The Patricia Kailis Fellowship in Rare Genetic Disease

Your Perkins Supporter Newsletter | June 2024

HARRY PERKINS INSTITUTE
OF MEDICAL RESEARCH

IN THIS EDITION

Your support means so much to our family

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 and her team as they 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 Nigel and their team's vision 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 difficult to fathom that we are already approaching mid-2024!

2023 was another incredibly successful year for the research group in terms of research outputs and publications, winning grants and translation of our research findings. Thank you for partnering with us to ensure that our vital research can continue to go from strength-to-strength.

Since the start of 2023 we have published 27 manuscripts and preprints, including the description of six novel human disease genes, new guidelines for the molecular diagnosis of facioscapulohumeral muscular dystrophy (FSHD) and patient-derived induced pluripotent stem cell resources. These include publications in prestigious journals: *The New England Journal of Medicine*, *The American Journal of Human Genetics*, *Science Translational Medicine* and *Brain*. Your kindness has enabled this success – thank you so much!

I recently returned from Prague, where I attended the World Muscle Society Congress, and Tokyo, where I spoke at the 65th Annual Meeting of the Japanese Society of Neurology. I presented our work describing a rare form of adult-onset myopathy – oculopharyngodistal myopathy. The Perth team have worked on the genetics of this condition in a local family for many decades, and we have only in the last few years been able to identify the causative gene in these families. A true break-through! It's particularly awesome that we now know of families in France and the UK with the same genetic form of this myopathy.

Thank you for making Patricia's vision a reality – I really do believe that we have established the West Australian "hub" for rare genetic diseases that she always dreamed we would.

Ravenscroft

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

Chiara Folland has transitioned from a research assistant to a PhD student.

Chiara takes on a PhD and receives prestigious UWA scholarships

Chiara Folland has transitioned from a research assistant within the team to PhD student.

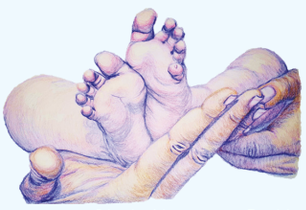
As a highly ranked PhD student applicant in the UWA Medical School, Chiara has been awarded multiple generous top-up scholarships including the *Jean Rogerson HDR Scholarship - Stipend Scholarship*, awarded to highly ranked applicants in the main application round, providing a stipend of $43,000 per annum. She also received the *Jock and Marjorie Hetherington HDR Top-Up Scholarship* which provides a living allowance stipend of $7,000 per annum in 2024 for students enrolled in full-time study. Chiara was also awarded the *Australian Government Research Training Program Domestic Fees Offset Scholarship* and *The University Club of WA Research Travel Scholarship*.

Chiara's proposed PhD project is entitled "*Exploring new bioinformatic approaches to identify hidden genetic variation underlying rare neurogenetic diseases*" and aims to identify the genetic causes of neurogenetic diseases in a patient cohort through re-analysis of existing short-read genomic data. One of Chiara's co-supervisors is A/Prof Mark Cowley, who leads the Computational Biology Team at the Children's Cancer Institute (Sydney). Chiara recently visited Cowley's Team in mid-October 2023 to foster this collaboration and was given a tour of their informatic platforms that holistically integrate multi-omics data, which will invariably assist Chiara in this project.

Passion project becomes reality

We now also have funding and ethics in place to begin a project that I'm really committed to, and that is exploring the utility of the optical genomic mapping approach in the context of unexplained recurrent pregnancy loss. Every day in Australia over 200 women experience a miscarriage, and tragically around 1-2% of women will experience recurrent miscarriages. The genetic diagnostic options available to these women haven't changed in decades, despite many new genomic technologies. Recruitment into this study has begun via private GP and fertility practices.

The team are really looking forward to seeing what insights this genomic mapping might provide to couples that have experienced recurrent miscarriage. We can't wait to keep you updated on our success in this area!



Drawing courtesy of Lab Alumnus, Dr Hayley Goullee

Third Annual Lab Retreat

In April we held our annual lab retreat at The Maali rooms at Perth Zoo.

We had a packed day discussing the grand challenges we face in the field of rare and neuromuscular diseases, our team values and culture, what we're doing well, areas for improvement and how we might make the most of ChatGPT. We learnt more about newer members of the team - Jeremy and Darcy both like baking and biking!

A team building activity saw us sharing our spirit animals which included turtles, raccoons, cats, meerkats, boobook owls, kookaburras, fat frogs, sugar gliders, eagles and dolphins. Some of us then tried to snap selfies with our spirit animals.

The Rare Disease Genetics & Functional Genomics Team and the Preventative Genetics Team enjoyed a productive and fun day on their annual lab retreat at Perth Zoo.

A sign in an area of the old cages talked about different ways of doing zoos and conservation. It really resonated with me. Likewise in science there is a new, kinder way of doing science and I hope our group is really living that.

