Auckland District Health Board

Research

Annual Report 2020

Haere Mai Welcome | Manaaki Respect | Tūhono Together | Angamua Aim High

TE TOKA TUMAI
Auckland DHB

He kano mātauranga whakatō, he hua mātauranga puta mai.

If the seed of knowledge is planted, the fruits of knowledge will emerge.

FOREWORD FROM THE CHIEF MEDICAL OFFICER

Tēnā koutou katoa

I am delighted to introduce this year's Annual Research Report.

This report higlights internationally recognized research activities that take place at Auckland DHB. Research is not just the process of testing a hypothesis but considering an important clinical problem, testing for the best solutions, and then offering a path to the translation of the research findings. Ultimately patients and communities benefit. Nowhere is that more evident than in the REMAP-CAP trial in which new evidence pertaining to COVID-19 therapies was rapidly published and translated into clinical practice in hospitals worldwide including Auckland City Hospital. Auckland DHB researchers are making a difference on the global stage with their research published in the highest order journals and leading to widespread change in clinical practice. That research spans the laboratory bench to the bedside and out into the community.

Successful research does not take place without funding, and we thank those funding entities, the big such as the Health Research Council, and small such as bequests and trusts. We also thank those who collaborate with colleagues half a world away. Our researchers have shown the value of international clinical trials collaboration with patients rapidly recruited into COVID-19 clinical trials thus generating research findings that can be applied in this outbreak. We also acknowledge our local collaborations through our partner universities. We say goodbye to the Medtech Centre of Research Excellence (CoRE) as its five-year grant comes to an end and welcome the Cardiovascular CoRE, profiling Professor Julian Paton in this report.

I would like to thank those who make research at Auckland DHB possible – the Research Office staff including those working in Starship, members of the both the Research Review Committee and Research Governance Committee who provide evaluation and oversight of our research activities, our research accountants and the A+ Trust for administering the research funds.

Aku mihi nui ki a koe

Dr Margaret Wilsher

Chief Medical Officer
and Head of Research, Auckland DHB

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Auckland DHB

Tēnā koutou katoa,

2020 was a year like no other but even when normal life as we knew it was at a standstill, research did not take a break. Remarkably, Auckland DHB researchers produced 854 original research articles in 2020, many in leading journals such as The Lancet, JAMA and New England Journal of Medicine. That's the greatest yearly output this organisation has ever produced, an increase of 180% from when I first prepared this report in 2011, and 200 more than 2019 which held the previous high score. Publication in peer-reviewed journals is an index of our researchers' skill in the elaboration of ideas, methods, and conclusions. This research output will obtain recognition for our people and build their reputations as experts in their fields both nationally and internationally and even more importantly, advance knowledge about healthcare and its application.

A sentinel example of new published knowledge making a difference can be seen with the publication in the New England Journal of the REMAP-CAP trial of tocilizumab and sarilumab for treatment of COVID-19 in intensive care. Auckland DHB intensivist Dr Colin McArthur and his international team of collaborators have proven the efficacy of this combination in reducing time needed on an ICU ventilator, an intervention that was life saving for 1 in 12 patients. To take on board the impact of this discovery, consider that there have been tens of thousands of COVID patients in high dependency units or ICUs around the world every day for the last 12 months. The vision, leadership and capability of the international team has enabled a second effective treatment for COVID to be found within 12 months of the declaration of the pandemic and rapid publication in the top journal in medicine, with all the worldwide attention that implies. Literally, thousands of lives will be saved because of this research.

Funding enables our scientists to be more productive. Dr McArthur's REMAP-CAP trial is supported by the Health Research Council (HRC), the elite funder of the best research proposals and the most promising individuals in the New Zealand health sector. HRC's prestigious Clinical Practitioner Fellowship programme is offered to just a few exceptional clinicians each year and enables them to operate as researchers within their clinical practice. In 2020 Dr Alison Leversha, Starship's Community Paediatrician, became our latest fellow. As a champion for the Collaboration for Child Wellbeing, Dr Leversha will spend her five-year fellowship working with the low decile school communities in the Tamaki Manaiakalani Kahui Ako. Her research will take a close look at school readiness screening and how the programme can be optimised to help ensure all children in the Tamaki area are healthy, socially, emotionally, and developmentally when starting school. Through collective impact, this collaboration will have implications for national roll-out of educational and health interventions targeting vulnerable children and families.

This report features the findings of two international clinical trials that were conceived and instigated by our people. The much-anticipated results of anaesthetist Dr Tim Short's Balanced study have been published in the Lancet. Dr Cynthia Sharpe's NEOLEV II appeared in Pediatrics, the highest ranked journal in the field. Both studies have yielded the answers to highly contested questions in medicine that will inform clinical practice for many years to come. This pair deserve special credit for managing the highly technical challenges of their research designs. Balanced required study anaesthetists to target different levels of sedation during surgery using EEG monitoring. NEOLEV II used state of the art continuous video EEG monitoring to detect and track baby's seizure activity. This meant considerable preliminary work for both researchers just to prove the many doctors and support staff needed to carry out their studies could acquire the skills to do so. And if ensuring the science was right wasn't enough, conducting trials at this level required a suite of more general abilities to cope with the enormous operational demands of engaging community, pleasing funders, overcoming critics, and satisfying regulators. These works represent more than a decade of enterprise by these researchers and their colleagues and have helped to define Auckland DHB as a world class research organisation.

I welcome you to find out more about our wonderful researchers and some of their achievements in 2020.

Dr Mary-Anne Woodnorth

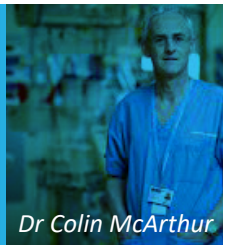
Auckland DHB Research Office

Auckland DHB Researcher Involved in Ground-breaking COVID-19 Discovery

A landmark worldwide COVID-19 trial involving New Zealand research leadership has discovered a treatment which significantly reduces the risk of critically ill patients dying from the virus, effectively saving the lives of one in every 12 patients treated.

As worldwide deaths from COVID-19 spiral alarmingly, the trial has confirmed that two anti-inflammatory drugs sometimes used to treat rheumatoid arthritis reduce the risk of intensive care unit (ICU) patients dying from the effects of the virus by a remarkable 24%. The findings mean doctors now have a second proven treatment for critically ill COVID-19 patients, following results last year, including from this trial, showing steroid treatment is also highly effective.

"In fighting the virus, the immune system can also cause damage to organs such as the lungs. These drugs work by stopping one of the protein signals that activate cells involved in the immune response".



Dr Colin McArthur

The trial results, now peer-reviewed and published in the prestigious New England Journal of Medicine (NEJM), show that critically ill COVID-19 patients treated with the immune-modulating arthritis drugs tocilizumab and sarilumab markedly reduced the time needed on a ventilator for organ support compared to patients who received neither drug, and that additionally, both treatments reduced mortality. The medications work by reducing the body's natural inflammatory response to the virus by modifying the immune system, speeding up recovery and reducing the time needed in intensive care.

One of the trial's senior researchers, Auckland City Hospital Intensive Care Specialist Dr Colin McArthur leads the New Zealand arm of the internationally acclaimed REMAP-CAP trial, being coordinated in this country by the Medical Research Institute of New Zealand (MRINZ).

"This is a truly significant finding" says Dr McArthur. "To find a second effective treatment for critically ill COVID-19 patients within a year of a global pandemic is remarkable. We always suspected that specifically targeting the body's immune response in the sickest patients was theoretically possible as a means of treatment, but we have now shown that it actually works. These findings will help critical care teams around the world improve outcomes for the most severely ill COVID-19 patients".

Trial patients were randomly assigned to receive either tocilizumab (353 patients), sarilumab (48 patients) or standard treatments alone (402) within 24 hours of being admitted to the ICU. The drugs yielded a 99.9% statistical certainty of superiority compared with the standard treatment group. Hospital mortality was 35.8% for the standard treatment patients but fell to 27.3% for those treated with tocilizumab or sarilumab – a 24% reduction in risk of death.

Dr McArthur says both drugs work by dampening down the body's natural immune response to COVID-19.

Dr McArthur says New Zealand's success in eliminating the community spread of COVID-19 means that so far, few New Zealand patients with COVID-19 have been admitted to our ICUs nationwide taking part in the REMAP-CAP trial. Nonetheless, he says our significant role in the running of the international trial means that local treatment guidelines can be kept right up to date with the latest evidence.

REMAP-CAP (Randomised Embedded Multifactorial Adaptive Platform for Community Acquired Pneumonia) is an ongoing, adaptive clinical trial, randomises patients to receive multiple combinations of treatments. It started in New Zealand in 2017, as a means of studying severe pneumonia. Designed to adapt in the event of a pandemic, the emergence of COVID-19 in early 2020 saw researchers promptly add in capability for the trial to evaluate different treatments for the virus. Those treatments included antivirals, drugs which modulate the immune response, and therapies that modulate or support other vital aspects of the body's response to the virus. The trial design means treatments can quickly be dropped if they are less effective than others or worse than standard care and others can be added to the study over time if need be.

"As a global collaboration, many patients and families have participated, enabling REMAP-CAP to provide evidence on a wide range of treatments for COVID-19" says Dr McArthur.

REMAP-CAP involves more than 5000 COVID-19 patients at more than 290 clinical sites around the world, including 11 ICUs within New Zealand. It is led by researchers in the UK, USA, Canada, Australia, the Netherlands and New Zealand.

