annual tradition and the Dobie family went on to raise an incredible $15,000 over the next four years for research into pancreatic cancer through the RAH Research Fund.

"We chose to host the fun days on the last Sunday of November each year as Brian's birthday was on the 28th and November is also Pancreatic Cancer Awareness Month. We had a different theme each year to keep it different and interesting; one year it was crazy hats and a beach theme the next. We couldn't be more chuffed with the amount of support and generosity we have received. I know that Brian would have been humbled and proud," Jean said.

"Raising the money and hosting these events has done me and I hope my family a world of good. It's been part of the healing process, putting our energy into something positive to help others."

The RAH Research Fund is so grateful for the support of Jean and her family and friends, we look forward to seeing what they achieve in the future!

Enhancing blood cancer therapies cont'd

> from page 1

of these AML cancer cells and what affect blocking them has," Alexander said.

"Hopefully I can then come up with different ways to block the sphingosine kinase and target the roots of the disease – the leukaemia cells that are missed by chemotherapy treatment.

"Being that chemotherapy is also quite gruelling for patients, if we can develop a targeted therapy to use in combination with it, we could lower the necessary dose and reduce side effects as well."

Similarly Melissa is hopeful her research could improve the effectiveness of the current treatment for multiple myeloma.

"I've found through targeting the sphingosine kinase protein through a particular inhibitor called K145 it actually enhanced the effects of the current treatment for multiple myeloma," Melissa said.

> **"Treating with a combination would ideally improve outcomes for patients and make them less resistant to treatment methods."**

Looking to the future, Alexander and Melissa are eager to push their findings to clinical trials in the hope of creating more targeted therapies for these heartbreaking cancers.

Solving the Snakebite Puzzle

Worldwide, at least 100,000 people will die each year from snakebites.

This is a frightening statistic and while the rate of deaths from snakebites in Australia is extremely low, Royal Adelaide Hospital (RAH) Emergency Physician and Toxicologist Dr Sam Alfred wants to make a difference in this area.

Through research he intends to grow knowledge in snakebite management in a bid to improve clinical management and reduce deaths across the globe.

Dr Alfred is part of the Myanmar (Burma) Snakebite Project, supported by the Australian Department of Foreign Affairs and Trade (DFAT) over three years in partnership with Australian antivenom producer, Seqirus (previously bioCSL), The University of Adelaide and the Myanmar Government. This international project is aimed at saving the lives of those who die each year from venomous snakebites in the South-East Asian nation of Myanmar.

Through his involvement with this aid project, Dr Alfred and his colleagues uncovered a number of unanswered questions about the management of antivenom in a clinical setting, which has led to research.

"I was so appreciative to receive funding from the RAH Research Fund for my proposed research project, which is now looking at the relationship between coagulation (blood clotting) screening and the presence of venom in the serum of a patient who has been bitten by a snake," Dr Alfred said.

When he isn't in Myanmar working on the Snakebite Project, Dr Alfred works at the Royal Adelaide Hospital as an Emergency Physician.

"The current situation for clinicians when someone presents to hospital with a snakebite is to try and determine if they have venom in their blood and giving these patients antivenom."

Dr Alfred explains that based on the current research and available literature, anywhere between 30 to 50 per cent of snakebites are dry bites, which produce no detectable envenoming in the patient.

"This presents a bit of a problem because we don't have a method of accurately identifying a patient with venom in the blood stream – you can't test for venom directly," said Dr Alfred.

cont'd on page 4

Growing Knowledge in the World of Allergy Research

As a recipient of a RAH Research Fund Mary Overton Early Career Research Fellowship, Dr. Kwok Ho (Dave) Yip is spending his post-doctoral fellowship investigating an area that impacts the daily life of so many Australians – allergies.

Dr. Yip's world of research is focused on mast cells, which normally mature and reside in a human's tissues, particularly those exposed to the external environment, including the skin, lung and gastrointestinal tract.

