How understanding the cell’s pathways will help us combat obesity.
When I visited a Grade 3 class to talk about science recently the teacher reminded the class that the theme of their science classes is “Why is it so?” This immediately brought to mind the sight and sound of the remarkable Julius Sumner Miller, who taught physics on television in the 1960’s. It also focuses on the underlying causes and mechanisms of events rather than their description. This is at the heart of what we do at SVI. We believe that understanding how diseases work at the molecular level can lead to improvements in everyday medicine. Innovation is the process of turning understanding into benefit.

Bruce Kemp, Greg Steinberg and Sandra Galic’s discovery of how the commonly prescribed anti-diabetic drug metformin works is described in this issue of The Edman. The work was published in one of the world’s most prestigious medical journals. Why did the editors of that journal think it was so important when metformin’s usefulness for the treatment of type 2 diabetes has been known for over 50 years?

Chance discoveries that certain plant extracts and chemicals improve illness without knowing why are part of the history of medicine. Metformin, derived from lilac plants, is one of many examples. In clinical medicine, practical benefit is the main priority when confronted with illness – application of existing knowledge is more pressing and immediate than thinking more abstractly about future developments. Chance discoveries are slow and random and they do not provide a path forward to progressive improvements in therapy. We have much more powerful tools to make discovery more targeted and precise. The task is to not only do the best we can for today’s patient, but also think about better treatment in the future.

Mathematicians are required to provide rigorous proofs of the solution to problems – not just get the right answer. Medical research, with its powerful array of technologies, can now deliver similar rigour and understanding. This understanding positions us to discover new, potentially more potent drugs, with less side effects, to tackle what metformin achieved by chance. This will not change the use of metformin today, but will undoubtedly contribute to innovations that will impact how type 2 diabetes and related conditions like obesity and polycystic ovary syndrome are treated in the future.

I wish you a safe festive season and thank you for your interest and support this year.

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2014 Diary

Risk factors for type 2 diabetes include genetics, obesity and lack of physical activity.

The total financial cost of type 2 diabetes is estimated at $10.3 billion.

Heart disease is the leading cause of death in people with diabetes.

Up to 60% of cases of type 2 diabetes are preventable.

Good blood glucose control and a healthy lifestyle can significantly improve diabetic complications.

People with type 2 diabetes do not produce enough insulin, resulting in excess sugar in their blood. When this is combined with a condition known as ‘insulin resistance’ where muscles become resistant to the effects of insulin, type 2 diabetes results. The majority of diabetics nationwide suffer from type 2 diabetes.

Obesity is a key risk factor for type 2 diabetes and heart disease, as well as for osteoarthritis and a number of cancers.

More than 67% of Australians are overweight and more than 18% are classified as obese. In the last 20 years, Australia’s overweight rate has risen faster than that of any other developed country and the increases show no sign of abating.

Researchers at SVI are trying to find new ways of approaching the effects of Australia’s obesity epidemic by focusing on the body’s control of energy and by finding new ways of identifying people at risk of developing heart disease.
SVI IN THE NEWS

SVI’s Sandra Galic and Bruce Kemp received considerable media coverage in early November for their work on the role of the type 2 diabetes drug metformin.

The researchers, working in collaboration with Canadian colleagues, described for the first time the action of the type 2 diabetes drug metformin. This research answers decade-long questions about how metformin works and may help develop more effective therapies for the more than 1 million Australians currently living with type 2 diabetes.

Despite its front-line role in the treatment of type 2 diabetes, until now no-one has been able to explain how the drug lowers blood sugar for those patients living with the condition.

The team is the first to solve that mystery, with their discovery that metformin works by reducing fat in the liver. Their research was recently published in the prestigious journal Nature Medicine.

First author on the study, SVI’s Sandra Galic says, “Fat is likely to be a key trigger for pre-diabetes in humans. Our study indicates that metformin doesn’t directly reduce sugar metabolism, as previously suspected, but instead reduces fat in the liver, which in turn allows insulin to work effectively.”

