# focus



## LETTER FROM THE EDITOR

It is found in the cells of every living thing, however, very few people know what ribonucleic acid, or RNA for short, is. Described as the lesser known cousin of DNA, ribonucleic acid's best known role is as messenger to make proteins in the cell.

"If we think of DNA as our library – stable and locked away deep inside our cells – then RNA is a reference book from that library," explains SVI's Professor Carl Walkley.

"It's a copy of a tiny section of DNA with an important job: instructions to be used to create proteins."

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## • • • Living with joy

Eleven year old Ace's mother describes him as a joyful, healthy, happy child despite his tough start in life.

"When he was about three months old Ace was really unsettled and crying uncontrollably, so I took him to hospital," says Bianca. "They found some damage to the basal ganglia part of his brain, but they didn't know why."

It would take another five months for a diagnosis of Aicardi-Goutières Syndrome to be made.



Ace has calcification in his brain, with small and thin blood vessels putting him at risk of stroke. The disease means he has lack of control in some parts of his body, and problems with his fine motor skills

but nothing holds this little boy back.

"Originally, they thought that Ace would have to use his head to control his electric wheelchair, which he got when he was 9. But as soon as

Story continues page 3 ►



## **TOM SAYS**

Welcome to our first In Focus for 2023. It's been a little while since our last edition and, as always, quite a lot has been happening here at SVI.

We were very excited to have broken ground on the new \$206 million biomedical engineering facility, the Aikenhead Centre for Medical Discovery (ACMD).

The very best research comes out of collaboration and that is the primary purpose of the ACMD – bringing together a vast cross-section of researchers and clinicians to turbocharge innovation.

Our goal at SVI is purpose-driven research and to do this we need to support and develop the careers of our early and mid-career researchers. The next generation of bright young scientists, like Zhen who you'll read about in this issue, are already making significant contributions to medical research.

We are enormously proud of them all and very pleased they chose to begin their careers here at SVI. They are working alongside, and learning from, some of the greatest minds in Australian research. People like Carl, Natalie, and Stuart have been recognised as leaders in their fields and they share their labs with equally talented researchers. Research has always been a tough job, but it is even tougher at the moment, with low success rates for grants from traditional sources such as the National Health and Medical Research Council. Only a small percentage of applications are successful, and while it is our job to encourage Government to provide more funding, we couldn't give our researchers the support they need without you, our donors. Philanthropy is helping us to change the lives of all Australians.

The year ahead will be busy as we move full steam into new research while also continuing the success of our ongoing work. It's a very exciting time to be here at SVI and I very much look forward to seeing you throughout the year.

On behalf of all of us here, thank you for being a part of SVI.

#### Professor Tom Kay SVI Director

## LETTER FROM THE EDITOR continued.

RNA is not there to simply function as a direct copy of the DNA used to make proteins. RNA has important roles in many processes in the cell and can itself be modified by many enzymes in the cell. RNA can be edited – where the sequence is changed from the original sequence obtained from the DNA - which is great when the instructions are to create diversity in the immune response. It's another story, however, when the editing results in an error or gets disrupted altogether.

Fatal genetic childhood disease, Aicardi-Goutières Syndrome (AGS) is one such condition caused by a disruption to RNA editing. A devastating disease that affects the brain, immune system, and spinal cord, AGS can occur when there is a mutation in an RNAediting gene called Adenosine Deaminase Acting on RNA 1, or ADAR1 for short.

"AGS is degenerative disease with no known cure. Treatment options for the condition are also limited," says Carl.

"Diseases like AGS which are directly caused by RNA not doing what it is supposed to or doing it incorrectly were once impossible to treat because we didn't really understand how they occurred."

## • • • Living with joy continued.

they put him in, he was straight on the joystick and knew exactly what to do," says Bianca.

"He hasn't just mastered his wheelchair; he's also swimming twice a week and loves horse riding and bike riding. He also enjoyed for his first ever school camp to Sovereign Hill this year!"

During the Covid lockdown period, Ace surprised his family by learning to use a voice output device, which helps him to communicate with his classmates and join in conversations with his family <del>and make</del> requests for things he needs and wants.

"That is a milestone we can't quite believe he has reached in his lifetime," Bianca says. Understanding and, hopefully, one day finding a treatment for RNA editing errors is the focus of Carl's recently announced \$2.3 million NHMRC Investigator Grant.

"The goal then is to exploit this understanding to find new therapies for diseases like Aicardi-Goutières Syndrome and cancer."

Research of this calibre takes a cadre of people and a PhD student in his lab, Zhen Liang, is fascinated with the role of ADAR1 in disease. Zhen is the recipient of an SVI Foundation Top-up Scholarship.