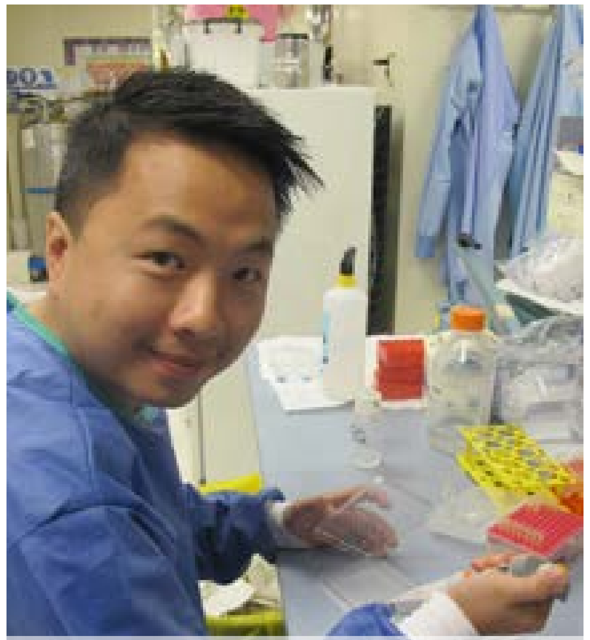
The Mary Overton Fellowship has enabled Dr. Yip to conduct his research, looking closely at these mast cells and finding out how to control them from triggering allergic responses without affecting their positive functions in the body.

"Receiving the Mary Overton Fellowship was really exciting for me and I am so very thankful for the people who donate to the RAH Research Fund," said Dr. Yip.

"The three year fellowship provides me with a stable position at the Centre for Cancer Biology, which means I can concentrate on my research without worrying about my funding situation."

Dr. Yip was interested in research in the area of allergies as he himself has suffered from eczema and he is passionate about looking into an area that impacts a large percentage of the population.

cont'd on page 5



Having suffered from eczema in the past, Dr Yip wanted to work in an area that impacts a large percentage of the community.

Solving the Snakebite Puzzle cont'd

> *from page 3*

A number of the dedicated individuals working on the Mynamar Snakebite Project including Dr Sam Alfred and his Australian colleagues.

FACT: Worldwide, there are more than 3,000 species of snakes, out of which about 600 are venomous.

"You also can't give anti-venom to everyone because it can potentially have quite serious side effects. Currently we use a screening process to try and identify which patients are likely to have venom in their bloodstream through indirect findings – like assessing for blood clotting abnormalities which are a common manifestation of envenoming post snakebite."

Dr Alfred says a lot of snakebites will trigger responses in the body that consume all of your blood clotting factors, so that you can't form any more blood clots. This results in a bleeding abnormality.

"There is an assumption that if you find the bleeding abnormality, there must be venom in the patient," he said.

"However, it's not entirely clear this is true because we don't have a solid understanding of how long venom stays in the blood stream and it seems this bleeding abnormality probably persists longer than venom is present. This means we don't really know if it's true that finding a blood clotting abnormality means you should give your patient antivenom."

Given the limited solid data on these issues, Dr Alfred's project will assess this process in snakebite patients, looking at the detection and relationship of envenoming (the process of a snake injecting venom into a patient) and its implications for snakebite management.

He explains that in an Australian setting, samples are sent to a laboratory where sophisticated blood clotting tests can be coordinated. These are not available in the vast majority of third world countries where these types of snakebites are common – they need an alternative method.

"In these sorts of third world settings, clinicians will put a little bit of blood into a glass test tube for 20 minutes and then tip it upside down to assess for the formation of a blood clot that would normally be expected to form during this timeframe –it's a useful test referred to as the 20 minute whole blood clotting test, but it's by no stretch of the imagination perfect," Dr Alfred said.

His research project will examine the relationship between this test and the more sophisticated clotting tests used in Australia.

"We're aiming to collect samples from patients in Myanmar and bring them to Australia and test what the formal clotting assessment is and look at the correlation between the whole blood clotting time and the more sophisticated test to try and analyse that relationship.

"Then we'll be looking at ways to detect venom in the plasma with various technologies on offer. If we're able to detect specific venom components and to look at things like whether the venom is affected by the anti-venom that's been administered, it gives us a means by which we can evaluate the traditional testing approach.

"We're also looking at South Australia, so looking at also enrolling snakebite patients at the Royal Adelaide as well for this project."

Dr Alfred is thankful for the community support through the RAH Research Fund and is optimistic about delivering some very useful clinical information about the value of the screening tests currently used and the timeframe venom stays in the human bloodstream.

"That's very useful clinical information that will make a big difference to how patients are treated pretty quickly!"

We look forward to giving you an update on this international research in the near future and wish Dr Alfred all the best with gathering samples and conducting his study!

