GILLIES McINDOE RESEARCH INSTITUTE
Pioneering future treatment of cancer

Newsletter Issue#22, October 2020

Pushing the boundaries and facing new challenges

As the world continues to grapple with the COVID-19 pandemic, we're very grateful that we've been able to keep on with our research. In our latest newsletter we share what we've been up to over the past few months and what we plan to accomplish next.

Pioneering research always has its challenges and we've faced a few more than usual recently, but we're still making good progress. We remain far ahead of where we'd thought we would be when the GMRI started seven years ago.

Thank you to each of our supporters for your dedication and generosity — our progress would not be possible without you.

Our new chief scientist brings new ideas and capabilities

In this newsletter, we welcome Dr Sean Hall to our team. Sean aims to build and lead our team to achieve our research goals using our greatest assets — our people. In his work, Sean will be identifying any bottlenecks in our research process and finding solutions. He'll also introduce state-of-the-art techniques and technologies to the GMRI that we wouldn't normally use. We look forward to sharing with you what he does next.

Investigating breast cancer and possible treatments for keloid disorder

We have two new researchers contributing to fundamental research at the GMRI. Dr Amanda Peacock is investigating cancer stem cells in breast cancer alongside our team — we're writing up the findings as you read this. Dr Sam Siljee will begin a PhD study investigating keloid disorder to see if we can use an effective low-cost method to treat keloid disorder. Currently, no effective treatment exists for this condition.

Progress, and ambitious plans for our clinical trials

Our glioblastoma clinical trial is going well and, with enough funding, we'll be able to move onto the next phase that would see us treating patients at an earlier stage in their cancer. Our second clinical trial is ongoing as we test our treatment method on patients with advanced malignant melanoma who have failed conventional treatment and immunotherapy. Subject to funding, we also have plans to begin clinical trials to treat other types of cancer.

Behind the scenes — a handy helper that makes our research more efficient

Here at the GMRI, we've had a lot of amazing helpers over the years — and not all of them are human. In this newsletter, we share with you how much of a difference some of the high-tech equipment in our laboratories can make to our research process. Since we started using it in 2013, the BOND RX Research auto-stainer achieves in a few hours what would otherwise take our team of researchers several days. This machine automates a process we use in almost all research that we publish in international journals and present at conferences.

For more regular updates, follow us on Facebook

Dr Swee Tan ONZM, MBBS FRACS PhD
Executive Director

Putting people first on the GMRI's journey to success

Meet Dr Sean Hall — our new chief scientist.

Success for the GMRI's new chief scientist, Dr Sean Hall, will mean two things: helping our team reach its research goals and setting a good example. 'If I'm able to accomplish this, then I'll be able to look back knowing I've put people first and achieved good outcomes.'

Following delays caused by COVID-19, Sean and his wife arrived in Wellington in September. He's come from Bern, Switzerland, where he was Group Leader at the Division of Thoracic Surgery at Bern University Hospital. Before that, he was a scientist and researcher at universities in Rotterdam and Harvard. And now that he's in Wellington, Sean is already adding his expertise to many of the GMRI's activities.

'Overall, I wear many hats at the GMRI. I am willing to take on any role that will ensure the success of our team.'

Rising to the challenge of building an effective team

The main focus of Sean's position is to help build and lead our team to achieve our research goals. Our goals focus on finding effective and affordable treatments for cancer, vascular birthmarks, and fibrotic diseases such as keloid disorder.

Sean believes our greatest asset is our people. From his perspective, we already have the great advantage of our existing team being world-class in many ways. He believes his task is to help our team develop even further, and to ensure we have the right environment to grow in.

Sean says he's hugely impressed by the GMRI team's dedication and the collegial atmosphere that exists.

'What also impresses me is the diversity of team members, ranging from academics, researchers, associates, nurses, students, and clinicians.

Each of these people has a unique set of skills that is critical to our success. They work so well together, supporting each other in achieving our common goal.'

Setting incremental goals to build on the GMRI's success

Sean says every scientist aims to be involved in cutting-edge research that eventually leads to treatments that relieve pain or suffering. To help us on this path, he believes in setting and building on incremental goals.

For Sean, one of these goals is to identify any research bottlenecks and find relevant solutions. Another is to introduce state-of-the-art techniques and technologies that are not yet part of the current research platform.

Sean will also recruit and train research fellows and PhD students by raising competitive, peer-reviewed funding. And he'll introduce new research ideas that our team can develop.

Connecting the public with the GMRI's journey

The public play a very important part in our success, not to mention our mere existence. Sean will work with our team to increase dialogue between the GMRI and the public. He wants to bring the public closer to what's happening at the GMRI.