[Original article courtesy of the Medical Research Institute of New Zealand]

Nurse-led Whare Hauora initiative for primary school health services

Sarah William's research follows on from her role running the Auckland DHB's nurse-led Mana Clinic at Wellesley Primary School. Studying for her Doctorate in Health Sciences at AUT and working as a nurse educator for Starship's Community Child Health service, her research project has examined the relationship between health services and education in primary schools from an education perspective.

Health and education are inextricably linked. To learn, a child or young person must be able to partake fully in the education opportunities that lie before them. Health issues play a major role in limiting or preventing learning opportunities for children and are a significant contributor to poor educational outcomes.

Whilst the interdependence between education and health is well described, less evident is what successful interagency collaboration looks like.

Preliminary findings have revealed a unique key stakeholder perspective of the relationship between education staff and health services including the barriers and facilitators to successful and sustainable interagency collaboration.

Sarah's experience carrying out her research cemented her conviction of the importance of having physical spaces for nurses in high need primary schools to provide health services.

Working in collaboration with Barfoot and Thompson, she initiated a project three years ago that led to the opening of Starship's first 'Whare Hauora', a partnership between health and education made possible through the support of the Starship Foundation. The Whare Hauora is an in-school, semi-permanent health clinic that provides a fit-for-purpose space for nurses to deliver health care to children at Panmure Bridge School.

"Experience had shown us that having a nurse available in the primary school space greatly supports children who have health issues that are preventing them attending school or engaging in learning activities," said Williams. ***"This approach works even better if there is an appropriate facility for our nurses and others to use."***

Williams said the Starship Community Nurses are working from the school three or four times a week and previously had to work from whatever space was available, which might not have been child or nurse friendly.

"In schools where you have a lot of referrals you need an appropriate space – if you are asking a nurse to work there for a full day, it needs to be a pleasant place to work in and an inviting place for children to come to as well."

Starship and its partners hoped to roll out two more Whare Hauora next year, working in collaboration with other high-needs primary schools.

The Whare Hauora contains a small waiting area, a private treatment space where patients are seen and office space at the rear for administration. It measures around 7.2 metres long and 3 metres wide and is like a shipping container, making it easily relocatable.

"Since the first facility was established at Panmure Bridge School, we have seen a noticeable decrease in health-related absenteeism suggesting a correlation between increased accessibility to healthcare and school attendance."

Sarah Williams

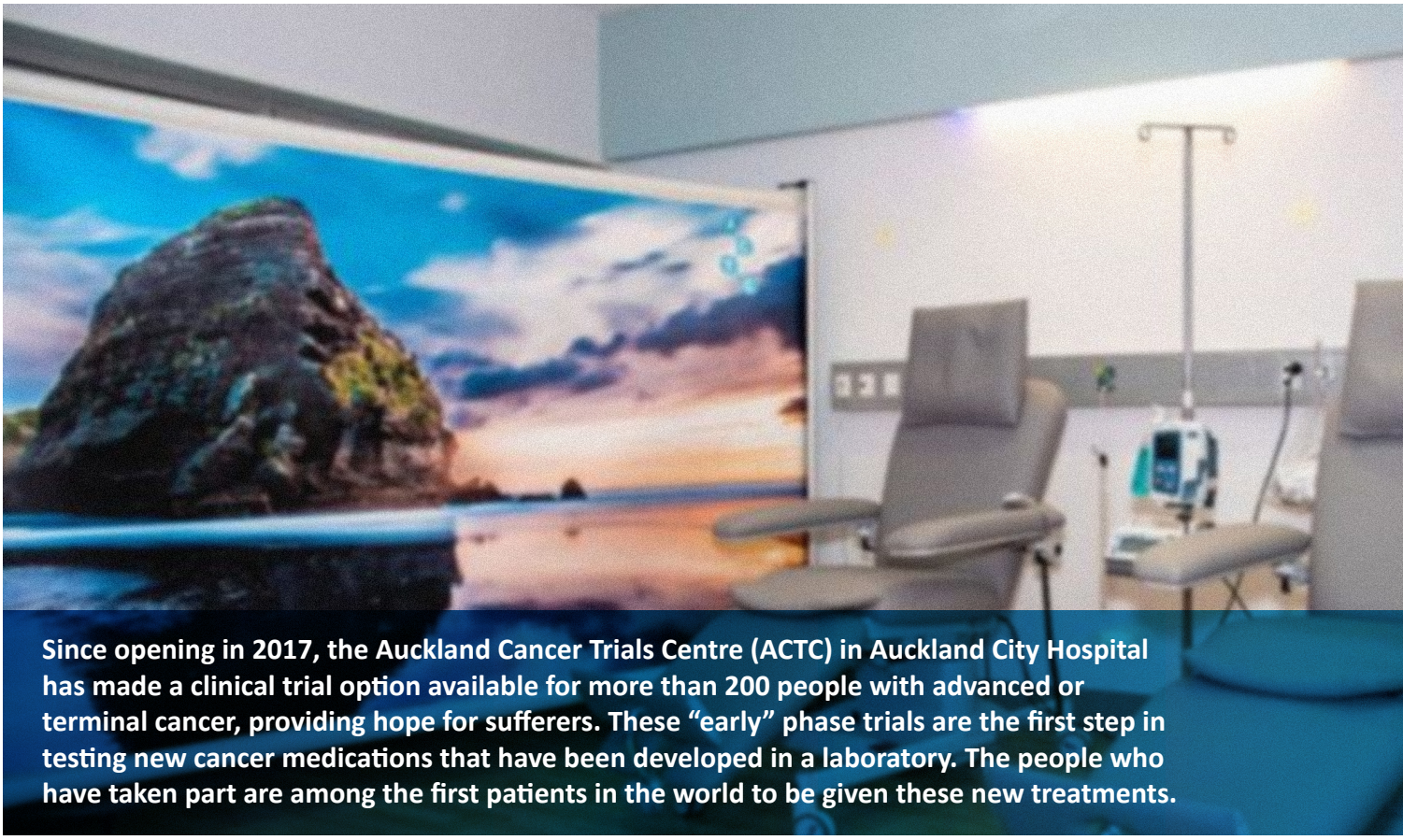
Paediatric Society of New Zealand Conference

Sarah Williams: People's prize for the best poster and awarded the Department of Paediatrics and Child Health Wilson Sweet Fellowship to complete her doctorate on the relationship between health and education in primary schools. The awards recognise Sarah's significant contribution to her field.

"We are very grateful for the support of the Starship Foundation, Barfoot & Thompson and to Point England School for sharing our vision and joining us in this wonderful collaboration".

Auckland Cancer Trials Centre celebrates fourth birthday

In an ideal world, every cancer patient would get a standard treatment option and a clinical trial option. Clinical trials give patients the ability to test a drug or a treatment combination which may not be approved or funded yet. For some, this could be their last option.



Since opening in 2017, the Auckland Cancer Trials Centre (ACTC) in Auckland City Hospital has made a clinical trial option available for more than 200 people with advanced or terminal cancer, providing hope for sufferers. These "early" phase trials are the first step in testing new cancer medications that have been developed in a laboratory. The people who have taken part are among the first patients in the world to be given these new treatments.

Prior to 2017, the focus of Te Pūriri o te Ora (Cancer and Blood) was on the conduct of larger phase 2 and 3 clinical trials. Establishment of the ACTC, a dedicated research facility, lifted the team's capability to run early phase studies as well. As New Zealanders have less access to publicly funded therapeutics than similar OECD countries research is one of the few ways patients can get to try cutting edge new medicines. ACTC can accept referrals from outside the Auckland region, which means improved equity with access to trials for patients across the motu.

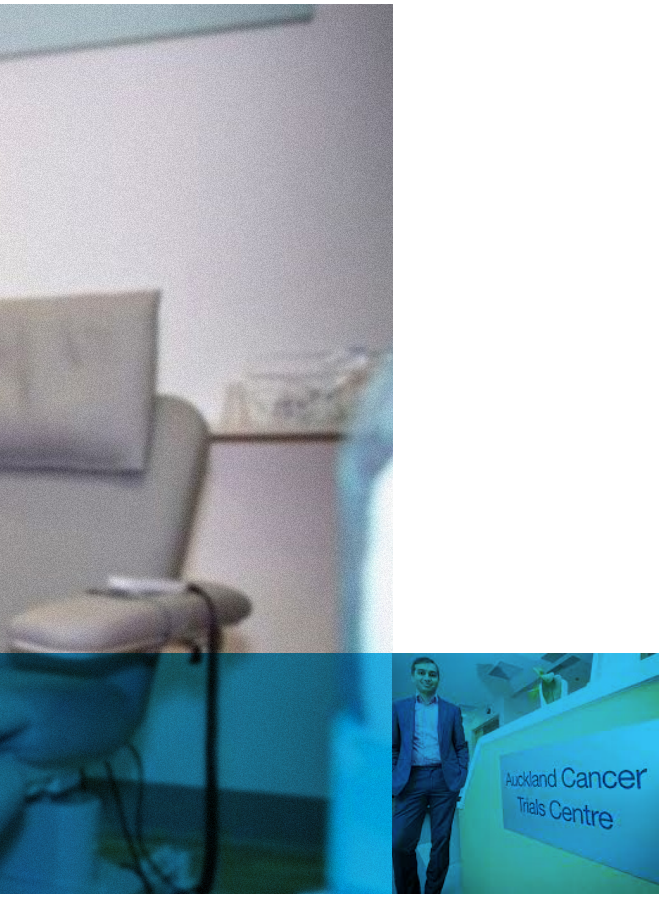
ACTC came into being as an initiative of the Auckland Academic Health Alliance, with the University of Auckland and Auckland City Hospital providing start up investment in the form of seed funding and infrastructure support. With the continued support of both organisations the next stage of planning is for growth, including more specialized staff, more dedicated researcher time, and a core fellowship programme.