Lending a Helping Hand

Immigrating from the UK to Adelaide in 1999, Cedric and Amanda Meyer have been a blessing to the South Australian community, donating two days a week to volunteer at the Royal Adelaide Hospital (RAH).

Initiated in 1971, the RAH Volunteers offers nine different services to patients ranging from laundry and driving to palliative care. All of these services are provided completely free of charge to those without support whilst in hospital.

Amanda herself has spent over 11 years as a devoted volunteer, splitting her time between Intensive Care and the Oncology Units.

"In both intensive care and oncology, we get involved with the families, helping them cope and understand what is going on," Amanda said.

"It's really quite rewarding, especially being able to help people who really need the support, such as single parents."

Cedric, who has a background in mechanical engineering, drives the scheduled shuttle bus between the RAH and The Queen Elizabeth Hospital on Tuesdays and on Wednesdays assists with administration jobs.

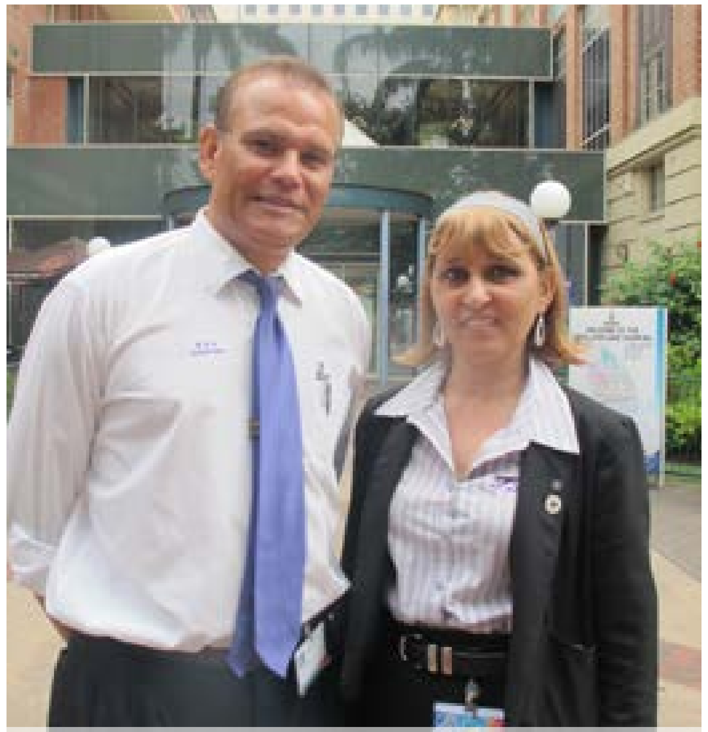
"I was initially a bit sceptical about becoming a volunteer, but then I realised the range of people who volunteer their time to provide these services – I fit right in," he said.

"The appreciation we get from patients and the respect we get from the staff at the RAH – it's very satisfying work," he said.

"Just getting a smile from someone can make your day."

With four grown up children and currently living in Morphett Vale, Cedric and Amanda spend their days not volunteering looking after one of their six grandchildren.

"We love being part of the RAH Volunteers and are excited to relocate to the new hospital," Cedric said.



Husband and wife Cedric and Amanda say that putting a smile on someone's face as part of their volunteer day is one of the best feelings!

If you ever see one of the RAH Volunteers while at the hospital, please don't hesitate to stop and ask them for a helping hand.

If you would like information about applying to be a volunteer, please contact RAH Volunteers Manager, Chris Iovino on ***08 8222 4637*** or ***chris.iovino@sa.gov.au.***

Growing Knowledge in Allergy Research cont'd

> *from page 3*

"Our primary focus is looking at how to restrain the hyper-activation of mast cells, which are a primary trigger in an allergic response," he said.

"Mast cells help to regulate immune responses and maintain homeostasis in organs, which means they keep different parts of the body at a stable condition."

"So our main research is to focus just on suppressing the hyper-activation of these cells without harnessing their normal functions."

Dr. Yip explained that his research team is now using human blood samples as a source of human mast cells for experiments in the lab.

"We routinely recruit either healthy volunteers or patients for blood samples, alternatively we can obtain blood samples from the Australian Red Cross, which is really helpful," Dr. Yip said.

Dr Yip hopes his research eventually leads to the development of a treatment for severe allergies that doesn't lead to side effects. Long-term treatment for people living with allergies, such as the use of steroids, will often result in a large number of side effects, some quite detrimental to a person's quality of life.