'It's really important that we involve the public to learn more about the research we're involved in, as they have a vital interest in our continued success.'

Sean will also dedicate time to developing working relationships with external partners such as academic, health, government, and community organisations.

We're very excited to have Sean on the team. We look forward to updating you on his work in coming newsletters.

Two passionate researchers and their exciting projects

Dr Amanda Peacock and Dr Sam Siljee have carried out research with our team and made interesting findings.

Dr Amanda Peacock is a plastic surgical trainee at Middlemore Hospital. She put her training on hold last year to take part in a six-month fundamental research programme at the GMRI, investigating breast cancer. Dr Sam Siljee was one of our summer students in 2014–2015 and 2015–2016. He's starting a PhD study on keloid disorder at the beginning of 2021.

Amanda investigated stem cells in breast cancer

Amanda often works on breast reconstruction and wanted to learn how to do quality research, as she feels there's more scope for it in plastic surgery. She worked with Dr Swee Tan, who is also one of the consultant plastic surgeons at the regional plastic surgery unit at Hutt Hospital. Her project investigated the characteristics of the cancer stem cells in breast cancer and the involvement of the renin–angiotensin system (RAS).

What Amanda discovered

Amanda identified and characterised cancer stem cells in breast cancer using certain stem cell markers. She found that these cells express components of the RAS. Our team is preparing a manuscript on her discoveries for publication in a peer-reviewed scientific journal. She is also writing a review article on cancer stem cells in breast cancer to update surgeons on this field of research.

Amanda has found the experience very rewarding and encourages fellow trainees to take part in similar research.

Sam is investigating a novel low-cost treatment for keloid disorder

Keloid disorder is a condition that causes skin injuries to form excessive scars that behave like a benign tumour. These scars continue to grow and cause problems. The team at the GMRI has previously discovered stem cells that express the RAS and vitamin D receptor in keloid disorder. Sam's PhD research will build on this work.

Findings from the project will also lead to a better understanding of Dupuytren's disease and other unsolved fibroproliferative diseases affecting organs such as the lungs, kidneys, and liver.

The effects of keloid disorder

Keloids can have a big impact on people's lives — as well as being disfiguring, they can cause joint contracture, pain, and itching. Keloid disorder affects all racial groups, but is more common in people with darker skin. It affects 2% of Caucasians and a larger, but unknown, proportion of Māori and Pasifika.

This project aims to develop treatment for keloid disorder with existing low-cost medications

We don't fully understand what causes keloid disorder, so current treatments are ineffective with very high recurrence rates following surgery. Sam's project will investigate how exactly the RAS and vitamin D influence the stem cells of keloid disorder, and determine if we can treat it with existing low-cost medications, such as vitamin D and anti-hypertensive drugs. If proven successful, the project will benefit everyone with keloid disorder.

These low-cost medications are widely used for other purposes and their safety profile is well known.

We'll investigate keloid disorder through an 'ex-vivo' model

Part of the project will involve developing a model system that replicates the features of keloid lesions so we can identify their vulnerabilities and test new treatments. This model will be an *ex-vivo* organ culture, meaning it will offer results that are as close as possible to experimenting on real keloid lesions.

Our clinical trials are making steady progress

Cancer stem cells are like ‘queen bees’ that produce ‘worker bees’ (cancer cells). These stem cells also produce new queen bees that create new ‘hives’ (new tumours in other parts of the body).

Our clinical trial programme is testing the GMRI’s novel treatment approach by targeting cancer stem cells, the proposed origin of cancer. We are currently running two trials, focusing on patients with glioblastoma and patients with advanced malignant melanoma who have failed conventional treatment. The glioblastoma clinical trial is well underway and the early results are promising.

We have shown that cancer stem cells in 14 types of cancer express the renin-angiotensin system (RAS) and the converging pathways. These pathways can be blocked by commonly available, low-cost, off-patent oral medications, including those used for treating high blood pressure, diabetes, and arthritis. These medications have been used for many years, and their safety profile is well understood. They cost about $4,000 per patient per year — substantially less than conventional treatment for glioblastoma, which can be $80,000 to $100,000 per patient.

With more funding, we can move to the next phase and treat patients earlier

The next phase of our clinical trial for glioblastoma would involve starting the treatment at an earlier stage, which may achieve better outcomes.

We currently have limited funding, so we can’t begin this next phase yet. We also have plans to extend our clinical trial programme to include other types of cancer, but need more funding to make this possible.

We have a new clinical trial coordinator

Meet Ruth Watson-Black — our new clinical trial coordinator.

