The Patricia Kailis Fellowship in Rare Genetic Disease

Your Perkins Supporter Newsletter | June 2023

Firstname, your support is helping to uncover answers inside...

25 YEARS DRIVING DISCOVERY

Perkins
HARRY PERKINS INSTITUTE OF MEDICAL RESEARCH

IN THIS EDITION

Our family continues to be so very proud of its association with Associate Professor Gina Ravenscroft at the Perkins. We feel very honoured that we, with the support of so many in this wonderful community of generous donors, can ensure that the Dr Patricia Kailis Fellowship in Rare Genetic Disease provides financial stability and back-up for Gina as she and her team continue to progress this vital research into rare genetic diseases.

Thank you for partnering with us and for helping to make our Mother's legacy possible.

Maria Kailis **Amanda Kailis**
on behalf of the Kailis Family

Thank you so very much for your amazing, and continued, support of the Dr Patricia Kailis Fellowship in Rare Genetic Disease

Your generosity ensures that Associate Professor Gina Ravenscroft and her team can continue their ground-breaking research without the risk, faced by most researchers in Australia, of very limited access to funding from government grants. Your support provides reassurance that this important work can continue, no matter how long it might take.

We remain especially grateful to Patricia's family, Maria, Amanda, Alex and George, for their continued support of the Dr Patricia Kailis Fellowship, for believing in Gina and the vision she has for this research – something for which Patricia so passionately advocated.

Our heartfelt thanks and appreciation to the Kailis family – and you – for the loyalty and friendship afforded to us at the Perkins.

We present this update to you with our thanks and our very best wishes and we look forward to hosting you at the Harry Perkins Institute of Medical Research again soon.

Happy reading!

Warm regards

Shelley Mason
Key Relationships Manager

An update from

Associate Professor Gina Ravenscroft,
Dr Patricia Kailis Fellow in Rare Genetic Disease

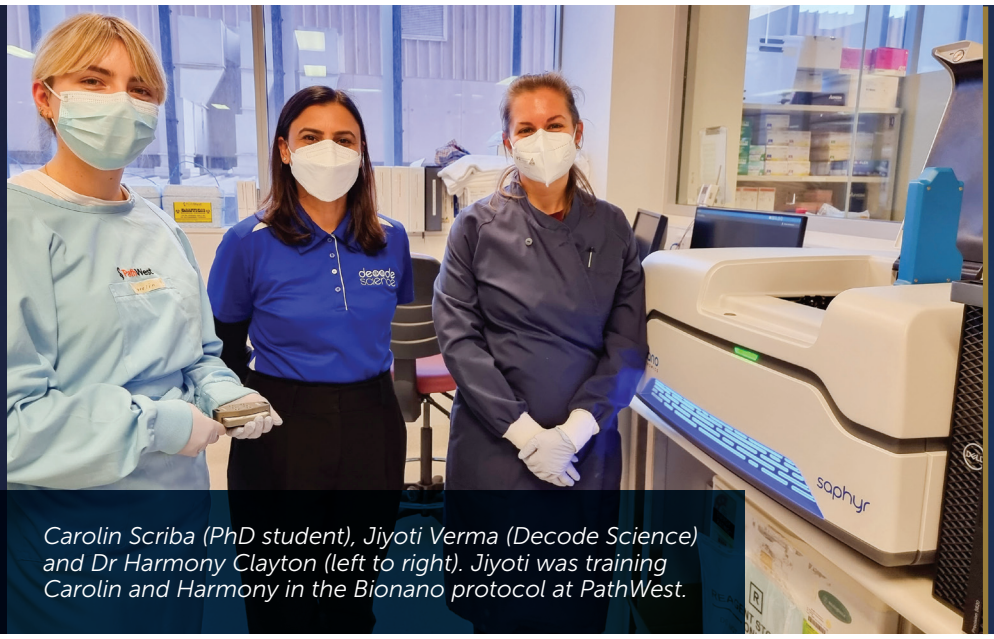
It is hard to believe that we are almost into the middle of June already!

2022 was another highly successful year for our research group which saw a return to international travel and in-person conferences. In 2022, we published 21 papers including first-author publications by research assistant Chiara Folland and students Lein Dofash and Isabella Suleski. This included the description of novel human disease genes, including a new genetic cause for a severe, life-threatening muscle disease called rhabdomyolysis, published in the prestigious journal Brain.

We also played a key role in the discovery of a novel repeat expansion causing cerebellar ataxia, an adult-onset neurodegenerative disease which leads to vertigo, speech difficulties and loss of coordination. This work was published in the highly prestigious *New England Journal of Medicine*. This was a collaboration between my team in Perth, and colleagues in Germany, India and the USA, and was led by our colleague Prof Bernard Brais in Montreal.

This discovery can now lead to a more accurate genetic diagnosis for these patients, and they can plan for their future knowing what to expect. And now that we know the genetic cause, the next stage will be to work on possible treatments.

