

SUMMER 2020

HUDSON NEWS



Welcome to *Hudson News* summer 2020.

What a year 2020 has been. I hope you and your loved ones have remained safe and well despite the COVID-19 pandemic, which has been keenly felt in Victoria, especially Melbourne, the home of our Institute.

Many of you, like us, have had to adapt to the challenging and changing circumstances of 2020; working from home, juggling work with remote learning for school-age children, perhaps suffering employment pressures, and coping with isolation from friends and family.

I'm proud to tell you that our research into treatments for COVID-19 has progressed since our last edition. We have several projects underway, including clinical trials based on our discoveries. You can read about these in the update provided on the opposite page.

While we are working hard to progress our work on treatments for acute cases of COVID-19, I am mindful the pandemic has sadly wrought a toll on millions of lives around the globe. Not only in terms of death, but also in lingering symptoms arising from the long-term impact of severe inflammation. This is an issue that will need further clinical research and trials in the coming months and years.

Aside from the threat to our health, the major disruption to our everyday life caused by the pandemic has thrown the careers of many medical researchers into doubt. Women and early-to-mid-career researchers have been disproportionately affected as many juggle caring responsibilities. This is compounded by the uncertain economic climate adversely affecting fundraising and philanthropy.

In our Institute, I have watched my colleagues strive to continue working

while caring for babies and toddlers or homeschooling young children. You can learn more about how we coped with this, and even found some silver linings, in our Q&A with researchers in the following pages.

While COVID-19-related research is of utmost priority for the world, we also need to remember that fundamental research across all disease areas must continue. Cancer patients still need and deserve hope for treatments and cures. In this edition, we have highlighted the work of Dr Jason Cain and his team, who have made fantastic inroads into finding a target for emerging therapies to treat cancers, including small cell lung cancer and childhood tumours.

The support of the community means everything to us, and now more than ever the community has looked to science to combat the threat of the COVID-19 pandemic. We were particularly thrilled to receive letters from the students of Malvern Primary School in Melbourne sending us messages of appreciation and resilience. You can also enjoy some of these in the following pages.

To ensure the work of all our researchers can continue, we would be grateful if you could consider any financial support you might be able to offer. Any donation, large or small, is welcome and could make a huge difference to the lives of many.

It might just be the greatest gift you give this festive season.

We wish you and your loved ones a safe and happy holiday.

Professor Elizabeth Hartland
Director and CEO

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Progressing our COVID-19 research for patients

As the second wave outbreak in Melbourne clearly showed, the new coronavirus is highly infectious and affects the most vulnerable in our society, particularly the elderly and those with pre-existing health conditions. COVID-19 can also leave healthy people with lingering debilitating symptoms. Without safe and successful treatments, the threat of SARS-CoV-2 infection is particularly foreboding, with implications not only for the most vulnerable, but potentially for all our loved ones – young and old.

As scientists around the world race to deliver a COVID-19 vaccine, Hudson Institute researchers are using their world-leading inflammation research expertise to develop treatments to mitigate the deadly inflammation caused by SARS-CoV-2.



Dr Michael Gantier



Associate Professor Rebecca Lim



Professor Paul Hertzog

Clinical trial starts in Europe

The first clinical trial of a potential COVID-19 treatment involving a discovery by Hudson Institute researchers received approval in September.

The end-stage prostate cancer drug Veyonda will be tested as a treatment in COVID-19 patients, following a discovery by Dr Michael Gantier and his team that the drug has potent anti-inflammatory activity.

The trial will involve approximately 40 patients in hospitals in Ukraine and Moldova, two countries experiencing high rates of SARS-CoV-2 infection and hospitalisation.

COVID-19 facts

Australia

- > 27 000 cases (20 000 in Victoria)
- > 880 deaths

Globally

- > 33 million cases
- > 1 000 000 deaths

Placental cells to fight COVID

Associate Professor Rebecca Lim is exploring the use of placental cells (from the amniotic sac), which have potent anti-inflammatory and regenerative effects, to treat COVID-19. A/Prof Lim has been investigating the use of these cells to treat a serious form of lung disease in extremely premature babies, called bronchopulmonary dysplasia, as well as liver disease and stroke.