The ability to take research from the laboratory bench to the clinic is a key priority for the ACTC. Performance so far has given proof to the capability of Te Pūriri o te Ora and the University of Auckland to operate a successful integrated academic cancer unit without layout on bricks and mortar. While the majority of ACTC's trials so far

have come from the pharmaceutical industry, collaboration with the University's "heavy hitter" cancer biologists means the Centre can play an integral part to discover, trial and bring new anti-cancer drugs and screening tools into clinical use.

According to ACTC's Medical Director, oncologist Dr Sanjeev Deva, "As an early phase cancer trials unit, ACTC has been precocious since its inception, with recognition from all the key stakeholders that we have created a world class facility in a relatively short space of time."

"The value of ACTC is many fold. Firstly, patients now have access to an additional line of therapy. This treatment can be (and has been) transformative for a patient's health outcomes. We are strategic in terms of trial selection, not only picking those of academic interest, but trying to select studies that would be of value to our patient population."



Dr Sanjeev Deva

"ACTC has been an avenue that has strengthened the connection with the University of Auckland. We have a number of translational projects with local scientists and many more in the pipeline. The archetypal ACTC physician is a true Clinician Scientist, one who is able to span both sides of Park Road."

"Cancer remains a devastating illness and we can only make collective gains from learning from our patients. We can only achieve this through clinical research and trials. I admire the courage of those patients who have taken part in the trials in ACTC. It is these people who will make tomorrow a better place ."

MoST-NZ brings biomarker-guided treatment platform to ACTC

Biomarker directed therapy has huge potential benefit for many patients and has helped patients live longer and better.

Genome sequencing, the process of determining the entirety of a person's DNA, is now being used to profile a patient's tumour on a molecular basis with the primary goal of identifying mutations of clinical relevance to guide ongoing treatment decisions and match to novel targeted therapies. The increasing identification of specific DNA mutations that drive cancers leaves us on the threshold of a new era of "personalised cancer medicine" in which biomarkers will be used to direct targeted agents to only those patients most likely to respond. The potential medical, scientific, and long-term economic benefits of such a personalised approach to cancer therapy are immense. The MoST-NZ study investigates how genomic testing can be delivered in the NZ context in a patient-centred and culturally acceptable way to improve the burden faced by Māori patients and their whanau.

Matched therapy has led to consistently superior response rates in Phase I clinical trials, ranging from 22% to 27%. This contrasts with the classically reported response rates of 5%. This approach carries an expectation of a much more dramatic effect and benefit, provided the selection and matching strategy is accurate.

MoST-NZ will modify and adapt a novel framework, that has been proven successful internationally, to suit our New Zealand population. This will facilitate molecular screening of 500 patients with an enriched Māori population. Patients will have the opportunity to be linked efficiently to a suite of early phase clinical trials for biomarker-driven treatments. This design will facilitate the testing of potentially ground-breaking therapeutic concepts, while rigorously evaluating safety and response. New Zealand-specific questionnaires will enable assessment of patients' expectations and understanding of genomic testing to impact clinical care delivery in the future and identify barriers hindering advancement of patient care. With a dedicated Māori cohort, this model can tackle some of the facets that contribute to the inequity in patient outcomes.

With genomics so central to precision oncology, MoST-NZ has the potential to offer novel therapies in a timely more cost-effective model. It also will explore models to reduce geographical inequity by offering the genomic testing component at three DHBs. This has national ramifications.

According to the study lead investigator, medical oncologist Dr Michelle Wilson, one of the strengths of MoST-NZ is our Māori patient population. The team, which includes Māori cancer biologist Dr Kimiora Henare (Te Aupōuri, Te Rarawa) are planning to concentrate on Māori and will work with an advisory group to look at ways to increase Māori recruitment and develop education resources that are relevant.

"In Aotearoa the burden of cancer is not shared equally. Māori are 20 per cent more likely than the rest of the population to develop cancer and nearly twice as likely to die from it. Genomic testing is integral to identifying those patients who will benefit the most. We have recently shown that Māori are underrepresented in clinical research. MoST-NZ has the ability to advance Māori health by challenging this paradigm."

Dr Michelle Wilson

Auckland City Hospital leads ground-breaking anaesthesia trial that will inform practice worldwide

The current practice of general anaesthesia emphasises giving adequate doses of anaesthetic drugs to ensure that all patients are unconscious. This approach is effective and safe for most of our patients. However, the dose of anaesthetic that ensures unconsciousness for all patients means those who are sensitive to anaesthetics receive significantly more drug than necessary.

Reducing the dose towards the threshold for consciousness becomes a matter of judgement, unless monitors that process the frontal lobe electroencephalograph (EEG) to track anaesthetic depth are used. These monitors make it possible to titrate anaesthetic dose more precisely according to individual patient requirements. Marketing of these monitors has emphasised their use to ensure sufficient anaesthetic administration to prevent awareness. Their use to reduce unnecessarily deep anaesthesia is more controversial. Deep general anaesthesia has been associated with worse outcomes, including death, than light general anaesthesia in observational studies, but until now no high-quality large randomised controlled trials had been undertaken.

The much-anticipated results of the landmark Balanced Anaesthesia Study have now been published in the prestigious medical journal The Lancet. The study was run by the Australian and New Zealand College of Anaesthetists Clinical Trials Network, with Auckland City Hospital's own Dr Tim Short as the lead investigator. Balanced is an international randomized controlled trial of deep and light volatile-based general anaesthesia undertaken in 78 centres in eight countries. The study included 6,640 patients who were aged 60 years and over, with significant co-morbidity, randomised them to deep or light general anaesthesia and followed them for one year. Mortality was similar in the two groups (7.2% in the deep group versus 6.5% in the light group). There were no differences in any of the secondary outcomes, and there was only one case of awareness during anaesthesia.

Balanced has been described as by far the largest and most robust trial of anaesthetic depth on intermediate-term postoperative mortality ever conducted. The Lancet publication brings to fruition 10 years of intense effort by the study team at Auckland City Hospital and the ANZCA Clinical Trials Network. Congratulations to the whole team for the colossal effort involved in undertaking a trial of this magnitude and rigour.

Among older patients at increased risk of complications after major surgery, light general anaesthesia was not associated with lower one-year mortality than deep general anaesthesia. This was greatly reassuring to anaesthetists worldwide who had been concerned about the safety of their practice. The trial defines a broad range of anaesthetic depth over which anaesthesia may be safely delivered when titrating volatile anaesthetic concentrations using a processed EEG monitor.

These results are great news, because they show that deep anaesthesia is safe and can be used if indicated for individual patients. Anaesthetists worldwide now have definitive evidence to guide their practice. They are also another example of the power of collaboration in delivering evidence that guides care and helps in improves patients' lives.

Impact tracker Altmetric has tracked 17,776,174 research outputs across all sources so far. Compared to these Balanced has done particularly well and is in the 99th percentile: it's in the top 5% of all research outputs ever tracked by Altmetric. Attention score 151.

Phenobarbital and phenytoin are often used for neonatal seizures.

There is no FDA approved drug. Levetiracetam may be safer, but does it work? Trial led by Starship Child Health answers this question.

Seizure activity in an infant must be diagnosed and treated immediately because seizures are dangerous and can cause nerve cell injury and kill brain cells. Seizures may also adversely alter brain function in other ways like rewiring brain circuitry. Babies' brains are hyper-excitable, and it is no surprise that seizures are more common in neonates than in other age groups. The risk for neonatal seizures is highest in the first week of life and especially in the first 48 hours of life. But unlike older children and adults, there has been limited choice to treat seizures in this age group, as newer antiepileptic drugs have not been adequately tested on this vulnerable population.

Seizures in neonates are often subtle and difficult to recognize from clinical observations at the bedside. Continuous electroencephalographic (cEEG) monitoring is the gold standard for detecting seizures and a critical tool to avoid both under- and over-diagnosis. While managing neonatal seizure, not only short-term seizure control is desirable, but also protection of long-term cognitive outcomes. Several of the anti-epileptic drugs used to treat newborns are known to cause brain cell death and brain atrophy.

Although phenobarbital is used as first line agent in neonatal seizures there are concerns of its short- and long-term toxicity, particularly on developing brains. In recent years, levetiracetam has emerged as an alternative to phenobarbital due to its favourable safety profile and effectiveness against paediatric status epilepticus. However, there has been no consistent data to support its use in neonates. Well-designed high-quality evidence from clinical trials was crucial to establish the most effective and safest treatments to protect these babies' brains.

The NEOLEV II study (efficacy and safety of levetiracetam in comparison to phenobarbitone for management of neonatal seizures) is the brainchild of Starship Child Health's Dr Cynthia Sharpe and her Californian colleagues.

The study recruited and performed continuous video EEG monitoring on 270 high risk newborns from Starship and paediatric centres around California. 106 of these babies were treated for seizures. In the final intention to treat analysis 28% of the 53 babies in the levetiracetam group and 80% of the 30 babies in the phenobarbitone group remained seizure-free for 24 hours. Response to levetiracetam was not sustained with only 17% seizure-free for 48 hours, while 64% of babies remained seizure-free for 48 hours in the phenobarbitone group. These results showing greater efficacy of phenobarbital were highly statistically significant

The study has been described as a landmark study in that it is the first randomized controlled trial of treatments for neonatal seizures since 1999 and the first ever to use real time state of the art continuous video EEG monitoring. Previous studies which have used continuous video EEG monitoring have reviewed the monitoring and implemented treatment of seizures with up to a 24-hour delay. The rapidity of detection and treatment of seizures in NEOLEV2 may explain the much higher than previously observed efficacy of phenobarbital.