Professor Bruce Kemp, who has worked closely on the project with former SVI researcher Associate Professor Greg Steinberg now at McMaster University, said, “This work, the result of a great international collaboration, has the potential to help develop more effective treatments for type 2 diabetes, which currently affects 4% of Australians and represents an ever growing burden on our health system.”

Research at SVI has been boosted by almost $4 million in funding announced in the most recent round of the Federal Government’s National Health and Medical Research Council (NHMRC) grants.

The NHMRC’s Project Grants Scheme is the main avenue of support for individuals and small teams of Australian researchers undertaking biomedical, public health and health services research.

The funding, announced on October 23, includes six Project Grants awarded for research into type 1 diabetes, metabolism, bone cancer and osteoporosis.

Of particular note were two grants awarded to Professor Bruce Kemp and colleagues Jon Oakhill and Sandra Galic for their research into the body’s method of regulating its energy usage via an enzyme called AMP kinase. Bruce has held more than 30 Project Grants over the last 20 years, a testament to the relevance and quality of his work.

He says, “Many of the most serious diseases of Western societies, including obesity, type 2 diabetes, cancer and heart disease, have metabolic dimensions. Our work is aimed at understanding how the enzyme AMP kinase balances energy demand with nutrient supply. Hopefully, by increasing our understanding of how the body coordinates these pathways, we will be able to develop better treatments for these diseases.”

Dr Stuart Mannering, from SVI’s Immunology and Metabolism Unit, will use his grant to profile the immune cells responsible for killing insulin-producing cells in human type 1 diabetes. His colleague, Dr Esteban Gurzov, received a New Investigator grant to research how the insulin-producing cells contribute to their own demise in type 1 diabetes.

Dr Carl Walkley, from the Stem Cell Regulation Unit, received support to understand the role of a gene that has been implicated in a familial cancer syndrome, in which affected families have higher rates of the bone cancer osteosarcoma. Bone experts, Associate Professor Natalie Sims and Professor Jack Martin will receive $626,894 to further their work into manipulating genes to increase bone formation and develop new therapies for osteoporosis.

Of note, two of SVI’s former PhD students, David Ascher and Hayley O’Neill, received funding from the NHMRC to carry out their postdoctoral studies, in London and Queensland, respectively.
One in five members of the community will develop heart failure, a serious condition in which the heart is unable to pump sufficient blood for normal daily activities. In addition to the poor quality of life and premature death that result, hospitalisations for heart failure cost more than $1 billion per year.

A particular concern, given the obesity epidemic, is that obese people are more likely to develop heart failure, and their increased risk of heart failure is independent of age, high blood pressure and diabetes.

To understand why obese people develop heart failure, SVI’s Associate Professor Jock Campbell studied heart muscle biopsies from patients undergoing open-heart surgery. This research was done in collaboration with the heart surgeons and cardiologists at St. Vincent’s Hospital, and the heart muscle biopsies were taken with the patients’ consent.

Jock’s research showed that heart muscle from obese people has fewer small blood vessels in heart muscle of obese people means that their heart muscle cells do not receive sufficient oxygen and fuel to work effectively.

This demonstration of fewer small blood vessels in heart muscle of obese people provides new understanding of why these subjects are more likely to develop heart failure. The first approach to prevention and treatment of heart failure in obese people is lifestyle advice to reduce weight. Jock’s research also opens the door to new therapies aimed at restoring the number of small blood vessels to heart muscle. Such therapies may help not only obese people with heart failure but also non-obese people with heart failure and people who have heart attacks.

Jock says, “To a large extent, our heart health is in our own hands. The recipe to a healthy heart is a Mediterranean-style diet and regular exercise, with maintenance of a healthy weight, avoidance of cigarettes and treatment of high blood pressure if present. My research would not be possible without patients agreeing to the surgeon taking a small piece of their heart muscle for research during their heart operation. It is a wonderful example of how patients are helping us make discoveries that will benefit the whole community.”