A/Prof Lim and Professor Euan Wallace (Head, Monash University Department of Obstetrics and Gynaecology; Research Group Head, The Ritchie Centre, Hudson Institute) have begun a clinical trial to investigate whether these cells could also help treat patients with serious respiratory disease due to COVID-19.

The team is working closely with intensivists at Intensive Care Units from Monash Health, Austin Health and Western Health to deliver a Phase 1b/2a clinical trial for COVID-19 positive patients requiring ventilatory support.

Funders Victorian Medical Research Acceleration Fund (amniotic exosome therapeutics to treat BPD in extremely premature babies, and potentially other respiratory conditions including COVID-19).

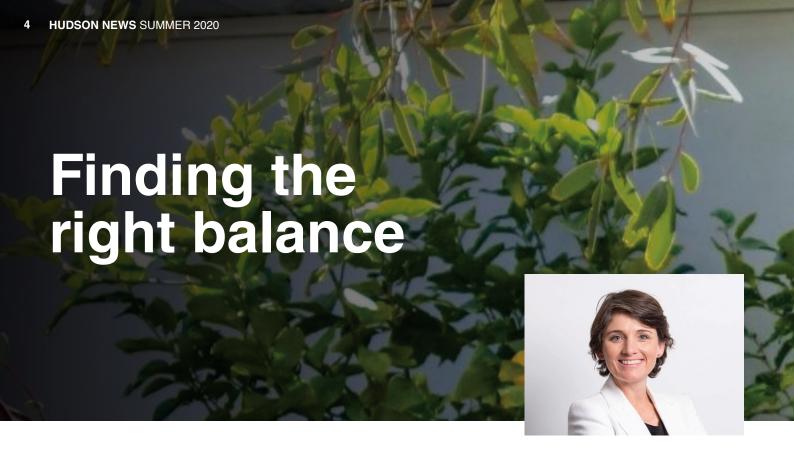
Medical Research Future Fund (stem cell therapies for liver disease).

COVID-19 immune response

Previously, we told you about a research project studying the innate - initial - immune response of COVID-19 patients admitted to Monash Health. We are pleased to report that this is now underway involving our worldleading innate immunity, microbiome and paediatric immunology researchers: Professor Paul Hertzog, Dr Sam Forster, Professor Marcel Nold and Associate Professor Claudia Nold. The study is comparing the status of the immune response and microbiome composition in COVID-19 positive patients of different ages, disease severity and outcomes; e.g. recovery or intensive care with samples processed in our newly upgraded clinical research lab.

Fundamental research like this, with your support, will help us to better understand the virus and how best to optimise our immune response to fight it.

- Collaborators Professor Paul Hertzog, Dr Sam Forster, Professor Marcel Nold, Associate Professor Claudia Nold, Professor Phil Bardin, Professor Jim Buttery and Dr Ben Rogers.
- Funding This project requires funding for analysis using hi-tech equipment and procedures.



The coronavirus pandemic is having far-reaching consequences on employment, the economy, education and mental health. Our scientists are not immune.

Melbourne's first and second wave of infections and subsequent lockdowns affected laboratory work, funding and the ability to juggle childcare and homeschooling with work and career. Many mourned the loss of work and home life balance.

We asked four of our scientists how COVID-19 affected them.



Dr Jaclyn Pearson Research Group Head, Host-Pathogen Interactions

WORK-LIFE As a lab we are operating at about 40 per cent capacity. Personally, I can only manage shorter experiments, which heavily restricts what I can achieve. On the plus side, I get more time to think and write when working from home.

This pandemic has literally stopped many scientists in their research tracks and generated an immense amount of uncertainly about their future. For some though, I can see it has generated a once in a lifetime opportunity to contribute to one of the biggest public health crises the world has ever seen.