NEOLEV II has given class 1 evidence for first-line anti-epileptic drug treatment of neonatal seizures. Phenobarbitone has superior efficacy for seizure control in comparison to levetiracetam. But the story of levetiracetam is not over. Dr Sharpe and team found that phenobarbital was more effective but also more toxic than levetiracetam. Further studies with a higher dosage of levetiracetam will be the next major target of research in this field. Until then, this much anticipated study has justified why phenobarbitone should remain the gold standard for neonatal seizure.

The Altmetric attention score 84 puts NEOLEV II in the top 5% of all research outputs scored by Altmetric

Read the original paper: Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial. Pediatrics. 2020 Jun;145(6):e20193182.

And additional publications describing how a real time response to seizures was achieved within the study:

Sharpe C, Davis S, Haas R, Reiner G, Lee L, Gold J, Nespeca M, Wang S, Joe P, Kuperman R, Gardner M, Honold J, Lane B, Knodel E, Boutin M, Battin M, Rowe D, Bridge R, Rasmussen M, Arnell K, Harbert M. Assessing the feasibility of providing a real time response to seizures detected with continuous long term neonatal EEG monitoring. J Clin Neurophysiol 2018;00: 1–5.

And an additional important publication which identifies the first hour of cEEG monitoring as something which can identify babies who need closest monitoring with high sensitivity and specificity

Macdonald-Laurs E, Sharpe C, Nespeca M, Rismanchi N, Gold J, Kuperman R, Wang S, Le M, Michelson D, Haas R, Reed P and Davis S.L. Does the first hour of continuous electroencephalography (cEEG) predict neonatal seizures? Arch Dis Child Fetal Neonatal Ed 2021;106:F162–F167.

Whānau room rejuvenation – success by co-design

At the construction of the "new" building in the early 2000s, Auckland City Hospital became one of the first hospitals in the world to have whānau rooms integrated into each adult inpatient ward. These spaces were designed to manaaki whānau and meet the needs of Tikanga Māori, especially around death and dying. They provided a culturally safe space for whānau to gather and grieve all together with their Tūpāpaku, with privacy from a 4-bedded ward room.

Over time these spaces became run down and a project was initiated to rejuvenate them, sponsored by the Chief Nursing Officer, and fundraised for by the Auckland Health Foundation. We at Ara Manawa, a multidisciplinary design and innovation team within Auckland DHB, were asked to explore solutions to breathe new life into these cherished spaces.

ARA MANAWA

Ara Manawa is a team in the Auckland DHB championing the needs of users in the design of new spaces, services, experiences, and products via the application of human centred research methodology.

"Ara Manawa has two components; 'Ara' to create, find, or forge a path. Think of a whale finding its way through the ocean or a bird navigating to a destination. 'Manawa' means heartbeat, capturing intelligence, or a psychic knowing. Thereby reflecting the creativity of the team."

Dame Rangimarie Naida Glavish

We knew that, traditionally, groups of managers, clinicians and service planners sit down and review or plan a new service based on their experience and expertise. Every year countless opportunities are lost in initiatives that fail to create meaningful benefits because researchers have not consulted with patients, whānau, clinicians, and other end-users.

Experience-based co-design is a method for turning this around and partnering with patients, consumers, and service users right from the beginning of service planning to ensure a closer alignment of service delivery with what will work best for service users.

Experience based co-design offers a methodology that brings health workers and consumers together in an authentic partnership to create services that deliver an improved experience. Co-design challenges traditional research paradigms that have tended to treat patients and their whānau as passive recipients of health services. Instead, it encourages patients to take an equal role in the review and development of services and focuses strongly on designing services around patient experiences.

The six phases of co-design

Engage:

proactively establishing and maintaining meaningful relationships with patients (and staff) to understand and improve health services.

Plan:

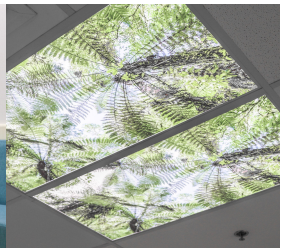
working with patients and staff to come up with ideas about the goals of the improvement work and how to go about doing it.

Explore:

learning about and understanding patient and staff experiences of services and identifying things that can be improved.

Co-design is a very new methodology and was unexplored in New Zealand until only a decade ago. Since then it has gained traction and is now part of Ara Manawa's research toolkit. The whānau rooms refurbishment project used an extensive co-design process, bringing together patients, whānau, staff, designers, Māori specialist architects and hospital architects to explore together what the future of these spaces could look like. As there are 45 whānau rooms across adult inpatient services at Auckland DHB, eight wards with complex/high needs were chosen to be involved in the co-design process. At the same time, an operational group from across all levels of Auckland DHB pulled together a policy to honour the original kaupapa and protect the use of these spaces going forward.

Running the co-design process with these eight pilot wards enabled us to create a 'kit of parts' to progressively refurbish our 45 whānau rooms as funding became available. The kit of parts details the elements that will be implemented consistently across the hospital – such as a wood look vinyl flooring, a diurnal lighting system and an entrance mural designed by TOA architects depicting te ara a tane o te waiora which signposts the location and intent of the room. Following on from this, the kit of parts provides each ward team with a complementary range of options to choose their furniture style and colour, wallpaper options and co-design elements. This enables consistency in look and feel, whilst ensuring the ward design team can flex to meet the needs of their specific patient cohort.



Develop:

turning the ideas into specific improvements.

Decide:

choosing what improvements to make and how to make them.

Change:

turning improvement ideas into action.

Where we are now:

As of July 2021, the first tranche of six whānau rooms have been completely refurbished and the Auckland Health Foundation is actively fundraising for the remaining 39 rooms to be refurbished over the next 2-3 years. The re-establishment of the whānau room purpose demonstrates Auckland DHBs adherence to Te Tiriti o Waitangi in action. Visibly demarcating the rooms as Māori is important as it creates a safe space in a health system that has historically not been so. It acknowledges the essential role whānau play in a patient's hauora, and by providing facilities for them to spend time together in often highly stressful hospital stays health outcomes are improved. These spaces are visibly Māori, but in line with the gifting of the land that Auckland City Hospital sits on from Ngāti Whātua tupuna, they exist to manaaki patients and whānau of all ethnicities.

In 2020 Auckland DHB researchers and their colleagues have enjoyed considerable success in obtaining funding in the millions for their research from a variety of charitable and public-good sources.

A+ Trust Research Grants

The hallmark of a great hospital is having a research programme of excellence. The Auckland DHB Charitable Trust (the A+ Trust) is a major supporter of research and the culture of research and innovation. This culture is helping reshape healthcare for our patients to ensure that they receive the best care possible. A+ Trust Research Grants have been awarded annually via a contestable funding round since 2007. The funding has supported Auckland DHB researchers from all disciplines to undertake research across the health spectrum, from patients to population, disease to prevention, and service delivery. Here are the successful applications for 2020.

A+ Trust Project and Small Project Grants

Varsha Asrani (Nutrition and Dietetics) GastroIntestinal DysFunction in CriTical Illness- The Role of Gut BiOmarkers ($50,000)

Mark de Hora (LabPlus Specialist Pathology) Development of a Liquid Chromatography Mass Spectrometry Research Method for Adrenal Steroids in Bloodspots ($30,000)

Katie Groom (National Women's Health Maternal Fetal Medicine) The C*STEROID Trial: Safely improving outcomes for babies after birth by planned caesarean section at 35+0 to 39+6 weeks ($48,782)

Anil Joshi (Adult Emergency Department) Does wearing a surgical mask influence face touching by healthcare workers?- A Case Control study during the SARS-CoV-2 pandemic ($9,500)

Alison Leversha (Starship Community) LEAP: Language, ENGAGE and Play. Building self-regulation through Play ($14,880)

Cosima Santhakumar (NZ Liver Transplant Unit) Immune microenvironment in liver cancer ($35,000)

Jithendra Somaratne (Cardiology) MINOCA-bat (Randomized Evaluation of Beta Blocker and ACE-Inhibitor/ Angiotensin Receptor Blocker Treatment in MINOCA patients) ($17,000)

Nigel Wilson (Starship Paediatric and Congenital Cardiac Service) The New Zealand Rheumatic Heart Disease Registry ($50,000)

Trust funding vital next step to reverse disease burden of rheumatic heart disease

The 2020 A+ Trust award made to Dr Nigel Wilson, a children's heart specialist at Starship Hospital, will continue a vital research programme that commenced in 2017 with funding from the National Heart Foundation. Nigel and his colleagues have found recurrences of rheumatic fever are linked to people not keeping up with their medication, with adolescents and young adults most at risk. The problems are worse among Māori and Pasifika communities.

Rheumatic fever is a serious illness that can lead to heart damage (rheumatic heart disease). It often starts with a sore throat caused by strep bacteria, and can cause swelling and pain in sufferers' hips, knees, ankles, elbows, and wrists. Recurrences are prevented with regular penicillin injections, about every 28 days, administered by a community nurse, district nurse or public health nurse.