Our new Clinical Trial Coordinator, Ruth Watson-Black, has managed medical trials in the United Kingdom and New Zealand, and has experience of project managing clinical trials at a global level.

Ruth is the main point of contact for patients. She coordinates the GMRI's clinical trials and their daily activities. Her role breaks down into two elements — patient relations and project delivery. In the first part of her role, Ruth organises the logistics of all the patients' visits and checks that we're giving patients good care. She also ensures we're keeping them safe and following the process of collecting data, such as study outcomes and blood pressures.

Ruth has worked in the pharmaceutical industry in the United Kingdom and New Zealand. For almost a decade she specialised in clinical trials, supporting local clinical trial centres and project managing clinical trials in the UK, Europe, North and South America, Asia, and Australasia.

During this time, Ruth was responsible for Phase 1 to Phase 4 projects in a wide range of therapeutic areas, including:

- breast cancer, gastrointestinal stromal tumours and paediatric oncology
- attention impairment
- influenza and hepatitis C
- cystic fibrosis and haemophilia
- diabetes
- multiple sclerosis
- rheumatoid arthritis and osteoporosis
- renal dialysis

Ruth's other previous role as a childbirth educator has honed her interpersonal skills. She draws on this experience to ensure we give medical information to patients in language they can easily understand.

Our handy helper — thanks to you

Our BOND RX Research auto-stainer.

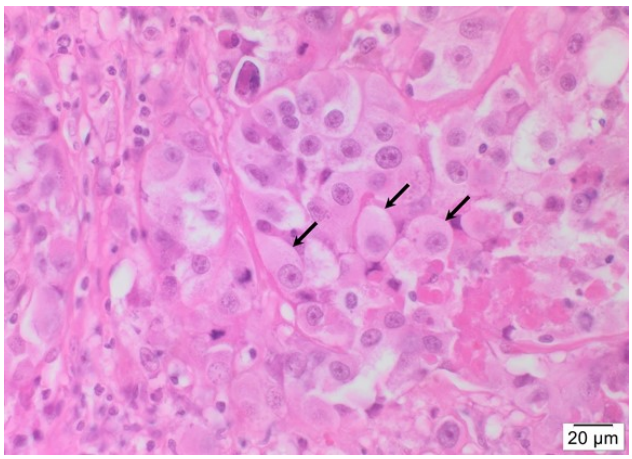
Our laboratories have a range of high-tech equipment thanks to donations and philanthropic support. We wanted to show you how one vital piece of equipment can help us so much. In just a few hours, our BOND RX Research auto-stainer does what would otherwise take us two days, and we use it in almost all of our research.

Most of our research relies on staining tissue samples

Our research usually requires us to identify key components of cells and tissues. We use staining to help us identify specific properties that characterise the diseases and cancers we investigate.

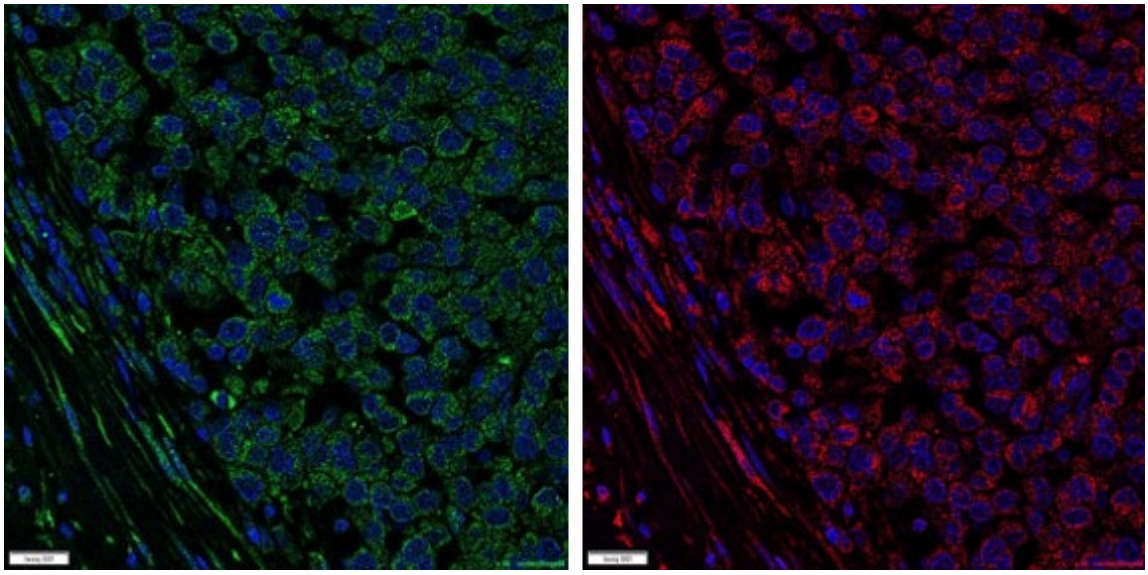
Our auto-stainer uses a variety of antibodies and diagnostic markers to stain sections of diseased human tissues. It identifies specific components unique to the cells and tissue samples of certain diseases, using different immunohistochemical techniques.