HOME-LIFE It has been quite an intensive time for us as a family, as my wife is the Director of Microbiology at Royal Melbourne Hospital – one of the first labs to develop a testing platform for SARS-CoV-2. She was also seconded to the Victorian health department three days a week. As a family we have tried to rally around her in her very long days, after hours work commitments and constant pressure to deal with a very real problem. We are all very proud, but at times we miss her very much.

For balance, we take time at weekends to walk, have nice dinners at home, laugh and spend time with our kids. ABC Kids has been a lifesaver! But also, it's been about letting go of being precious about the house, letting the kids go outside, get messy, play in the sand, do some painting, spray the hose everywhere – that has been the key to us getting through.



Dr Beth Allison

Senior Research Scientist, Perinatal Transition

WORK-LIFE COVID-19 and the related stress has impacted my research. Several times I have been unable to attend experiments, because either myself or the kids were unwell. But my team rallied to make sure this work continued where possible. I have analysed data, which has been awaiting my attention. However, one drawback is the reduced amount of philanthropic funding available for research.

HOME-LIFE There was a COVID-positive case at our daycare centre, which meant we were unable to send my daughter for several weeks. This compounded the stress associated with using these facilities! I have had quite bad anxiety, which I have never experienced before.

Unfortunately, I feel like the work-home life balance is lost. These are now melded together. My husband and I attempt to have protected work time each day, however this is incredibly difficult as we juggle caring for the kids. We work in the evening and on weekends to keep up. Our kids are quite excited when we say we have an important meeting – this generally means ABC Kids time!

A big positive is having the time with the children. I have worked close to full-time for most of their lives, so having this time together is precious.

Associate Professor Michelle Tate

Research Group Head, Viral Immunity and Immunopathology, COVID-19 researcher

WORK-LIFE I have been busier than ever collaborating with commercial partners and performing experiments to facilitate drug development. The battle to find new treatments for COVID-19 infections is a global effort. It's exciting to contribute by leading preclinical studies and collaborating with commercial partners.

The impact a pandemic can have, not just on public health, is now much clearer. The threat of a bird flu pandemic, which carries a potential 50 per cent mortality rate, will now hopefully be taken more seriously. COVID-19 and influenza viruses similarly induce hyperinflammatory responses leading to tissue damage and severe disease. There is now a greater need to identify new drugs that limit inflammation and treat severe respiratory virus infections. COVID-19 has cemented the importance of my research and provided a greater sense of ambition.

HOME-LIFE I have had to juggle increased work hours and pressures with family life. I regularly sneak off to work on weekends while my son has his nap. I am lucky to have an extremely supportive partner who has increased caring responsibilities, especially with the loss of childcare access during Stage 4 restrictions.

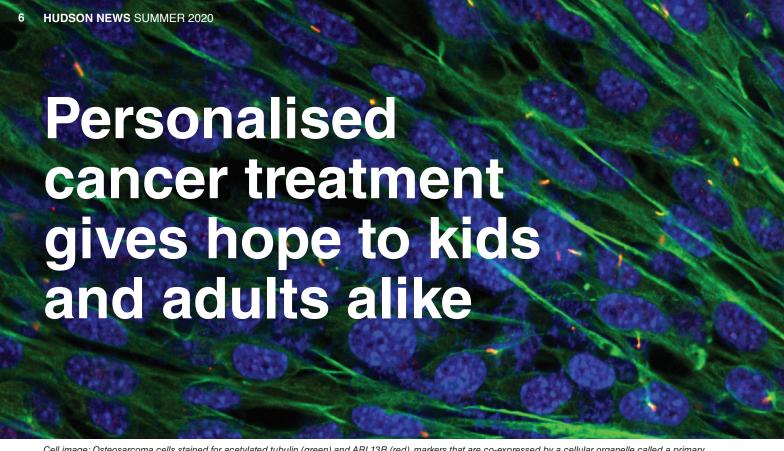
Dr Michael Gantier

Research Group Head, Nucleic Acids and Innate Immunity Research group Working on treatment for COVID-19, repurposing existing cancer drug

WORK-LIFE The next round of grant applications is critical for my lab. Our funding ends in December. The pandemic has changed the grant evaluation process, meaning funding outcomes will be even more uncertain. On the other hand, the situation has created novel grant and commercial opportunities, which may help my team stay afloat. Any further funding for my laboratory at this very stressful time could be the difference between our vital COVID-19 research continuing or ceasing.

