THE IMPACT OF GIVING 2019/2020
All photos used in this report that include two or more people were taken prior to social distancing guidelines being implemented at the Institute and in Australia.

We acknowledge the traditional owners and custodians of the land on which our campuses are located, the Wurundjeri people of the Kulin Nation, and pay our respects to their elders past, present and emerging.

Artwork (left): In Your Hands by Robert Young, commissioned by the Walter and Eliza Hall Institute.

The Walter and Eliza Hall Institute of Medical Research. ABN: 12 004 251 423.
Vision

To be an innovative medical research institute that engages and enriches society and improves health outcomes through discovery, translation and education.

At a glance 2019

In 2019 the Walter and Eliza Hall Institute of Medical Research received $18,863,000 in philanthropic donations, grants and bequests from passionate individuals, community organisations, companies and trusts and foundations.

Five things you made possible in 2019

- Supported innovative research on important cancers. Read more on pages 6 & 7.
- Helped us design new diagnostics test for Parkinson’s disease and dementia. Read more on pages 8 & 9.
- Progressed personalised oncology treatments. Read more on pages 10 & 11.
- Established a new world-class drug discovery centre. Read more on pages 12 & 13.
- Supported advancement in epilepsy research. Read more on pages 14 & 15.

Thank you for your generous donations

Total donations, grants and bequests received in 2019: $18,863,000. The Institute ensures that 100% of your donated funds go to the area of research you have agreed to support.
It has always been wonderful to meet WEHI’s donors and hear their reasons for supporting researchers at the Institute. As a scientist, I also know how inspiring it is when a member of the community supports a scientist to progress their research.

In 2020 we have all been impacted by COVID-19. It has been a time of fear and uncertainty. Much of the Institute’s workforce has had to adapt to working from home while a group of researchers have quickly adapted their research and applied their expertise to tackling COVID-19.

This edition of *Impact of Giving* looks back at 2019 – a different world in many ways to today.

You can read about how WEHI’s supporters have brought new tests and treatments for cancers one step closer, and helped to solve mysteries about the causes of epilepsy and asthma.

WEHI’s supporters have been instrumental in the establishment of two major new centres – the new Colonial Foundation Healthy Ageing Centre, bringing together research into dementia, Parkinson’s disease and other age-related disorders; and the National Drug Discovery Centre, which is now providing researchers from around Australia with the necessary infrastructure and expertise to develop much-needed new medicines.

We understand that you, as a valued WEHI supporter, have a range of motivations for contributing to medical research, either through a donation or making a gift in your will. You might have experienced the challenges of seeing a loved one live with a disease – or lived with that disease yourself – and know that medical research promises a better future for you, people like you, and your loved ones.

This was the case for sisters Ellie Rogers and Lisa Bardas, who were motivated by their own family’s experiences of breast cancer to organise a fundraising ball in 2019 that raised more than $1 million dollars for WEHI’s medical researchers.

Some supporters have experienced first-hand the positive outcomes of WEHI’s research, whether that be research that underpinned the development of a new medicine or a new diagnostic test.

Like you, all of our supporters are united by a passion to make the future better.

Please be assured that WEHI’s scientists share your passion. Our focus is on improving the understanding of how our body works and what goes wrong in disease, so that we can develop new medicines, prevention strategies and diagnostic tests that will improve the lives of people here and around the world.
Thank you for investing in the future. By supporting life-changing research at the Walter and Eliza Hall Institute, together we can tackle the biggest health issues affecting humanity.

From cancer, immune disorders, healthy development and ageing to infectious diseases, your support is vital to make the next discoveries.

There are many ways for you to learn more about WEHI’s research, either through the Illuminate newsletter or following us on social media. I hope you will also have the opportunity to meet WEHI’s researchers and inspire them with your stories about why you choose to support them.

Thank you for the trust you have placed in the Walter and Eliza Hall Institute. We promise that your support will enable our scientists to make discoveries that improve health, ultimately bringing about a better future.

Professor Doug Hilton AO
Director, Walter and Eliza Hall Institute

Above: Institute director Professor Doug Hilton.
Right: (l-R) Dr Hai Vu Nguyen, Professor Suzanne Cory and Dr Cassandra Vandenbarg; Dr Kym Lowes; Dr Paola Favuzza.
Case study #1

Cellular barcoding: understanding how breast cancer spreads

In 2019, Institute researchers revealed they could tag, track and pinpoint cells responsible for the spread of breast cancer from the original tumour using a technique called ‘cellular barcoding’. This year they expect a study to be published on an exciting new tool that advances this work.

Dr Shalin Naik, who co-developed cellular barcoding in the Netherlands in 2013, and Professor Jane Visvader, who specialises in breast cancer research, led the first study. It also showed that chemotherapy temporarily shrinks the tumour arising from individual cells, rather than eliminating them, explaining how the cancer could later relapse.

