The surprising double life of a DNA damage response protein

Developing lung of a 12.5 day old mouse embryo
(Ian Smyth, Monash University)
Stacking THE DECK

There’s a whiteboard behind the desk of Tom Brodnicki, head of SVI’s Immunogenetics laboratory. It’s covered in a dense jumble of scribble, numbers and formulae, and words by the dozen, urgently expressed in black spidery marker.

Then, with a complicated array of circles, brackets and arrows that sweep from one side of the board to the other, some sort of order is imposed.

In Tom’s world of genetics, things are complicated. Tom and his group attempt daily to unravel the complexities of our DNA. He describes himself as a gene hunter, and his research interest is the genes that contribute to the development of type 1 diabetes.

In conversation, with a Midwestern American accent that does not seem to have been tempered by 14 years in Australia, Tom describes his work. “Type 1 diabetes is a complex genetic disease – this means that different combinations of genes can affect an individual’s risk of developing the disease. However, because of the diversity of the human population, isolating the genetic variants that actually cause the disease has been a real challenge.”

To avoid the complication of genetic diversity, Tom and his colleagues have used selective breeding of a particular type of diabetic mouse in order to narrow down one of 25 genomic regions associated with increased risk for diabetes to a single gene of unknown function. “We actually got a bit lucky in identifying a mouse gene that hadn’t been studied before”, he says.

The discovery has recently been published in the journal Genome Research. Tom describes how selective mouse mating in inbred strains shuffles small pieces of DNA between mice, analogous to shuffling a deck of cards, revealing which piece of DNA encodes a disease-related gene. “In our case, a unique chromosome feature, called a recombination hotspot, stacked the DNA deck in favor of finding a gene that appears to be involved in diabetes susceptibility.”

Tom says that it is not yet known if the mouse diabetes gene has an equivalent in humans, and exactly how the gene confers type 1 diabetes susceptibility remains unclear. “Our ongoing work is aimed at defining the function of this gene in mice and humans to determine how it might be used to help in preventing type 1 diabetes.”

2 Minutes with Nicole

Nicole Walsh, postdoctoral fellow in the Bone Cell Biology and Disease Unit was recently awarded her first NHMRC Project Grant.

**My childhood ambition was to...** be a teacher.

**My first job was...** from the age of 12 through high school, I delivered milk.

**My worst job was...** not a paid job as such, but during my PhD I was responsible for milling very thin slices of dentine from a set of very smelly cows teeth.

**My happiest moment was...** most recently, finding out that my NHMRC project grant was funded.

**I got into research because...** of two things: A year 11 trip to Canberra where we were introduced to scientists from many different fields who shared with us their enthusiasm for their jobs. I also did a second year vacation project at UQ in a lab growing osteoclasts, (the cells that eat bone). I thought these large multinucleated cells were the coolest things, and I wanted to know more about how they worked.

**The hardest thing I have ever done was...** finishing my PhD.

**My scientific role model...** share the following traits: they are passionate about their research and sharing it with others, but also recognize life is important too; they appreciate that sometimes the answer is more grey than just black and white; they can see the silver lining when experiments don’t work out, or when they yield more questions than answers.

*Jeff Clifton*  
Feb 21, 1949 – Oct 18, 2010

Jeff Clifton passed away on the 18th of October after a long illness. Jeff made a great contribution to SVI, serving on the Board for 6 years.

He brought to the Board his business acumen, developed after more than 35 years in the property industry.

These skills were particularly appreciated at the Institute during its re-development some years ago.

An astute businessman and talented sportsman, Jeff was particularly well known for his outstanding contribution to the Collingwood Football Club both as a player and more recently, by supporting retired footballers.

His generous and genial nature will be sorely missed by all.

The Institute offers its sympathy to Jeff’s wife, Sue and his children Chris, Rob and Kath.
TOM SAYS

As well as Christmas, school break-ups, exam results and all the other seasonal preoccupations, as the year draws to a close medical researchers find out the results of their all important applications to the National Health and Medical Research Council (NHMRC). SVI did well again this year with about 40% of our grants funded in an increasingly highly competitive environment, in which just over 20% of all grants are successful. This is a great credit to our excellent team. NHMRC and other competitive funding remains the core source of SVI’s income.

We also had a successful year with philanthropic fund-raising. In particular we raised over a million dollars for research into prevention of heart disease and for renewal of our advanced mass spectrometry facilities. Generous support for these instruments was provided by several Trusts and Foundations as well as individuals, and the University and St Vincent’s Hospital also contributed. It has of course been a difficult period for fund-raising in the community so this support is very welcome. Philanthropy is a critical part of how the Institute is funded. We use it to support young peoples’ careers, buy specialized equipment and seed new projects. However, the capacity of philanthropy to compensate for inadequate government funding is limited. Our core support still needs to come from government.

Medical research is a great use of tax payers’ dollars. It is directed to the health of our community and creating high value jobs for current and future generations. Not surprisingly, we very much support and encourage the Government’s spending on health and medical research with the goals of preventing and curing diseases and limiting the spiraling cost of disease treatment. Research is a mere 2% of the health budget but it is strategically enormously important in the global effort to combat disease and domestically in having continuously improving and evidence-based health care. The community expects the Government to return the Budget to surplus, but hopefully not at the expense of valuable and successful activities like medical research.

