March 2018 edition 33

QUT ihbi
Institute of Health and Biomedical Innovation

IHBI ADVANCES

IN THIS ISSUE

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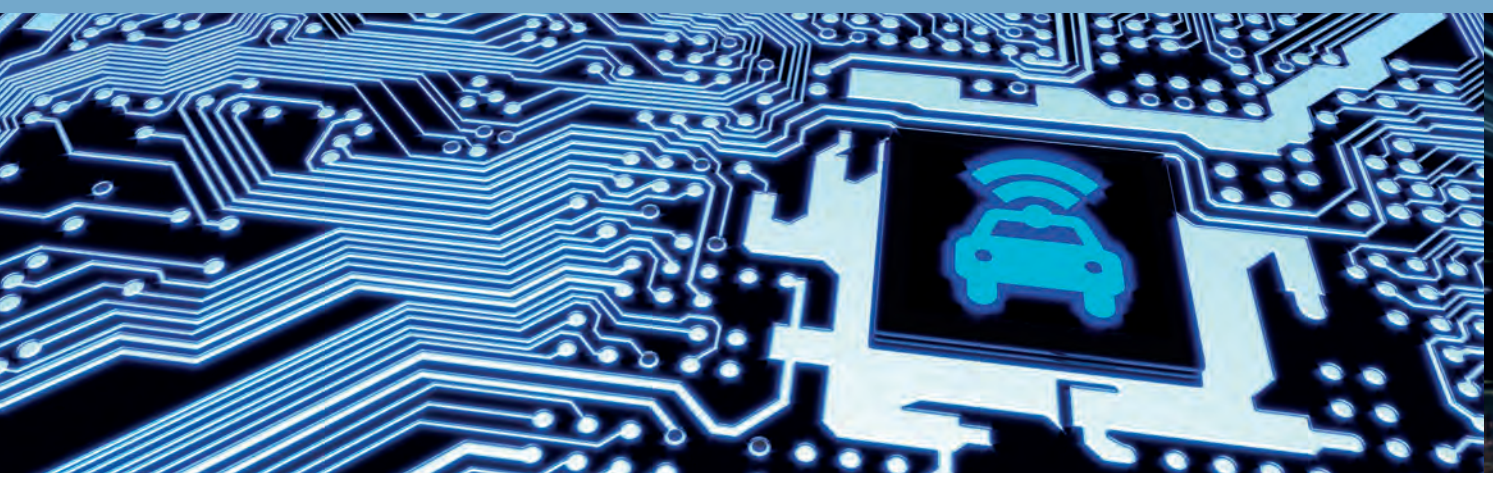


Professor Andry Rakotonirainy

Driver behaviour a focus in test of cooperative vehicle technology

While road deaths continue to decline in Australia each decade, driving remains one of the most dangerous activities a person can perform. IHBI researchers are part of a collaboration investigating use of technology such as connected cars to further improve safety.

IHBI's Professor Andry Rakotonirainy is leading a QUT study as part of the iMOVE Cooperative Research Centre, a consortium of 44 industry, government and research partners engaged in a 10-year effort to improve Australia's transport systems.

The Queensland Department of Transport and Main Roads (TMR) is delivering an on-road test of a number of Cooperative Intelligent Transport Systems (C-ITS) technologies fitted to about 500 public and fleet vehicles in Ipswich, from late 2019.

COOPERATIVE VEHICLES

Equipped with specialist technology and devices, along with wireless/3G/4G internet access, cooperative vehicles are able to 'talk' to each other, roadside infrastructure and road operations systems.

Internet access allows cars to communicate with each other and the world around them. While cars are already connected, with navigation systems including connected car functions such as dynamic route guidance, the difference with cooperative vehicles is the addition of wireless communication between cars, infrastructure and cloud based data sharing systems.

THE DRIVER'S ROLE

A cooperative car supplies useful information to a driver to help make safer or more informed decisions. The car is not making choices for the driver but supplies information to the driver, including potentially dangerous situations to avoid.

AUTONOMOUS VEHICLES

Some cars are already being deployed with autonomous functions, such as self-parking or auto-collision avoidance features. But they are not considered a true autonomous vehicle until it can drive itself independently. A fully autonomous vehicle does not require a human driver—rather, they are computer-driven.