Dr Wilson explains;

"Around the country, each region has their rheumatic fever registers, so the nurses know who needs their penicillin that week or that day. That system doesn't work for adults because the registers are for children. Once a young person leaves that system, it is up to them to find a healthcare provider who can administer the penicillin injections. However, it is not the provider's job to chase down patients the same way as they did with young children on a register. Young adults can fall through the gap. If regular injections are missed for five or six weeks the chance of a rheumatic fever recurrence increased, and so did the risk of rheumatic heart disease."

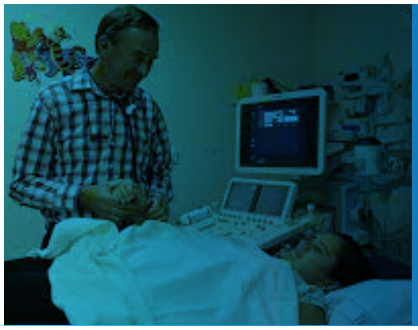
"There's a very low rate of recurrence in children. Only four percent of children in the study time period- 2010 to 2014, were recurrent cases. All the rest were new cases of acute rheumatic fever. But once over the age of 21, recurrences in that age group...25 percent were not first episodes, they were recurrent episodes."

"Previous work in the last couple of years showed that engaging with health services is not always user-friendly. Health is not always a huge priority and so the adolescents and young adults make their own decisions."

Dr Wilson says cost and time were barriers. "People are busy. Just making the appointment to have the injection can be a barrier." He said the mobility of young people, who moved towns and regions in search of work and new lives, was also a problem for them keeping up with much-needed medication.

He said the results of the study showed where the emphasis was needed on improving outcomes.

"For over 10 years now we've been saying that having a national rheumatic heart disease register would be very helpful so that if someone moves town and turns up to a different accident and emergency department for example, then a light comes up on the patient information sheet that says they're on penicillin and should be getting an injection every 28 days."



Dr Nigel Wilson with young patient

Professor Wilson said it was rare to see new cases of rheumatic fever in non-Māori and Pasifika populations. "It really is a problem for Māori and Pasifika, and so by having a very good secondary prophylaxis (antibiotic), you're decreasing the recurrences and therefore decreasing the long-term rheumatic heart disease and the consequences of that."

Praise for Dr Nigel Wilson and his colleagues- Reviewer for the National Heart Foundation 2017 “One definition of institutionalised racism is “inaction in the face of need”. It seems that despite a great need for research and improved care that rheumatic heart disease has suffered a great deal of inaction. As such this study can be seen as an anti-racism intervention and I would like to see it funded ”.

A+ Trust Summer Student Grants

Jocelyne Benatar (Cardiology) Change in Ejection Fraction Study

Jonathan Bishop (Starship Paediatric Gastroenterology) Ultrasound Elastography in Cystic Fibrosis- an Audit of practice since establishment of a new service

Harriet Cheng (Dermatology) Investigation of contact allergy due to plants

Barbara Cormack (Starship Paediatric Dietetics) A retrospective cohort study to investigate hypophosphataemia and clinical outcomes in children < 2 years of age cared for in Starship paediatric intensive care unit following surgery for cardiac conditions.

Kevin Ellyett (Respiratory Physiology) Correlation between clinical history and exercise oscillatory ventilation evaluated using a novel application of Poincaré analysis: Investigation of the association between unstable ventilatory patterns and history of cardiac disease.

Cameron Grant (Starship General Paediatrics) Modifiability of sleep duration in relation to childhood obesity- A systematic review and meta-analysis of randomized controlled trials

Alison Leversha (Starship Community) Early engagement and timeliness of interventions for pregnant women referred to Noho Āhuru- Healthy Housing

Paul Monk (Orthopaedics) Design and validation of smart feeler gauge for use in uni-compartment knee arthroplasty

Jeanine Nunn (Te Puaruruhau) Family Violence Survey Development Project

Steve Waqanivavalagi (Adult Emergency Department) Cardiac Arrest in the Auckland Region: Development of a Comprehensive Database

Miriam Wheeler (Cardiology) INR monitoring and secondary prophylaxis after heart valve replacement for Rheumatic Heart Disease: What are we doing and are we doing it well?

Cancer Research Trust

Anne Fraser (Oncology) LuCaS (Lung Cancer Surveillance) Study: surveillance models for non-curative lung cancer patients. ($133,653)

Anna Waylen (Anaesthesia and Perioperative Medicine) The Volatile Anaesthesia & Perioperative Outcomes Related to Cancer (VAPOR-C) Trial ($80,000)

Green Lane Research and Education Fund

The Green Lane Research & Educational Fund was established at Green Lane Hospital in 1971 and incorporated under the Charitable Trusts act in 1976. Its aims then and now are to advance research and education within the departments of Cardiology, Cardiothoracic Surgery, Paediatric Cardiology and Surgery, Cardiothoracic Anaesthesia and Respiratory Medicine, within the Auckland District Health Board.

The Fund supports a Senior Research Fellowship, annual large and small project grants on a merit contested basis, a PhD Scholarship, conference support for nurses and technical staff and salary support for specified research positions. The Fund hosts an annual Scientific Session followed by the Green Lane Dinner, at which a past member or members' professional achievements are honoured.

Jocelyne Benatar (Cardiovascular Research Unit) Long term outcomes in patients who were in the FRAILTY study ($50,000)

Alan Merry (Anaesthesia and Perioperative Medicine) Timing In. Evaluating the potential for a patient-centric modification of the WHO Surgical Safety Checklist ($47,912)

Jithendra Somaratne (Cardiology) Myocardial infarction with nonobstructive coronary arteries (MINOCA) – research for better evidence-based treatments ($13,800)

Health Research Council of New Zealand

Dr William Abbott (NZ Liver Transplant Unit), Dr Tien Huey Lim, Dr Klaus Lehnert HBsAg mutations and pathophysiology of chronic hepatitis B ($150,000)

Dr Malcolm Battin (Neonatal Intensive Care Unit), Professor Alistair Gunn, Dr Lynn Sadler (National Women's Health), Professor Ngaire Stott (Starship Paediatric Orthopaedics) Improving care and outcomes for babies at risk of brain injury ($823756)

Dr Angela Beaton, Nicole Pihema, Dr Jeff Foote, Dr Lynn Sadler (National Women's Health) Activating communities to improve outcomes for wāhine Māori ($30,000)

Professor Ian Bissett, Professor Gregory O'Grady (General Surgery), **Dr John Woodfield** Randomised trial of a novel chyme reinfusion device for temporary ileostomies

Professor Frank Bloomfield (Neonatal Intensive Care Unit), Professor Lisa Stamp, Associate Professor Matire Harwood, **Associate Dean Collin Tukuitonga, Dr Christine Walsh, Dr Cameron Lacey, Dr Colin McArthur** (Critical Care Medicine), **Professor Katrina Sharples, Professor Stuart Dalzie**l (Starship Children's Emergency Department), **Dr Irene Braithwaite, Professor Mark Gahegan, Dr Deborah Schlichting, Professor Dr Nicolette Sheridan, Dr Sarah Benge, Professor Ngaire Kerse MNZM, Professor Christopher Bullen, Associate Professor Conroy Wong, Professor David Baxter, Associate Professor Garry Nixon, Mr Charles Stratton** Towards a national, equitable & sustainable clinical trial system in Aotearoa NZ

Associate Professor Mark Bolland (Endocrinology), Dr Deborah Schlichting, Mr Gregory Gamble, Dr Anne Horne, Associate Professor Andrew Grey, Professor Ian Reid (Endocrinology) Zoledronic acid and fracture prevention in early postmenopausal women

Dr Gary Cheung (Mental Health Services for Older People), **Dr Makarena Dudley, Dr Tai Kake, Dr Kathryn Peri** Getting ready for the first clinical trial for Māori with dementia

Associate Professor Katie Groom (National Women's Health Maternal Fetal Medicine), **Professor Caroline Crowther, Professor Frank Bloomfield** (Neonatal Intensive Care Unit), **Dr Arier Lee, Professor Jonathan Morris, Dr William Grobman** Safely improving outcomes for babies after birth by planned caesarean section

Dr **Nishi Karunasinghe, Dr Jonathan Masters** (Urology), **Professor Lynnette Ferguson, Professor Dr Benji Benjamin** Relationship building: Study on stratified PSA for prostate cancer detection

Dr Alison Leversha (Starship Community) Collaboration for child wellbeing ($890,709)

Dr Alison Leversha (Starship Community), **Dr Anneka Anderson, Dr Teuila Percival, Ms Jacinta Fa'alili-Fidow, Professor Suzanne Purdy, Professor Trecia Wouldes, Associate Professor Bridget Kool, Dr Dug Yeo Han** Reducing inequities in Well Child Tāmariki Ora developmental surveillance ($1,350,785)

Dr Joanne Lin, Associate Professor Suresh Muthukumaraswamy, **Dr Nicholas Hoeh** (Taylor Centre), Associate Professor Frederick Sundram, Dr Scott Graham, Dr Alana Cavadino Low-dose naltrexone as an adjunctive treatment in major depressive disorder

Dr Christopher McKinlay, Associate Professor Jane Alsweiler, Professor Jane Harding, **Professor Wayne Cutfield** (Starship Paediatric Endocrinology), Ms Jennifer Rogers, Professor Geoff Chase, Mr Gregory Gamble Neonatal Glucose Care Optimisation (NeoGluCO) Study

Starship researcher to assess the effectiveness of the free universal Well Child Tāmariki Ora programme

Dr Alison Leversha

September 15 2020 – Today the Health Research Council announced more than $14M in funding to research aiming to improve the delivery of healthcare services in Aotearoa.