“We’ve developed this methodology and proved that it actually works ... we now want to apply it to cancer.”

The next phase is to understand why some cells from the original tumour grow and metastasise (spread) and others grow but don’t metastasise. Most deaths from breast cancer are caused by the metastasis of cancerous cells into other organs.

“We want to know why this particular behaviour occurs: is it random or is it something that is programmed within cells?” Dr Naik said.

To find out, Dr Naik’s team developed a new method called SIS-seq, a molecular ‘time-machine’ that allows scientists to track a barcoded cell in the tissue it came from. In this way, they can see what genes are necessary for it to change from one type of cell to another type.

“Now we can find out which gene correlates to which function,” he said.

“We’ve developed the methodology and proved that it actually works applying it to stem cells; we now want to apply it to cancer as well.”

The ultimate hope is for new targeted treatments for breast cancer.

“This technique is powerful,” Professor Visvader said. “I think it’s going to have many applications, particularly given the advances Shalin and his team have been making.”

First authors on the 2019 paper were Dr Delphine Merino (now at the Olivia Newton-John Cancer Wellness & Research Centre) and Dr Tom Weber.
Pancreatic cancer has one of the lowest survival rates of all cancers: only six to seven per cent of Australians with the disease will survive beyond five years. No screening is available for it, and unfortunately by the time most people are diagnosed, the cancer is already well advanced.

Dr Belinda Lee established the PURPLE pancreatic cancer translational registry to look for solutions. The web-based registry, a forerunner in Australia, has already collected longitudinal comprehensive treatment and outcome data on 1600 patients (and growing) at more than 27 cancer centres across Australasia.

“The registry concept is about big data,” Dr Lee said. “The more data we can put together the more insights we can get. Often when you have larger numbers you start to see patterns which wouldn’t be evident with smaller numbers.”

Dr Lee is actively using the registry data to support several research projects. One is collecting tissue and blood samples to explore potential molecules to act as ‘biomarkers’, indicating the presence and extent of disease. These could be used to screen for early stage cancers and to predict whether a planned treatment is likely to work in an individual patient.

She is particularly interested in immunotherapies, which help the body mobilise its own immune cells to fight cancer. Although immunotherapies have been successful in many other solid tumours, particularly in lung cancer and melanoma, they have been disappointing in pancreatic cancer.

“We’re breaking down the subsets of different types of immune cells to see if we can identify a particular immune cell population that might predict a better treatment response,” Dr Lee said. “We’re excited by the possibility that there are alternative populations of immune cells that might be more helpful in fighting pancreatic cancer.

“With very limited treatment options we urgently need to find better alternatives to what we’re using.”
Neurodegenerative diseases such as Parkinson’s disease and Alzheimer’s disease are characterised by clearly defined symptoms, but signs of these diseases are often present in people for years or even decades before symptoms appear.

To counter this, the new Colonial Foundation Healthy Ageing Centre is aiming to develop blood tests to detect neurodegenerative diseases early. The tools would revolutionise diagnosis.

The multidisciplinary centre, co-led by the Institute’s Associate Professor Andrew Webb and Professor Frank Bowling, Director of Pathology at The Royal Melbourne Hospital, takes Institute discoveries to Professor Bowling’s pathology team, which carries out the processes necessary for them to be used with patients.

“We intend for all our discoveries to have clinical applications,” Associate Professor Webb said.

The five-year project, funded by the Colonial Foundation, is currently building prototype robots to automate the handling of samples from patients.

Professor Bowling said work by the new translational centre, believed to be the first of its kind in Australia, could significantly shorten the time it takes for a patient to get the right treatment.

“If you introduce a trial for a patient you may have to wait years to see a change in symptoms, whereas if you’re measuring the molecules related to the disease – which is our approach – you may see changes to the molecules early in the course of treatment,” he said.

“These cutting-edge tools could also potentially unlock important insights in how diseases of the brain develop and progress,” said researcher Dr Andrew Evans, a neurologist at The Royal Melbourne Hospital who specialises in movement disorders including Parkinson’s disease.

The centre also aims to map out a biological model of both healthy ageing and dementia – a ‘trajectory of ageing’ – to help understand the biological mechanisms and pathways of disease and to develop new therapeutics.
Although dementia is commonly thought of as a single condition it is actually an umbrella term for several diseases, including Alzheimer’s disease.

Correctly diagnosing dementia subtypes is essential to managing a patient’s symptoms, clinician neuroscientists Associate Professors Rosie Watson and Nawaf Yassi stress. The need is pressing: more than 447,000 Australians now live with dementia with 250 new cases diagnosed each day.

“This is the sort of research that would have massive implications if we could develop such a blood test.”