This is the first time in ages that science is at the top of news bulletins, every day. The only way out of this pandemic is biomedical research.

HOME-LIFE Working at home with my three-and-a-half-year-old son and seven-year-old daughter has been challenging. Homeschooling my daughter has taken its toll on my productivity writing grants and publications, as my partner is also working full-time from home. We make it work, but I am not sure there is any balance! I gave in on two things this year – a trampoline and a puppy!



Cell image: Osteosarcoma cells stained for acetylated tubulin (green) and ARL13B (red), markers that are co-expressed by a cellular organelle called a primary cilia. The primary cilia are required for the Hedgehog signalling pathway.

This year, about 1000 children and adolescents in Australia will have been diagnosed with cancer and 5600 will have continued their treatment. Any cancer diagnosis, for yourself or a loved one, is heart-wrenching. For children, who have a lot of life to live, it seems profoundly unfair.

But, what if we could literally stop cancer in its tracks? This is the ultimate goal of researchers at the Institute who study biological pathways associated with cancer.

Dr Jason Cain's laboratory investigates lung cancer and paediatric cancers including brain tumours, to develop new treatments with fewer side effects. The team is specifically interested in studying the most insidious cancer types with low survival rates.

World-first discovery

Dr Cain's laboratory's latest world-first discovery – in developmental and small cell lung cancer (SCLC) models – has implications for childhood cancer, with further research findings slated for publication. Thanks to your generous support funding this research, the team recently discovered two potential genetic markers that could be used to provide more personalised cancer treatments.

"This discovery could help us learn which patients, and which tumours, are likely to respond to an emerging cancer therapy," said Dr Cain, Head of the Developmental and Cancer Biology Research group.

The team discovered that changes in two genes, TP53 and RB1 (which act as tumour suppressors), played a role in activating a developmental pathway called Hedgehog signalling, which is associated with a wide range of cancers.

These two genes could act as genetic biomarkers in tumours that are likely to respond to new cancer treatment drugs, known as Hedgehog inhibitor therapies. Many of these drugs are in clinical trials, with a small number approved to treat specific cancer types.

Next steps

The next step is to conduct a retrospective study, analysing cancer tissue samples for the biomarkers, in patients who have received Hedgehog inhibitor therapy.

"We could then correlate the biomarkers with how the patient responded to therapy. That would provide some strong evidence as to whether to proceed to a prospective clinical trial, which would actively recruit patients with changes in TP53 and RB1 genes, to receive Hedgehog inhibitor therapy," Dr Cain said.

Continued on page 8



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Kids thank their scientist superheroes

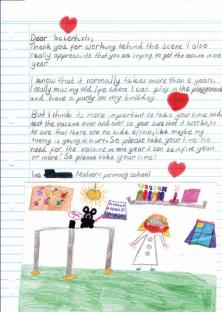
As 2020 comes to a close, we reflect on the acts of kindness and gratitude that have shone through what sometimes felt like an endless stream of bad news. That's why we wanted to share with you a heartwarming project. Children from Malvern Primary School in Melbourne created 650 thoughtful letters, which were delivered to scientists at Hudson Institute and researchers around Australia, in a much-appreciated morale boost.