One of the projects with a strong focus on achieving health equity for Māori and Pacific peoples was awarded to Dr Alison Leversha. Alison, who works at Starship Children's Hospital as a community paediatrician, and her team will examine the Well Child Tāmariki Ora (WCTO) programme, which is New Zealand's primary way of detecting developmental and behavioural problems in children.

Despite high rates of enrolment, the programme is only picking up problems in half as many children as other countries. This project will investigate why so many cases go undetected and why children who could have been treated earlier are starting school already behind their peers. Alison hopes the new knowledge will help make the programme more effective.

"Inequities in learning, development and health are evident when children start school, and these trajectories track into adulthood with poorer educational, health and social outcomes. If problems are identified and interventions made early, many of these problems can be prevented or reduced," says Dr Leversha.

She says anecdotal and some research evidence suggests that the WTCO programme may be exacerbating inequalities.

"Emerging evidence suggests that the WTCO programme may not be identifying a significant proportion of children with developmental or behavioural needs. This is particularly true for Māori and Pacific children and those from disadvantaged communities for whom the current developmental screening tool is not fit for purpose. Improving the way we identify children's needs will ensure we can support caregivers and whānau/aiga, and that all children reach their potential," she says.

"The questionnaire used for the WCTO developmental surveillance (PEDS) is a series of ten questions that asks parents if they have any concerns about their child's development; for example: Do you have any concerns about how your child talks and makes speech sounds? Across New Zealand, only 5% of children are identified as being in pathway A: at high risk of developmental difficulties. This is only half the rate identified in every other country around the world. We are exploring why this is the case. Is it because parents don't report concerns to a nurse they've only just met? Is it that parents aren't aware that their child isn't meeting their developmental milestones?"

"As it stands, we are overlooking children with reasonable significant concerns, and this is disproportionately impacting Māori and Pacific children. Being 'the same as other children in the community' is not the same as being developmentally on track."

"The first few years of a child's life are critical as a platform for lifelong success. If we can identify things early and we can get appropriate support and interventions early, we get better outcomes."

Findings will directly impact the redesign and future delivery of the WCTO programme to ensure that it reduces inequities and achieves better outcomes for all tāmariki.

In a rare double, Alison also won an HRC Clinical Practitioner Fellowship in 2020. This prestigious award is made to only two clinicians a year. She'll use the ring-fenced research time paid for by the Fellowship to take the helm of the Collaboration for Child Wellbeing, a partnership of clinicians, academics, and schools in the Tamaki Manaiakalani Kahui Ako, working together to make a collective impact for disadvantaged communities. In addition to the WCTO work the collaboration will pool its expertise to improve children's self-regulation by studying a play-based programme (ENGAGE).

Developed by researchers at the University of Otago, ENGAGE is a promising tool for enhancing self-regulation, a cognitive skill set that can be improved with training. Self-regulation is a better predictor of future health economic, educational, and social outcomes than IQ. Given the high prevalence of language disadvantage, low working memory and poor motor planning in Tamaki new entrants, the team will collaborate to adapt ENGAGE to an appropriate developmental level for these tamariki.

Alison is working with great team of clinicians and academics from the University of Auckland: School of Population Health, Speech Science, Psychological Medicine, and Te Kupenga Hauora Māori; Moana Research; Auckland University of Technology: Occupational and Physiotherapy Clinical School; Starship Community and principals and teachers in the Manaiakalani Community of Learning.

Dr Tess Moeke-Maxwell, Professor Linda Waimarie Nikora, Professor Merryn Gott, Associate Professor Janine Wiles, Dr Lisa Williams, **Dr Jackie Robinson** (Palliative Care), Dr Tatiana Tavares Health equity and wellbeing among older people's caregivers during COVID-19

Dr Tess Moeke-Maxwell, Mr Rawiri Wharemate, Professor Merryn Gott, Dr Melissa Carey, **Dr Jackie Robinson** (Palliative Care), Dr Lisa Williams Tupu Tika: Building whānau capacity to carry out end-of-life and end-stage care

Associate Professor Nicole Moreland, Dr Amy Chung, **Associate Professor Nigel Wilson** (Paediatric and Congenital Cardiac Service), Dr David Crossman, Professor Michael Baker

Miss Malia Pateli, Dr Julie Lim, **Dr Rachael Niederer, Dr William Cunningham** (Ophthalmology) The prevalence of vitrectomy and cataract post vitrectomy in Pacific and Māori

Associate Professor Rachael Parke (Cardiothoracic and Vascular Intensive Care Unit), Dr Aileen Collier, **Dr Jackie Robinson** (Palliative Care), Dr Tess Moeke-Maxwell, **Ms Eileen Gilder** (Cardiothoracic and Vascular Intensive Care Unit), Professor Dr Bridget Johnston, Dr Deans Buchanan, Professor Dr Judith Sixsmith, Professor Merryn Gott New Zealanders' experiences of hospital 'visiting' during COVID-19 restrictions

Professor Anthony Phillips, Professor Colin Green, **Professor John Windsor** (General Surgery), **Dr Colin McArthur** (Critical Care Medicine), Mr Fred Astle Reducing organ failure in critical illness

Professor Anthony Phillips, **Professor Gregory O'Grady, Professor John Windsor** (General Surgery), Mr Fred Astle Improving nutrition delivery

Professor Anthony Phillips, Dr Kevin Stewart, Dr Jiwon Hong, **Professor John Windsor** (General Surgery) Lung protection during critical illness

Dr Christopher Pook, Ms Mariana Muelbert, **Professor Frank Bloomfield, Dr Barbara Cormack** (Neonatal Intensive Care Unit), Suzanne Butler Curds and whey in preterm babies: does fortifier adversely affect mother's milk?

Dr Raewyn Poulsen, Dr Jade Tamatea, **Professor Nicola Dalbeth** (Rheumatology) Turning off the cellular energy supply to treat osteoarthritis

Dr Rodrigo Ramalho, **Dr Gary Cheung** (Mental Health Services for Older People), Dr Yan Chen, Dr Mark Lawrence, Dr Mataroria Lyndon, Dr 'Etuini Ma'u e-Mental health in Aotearoa: sector engagement and research agenda priorities

Dr Rohit Ramchandra, Professor Julian Paton, **Associate Professor Nigel Lever** (Cardiology), Dr Julia Shanks Respiratory modulated pacing to improve outcomes in heart failure

Associate Professor Jacqueline Ramke, Dr Arier Lee, Dr Peter Carswell, Associate Professor Matire Harwood, **Dr Corina Grey** (Pacific Health Data and Insights)**, Associate Professor Rinki Murphy** (Auckland Diabetes Centre), **Dr David Squirrel**l (Ophthalmology), Mrs Tarati Blair-Hunt, Dr Carol Barker Improving equitable access to diabetes eye services

Dr Lisa Reynolds, Associate Professor Suresh Muthukumaraswamy, **Dr Nicholas Hoeh** (Taylor Centre), Associate Professor Frederick Sundram, Dr Alana Cavadino, **Dr Nicola Lawrence** (Oncology) Psychedelic-assisted therapy in advanced-stage cancer patients

Dr Stephen Ritchie, Associate Professor Mark Thomas (Infectious Diseases), Ms Susan Reid, Dr Sandra Thaggard, Associate Professor Robyn Whittaker, Dr Lily Fraser, **Dr Amy Chan** (Pharmacy), Dr Arier Lee, **Dr Emma Best** (Starship Infectious Diseases), Professor Bruce Arroll Reducing antibiotic usage in people with self-limiting viral illness

Dr Jackie Robinson (Palliative Care), Ms Ying Huang, Professor Merryn Gott, Associate Professor Daniel Exeter, Dr Jinfeng Zhao, Dr Andrew Old, Dr Tess Moeke-Maxwell, Dr Lisa Williams, Associate Professor Janine Wiles Dying as a health and social justice issue: exploring the impact of deprivation

Dr Peter Saxton, Professor Patricia Priest, Dr Susan McAllister, **Dr Stephen Ritchie** (Infectious Diseases), Dr Janine Paynter, Dr Sarah Morley, Dr Kim Southey, Dr Jason Myers, Mr Mark Fisher Improving blood safety and donor selection

Assistant Professor Julia Slark, Professor Merryn Gott, **Dr Jackie Robinson** (Palliative Care), Dr Jennifer Parr, Dr Tess Moeke-Maxwell, Professor Denise Wilson Optimising compassionate care in acute hospitals: building the foundations

Dr Simone Watkins, Dr Monique Stein-de Laat, **Professor Frank Bloomfield** (Neonatal Intensive Care Unit), **Dr Thomas Gentles** (Paediatric and Congenital Cardiac Service), Dr Teuila Percival, Professor Dr Sue Crengle, Dr Elza Cloete, **Dr Lynn Sadler** (National Women's Health) Why do outcomes of critical congenital heart disease in NZ differ by ethnicity?