> **"I really love working in an area that can help to improve the wellbeing of a lot of people and we look forward to understanding and exploring the role of mast cells more."**

"It's challenging as mast cell research is not just limited to allergies, there is also more to explore in their role in other disease settings, such as autoimmune diseases and cancer progression."

Understanding Congenital Heart Disease

Kick starting her three year post-doctoral Mary Overton Early Career Fellowship from the RAH Research Fund, Dr Sophie Wiszniak wants to provide a better understanding of a disease affecting one per cent of Australians at birth.

Dr Wiszniak is investigating the origins of Congenital Heart Disease (CHD), a problem in the structure of the heart present at birth, arising from a problem with embryo development. This is usually caused by a genetic defect of a mutation in a gene.

"In my research I am looking at the normal processes of heart development to understand what goes wrong to give rise to a heart defect," Dr Wiszniak said.

"In addition to affecting one percent of all births, CHD is also responsible for 20 per cent of miscarriages; it is quite a prevalent disorder. That's why it's so important for us to work out what is going wrong and why."

Dr Wiszniak is passionate about her research and wants to be able to grow knowledge about this heartbreaking disease.

FACT:
CHD is the biggest killer of Australian children under one

To gain an understanding of the heart's development Dr Wiszniak's research is centred on analysing neural crest cells, a group of cells that play a large role in a baby's development in the womb.

"The focus of my lab is on these neural crest cells which are present in the embryo and differentiate into lots of different cell types within the body to give rise to different organs," Sophie said.

"The neural crest cells come from the neural tube which is the precursor to the spinal cord and the brain. During development these cells migrate through the body turning into different cells, including those in the heart.

"I'm looking to see if there are issues with how the normal neural crest cells migrate, develop and interact with other cells in the heart leading to a defect."

In the early stages of her research, Dr Wiszniak has begun analysing and identifying certain genes within the neural crest cells that may be playing a role in disrupting the function of the cells, resulting in a heart defect.

"We are now underpinning the important genes in the neural crest cells that are causing the heart to have a defect. Based on these findings we can then look at other pathways and interactions of those genes that may be inhibiting the neural crest cells from functioning properly."

With a lot of work still to come, Dr Wiszniak is hopeful her research will help better inform patients on why they have CHD and what their chances are of passing the disease onto their children.

"If we can identify new genes that are important and find people that do have mutations in certain genes, doctors may be able to inform these people on the likelihood of passing these defects onto their children.

> **"We are never going to be able to cure CHD without an understanding of how the defect arises in the first place."**

Finding her niche research area, Dr Wiszniak is eager to see where the next three years and beyond take her.

"It is fascinating that these cells can be involved in so many aspects of how a baby develops. There is so much more to know in this area of research – I am looking forward to the next three years!"

Intervening on a Global Problem – Lower Back Pain

Affecting an estimated 84 per cent of people at some stage of their lives, lower back pain has become an area in dire need of research and clinical intervention.

PhD candidate and physiotherapist Emma Karran, is thrilled to be supported by a Royal Adelaide Hospital (RAH) Research Funds Dawes Scholarship, enabling her to investigate the psychological and physical characteristics that are linked to poor outcomes for patients experiencing lower back pain.

Emma would also like to acknowledge the support received from Matthew Beard and Naomi Haensel (Physiotherapy) and her supervisors Dr Yun-Hom Yau and Professor Lorimer Moseley.

"Lower back pain is the leading cause of disability globally and costs the Australian economy about $1 billion each year."

Having previously worked in the Spinal Assessment Clinic at the RAH, Emma's interest in this area was stirred after seeing patients who could benefit from better information about their back pain at an earlier stage.

"It made sense to me that if we could identify at an earlier stage, patients who were going to recover poorly, we could better target management to those people who need it most," she said.

"We have to appreciate that a person's experience of pain is determined by a lot more than just the physical pathology – it's quite a lot more complex than that.

"A patients beliefs about what's wrong with their back, their likelihood of recovery and factors such as depression and anxiety are also important to consider.

"Certainly a lot of the patients that we see in the spinal assessment clinic have quite complex problems with a long history of pain.

"They are often very fearful of moving because they believe it is dangerous to do so - and this can lead to deconditioning and even poorer tolerance of activity."

For her research project Emma has recruited 280 patients who are on the RAH Spinal Clinic's waiting list, sending them three different questionnaires, which have been used in other settings to help predict who is going to recover poorly.