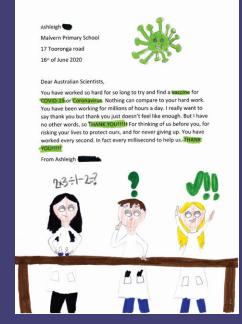
The Gratitude Project, the brainchild of Hudson Institute researcher Dr Sarah Meachem, invited children during the first remote learning period to write letters thanking scientists for their work improving people's lives, including on the coronavirus. The story featured in the Herald Sun newspaper.

We hope you enjoy the selection of children's letters as much as we have.



Dr Sarah Meachem





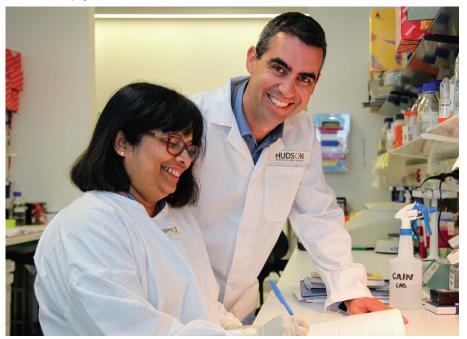
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L-R: Dr Samantha Jayasekara and Dr Jason Cain

Quick facts

- Each year, >2 million people worldwide are diagnosed with lung cancer. About 15 per cent of these are small cell lung cancer and 85 per cent are non-small lung.
- In Australia, it is estimated that 13 258 Australians will be diagnosed with lung cancer and 8641 will die from their disease.
- Brain tumours are the most common solid tumours in children and the leading cause of cancerrelated death.
- In Australia, ~100 children are diagnosed with brain or spinal cord tumours every year.

What is Hedgehog signalling?

The Hedgehog signalling pathway is a developmental pathway activated in embryonic stem cells, playing a crucial role in babies' growth in the womb.

After its development role, the pathway is essentially turned off and lies dormant, unless there is a tissue injury in the body, which can switch the pathway back on as part of the healing process. Problems occur when the pathway is activated in healthy tissue, which is associated with the development and progression of

Your support will help

us save lives and

protect everyone from

the lasting effects of

COVID-19.

"Any further funding at this

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Dr Michael Gantier

Dr Vijesh Vaghjiani, a co-first author on the study published in The Journal of Clinical Investigation, said it may be possible to selectively screen for these gene mutations in cancer patients' tumour tissue (such as those with SCLC) to determine whether personalised treatment with Hedgehog inhibitor therapy would work.

"Taking this discovery from the laboratory to hospitals could be absolutely life-changing for cancer patients," Dr Vaghjiani said. "It's why we do what we do.'

Silver linings in the COVID-19 cloud

Dr Cain says: COVID-19 has definitely restricted our research activities. During the first lockdown, almost everything stopped. Our return to work since then has been in a limited capacity, for wet lab work only, and this largely continued through the second lockdown. We're still very productive thanks to the efforts of my brilliant staff and students.

Since I don't spend as much time at the lab bench as I used to, I am exclusively working from home while my staff and students progress essential experiments. All my meetings are conducted virtually on Zoom. Despite this, I am busy writing grants,

papers, analysing data and planning experiments with my lab members.

My wife is a midwife at Monash Health, so her work continued while I stayed at home with the kids (Grade 6 and Grade 4), supporting their schooling and cooking meals.

There are many silver linings to this unusual year. This period has enabled me to really think about our research, come up with important ideas, plan exciting experiments and write papers. But equally importantly, it allowed me to spend more time with my family eat lunch with them, go on walks and bike rides, help with schoolwork - all of which I don't normally get to do.



Funders Victorian Cancer Agency, Cancer Council of New South Wales, Children's Cancer Foundation, Bailey's Day, Australian Government Research Training Program, Monash University Postgraduate Publication Award, Science and Industry Endowment Fund STEM+ Business Fellowship in partnership with Mayne Pharma, Petre Foundation, National Health and Medical Research Council of Australia and Victorian Government's Operational Infrastructure Support





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Professor Elizabeth Hartland Director and CEO, Hudson Institute



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