Times have changed and the next generation are fierce advocates for a different way of doing research.

The AICC(WA) Dr Patricia Verne Kailis Women of Achievement Annual Event

Members of our team greatly enjoyed the 2023 Australia Israel Chamber of Commerce Dr Patricia Verne Kailis Women of Achievement lunch.

The highlights included networking with inspiring women and hearing from Dr Vanessa Guthrie AO. She shared insights into her career as a pioneering woman in the mining sector and her journey from activist to successful advocate.

It was a wonderful event and a welcome opportunity to take a break with some of the team, to be inspired and to reflect.

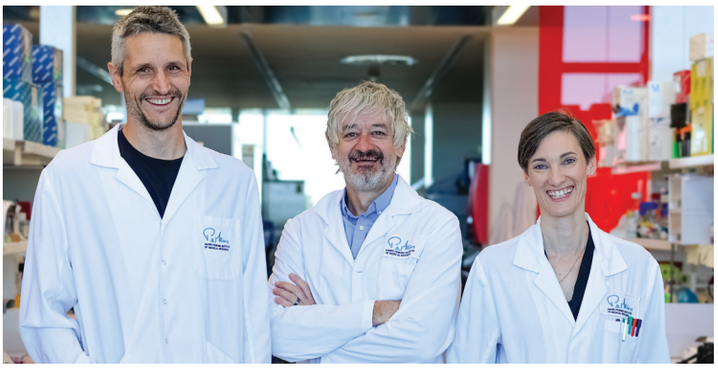
Members of our team enjoyed catching up with Ms Mandy Loton OAM.

Funding boost for development of disease models and treatments for congenital muscle diseases.

Dr Rhonda Taylor is the team leader of the Disease Models and Therapies research theme which spans the Rare Disease Genetics and Functional Genomics (Gina's group) and Preventive Genetics (Nigel's group) at the Perkins.

Rhonda's team aims to develop new patient-centric cell models of muscle diseases that can be used to develop and test new treatments for this currently incurable group of rare muscle diseases.

In December 2023, Rhonda was awarded one of two prestigious Safe Harbour Fellowships which were established to offer support to high achieving Early-to-Mid-Career Researchers at the Perkins.



Dr Rhonda Taylor pictured with the Perkins Safe Harbour Fellows Dr Olivier Clement (L) and Dr Chuck Herring (R).

Additionally, Rhonda was also awarded a research grant by the Channel 7 Telethon Trust to support the screening of a range of new treatment options being developed by Rhonda's team. Collectively, these sources of funding will allow Rhonda to generate the first evidence of treatment feasibility for a subset of specific muscle diseases. Studies are now underway and it is a very exciting time – we can't wait to share what comes of this research with you soon!

Thank you so very much

The Patricia Kailis Fellowship in Rare Genetic Disease was launched in 2019 with a campaign target of $1.5 Million. We are thrilled to confirm that since that time $744,195 has been raised thanks to your kind and generous support. When you donate to the Patricia Kailis Fellowship you are not only ensuring that Associate Professor Gina Ravenscroft has a safety net to fall back on (in the event there was ever a gap between her salary and the grant funds she has secured) but you are supporting the many research projects this amazing team are carrying out under Gina's and Nigel's leadership. Your gift helps to ensure this life-changing medical research can continue. Thank you from the bottom of our hearts for your continued loyalty and care!

We loved seeing you! Thank you for joining us at the Perkins for dinner and on the *Manitoba*. Our sincere gratitude to the Kailis family for their warm and generous hospitality.

Emeritus Professor Nigel Laing AO in the lab.

A few words from Emeritus Professor Nigel Laing AO

Genetic carrier screening informs couples of their chance of having a child affected by a recessive genetic disease before they have children.

Dr Patricia Kailis invented carrier testing for known Duchenne muscular dystrophy families in the 1960s, while I first became interested in carrier screening in the late 1980s. The carrier testing that Patricia invented is called cascade carrier testing now and can only be applied in a family that has already had an affected boy. The carrier screening that I became interested in in the late 1980s was to screen couples before they had any children. Really, the technology to do such screening only became available with the invention and large-scale clinical application of next generation DNA sequencing in the 2010s. I along with a number of other researchers and clinicians started to advocate for researching such carrier screening in the mid 2010s.