"I then followed these study participants up four months later to see how they have gone," Emma said.

Emma is excited for a big year ahead, travelling to two international conferences to present her findings.

FACT:
Lower back pain is the leading cause of disability globally.

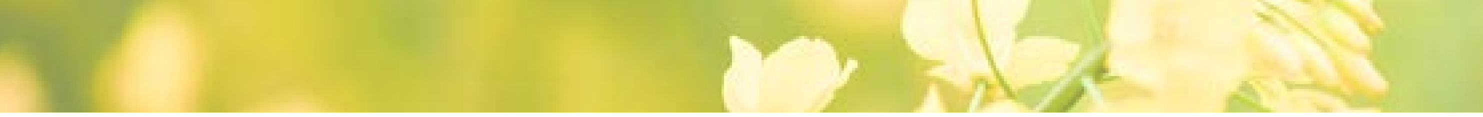
"My initial findings are showing that the majority of them have not recovered well."

Later in the year, Emma's research will lead to an intervention to be delivered in the RAH's spinal clinic. This will involve patient education, and provision of a booklet – which largely aims to reassure patients and promote activity.

We would like to change the way people understand the 'wear and tear' which shows up on their scans. Many of the findings are very common and quite normal - and if we can present this information in a positive way it may help encourage people to keep active," she said.

> **"I am also involved in some research that is investigating how radiologists report their imaging of lower back problems and the way practitioners, GPs and physios are communicating these outcomes to their patients."**

2016 will be a busy year for Emma who is heading to the UK and Japan to present at two international conferences. We look forward to updating you on this exciting research in the future!



WE HONOUR THEIR MEMORY

Donations were received between 7 December 2015 and 5 February 2016 in memory of the following people:

Joyce Doreen Grant
Horrie & Brian Martin
Daniel Craig Hibbert
Donald (Don) Crick
Carol Monaghan
James Hughes
Gerri Lou Bailey
Sandra Elizabeth Corboy
Sylvia Radestock
Melville Bowyer
Barbara Elaine Goldsmith
Allan Richard Tiller
Raymond Sau Kin Wong
Charles Murray Thompson
Owen Stanley Butler
Lorraine Heather Jan Page
Anna Alexakis
Edward Launston Christopher (Chris) Phillips
Robert John (Bob) Williams
Susan Linda Cope
Clelia Fragnito
Angelo Megetto
Timothy James Marks
Oliver (Declan) Kenny
Clara (Claire) Elizabeth Lowe

Have you been treated at the Royal Adelaide Hospital and would like to share your story?

We're always on the lookout for patients or supporters who are willing to talk to us about their experience. This is a great way to become involved and connect with our very friendly community.

If you're interested in sharing your story, please contact us on ***08 8222 5281***
EMAIL: ***RAHResearchfund@sa.gov.au.***

2016/17 Entertainment Books

Pre-Order your Entertainment™ Books and Entertainment™ Digital Memberships before 9th April 2016 and you'll receive over $200 worth of Early Bird Offers which you can use straight away! (Subject to availability).

You can reserve your copy today with a credit card by phoning ***8222 5281*** or via this link: ***www.entertainmentbook.com.au/orderbooks/160x892***

With your purchase you are also helping our researchers, doctors and nurses to continue to be lifesavers.

$13 from every book sale go towards our research programs.

Become a Hospital Hero!

You can join an exceptional group of people who help make the Royal Adelaide Hospital (RAH) the best place for you and your family to access the most advanced treatments and hospital care informed by world leading medical research.

As a Hospital Hero you will enable us to fund major medical research programs, purchase highly specialised research equipment and develop lifesaving treatments and potential cures. We would love for you to join us!

You may already support us regularly. Thank you! We can now make it even easier for you. As a Hospital Hero your monthly gift will be deducted automatically and you will receive one receipt in July each year to help you claim your tax deduction. Your monthly gift also allows us to reduce our administration costs, supporting more research and further enhancing patient care at the RAH.

We are also offering our Hospital Heroes the opportunity of a tour of the new RAH and are currently taking names for a special tour prior to opening!

To become a Hospital Hero, please fill in the enclosed form and send it back in the reply paid envelope or phone us on ***08 8222 5281.***

Joining our special group will ensure the very best care and treatment is available at the RAH when you or your loved one need it the most.