Symptoms of dementia can vary widely. Patients with Lewy body dementia experience visual hallucinations and a slowing of movements similar to Parkinson’s disease; those with vascular dementia, which can occur after a stroke, have problems with attention and the ability to plan, whereas short-term memory loss is a hallmark of Alzheimer’s disease.

To improve diagnosis, the Watson/Yassi lab is developing a blood test to look for trace amounts of proteins that have accumulated in the brain and cause damage. In Alzheimer’s disease, for example, these are amyloid-beta and tau. The researchers are using a new machine called a Simoa to accurately measure very low concentrations of these proteins.

The researchers said the generous support of philanthropic groups including the Yulgilbar Foundation, Besen Family Foundation and Portland House Foundation had enabled them to invest in this technology and advance their work.

“This is the sort of research that would have massive implications if we could develop such a blood test,” Associate Professor Yassi said. “The tests available now are either in research application only, prohibitively expensive and only available in very highly specialised centres, or require invasive procedures such as lumbar punctures.”

A new blood test would be inexpensive, less invasive and readily available to people living in rural or regional areas – the vision of the Yulgilbar, Besen Family and Portland House Foundations.

“We also need appropriate diagnosis as we move towards trying to develop new disease-modifying treatments as well as effective symptomatic treatments,” Associate Professor Watson said.
What makes one person’s immune system more effective at fighting cancer than another’s is a question that may hold the key to creating new or improved immunotherapies for cancer.

Dr Justin Bedo and Dr Holly Barker in the Stafford Fox Rare Cancer Program are investigating ‘super responders’ – cancer patients who defy the odds to thrive when they would otherwise be expected to succumb to the disease.

Tissue from the tumour of a woman with aggressive ovarian cancer, a test case for the research, is yielding valuable clues.

“This patient has a highly active immune system – her tumour is packed with immune cells,” Dr Barker said.

Bioinformatician Dr Bedo has used mathematical modelling to identify antigens – substances that cause an immune response in the body – on the surface of the tumour cells that could be recognised by an immune cell.

“We found she may have developed a T-cell response towards one particular antigen – a finding we are still analysing,” Dr Bedo said.

The results still need validating but their potential is exciting, he said.

Dr Bedo, who said his work was helped by improved sequencing programs, is preparing a list of other antigens which may also be candidates for use in new treatments.

“If we find the right antigen that is specific for a particular tumour, a vaccine could be developed for this patient if she suddenly stopped responding to therapy. This could also help therapy or for other patients who don’t respond to treatments,” Dr Barker said.

“Immunotherapy is a field with huge potential,” she said. “It’s really exciting.”

The work on ‘super responders’ has been supported entirely by donors.

Case study #5
Harnessing the immune system to fight cancer

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“Immunotherapy is a field with huge potential,” she said. “It’s really exciting.”

The work on ‘super responders’ has been supported entirely by donors.
For the one in nine Australians who have asthma, current treatment options centre on airway reliever inhalers and anti-inflammatory steroids with sometimes unpleasant side-effects. Both approaches help relieve the symptoms – chest tightness, shortness of breath and coughing – but do not treat the disease itself.

In a triumph of basic science, Institute researchers have identified an enzyme that is critical to the immune T cells that initiate the lung inflammation that causes asthma. They are now investigating a small molecule inhibitor or drug that inhibits this enzyme.

The research is led by the Institute’s Dr Christine Keenan, Associate Professor Rhys Allan and Professor Stephen Nutt, along with collaborators at the University of Newcastle.

Dr Keenan said the team had been trying to understand the basic mechanisms behind what starts an allergic response when they found that the immune T cells needed the enzyme Ezh2 to function.

“If we remove or inhibit this enzyme with a drug we can actually stop that particular cell type from responding and shut it down very quickly. This ‘switches off’ the allergic reaction that leads to the uncontrolled inflammation,” Dr Keenan said.

While the studies were in the preclinical stage, the potential of the pre-existing inhibitory drug was “super exciting”, she said.

Samples from patients with a variety of allergies would now be tested against the inhibitor.

“The drug, which is very selective for this enzyme, has been tested in clinical trials on a range of cancers and found to be safe – but it’s not very effective in controlling cancer,” Dr Keenan said.

“As the drug is fast acting, it could actually reverse inflammation that had already set in after an immune response.

“I think it could potentially be transformative for people with asthma, particularly for people with severe asthma that doesn’t respond to current therapies,” she said.
A chemical compound developed by Institute researchers that stops cells dying, keeping them healthy and functioning, is attracting keen interest from pharmaceutical companies.

The new ‘cell death blocker’, which has been tested in the laboratory, acts early in the process of programmed cell death, or apoptosis, before irreversible cell damage occurs. Its potential applications include preventing degenerative diseases, stopping damage to brain cells after a stroke or heart muscles after a heart attack, or preserving organs for transplants.