To begin the identification process, we slice very thin (about 4 micrometre) sections of tissue samples from a particular disease, such as cancer, we're investigating. We place these sections on glass slides. We use a different piece of equipment to stain the tissue, changing it from white to pink-purple — like in the image below. This initial staining means we can identify the type of cancer or disease and its properties.



A haematoxylin and eosin stain of a metastatic malignant melanoma showing cancer cells (arrows), magnified 400x.

Next, we use the auto-stainer to identify more specific properties of the tissues using techniques like the one in the images below. We can customise the settings of the auto-stainer so it identifies specific markers or tags. These results form a large part of the research our team publishes in international journals.



Images of a metastatic malignant melanoma stained using fluorescence dye, showing cancer stem cells (in green) that express pro-renin receptor (in red), which is a component of the renin-angiotensin system. Magnified 400x.

The auto-stainer makes our research process very efficient

It works quickly — we can stain up to 30 slides at the same time, using different customised settings. Each run can take up to four hours to complete, depending on the settings. This means we can stain up to 60 slides in a day, compared with four slides over two days by hand staining.

We can also run the auto-stainer overnight, so our research team doesn't have to do overtime. For example, the stains using immunofluorescence tags (like the images above in green and red) usually take 11 hours using the auto-stainer.

Back in the past we had to stain cells by hand

Without this vital piece of equipment we would have to stain by hand and follow multiple steps. It usually takes two days to produce four slides — a fraction of the amount of slides the auto-stainer turns out. Sometimes we would get inconsistent results because multiple steps and sometimes multiple people were involved in the staining procedure, which could vary from one person to another.

We acquired our auto-stainer at the end of 2013. It was the first installed in New Zealand and one of the few that can be used for research applications. Leica, the auto-stainer's manufacturer, provides excellent servicing with technical experts that we can contact readily.

Many labs around the world still stain tissue samples by hand. We're very fortunate that the funding we've received allows us to use this fantastic piece of equipment — and others like it.

Your opportunity to make a real difference

Join us and become a GMRI donor. By supporting our research, you'll play a part in making a real difference in the lives of people suffering from cancer.

As a charity, our goals are unashamedly aspirational — the Gillies McIndoe Research Institute exists to reduce human suffering and improve lives. With your help we can achieve our goals.

What we're trying to achieve

Our cutting-edge research is working towards making cancer treatment more effective, less invasive, and more accessible and affordable. Our team has developed a novel cancer treatment that repurposes existing generic low-cost medications. If proven effective, this treatment method will reduce the need for surgery, radiotherapy, and chemotherapy, and help reduce the treatment disparities that currently exist.

We're a team of world-class experts dedicating our knowledge and time towards reaching our goals. One of our biggest challenges, however, is securing funding to carry on with our research and clinical trials.

That's where you can play a part and help us achieve better outcomes for cancer treatment.

Why we need your help

Our research shows enormous promise and could transform how cancer is treated. But we have a lot more work ahead of us yet. We need to undertake clinical trials over several years to test our proposed cancer treatment on different types of cancer — glioblastoma (a type of brain cancer), malignant melanoma, mouth cancer, and metastatic squamous skin cancer. Clinical trials and the research that supports them are expensive, costing us $1 million per trial per year to complete. Unfortunately, many businesses aren't very interested in funding research into using low-margin generic drugs to treat cancer, because the usual commercial incentives aren't present.

To reach our goals, we need a shared funding solution involving the government and public sector agencies, businesses, charitable organisations, and donations from people like you.

How you can make a difference

By supporting our research, you could make a transformational difference in the lives of people suffering from cancer. Imagine if cancer treatment was gentle and affordable, and involved minimal time away from home. That's what we're aiming for. Your support and donation will progress our work.

We are deeply grateful for all donations in support of our cancer treatment, whether they are small or large, regular or one-off, anonymous or recognised — all are vital and are valuable to our mission. As the GMRI is a charity, all donations over $5 are eligible for a tax rebate following the usual IRD rules.

Email us to find out more

Become a GMRI Donor