I wish you all a safe and happy Christmas break and look forward to staying in touch next year.

During that time, Nana Sims fell in the garden and broke her shoulder; the result of a process of bone thinning, which is such an accepted part of ageing that it was not further investigated, or treated.

“She took a long time to recover from the accident, and felt the effects for years afterwards”, says Natalie, “She often used to tease me by asking, ‘Haven’t you found a cure for this yet?’”

Natalie says that her Nana’s condition fueled her interest in bone and how the cells of bone communicate with each other.

Natalie’s work has recently been acknowledged with a prestigious Fuller Albright Award from the American Society of Bone and Mineral Research. The Award is given in recognition of meritorious scientific accomplishment in the bone and mineral field to a researcher under 41 years of age. Natalie is the first Australian-based researcher to receive it.

The Award recognizes Natalie’s achievements in skeletal research, including discoveries of new factors that change the way that cells of bone behave, which has implications for arthritis and osteoporosis treatments.

Arthritis and osteoporosis are among the leading causes of pain and disability in Australia. Arthritis affects over 3 million Australians, including more than one-third of people aged 65 or over. Almost 600,000 Australians have been diagnosed with osteoporosis, with this number likely to be a substantial underestimate of the true extent of the problem.

Sadly, when Natalie was undertaking postdoctoral work at Yale, she received the news that her grandmother had fallen and broken her hip and had died less than 24 hours later.

By reducing the impact of these diseases, Natalie hopes to help people like her grandmother to live longer and healthier lives.

Natalie says “We need new treatments to prevent fractures in osteoporosis and cancer and to relieve the pain and disability of arthritis; this Award shows that we are on the right track”. 

Sitting on Natalie Sims’ desk, sandwiched between her computer and a teetering pile of paperwork, is a photo of a younger Natalie in a graduation gown, flanked proudly by two older ladies, complete with cardigans and hair obviously set for the occasion.

Natalie was particularly close to one of these ladies, her ‘Nana Sims’, with whom she lived while completing her studies at Adelaide University.

Mouse vertebrae
SVI researchers have been awarded approximately $5.4 million in the latest round of National Health and Medical Research Council (NHMRC) Project Grants. These grants fund specific projects over a period of three to five years. SVI had 37% of its submitted grants funded, compared to a nation-wide success rate of 23%.

Congratulations to the following researchers:

Jörg Heierhorst, who was awarded two project grants
Bruce Kemp and Jon Oakhill
Bruce Kemp and Greg Steinberg
Louise Purton
Suzanne Rogers, Sean McGee and Greg Steinberg
Boris Sarcevic and Helena Richardson
Natalie Sims, Jack Martin and Nicole Walsh
Boris Sarcevic and Greg Steinberg
Louise Purton
Suzanne Rogers, Sean McGee and Greg Steinberg
Natalie Sims, Jack Martin and Julian Quinn
Nicole Walsh, Natalie Sims and Evange Romas
Louise Purton was also awarded a Fellowship from the NHMRC to further her research into the uses of vitamin A products to improve the treatment of patients with blood cell diseases.

In other grant news, Ms Hui Peng Lim was awarded a Leukaemia Foundation scholarship to look at the effects of the bone marrow environment on the development of leukaemia, under the supervision of Louise Purton, Carl Walkley and Harshal Nandurkar.

Congratulations also goes to Dr Lorien Parker, whose thesis “Crystallographic studies of the recognition of anti-cancer compounds by Glutathione Transferase Pi” was recognised as of outstanding quality by the Australian Synchotron Thesis Award Committee.
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You can make a difference. 100% of all donations received will directly fund medical research.

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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 SVI 1000 Club
- Join the $10,000 Discovery Fund

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- Organise a fundraising event for SVI
- Give to SVI through Workplace Giving
- Donate in Memoriam
- Information on the 1000 Club
- Information on the SVI $10,000 Discovery Fund

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SVI 2010 Charity Golf Day

The SVI 2010 Charity golf day at the Albert Park Golf Course was a huge success, with over 100 players raising $50,000 for heart research at SVI. The winner of the inaugural Jack Holt Trophy was Athol Marks from Newcrest Mining.

Thanks to the Golf committee: Michael Dwyer, Leon Wiegard, Michael Kay, Barry Holbrook, Mark Kerr and Charlie Happell. We would also like to thank pro bono sponsors and Darryl Foley for her hard work on the day.

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THE SVI SUPPORT GROUP

The Annual SVI Support Group Dinner, led by Claire O’Callaghan, this year raised $30,000 to support student scholarships at SVI. At the dinner, PhD student Walter Pfister explained his reasons for pursuing a career in medical research.

Walter said, “The financial support through this special award means a lot to the students at SVI. It enables us to put our undivided focus on research and it gives us the flexibility to plan our time. Results don’t come easily. Research is hard work and it requires dedication, a great mind and the patience of an angel. Your generous contribution helps develop students into top researchers, and together it takes us closer to new insights and new solutions to fight diseases that affect all of us.”

Thanks to everyone who has donated to student scholarships, and especially the SVI Support Group, who are outstanding long-term supporters of SVI.