Dr Karen Wright, **Professor Ngaire Stott** (Starship Paediatric Orthopaedics)**, Dr Anna Mackey, Ms Alexandra Sorhage** (New Zealand Cerebral Palsy Register), Dr Sian Williams Cerebral palsy and Māori health inequities in New Zealand

Mercia Barnes Trust

Lucy Prentice (National Women's Health) The FIIX study – The Fertility and IVF and Intrauterine Insemination trial in couples with unexplained infertility ($25,000)

National Heart Foundation

Sergej Cicovic (Cardiology) Fellowship in International Cardiology

Mark Webster (Cardiology) Prasugrel versus ticagrelor in acute coronary syndromes ($184,402)

Neurological Foundation of New Zealand

Richard Roxburgh (Neurology) Characterising VIIIth cranial nerve involvement in Charcot-Marie-Tooth disease 1A ($90,852)

Starship Foundation Clinical Research Fund

Starship Child Health and the Starship Foundation share a vision to create, at Starship, an environment of world-class research, training and innovation that will better the lives of kiwi kids faster. In 2016, that vision took an important step forward with the announcement of a significant new investment in paediatric clinical research. Since then, over $2.0m has been committed by the Starship Foundation to projects now underway. This investment enables our national children's hospital even greater ability to lead the way in evidence-based care and improved health outcomes for New Zealand's children. The Starship Foundation is proud to fund projects that save and extend lives, lift spirits, and reduce discomfort, ensure better outcome, faster recovery, and less invasive treatments, and are focused on equity and prevention to accelerate the pace of change at our national children's hospital.

Clinical Research Project Grants awarded In 2020

Malcolm Battin (Newborn Services) Facilitating early identification of infants with cerebral palsy within the Neonatal Intensive Care Setting: an implementation science study ($99,947)

Emma Best (Starship Infectious Diseases) Understanding measles; severity and sequelae ($97,056)

Tom Gentles (Paediatric and Congenital Cardiac Service) Major Congenital Heart Disease in New Zealand: Inequities and time-related trends in diagnosis and outcome ($50,000)

James Hamill (Starship Surgery) Mixed methods study on how multidisciplinary action teams learn and how to debrief ($92,120)

Elaine McCall (Safe Care Programme) Children's pain prevalence, intensity, and treatment at Starship Child Health: Point of prevalence study ($29,023)

Diana Purvis and Georgina Harvey (Starship Dermatology) Aotearoa Healthcare Equity in Atopic Dermatitis (AHEAD Study) ($47,360)

Michael Shepherd (Children's Emergency Department) The Adjunct for Endotracheal Tube passage in Simulated Paediatric Airways ($21,100)

Claire Spooner (Starship Neurology) Paediatric Acute Code Stroke Study

Sue Stott (Starship Orthopaedics) Respiratory health for tamariki with cerebral palsy in New Zealand ($99,724)

Rachael Webb (Starship Infectious Diseases) SNAP-PY: Staphylococcus aureus Network Adaptive Platform trial: Paediatrics and Youth ($195,767)

Melissa Wilson (Safekids Aotearoa) Disparities in Dog Related Injuries in New Zealand Children ($96,600)

Nichola Wilson (Starship Orthopaedics) SCIENCE – Surgery or Cast for Injuries of the EpicoNdyle in Children's Elbows ($100,000)

The Auckland Academic Health Alliance (AAHA) formalises a research, teaching and clinical delivery relationship spanning almost five decades between the Auckland DHB and the University of Auckland.

Auckland Academic Health Alliance takes aim at health disparities

It is known that speaking te reo increases

- self-worth and self-esteem
- confidence
- happiness
- pride
- determination
- courage

All these are indicators of a person's emotional, mental, and psychological wellbeing (hinengaro). This research will explore the relationships between te reo Māori speakers' hinengaro, tinana (physical), and wairua (spiritual), and whanau health and wellbeing.

About the team

Dr Helen Wihongi is a community psychologist and Director of Māori Health Research at Auckland DHB. Associate Professor Daniel Exeter is a health geographer with the University of Auckland. Helen brings to the collaboration a background in Māori health, health policy, a systems and ecological approach, funding and planning experience and knowledge of kaupapa Māori research methods. Daniel uses big data sets to research geographical variations in health outcomes, particularly the identification of and potential solutions to health disparities due to socio-economic conditions, area disadvantage and ethnicity.

What's the science?

We will interrogate Stats NZ's Integrated Data Infrastructure (IDI). The IDI is a large research database. It holds microdata about people and households collected by government agencies and includes information from the NZ census and Te Kupenga. In the IDI the data from various sources are linked together. Researchers use this resource to gain insight into our society and answer complex questions.

IDI is a 5 Safes resource (safe people, safe projects, safe setting, safe data, and safe outputs) and the identities of individuals in a study are not disclosed to researchers, or any other data that could be used to re-identify them.

Since 1996, the census has asked New Zealanders: "In which languages could you have a conversation about a lot of everyday things?" of which te reo Māori is one response option. In 2013, Stats NZ carried out Te Kupenga, its first survey of Māori well-being. Te Kupenga collected information from 5,500 Māori on a wide range of topics to give an overall picture of the social, cultural, and economic well-being of Māori in New Zealand. The survey included questions about respondents' ability to speak, listen, read, and write in te reo Māori and the environments in which they used the language. We will link data about people's use of and proficiency in te reo from the census and Te Kupenga to health data, such as hospitalisations and medicines dispensed.

What will the study achieve?

We hope to identify the extent to which health outcomes for Māori can be associated with engagement in te reo Māori and wider measures of wellbeing. Our study may provide support for new ventures to lift te reo in our communities, and in particular te reo Māori activities in Auckland DHB. Given the persistent and widening gaps in health outcomes for Māori, we hope to use this new knowledge to disrupt this continued trend of persistent negative health outcomes.

The study sits with in te ao Māori and te ao Pākehā. Taking these into account the study team have experience working with Māori data and have led significant changes to the way StatsNZ gather data. The team have also all been instrumental in changing health policies and in two cases health legislation in an endeavour to improve Māori health gain.

Experts in the IDI lead the analysis of the data. Associate Professor Dan Exeter will lead work on identifying health outcomes in the IDI while Conal Smith and Luisa Beltran-Castillon (Kōtāta Insight) will lead analysis of Te Kupenga and integration of Te Kupenga data with health outcomes. Dame Rangimarie Naida Glavish, Professor Tania Ka'ai, Dr Helen Wihongi and Tania Smith will act as kaitiaki over the data and its analysis.

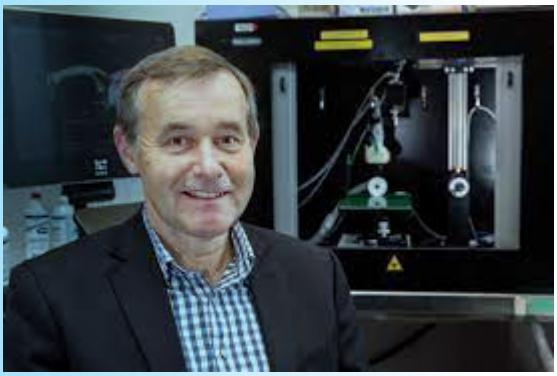
The methodology builds on previous research by Kōtāta Insight – Ngā Tamariki o Te Kupenga – which studies the relationship between cultural connection and educational outcomes for tamariki Māori.

At Auckland DHB we believe that improving healthcare for our patients comes through evidence-based research. To this end, a number of exciting new initiatives have emerged recently.

New opportunities for heart research - Healthy Hearts for Aotearoa New Zealand

Introducing Auckland DHBs esteemed collaborator Professor Julian Paton. Julian is Professor of Translational Physiology and Director of Manaaki Mānawa – The Heart Research Centre of the University of Auckland.

"Cardiovascular disease is Aotearoa's biggest killer and responsible for the shorter life span in Māori and Pacific people. High blood pressure is the biggest risk factor for cardiovascular disease – the leading cause of death globally – and it's clear we don't yet know everything about controlling it".



Professor Julian Paton

Julian is a world-leading physiologist who has made outstanding contributions to knowledge in the area of cardiovascular and respiratory control. He has pioneered new technical approaches surrounding neural control of circulation and breathing. His unique technical research and contribution of new scientific concepts in cardio-respiratory diseases has resolved a major controversy surrounding respiratory complications. Julian's discoveries have had a significant impact on understanding how hypertension, heart failure and sleep apnoea develop and progress.

Manaaki Mānawa is the host of Healthy Hearts for Aotearoa New Zealand (HHANZ), the new Centre of Research Excellence (CoRE) that's an integrated national network of heart researchers, clinicians, and community experts from around the country. The name means 'preserving the life force of the heart' and was gifted by Auckland DHB's Dame Rangimarie Naida Glavish.

"The government has recognised the chronic issue around cardiovascular disease, particularly the inequity around Māori and Pacific,"

says Julian.

CoREs are major awards granted to enhance collaboration and impact of a particular area of research. This was the third attempt for securing a CoRE in heart research and presents a historical landmark and unprecedented opportunity for Aotearoa New Zealand.

The focus of the CoRE is equity. "Founded upon and upholding Te Tiriti obligations, we have worked together with Māori and Pacific Peoples to develop our governance, strategy and leadership."

says Julian.

An important part of the CoRE's mission is capability and capacity enhancement in the heart research workforce. It supports the training via clinical fellowships for Auckland DHB doctors, nurses, and other health professionals to achieve PhD and MD degrees. There are also have ring fenced fellowships for Māori and Pacific fellows.

With members of Auckland DHB's cardiothoracic surgical team a cardiopulmonary bypass sheep model is being developed for testing of new cardioplegia and new open-heart procedures including testing of new heart valves for rheumatic disease patients.

The CoRE will fund the creation of a national clinical cardiac research network that piggy backs on the existing national cardiac service network. This will be driven by a new part time position to assist in patient recruitment for trials hosted at Auckland DHB.