MORE INFORMATION

Visit imovecrc.com

The technologies include warnings that alert drivers to upcoming hazards involving other vehicles on the road network. They include vehicles braking hard some distance ahead, pedestrians or cyclists crossing at an intersection, hazards on the road such as water or debris, road works, a change to speed limit and congestion that is not visible to a driver.

Professor Rakotonirainy brings to the collaboration his expertise in human factors and road safety, complementing QUT project manager Dr Andy Bond's focus on the future of transport, new technology and patterns of use based on work in road safety, law and robotics.

Another 10 QUT researchers contribute to the collaboration, covering disciplines such as psychology, human behaviour and communications, mathematics, traffic engineering, statistics and computer science.

Professor Rakotonirainy says the collaboration will consider multiple aspects, including planning and design of future transport networks and services; driver behaviour and responses to the technology and warnings; and strategies for enhancing driver acceptance and adoption.

'The evaluation findings will be used by transport agencies – local, state and federal – to support the investment in infrastructure, both digital and physical, that supports the emerging C-ITS need,' Professor Rakotonirainy says.

'The ultimate goal is to conduct evidence-based research to inform government about the benefits of C-ITS deployment.'

The research has funding from the iMOVE CRC and support from the Cooperative Research Centres program, an Australian Government initiative.

During the 12 months ended December 2017, there were 1225 road deaths in Australia.

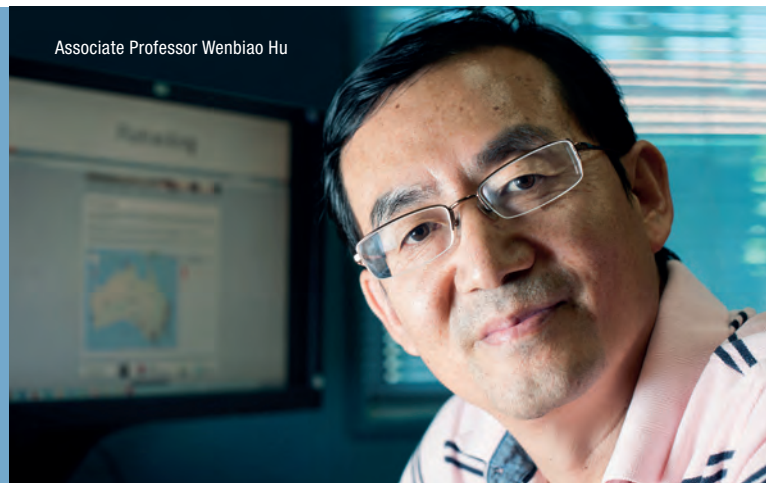
Although that is a 5.3 per cent decrease compared to the total for the 12-month period ended December 2016, serious injuries continue to increase, with more than 6000 people in Queensland taken to hospital each year due to road trauma. On average, each injury costs the Queensland community $600 000. Those involving brain and spinal injuries cost the community an estimated $8 million per injury and have lifelong repercussions for crash victims.

The C-ITS Pilot project is part of the larger Cooperative and Automated Vehicle Initiative (CAVI) that TMR is delivering to help prepare for the arrival of new vehicle technologies with safety, mobility and environmental benefits on Queensland roads.

The CAVI project will also include the testing of a small number of cooperative and highly automated vehicles on South East Queensland roads, as well as investigate options for using emerging technologies to benefit pedestrians, cyclists and motorcycle riders.

Understanding climate a major part of Asia-Pacific dengue study

Climate and health are known to be linked. The impact of future climate change is likely to impact the distribution, burden and costs associated with infectious diseases such as dengue virus.


Associate Professor Wenbiao Hu

IHBI's Associate Professor Wenbiao Hu is using modelling that takes into account time and space to project the likely impact of dengue in Australia and five other countries in the Asia-Pacific region. The research will inform public health policies for enhancing dengue surveillance and risk management programs.

With funding from a National Health and Medical Research Council Project Grant, Associate Professor Hu is leading research that aims to harness advances in technology to develop an innovative early warning system for dengue.

Associate Professor Hu is collaborating with researchers from Sun Yat-sen University in China, London School of Hygiene and Tropical Medicine, the University of Queensland and the Mosquito Control Laboratory at QIMR Berghofer Medical Research Institute. The researchers will work closely with government departments in each of the six countries and obtain data from the Intergovernmental Panel on Climate Change.