Associate Professor Gina Ravenscroft
Dr Patricia Kailis Fellow in Rare Genetic Disease



Carolin Scriba (PhD student), Jiyoti Verma (Decode Science) and Dr Harmony Clayton (left to right). Jiyoti was training Carolin and Harmony in the Bionano protocol at PathWest.

Facioscapulohumeral muscular dystrophy (FSHD), Lindt and Bionano optical mapping

FSHD is the second most common neuromuscular disease, affecting around 1 in 5000 people.

The cause of FSHD is a contraction of a segment of DNA on chromosome 4. This genetic cause of FSHD is difficult to diagnose but a new test – Bionano optical genomic mapping – can easily and reliably identify its genetic cause. In 2022, together with PathWest, we obtained funding from FSHD Global, an Australian based charity established by businessman and FSHD-sufferer Bill Moss AO, to purchase the Bionano instrument and set up diagnostic testing for FSHD. Dr Harmony Clayton is now employed part-time at PathWest to establish this new diagnostic test so that Australian patients can receive a genetic diagnosis. This is a really important step for the FSHD community as clinical trials are on the horizon for FSHD and Australia needs to be ready to take part in these trials.

As a result of our collaboration, I was invited to join the Scientific Advisory Board of FSHD Global and attend a meeting in Sydney that coincided with the 11th FSHD Global Sydney Chocolate Ball. This fundraising event, sponsored by Lindt, raised more than $1 million for FSHD research.

Some quiet time at home

I enjoyed the Christmas shutdown period, taking trips to the beach with my family, and catching up with friends. I also got to do some experiments with my kids at home.

Experimenting with colours with my 5-year-old daughter Lucia and Cinderella, both in their custom-made lab coats. As I regularly like to say - "You can't be what you can't see"!

Dr Mridul Johari joins the team

In November 2022, Dr Mridul Johari joined our group at the Perkins and will work on identifying genetic causes of myopathies.

Mridul on the day his PhD was conferred. In Finland, all new PhD holders are given a traditional PhD Sword and PhD Hat during a Conferment Ceremony. The sword and hat symbolise the freedom of research and the fight for what is good, right and true.

Dr Johari completed his PhD in 2021 in the laboratory of Dr Bjarne Udd in Helsinki, Finland. Mridul's PhD focused on the genetics of muscle diseases in adults and the elderly. Inclusion body myositis (IBM) is the most common acquired myopathy in people over 45 years of age (IBM is characterised by chronic, progressive muscle inflammation and muscle weakness). Mridul's research focused on understanding the genetic risk in the Finnish population where the prevalence of IBM is around 70 per million. His research also included the description of a novel muscle gene – small muscle protein X (SMPX). Mutations in this gene on the X-chromosome cause a myopathy in men. Bjarne and our own Emeritus Professor Nigel Laing AO have collaborated for more than 20 years and Dr Johari's addition to the Perkins team represents the next generation of Perth-Helsinki collaborations. We're excited to see what Mridul achieves during his time here.

Inaugural retreat

The Rare Disease Genetics and Functional Genomics team held our inaugural group retreat at the UWA Water Sports complex on the banks of the Swan River (Derbal Yerrigan).

It was a great opportunity to come together in person, update each other on our individual research activities and goals, and allow new members of the team to get a sense of the overall group and the history of neuromuscular disease research in WA.

Following this retreat we mapped our team's core research and culture values. Our research values are **collaboration, curiosity, excellence and integrity.** Our culture values are **inclusiveness, growth, respect and fun!** All these values combine to set a solid foundation for future progress in our field and ensure an integrated approach to further discoveries.

Gina and her team (and Emeritus Professor Nigel Laing AO) on thier inaugural retreat.

Mediterranean islands contribute to our understanding of the genetics of muscle diseases

In two studies published last year, founder mutations arising on islands in the Mediterranean have allowed us to characterise muscle diseases.

We described a novel mutation in CHRNA1, a gene involved in transferring the nerve impulse to the muscle, in patients from Malta, Italy and Spain, including patients in Perth from a small island off Sicily. During his PhD, Mridul identified a founder mutation in the gene ANXA11, which causes adult-onset muscular dystrophy, in four large families from the Greek island of Ios. It is very likely that both these founder mutations will contribute to disease in the Mediterranean diaspora.

WMS Executive Board

Perth team shines at the 27th Annual Congress of the World Muscle Society in Halifax, Nova Scotia

It was wonderful to travel again and reconnect with colleagues and friends after so long.

At this conference, Lein Dofash and Dr Mridul Johari presented research posters, and Chiara Folland's abstract was selected for an oral presentation.