"My research is on the fundamental aspects of the immune system and a key to the puzzle is ADAR1," she said.

"With Aicardi-Goutières Syndrome affecting mostly babies and young children, it makes research into finding new treatments feel more urgent."

"I'm proud of the work we're doing and all that I am learning in Carl's lab and under Jacki Heraud-Farlow, my PhD supervisor. Understanding these disease pathologies brings us a step closer to finding treatments."

"He's now 11 and we look back on that and think that all things considered, he's a very healthy child. He doesn't have hospital admissions, he doesn't get sick. We're so grateful he surpassed the 10-year mark. Others in our position haven't been as lucky as we have."

Bianca says that it gives her hope that research is actively focused on understanding the causes of the disease. "We're just a normal family. Ace's condition is genetic, so what happened to us could happen to anybody."

"Despite everything, Ace has allowed us to do some really great things that wouldn't have been possible if he wasn't who he is."

## **THE BONE LIBRARIAN**

The study of human anatomy has been occurring since at least the second century when Greek physician, Galen sought to better understand the workings of the human animal. With so long spent examining the complex machinery of the body it may come as somewhat of a surprise to learn that we still actually know very little about the scaffold on which it is all built, our bones.

At a microscopic level, bone cells resemble brain cells. They also function in a similar way, firing off messages and reacting to stimuli.

We have all heard the message that we need to do weight-bearing exercise in order to maintain healthy bones, but not many of us know that it's because the bone cells know when they are under pressure from weight or impact and respond by building more bone. This is how bones get stronger. Less impact means the cells don't bother, so the bone gets weaker.

Much more than simple, hard structures for the more complex systems to adhere to, our bones are actually living eco-systems, constantly replenishing and changing as we age.

But just how our bone ages is something we don't know a whole lot about.

"A part of why we still don't really know how bones age at a microscopic level is because it is very hard to get bone samples to study. It's not like giving blood," said SVI's Professor Natalie Sims.

Better understanding ageing bones is the first step to finding new treatments for conditions like osteoporosis.

"We've known for almost fifty years that bone gets





more porous as we age, but we still don't understand how this happens or what drives it," she said.

That's why access to a large collection of bone samples from people who died unexpectedly is critical for research.

"Bone scans can only tell us so much. They can show us how much bone someone has but not the quality of it. The Melbourne Femur Research Collection is changing the game for bone research."

The collection was originally started by Forensic Odontologist, Professor John Clement, whose work trying to identify skeletal remains in mass graves or at sites of natural disasters led him to see if he could estimate the sex and age of a person at the time they died.

Although the bones samples he collected through donation from the families of people who had unexpectedly died didn't prove as useful as hoped in this way, the large collection has been critical for other types of research.

"We can use advanced imaging techniques on the bone samples to get a really good look at what's going on. The bone collection is opening up a lot of pathways for us to develop new treatments for agerelated bone conditions."

"The problem we have now is having enough people to do actually do the research. It's not simple, and it's

"The bone collection is opening up a lot of pathways for us to develop new treatments for age-related bone conditions."

# About SVI's Catalyst Circle

Ground-breaking medical research takes more than skill; it also requires infrastructure - laboratories, tools and technologies. Without this, the ideas and theories generated by even the brightest minds will never be translated into effective treatments.

By joining the SVI Catalyst Circle, you can help create the high-tech environment our researchers need to excel and to break new scientific ground.



Image: Microscopic image of the osteocyte network the cells responsible for regulating bone turnover.

incredibly time consuming because it's such exacting work. You have to look at tiny little slice after slice of bone structure."

"Despite all of our medical advances, this type of research is very dependent on people power."

Natalie and her team were recently awarded an Australian Research Council grant to advance her work. This will not only drive new treatments for osteoporosis, but will also lead to engineering better load-bearing materials for improved surgical implants for knee and hip replacements.

"Bone really is a completely fascinating substance," laughs Natalie.

We couldn't agree more.

Natalie has received a three-year Australian Research Council Discovery Project grant to further her research on understanding the mechanisms of agerelated bone deterioration.

Donors to the Catalyst Circle help fund the purchase of powerful equipment and instrumentation.

Joining the Catalyst Circle is your chance to lay a vital foundation for world-class research that will change lives.

For more information, contact the SVI Foundation: foundation@svi.edu.au or 03 9231 2480

## IF NOT, WHY NOT?

Associate Professor Stuart Mannering ponders some pretty big questions. One of the biggest though is why some people get type 1 diabetes while others don't.