2 MINUTES IN OXFORD

Dr Xianning Lai completed her PhD in SVI’s Molecular Genetics Unit in 2012.

Where are you working now? I am doing my postdoctoral work at the Gray Institute for Radiation Oncology and Biology at The University of Oxford.

What are you working on? I am investigating how factors involved in DNA repair contribute to the establishment of the protein structures that protect the telomere: the tiny caps at the end of the chromosomes that become frayed and damaged as we age. These studies will be important to understand how components of this protein complex contribute to tumour suppression.

What are your reflections on your time at SVI? It was a pleasure working at SVI. The environment was very conducive to learning, and it was really comfortable and friendly. All the necessary infrastructure and resources were available to facilitate research. My time at SVI equipped me with all the practical techniques and analytical skills that I can now apply in my new lab.

What did getting a SVI Foundation Top-up scholarship mean to you? The Top-up Scholarship greatly aided me during my PhD by enabling me to rent accommodation closer to the lab, reducing the amount of time I had to spend travelling to and from work.
This year was a big year of change for the Foundation, with the retirement of two long-term staff members, Beth Castles and Clare Lacey, both of whom had dedicated over 10 years to SVI.

There have also been some changes amongst the Foundation Board members, with the departures of Jan Spooner, Bruce Guthrie, Suzan Morlacci, Tony Burgess and Sam Tarascio. All of these people have made fantastic contributions to SVI and we look forward to continuing our involvement with them in the future.

In June 2013 we welcomed Bernadette Dennis to the SVI Foundation Board. Bernadette’s appointment represents a formalisation of her involvement with the Institute over many years.

SVI Foundation events have continued to help promote SVI amongst our donors and the community, with the Women In Research Award being launched this year at the inaugural Susan Alberti Medical Research Foundation Mother’s Day Luncheon at Leonda, with Ita Buttrose as guest speaker.

The Susan Alberti Medical Research Foundation Signature Ball was a great success in 2013, raising $160,000 for SVI. The SVI Charity Golf Day raised a record $111,000, as did the SVI Support Group, with a total of $60,000 raised at their annual dinner.

The $10,000 Discovery Fund continues to gain new members through the tireless work of Christine Tarascio and her committee. The SVI Breakthrough Committee has worked to help promote SVI to a new younger audience, running movie nights, wine tastings and dinners throughout the year. The Jack Holt Society, launched at the end of 2012, now has ten confirmed bequestors amongst our supporters.

We thank you all for your support of the Institute and hope that you will continue to work with us in 2014 to support the great medical research at the Institute. Wishing you a healthy and happy Christmas break.

Madeleine Whiting
Development Director

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SVI researcher Dr Jon Oakhill has been awarded a Future Fellowship from the Australian Research Council (ARC) to investigate the role of the protein AMP-activated protein kinase (AMPK), the body’s master regulator of cellular energy.

The Future Fellowship outcomes were announced on the 8th of November, with 201 research projects funded to the tune of $152 million. The scheme promotes research in areas of critical national importance by giving outstanding researchers like Jon incentives to conduct their research in Australia.

Jon says, “The incidence of type 2 diabetes has escalated in Australia in recent decades. Over that time, AMPK has emerged as a major player in human disease, with important roles not only in metabolism, but also in cancer, heart disease and neurodegenerative diseases. I am thrilled to have been selected to receive a Fellowship, and look forward to making an impact with my research.”

Jon and the team at SVI have played a major role in identifying the importance of AMPK within the body.

Jon’s research is based around their recent work on AMPK, published in two major research articles. In 2010 and 2011, the team turned knowledge of how the body regulates its use of energy on its head, by providing insights into how AMPK signalling is initiated in response to energy deprivation. In doing so the group solved a 40 year-old problem that had eluded the best efforts of multiple international laboratories.