On the last day, in the "Late Breaking" session, three of the nine presentations were novel disease genes identified by our group from the Perkins. Lein presented her PhD work on a new genetic cause for rigid spine myopathy and I presented our work on a new genetic form of oculopharyngodistal myopathy (a rare, adult-onset hereditary muscle disease which affects the eyes and throat), which presented in two large Australian families; one with over 100 people marked in the family tree.

Some Personal Achievements to Share

I want to share some of the personal success I enjoyed this year, thanks to your support.

After being promoted last year to Associate Professor at UWA, I was awarded the Mid-Career Researcher Award at the 43rd Annual Lorne Genome Conference, and I was elected onto the Executive Board of the World Muscle Society.

After many years of advocating for better gender equity in grant funding through the National Association of Research Fellows and the Equity in Australian STEMM group, the major funding body of Australian health and medical research, the National Health and Medical Research Council (NHMRC), announced that they will split the funds for one of their schemes, the Investigator grants, by gender. I am now also a member of the NHMRC's Women in Health Sciences Committee.

Emma Weatherley, Managing Director of FSHD Global, and Gina at the Sydney Chocolate Ball

What's been happening in 2023 so far...

In 2023, we are looking forward to continuing to identify new genetic causes of disease, investigating new types of mutations that have remained elusive until now, and implementing new diagnostic tests for Australian patients in collaboration with PathWest.

Thanks to your support, we'll be able to continue our numerous collaborations and ongoing studies and strive for excellence and integrity with a side measure of fun. And with Nigel now an Emeritus Professor, he has more time to get back to the research (please read on for his own update below).

A few words from Emeritus Professor Nigel Laing AO

I am happy to report that I was made Emeritus Professor by UWA last year. The title Emeritus Professor means that the professor is no longer paid. Emeritus Professor is an honour awarded to retiring professors who apply to continue their association with the university, especially if they want to continue researching. It is not awarded to all the retiring baby-boomer professors, with, for example, only seven professors awarded Emeritus by UWA last year. I am still adjusting to this new stage in my life. Being Emeritus makes it very easy to say "No" to things I do not want to do (!) and therefore makes it easy to devote my time to what I want to do – which is the research.

My research has been by far and away my major hobby. I used to be paid to do my hobby, but now my research is simply my major hobby. This is a relief to my family who worried about what I was going to do when I retired because of my general lack of hobbies!

The funding for Mackenzie's Mission, the Australian Reproductive Carrier Screening Project that I co-led, finished at the end of 2022. All the research work was completed. Over 9,000 couples, spread across the whole of Australia, were tested for their carrier status for 1,300 genes associated with 750 recessive diseases. One of the KPIs of Mackenzie's Mission was to apply to the Federal Health Department's Medical Services Advisory Committee (MSAC) for funding to have Medicare rebates for this carrier testing. The response from MSAC was that there was a significant unmet need for funding for this testing, but that they were not sure whether it should be funded by Medicare rebates or as a national screening program. Mackenzie's Mission is tasked now with exploring these two options with the Federal Department of Health.

I had 17 publications in 2022, eight of which were joint publications with Gina.

I am looking forward to continuing my new Emeritus status in 2023 and beyond.

Emeritus Professor Nigel Laing AO in the lab

Channel 9 visited the Perkins for a story on the MRFF funding announcement.

Medical Research Future Fund Announcement

I was so excited to hear about our success in being awarded a Medical Research Future Fund (MRFF) grant for further study into rare genetic diseases.

As part of a national consortium, MRFF awarded us $4.8m over 5 years to continue important research into blood cancers, intellectual disability, cerebral palsy, repeated miscarriages and neuromuscular diseases. For some sufferers these are inherited conditions caused by the presence of specific genes, not yet identified.

I will be leading teams from nine universities and institutes around Australia, all involved in seeking genetic causes for these diseases.

Despite the success of genetic analysis over the past 10 years, most rare disease patients still do not have a diagnosis, and with no accurate genetic cause, treatments cannot be designed and tested.

My research will help people like Susan and her husband.

Scan to read the full media release here

Susan Hall sought answers after repeated miscarriages. She hopes this research will help families find genetic links to recurrent miscarriages.

Answers for Susan

Susan Hall and her husband had their first baby in 2016. It was an uncomplicated pregnancy and birth, and the thought of anything going wrong with future pregnancies was far from mind.

However, in 2019 she experienced a miscarriage at 15 weeks with her second pregnancy. Her doctor said this was quite normal, and that one in four pregnancies end this way.

Later that same year she had a second miscarriage, and not long after, a third.

She wanted this to be investigated. Three miscarriages in a row seemed to say to her that something was wrong, but several doctors said there wasn't much that could be tested for. Susan felt as if she was being judged for persisting, for wanting to know what was happening.

Several years lapsed and to the family's delight, they had two more children in quick succession in 2022.

Susan has been part of a consumer group assisting Gina, providing patient input to her grant application and hopes that in future, families can find genetic reasons for recurrent miscarriages.

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