Type 1 diabetes occurs when the cells of the body's immune system attack the cells responsible for making insulin. This is a huge problem for a lot of very complicated scientific reasons but basically, insulin regulates blood glucose.

Blood glucose rises every time you eat and, when left to its own devices, is akin to a teenager in a parent free house for a weekend. The results are catastrophic.

Not everyone has or will develop type 1 diabetes and this is a conundrum because it points out that we don't really understand why the immune system decides to go on the offence in some people.

"We know that some people who have a genetic risk of type 1 diabetes, meaning there is a family history of it, don't ever end up developing it," said Stuart.

"If we can work out what is different about their immune systems we might then be able to work out how to delay or prevent the onset of type 1 diabetes."

Most current research is focussed on how and why people develop the disease so Stuart's work is taking an entirely new approach. "There is a clear gap in our understanding. To better understand the mechanisms of this disease we can't only ask why, we also need to ask why not?"

With funding from the Leona and Harry B Helmsley Charitable Trust, Stuart and his team are examining specific immune pathways and whether or not they are active in protecting the insulin-producing cells from whatever triggers the immune cells to attack.

"The immune system has several ways of stopping an immune response and there is also class of genes called HLA which both increase and decrease the risk of developing type 1 diabetes. If we can crack the code of how these pathways interact and behave differently in different people it could also lead to breakthroughs for other autoimmune diseases as well as type 1 diabetes."

"There is a clear gap in our understanding. To better understand the mechanisms of this disease we can't only ask why, we also need to ask why not?"

## SVI DONORS SHOW THEIR LOVE OF SCIENCE

Young scientists will be able to pursue new projects this year thanks to the commitment and generosity of SVI's philanthropic donors who attended the For the Love of Science dinner in November 2022. The Latin-themed 'Fiesta' dinner event, held at Butler Lane in Richmond, raised around \$240,000 to fund Rising Star Awards for SVI's early career scientists.

"We deeply thank everyone who attended and donated to the Fiesta event. It was our biggest dinner to date, and an absolute sell-out with 190 people attending," says Karen Inge, SVI Foundation Board Chair and member of the dinner organising committee.

"It was a fantastic night of food, music and entertainment. And everyone took great delight in hearing from the young scientists."

SVI's Dr Jacki Heraud-Farlow and Dr Jarmon Lees spoke about their research and how receiving a Rising Star Award has boosted their potential to gain competitive government grants.

"Your support gives us the confidence and the means to take our research to the next stage," Jarmon said. "That is a gift. On behalf of all current and future recipients of Rising Star Awards, we thank you."

## SVI extends our thanks to everyone involved in the dinner, and especially to:

**Event sponsors:** Pommery, Samsung, Crown, Flinders Hotel, Jeni Danks Jewellery, Victorian Opera, Melbourne Symphony Orchestra, Paradou, Four Pillars, Artvisory, Moke, Frank and Marina Russo and Rainbow Meats, Chancery Lane.

**Organising committee:** Karen Inge, Caroline Daniell, Kallie Blauhorn

Venue: Butler Lane

**Stylist extraordinaire:** Michael Strownix **Master of Ceremonies,** Jim Wilson **Live auction:** Paul Sumner, Director, Artvisory, South Yarra





## DONATING TO SVI

Please mail this slip in the reply-paid envelope to: 9 Princes Street, Fitzroy, Victoria 3065

#### To give online: svi.edu.au/support/donate

#### I would like to support SVI and allocate my gift to:

SVI Discovery Fund (research support)

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## **SVI UPCOMING EVENTS**

## Health Matters webinar - Osteoporosis

Every six minutes, someone is admitted to hospital with a fracture caused by osteoporosis. Known as the silent disease, osteoporosis isn't typically diagnosed until after a fracture has happened. This is because, up until this point, there are usually no signs or symptoms.

At this Health Matters webinar, you will hear from leading researcher Professor Natalie Sims, an internationally recognised bone biologist. Her team have identified new therapeutic targets that may be used to treat osteoporosis.

Guest speaker Dr Jasna Aleksova, a clinician and bone researcher will provide advice on prevention as well as the currently available treatments for osteoporosis.

### **Speakers**

**Professor Natalie Sims** an internationally recognised bone biologist

Dr Jasna Aleksova, a clinician and bone researcher

Host: Karen Inge, SVI Foundation Board Chair

Date: Wednesday 31 May 2023

Time: 1pm - 2pm

Location: Webinar

Tickets: Free

RSVP: By Monday 29 May 2023

For further information or to register, please contact Debbie Dervenis on 03 9231 3538 or email foundation@ svi.edu.au.



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