Jon will apply his expertise to understanding the potential of AMPK as a drug target with the aim of reducing the enormous financial and medical burden that conditions like type 2 diabetes and obesity place on the Australian economy. Jon has been awarded $727,370 over four years to undertake his research.

Image: SVI’s new Australian Research Council Future Fellow, Jon Oakhill.
The SVI/Macquarie Leasing 2013 Charity Golf Day was held on the 28th of October at the Albert Park Golf Course. The sixth year of this event saw ominous rain clouds quickly replaced by clear, bright skies just in time for tee off. With 28 teams competing from 22 organisations, we had a great turnout for the day.

The Melbourne Racing Club team of Wayne Sampson, Jake Norton, Ian Chapman and Dianna McKain finished first, winning the Jack Holt trophy. Runners up were SVI’s own Professor Jack Martin, with Joel Meek and Tom Hennessey from Newcrest Mining. The annual ‘Michael Dwyer Memorial Trophy’ was won by Michael Collins from Ernst & Young for the longest drive on Hole 6.

From the auctions, raffles and sponsorship, over $111,000 was raised in profit for SVI, setting a new record. All proceeds from the event will go to support medical research into diseases including type 2 diabetes, heart disease and cancer.

Success of the Charity Golf Day is dependent upon the support and commitment of a great many people and organisations. SVI would like to thank the Golf Committee for their dedication and time throughout the year.

We especially thank Gold Sponsor Macquarie Leasing and our long term sponsor Newcrest Mining as well as Silver Sponsors Deloitte, Ernst & Young, Jayco and Virgin Australia.
SVI FOUNDATION CHAIR RECEIVES GREAT AUSTRALIAN PHILANTHROPY AWARD

The philanthropic spirit of SVI Foundation Chair Sue Alberti was recognised at the 2013 Research Australia Awards night on the 13th of November, with the presentation of a Macquarie Group Foundation Great Australian Philanthropy Award.

Joining an illustrious list of previous winners, including Harold Mitchell, Clive Berghofer and the late Dame Elisabeth Murdoch, the award recognises Sue’s long and outstanding contribution as a philanthropist, particularly in the area of type 1 diabetes research.

Sue’s contribution to the community was also acknowledged in the second annual Australian Financial Review and Westpac Group 100 Women of Influence awards in October, at which she was announced as a finalist in the category of philanthropy.

Sue says, “I am honoured to receive these awards, and see them as a way of helping to deliver tomorrow’s medical discoveries, today.”

JACK HOLT’S BEQUEST

ONE OF AUSTRALIA’S TOP 50 PHILANTHROPIC GIFTS

The bequest that founded St Vincent’s Institute was recently announced as one of Australia’s Top 50 Philanthropic Gifts of all time. The top 50 recipients were revealed at The Wheeler Centre in Melbourne in October.

Standing shoulder to shoulder with the gifts that founded the CSIRO Parkes Telescope and the Miles Franklin Literary Award, Jack Holt couldn’t have imagined the impact his £200,000 bequest would make. His gift in 1958 was instrumental in founding St Vincent’s Institute.

Louise Walsh, CEO of Philanthropy Australia said; “The Australian philanthropic sector, and the organisations supported, have delivered amazing public benefits to the community. We hope that today will inspire many more Australians to support the projects they’re passionate about. Whether you start with $150 or $150,000, you can make a difference.”

For more information about the Top 50 gifts, visit: probonoaustralia.com.au/top50

If you would like to speak to someone about leaving a bequest to SVI, call us on (03) 9288 2480.

DON’S STORY

Twenty-eight years after Don’s heart surgery, he is still going strong.

“As it happens, heart disease proved to be a positive influence on my life!

At the age of 52 I had no symptoms to indicate illness but both my parents had died from heart disease so I was keen to know more about myself. After a stress test and angiogram, I was immediately admitted for surgery involving five coronary artery grafts. That was in 1986.

I was very fortunate as the steps I took, almost accidentally, to arrive at surgery meant that actual heart damage was prevented.