In 2020 Julian was elected to the Academy of the Royal Society Te Apārangi for his distinction in research. This is research that could save lives, improve the quality of life in people with high blood pressure, and dramatically reduce hospital admissions. Julian and his team have discovered a new organ (carotid body) that raises blood pressure, offering novel future treatment strategies, and built the world's first bionic pacemaker that reverses heart failure.

Key facts on heart disease:

- About one in 20 people are living with heart disease in New Zealand
- Every 90 minutes, a New Zealander dies from heart disease
- A quarter of people presenting to hospital with an event are under 55
- Heart disease is the greatest killer of women in Aotearoa
- Heart disease kills 3000 women in New Zealand every year
- Heart failure hospitalisation is 4.5 times higher for Māori vs non-Māori women

Rising Star – AAHA's Dr Annika Winbo awarded prestigious international prize for her cardiac disease research

A research collaborator with Auckland DHB-led Cardiac Inherited Disease Group (CIDG) since 2013, Annika has been awarded the prestigious, international award named the 'Heart Rhythm Society Young Investigator Award'. Hundreds of researchers from around the world submitted an abstract during the submission process. 60 applicants were considered in full and six chosen to be finalists.

Annika is the first New-Zealand based researcher to win the award since it began in 1990.

A key aspect of winning was that Annika and her team were also the first to successfully grow what is called human iPS-derived sympathetic neurons and heart cells together. Human iPS cells are derived from skin or blood cells that have been reprogrammed back into an embryonic-like pluripotent state that enables the development of an unlimited source of any type of human cell needed for therapeutic purposes. iPS-derived cells from patients with cardiac inherited diseases, such as long QT syndrome, harbour the genetic variants that underlie disease susceptibility, which makes them exciting targets for studying inherited conditions.

"Through a great deal of time and investment we have been able to increase our understanding of the complexities of this aspect of cardiac disease, some of which are unique to families in New Zealand," says Annika.

"The life-threatening arrhythmias in long QT syndrome typically are triggered by the 'fight or flight' response. That means sudden death can be triggered by fear, excitement, or a simple jump into the water. Our research enables us to study human heart cells and sympathetic neurons interacting (in a dish/in vitro), so that we can learn more about what triggers sudden death in families with Long QT Syndrome."

Annika's early research focused on clinical characterisation and risk stratification of long QT syndrome (LQTS) mutations common in the Swedish population. In 2013, she teamed up with Starship Child Health's Professor Jon Skinner, a paediatric cardiologist, with the common goal to further LQTS research by venturing into cellular heart research, with the aim to improve characterisation, risk stratification and patient-centred treatment strategies.

Professor Jon Skinner ~ "This is a truly remarkable achievement by Annika, who arrived from Sweden and has built around her a local and international team of scientists and clinicians. It is tough to move from being a medical doctor into basic science, let alone moving countries while doing so, and this acknowledgement speaks to how successful she has been. An important key to her success is also her wonderful supervisor, Johanna Montgomery, who has encouraged and supported Annika when the going was really tough. Hats off also to the Auckland Academic Health Alliance; her research was one of the first off the rank funded by this joint initiative between ADHB and Auckland University, and shows how important such funding is to translational science in Auckland.

We clinicians in the New Zealand national CIDG are very proud and pleased on behalf of our patients, to have been part of this."

The CIDG aims to better treat children who suffer cardiac inherited diseases, particularly long QT syndrome (LQTS), which mostly affects children and young adults with frequent faints, but sometimes results in sudden death. Each year, an estimated 100 people aged between one and 35 years die from sudden or unexpected cardiac death.

The CIDG draws on a registry of Kiwi patients, with genetic profiles unique to New Zealand.

Since its formation, the CIDG has become the gold standard for similar efforts around the globe and has proven instrumental in saving many young peoples' lives. The collaboration's work is now starting to help reduce life-threatening events across generations of LQTS families.


CELEBRATING OUR PEOPLE

Clarivate Analytics Highly Cited Researchers 2020

Drum roll!! Congratulations, yet again, to **Professor Ed Gane** (NZ Liver Transplant Unit) who made it onto Clarivate Analytics Highly Cited list for the FIFTH year running. As one of only 18 New Zealanders to make it onto this prestigious list in 2020, Ed is recognised among the world's most influential researchers of the past decade. Placement on this exclusive list is demonstrated by the production of multiple highly cited papers that rank in the top 1% by citations for field and year.

Professor Ed Gane

2020 Gluckman Medal

The Peter Gluckman Medal for Distinguished Contribution to Research is the premier recognition of research within the Faculty of Medical and Health Sciences at the University of Auckland. The awardee for 2020 was Auckland DHB rheumatologist and world-leading gout expert **Professor Nicola Dalbeth.**

Gout is a painful form of arthritis caused by urate crystals accumulating in joints. It affects one quarter of older Māori men and one third of older Pacific men in New Zealand. Nicola's work has challenged widely held beliefs about gout being caused by eating too much rich food. In fact, biological factors including age, being male, chronic kidney disease, genetic variants and some medications play a major role in development of gout. She has led initiatives to improve gout management within the community, particularly focused on destigmatisation and equity in gout management.

Nicola's work has re-defined central concepts of the disease including the language used to describe gout, how disease remission is defined, and standardised measurement in gout clinical trials. Her laboratory and imaging research led to understanding the pathways that cause bone and joint damage in gout, leading to treatments that prevent structural joint damage. She has led clinical trials showing that urate-lowering therapy early in the disease can reduce gout flares and joint inflammation.

Congratulations Nicola!

PUBLICATIONS

HOT Paper! First clinical evidence that CRISPR gene editing inside the body can be safe and effective.

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New Zealand patients with a deadly disease have recently become two of only six people in the world to have cells deep inside their body altered by the gene-editing tool CRISPR/Cas9. This was made possible by the collaboration between Auckland DHB's Professor Ed Gane [1] and New Zealand Clinical Studies, a state-of-the-art early phase research facility, also located in Grafton.

CRISPR has already been used to edit blood cells removed from the body and infused back in, as well as genes in the eye. But the trial In New Zealand was the first time anyone's whole body has been infused with the CRISPR tool. Gene-editing blood ***outside*** the body is useful, but it requires vast sums for specialist equipment and experts to run it. Gene editing cells ***inside*** the body opens the approach up to many more patients.

In this new study reported in the prestigious New England Journal of Medicine, participants suffered from hereditary transthyretin (TTR) amyloidosis (ATTR) with neuropathy. ATTR is a rare, rapidly progressive disease caused by a mutation in the TTR gene that results in the build-up of misfolded TTR and leads to clumps of proteins clogging up in the heart, gastrointestinal tract, and peripheral nerves. Life expectancy is about 3 to 15 years after the onset of neuropathy. Patients endure years of pain and progressive heart failure.

The study treatment known as NTLA-2001 was developed by Intellia Therapeutics of Cambridge, Massachusetts, a company founded by CRISPR-Cas9 pioneer and Nobel laureate Dr Jennifer Doudna, and Regeneron Pharmaceuticals Inc. of Tarrytown, New York. NTLA-2001 was infused into the bloodstream but designed to deliver its payload into the liver. There, the scissor-like CRISPR-Cas9 tool cuts and edits DNA and inactivates the TTR gene in liver cells to prevent misfolded TTR protein from being produced. The liver makes more than 99% of all circulating TTR.

It seems to have worked as planned. The one-time treatment appears to have turned off the TTR gene. Three participants who got a low dose of NTLA-2001 saw more than a 50% decline in their blood levels of the protein. The three who received a higher dose saw 87% and higher reductions.

It's too soon to know whether the treatment will reduce patient symptoms or extend their lives but experience from previous research has shown that the more the amyloid protein can be knocked down the better patients do.

While experts rightly urge no more than cautious optimism for a treatment that has been tested in only six people, if such CRISPR gene-editing continues to show as much promise, the results could herald a new era for transthyretin amyloidosis and dozens of other genetic conditions caused by "spelling mistakes" in genes.

"This is not an incremental advance – it's a wow!"

Professor Fyodor Urnov,
University of California, Berkeley .

"What was astonishing about this first-in-human study is not just that the treatment worked, but that it worked extremely well in patients, in one case turning off the disease gene close to 100%. It's like launching a rocket ship in the hope of just getting into orbit, but making it all the way to the moon on the first try."

Dr Kiran Musunuru,
University of Pennsylvania in Philadelphia .

Professor Gane has seen families "decimated" by the disorder as the misfolded protein deposits in their tissues. Once symptoms begin patients are at an age when they have already passed it on to their children. At the time of writing, he has now enrolled a further four participants into the study. All are family members of ATTR patients who needed life-saving transplantation from his Liver Service.

The CRISPR era has begun

[1] *Professor Gane is the Chief Hepatologist, Transplant Physician and Deputy Director of the New Zealand Liver Transplant Unit at Auckland City Hospital. He is a Member of the New Zealand Order of Merit for his services to medicine.*

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Directory

Research Office

Postal Address

Private Bag 92024

Auckland Mail Centre, 1142, New Zealand

Physical Address

14th Floor, Support Building

Auckland City Hospital

2 Park Road, Grafton

Auckland 1023, New Zealand

Email: researchoffice@adhb.govt.nz

Website: http://www.adhb.health.nz/health-professionals/research/

Mary-Anne Woodnorth	**Manager**
Helen Wihongi	Director of Māori Health Research
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This was the Auckland DHB Annual Research Report for 2020.

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Research

Annual Report 2020

AUCKLAND DISTRICT HEALTH BOARD
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