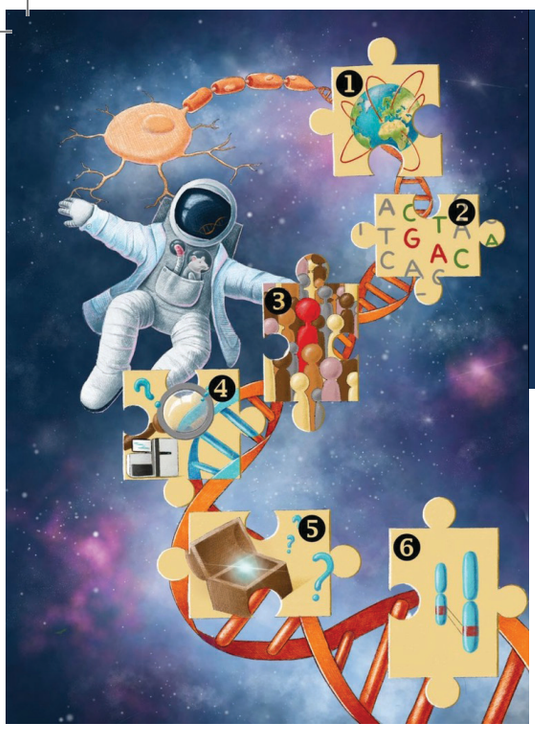
In May 2018, the Federal Health Department announced the funding of Mackenzie's Mission, the Australian Reproductive Carrier Screening Project and we were off and running. Mackenzie's Mission is now completed and it achieved what it was asked to achieve – demonstrate that carrier screening could be taken to every corner of Australia. On completion of Mackenzie's Mission, the Medical Services Advisory Committee (MSAC) recommended the Federal Department of Health explore the option of making Mackenzie's Mission-style carrier screening into a national screening program, like the breast and bowel cancer screening programs. The Mackenzie's Mission team is currently working on co-designing such a program with the Federal Department of Health.

Meanwhile, a Medicare rebate for reproductive carrier screening for three recessive diseases became available to all Australians on 1st November 2023. The three diseases covered by the rebate are cystic fibrosis, fragile X syndrome and spinal muscular atrophy – three of the commonest human recessive diseases. Carrier screening for these three diseases is now free to any Australian couple that wants to use it. There has been a very rapid uptake of the screening such that now approaching nearly 10,000 tests of this three-disease screen are being performed every month. The way this three-disease test has to be performed is that the female partner has to be tested first. After that, if the female partner is identified to be a carrier of cystic fibrosis or spinal muscular atrophy, the male biological partner is tested. This is a sequential test. The carrier screening performed in Mackenzie's Mission was a couple-based test where both the female and male partners were tested simultaneously. Sequential testing will not work in a national screening progran for the large number of genes (~1,300) tested in Mackenzie's Mission. When testing 1,300 genes, basically everyone is a carrier of something so the male partner would end up having to be analysed in almost every couple. It is therefore more efficient to perform couple-based screening for such a national screening program.

In Western Australia, PathWest is now offering the three-disease rebate-able carrier screen. It is also offering commercial testing for Mackenzie's Mission size expanded carrier screening. It is very gratifying to see both these in place.

I am sure Patricia would be delighted that carrier screening in WA has reached this point.

Thank you for your support of Gina and the wider team. I am so very proud of them all.



New Review on the progress and challenges ahead for inherited peripheral neuropathies.

Jevin Parmar, a third year PhD student in the team, recently had a review article accepted in the Journal of Neurology, Neurosurgery and Psychiatry.

Article title: The Genetics of Inherited Peripheral Neuropathies and the Next Frontier: Looking Backwards to Progress Forwards.

Inherited peripheral neuropathies (IPNs) are a group of rare inherited diseases affecting the peripheral nervous system with a wide range of symptoms, clinical severity and causes. Disease-causing variants in over 100 genes have been associated with IPN, with over 70 of these being associated with IPN in only the last 10 years. Despite the increase of reported disease-associated genes through diagnostics, improved bioinformatic analyses, and functional studies, around 50% of patients with IPN remain genetically unsolved.

This review explores the evolving genetic landscape of IPNs over the last ten years, including identification of disease-causing variants in novel genes and novel variant types that cause IPN. By extrapolating from challenges overcome to the challenges that still remain, we provide an outline for tackling the "The Final Frontier" of the missing genetics of IPNs, enabling a path towards accurate genetic diagnoses for the many families with IPN still to be solved.

This review was co-written with Professor Marina Kennerson at the ANZAC Institute in Sydney, one of Jevin's supervisors and a key collaborator in this space.

It includes this commissioned artwork *(above, left)* to accompany the review. Figure title: *Strategies to tackle "The Final Frontier" for the molecular diagnosis of inherited peripheral neuropathies.*

We hope this review will be a useful resource for those in the field of inherited peripheral neuropathies and we look forward to continuing to uncover some of the missing genetics of these diseases.

FSHD Diagnostic Test

Dr Harmony Clayton earlier this year applied to the National Association of Testing Authorities (NATA) to have Bionano optical genome mapping recognised as an accredited test for the molecular diagnosis of FSHD. NATA-accreditation of this diagnostic test is an important piece in the puzzle of getting Australia ready for clinical trials for FSHD, with many treatments currently under development and in clinical trials overseas.

Dr Harmony Clayton using the Bionano machine at PathWest

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