Since then I have had three stents inserted into various narrowings in the grafts. I regard these procedures as maintenance and accompanied by moderate exercise, I see the future of my heart health as excellent.

Several years ago I took up cycling and rode with a group in Laos on a fundraising mission for Care Australia. Since then I have regularly visited the Indo China Peninsula to cycle. This year I celebrated my 80th birthday and hope to ride in Vietnam in February 2014.

I believe medical research has made significant progress in heart disease. Stents are used far more frequently than the invasive surgery which was, more or less, the only option 30 years ago.

I like to hope that my success story offers encouragement to others and to the field of medical research."

For more information about the Top 50 gifts, visit: probonoaustralia.com.au/top50

If you would like to speak to someone about leaving a bequest to SVI, call us on (03) 9288 2480.
Over 160 guests attended this year’s SVI Support Group Annual Black Tie Dinner, which was held at The Athenaeum Club on the 10th of October. The evening raised over $60,000, with all proceeds going to the SVI Student Scholarship Fund.

At the dinner, PhD student Leni Green moved the audience with her speech, in which she explained her reason for embarking on a career in medical research.

Leni said, “When I was in early high school my father developed breast cancer. I can remember at the time I wasn’t really worried about it because he seemed fine but as he became sicker I saw first hand how diseases like cancer take hold. Sadly, my father passed away when I was sitting my year 12 exams. Because of this I developed an interest in medical science.”

She also explained how much her SVI Student Scholarship, donated by Margaret and Tony Reeves, means to her.

“My Top-up Scholarship gives me an additional $5,000 a year, without which I would have to work to cover the cost of my rent and living expenses. This would be on top of the 50 hours a week I already spend in the lab,” she said.

Since its inception, more than 14 years ago, the SVI Student Scholarship Fund has supported a total of 25 Honours and 26 PhD students, some of whom have now begun their independent research careers in labs around the world (see Two minutes in Oxford).

SVI Student Scholarships provide $5,000 to Honours students and boost PhD stipends by $5,000 per year. This relieves some of the financial strain on SVI’s committed young students, giving them the opportunity to dedicate themselves more fully to their studies.

For over 14 years SVI Foundation Board member Claire O’Callaghan and her dedicated group have been supporting students at the Institute and the group has raised more than $280,000 towards the cause.

SVI would like to acknowledge all those who have donated to scholarships at the Institute, and especially thank the SVI Support Group, whose outstanding long-term support of SVI is greatly appreciated.

If you would like to support the SVI Student Scholarship Fund, please fill in the donation panel attached to this newsletter.
Getting involved

There are many ways you can support medical research at SVI.

How you can help: (See over for payment details)

☐ Make a donation
☐ Join the Friends of SVI
☐ Join the $10,000 Discovery Fund

If you would like to:
(complete below and return)

☐ Make a bequest to SVI
☐ Donate in lieu of a gift
☐ Build a corporate partnership
☐ Sponsor an event or publication
☐ Organise a fundraising event for SVI
☐ Give to SVI through Workplace Giving
☐ Donate in Memoriam
☐ Information on the Friends of SVI
☐ Information on the SVI $10,000 Discovery Fund

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I want to make a single donation of:

☐ $25  ☐ $50  ☐ $100  ☐ $250  ☐ $500  ☐ $1000
☐ Other

2. Become a Friend of SVI
I want to make an annual donation of $1000 for:

☐ 3 years  ☐ 5 years  ☐ Other

3. Join the SVI $10,000 Discovery Fund
An investment in the $10,000 Discovery Fund is an investment in the future needs of the Institute. For more information contact the SVI Foundation on (03) 9288 2480

4. Leave a bequest to SVI
If you would like to talk to someone about making a bequest to SVI please contact the SVI Bequest Officer on (03) 9288 2480

See our website, www.svi.edu.au if you would like to make periodic payments from your bank account or credit card.

Donation payment details

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