The research was led by Professor David Huang, Professor Guillaume Lessene and Professor Benjamin Kile.

The compound, identified in a high-throughput screen of 240,000 small drug-like molecules, disables the protein BAK, which drives cell death.

“If this compound or others like it are powerful enough, we can think about a number of situations where we lose too many cells in our body and we want to minimise that so that we can preserve the function of the cells and the function of the organs,” Professor Huang said.

The project builds on the Institute’s landmark research on cell death, conducted over more than three decades.

“It was one of the projects we always struggled to find grant funding for. Although we started with commercial seed funding, the rest was largely supported by philanthropy,” Professor Huang said.

Professor Lessene, head of the Institute’s New Medicines and Advanced Technologies theme, said the work paved the way for the development of novel compounds active in human conditions involving the abnormal death of healthy cells.
Professor Kile, now Executive Dean of the Faculty of Health and Medical Sciences at the University of Adelaide, said scientists have been developing agents designed to kill cells, such as tumours, since the 1940s.

“It was one of the projects we always struggled to find grant funding for ... [it] was largely supported by philanthropy.”

“In contrast, maintaining the viability of healthy cells exposed to pathological stresses is a field in its infancy. We hope this is an important step forward,” he said.
Institute researchers have helped solve a decades-long mystery about the genetic causes of a rare form of epilepsy. Despite an international research effort over more than 20 years, the specific change in DNA causing familial adult myoclonic epilepsy (FAME) had remained elusive.

Late last year an international consortium studying FAME, including the Institute’s Dr Mark Bennett, Dr Haloom Rafehi and Professor Melanie Bahlo, announced that they had discovered two new genetic mutations connected to the disease.

The Institute researchers found one mutation in a gene called MARCH6 which causes FAME3, one of the six subclasses of the disease.

Moreover, they traced the origin of this mutation back to a European who lived an estimated 250 generations – or more than 5000 years – ago.

The researchers had developed highly specialised technologies that can detect specific mutations in patient DNA called repeat expansions, the type of mutation that causes FAME. Repeat expansions have previously been associated with other neurological diseases including Huntington’s disease. The first repeat expansion causing FAME was discovered two years ago, however this research only determined the cause of FAME in Japanese patients.

FAME affects people in different ways but patients characteristically experience a jerky tremor in their hands. It typically begins in their 20s or 30s and, in some cases, results in more severe seizures.

“It affects the quality of life, such as not being able to drive,” Dr Bennett said. “Having found the cause is great – it gives the families some understanding and can help if they’re planning a family.

“Now we know what we’re trying to target, it gives us hope that in the long term it will lead to potentially better diagnostic tests and treatments for the families living with FAME3,” he said.

“FAME has been studied for so many years, it’s incredibly exciting to finally have an answer.”

Case study #8
MARCHing towards understanding the genetic causes of epilepsy

“Now that we know what we’re trying to target, it gives us hope.”
Epilepsy is one of the most common neurological conditions, thought to affect about three in every 100 Australians. Yet for many of the patients whose disease has a genetic origin, the exact cause is unknown.

Epilepsy researcher Professor Melanie Bahlo and her team are using an innovative approach to probe tiny, hidden areas of the human genome that might harbour disease-causing mutations.

"With many epilepsy patients we can’t find what’s wrong genetically because they have contributions from many genes,” Professor Bahlo said. “We typically look in genes for the bits that are likely to be broken using very simple approaches but we know genes are very complicated.

“As well as a ‘protein coding’ region, genes also have what are called regulatory elements – regions near genes that affect how a gene functions,” she said.

Professor Bahlo said it had been hypothesised for some time that some of the causes of epilepsy were concealed in these regions but scientists had lacked the methods to identify them.

Dr Liam Fearnley, a postdoctoral researcher in her laboratory, has developed computational algorithms to search for statistical proof that regulatory elements are involved in some forms of epilepsy.

“Liam has done huge amounts of computational work pulling in data to try to pinpoint the portion of the gene, and especially nearby the gene, where some of these regulatory events might be happening,” Professor Bahlo said. “It all hinges on statistical argument.”

Dr Fearnley is collaborating with large research groups including Epi25, an international consortium with a data set of 25,000 epilepsy patients, mining their genetic data to see if he can demonstrate an ‘enrichment’ of mutations in the regions identified.

“With many epilepsy patients we can’t find what’s wrong genetically because they have contributions from many genes.”

“If there is something going on there, we’ll also then hopefully identify some of the causes of these epilepsies in these patients,” Professor Bahlo said.

While this research approach has been used in other diseases, the Bahlo lab is spearheading its applications to epilepsy.
Thank you

The advances in medical science at the Walter and Eliza Hall Institute are made possible thanks to your generosity. We are proud to acknowledge gifts and bequests received in 2019 (of $1000 or more).

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