Dengue is recognised as the world's most important arbovirus, a disease that mosquitoes transmit. The World Health Organisation estimates 3.9 billion people in 128 countries are at risk of contracting dengue. Not only is the number of dengue cases increasing as the disease spreads to new areas, but explosive outbreaks are occurring.

An estimated 50–100 million infections occur annually, accounting for 500 000 hospitalisations and 20 000 deaths.

'The large-scale re-emergence of dengue during the past few decades has renewed the disease status as a serious international public health problem, especially in tropical and subtropical areas in the Asia-Pacific region,' Associate Professor Hu says.

Dengue is prevalent in about 34 countries in the Asia-Pacific region. Although not naturally endemic to Australia, the dengue-transmitting mosquito *Aedes aegypti* is common in northern Queensland and outbreaks can occur when infected international travellers or residents returning from overseas provide an avenue for the virus to be transmitted to the local mosquito population.

Associate Professor Hu's collaboration builds on his previous research that suggests imported dengue cases trigger and enhance outbreaks in parts of Queensland under favourable weather conditions, especially in Cairns.

He says the geographical areas where imported dengue cases have been reported is expanding significantly in mainland Australia in the past decade.

'Our research will generate data that provides insight into the global origins of imported dengue and identifying Australian hotspots.'

There is an immediacy to the research, with global mean temperatures projected to rise between 1.1 and 6.6°C by the year 2100. Anticipated changes in the global temperature and rain patterns using present climate change scenarios will affect the biology and ecology of dengue-transmitting mosquitoes and increase the risk of transmission.

Rapid, unplanned and unregulated urban development, poor water storage and unsatisfactory sanitary conditions are also factors adding to the spread of dengue in the Asia-Pacific region.

Researchers will focus on Thailand, the Philippines, Vietnam, Indonesia and China, the countries with high incidence rates and the likely source of Australia's imported dengue cases.

Data will be compiled and linked for the countries, including meteorological factors such as temperature, rainfall, humidity, wind speed and direction; mosquito densities and control programs; and social and environmental factors such as population growth, urban development and vegetation.

Disease forecasting techniques used as part of the research will target specific communities with limited public health resources that are considered at high risk of an outbreak, with a view to improving health education and mosquito control and surveillance measures.

'The research will contribute to evidence-based policy making,' Associate Professor Hu says. 'The public health impact of climate change has not had sufficient prominence in government policies. Findings will provide important evidence on the benefits of reducing greenhouse gas emissions in the Asia-Pacific region.'

DENGUE VIRUS

A viral disease spread only by certain mosquitoes common in tropical areas around the world.

The world's fastest-spreading tropical disease.

Now present in more than 128 countries.

Symptoms may include a high fever, headache, vomiting, muscle and joint pains, and a characteristic skin rash. Recovery generally takes two to seven days. In a small proportion of cases, the disease develops into the life-threatening dengue haemorrhagic fever or dengue shock syndrome.


Dr Peter Lazzarini

Focus on feet aims to develop predictive tool for clinicians

Foot disease has a major impact on physical function, mental health and quality of life, but research related to hospitalisation has almost exclusively been conducted in populations of people with diabetes.

IHBI's Dr Peter Lazzarini is working to provide a more complete picture of foot disease, with the aim of developing a model that can predict which people are at risk of hospitalisation, amputation or even death.

Such a model has the power to enable clinicians, researchers and government agencies from around the world to measure, predict and take preventative actions.

Dr Lazzarini has a National Health and Medical Research Council Early Career Fellowship to support his research, in collaboration with experts from Brisbane Diamantina Health Partners, La Trobe University and the University of Amsterdam in the Netherlands.

Dr Lazzarini's research identified that only 40 per cent of people hospitalised for foot disease in Australia have diabetes, but most research in the field has almost exclusively focused on the disease.

'The research suggest that foot disease may be a much larger cause of all hospitalisation than first thought,' Dr Lazzarini says. 'In fact, we found it to be a top 10 cause of all Australian hospitalisations. It is vital that we investigate the incidence and predictors of foot disease hospitalisations.'

Dr Lazzarini's PhD studies found that 5 per cent of people in hospital had been admitted primarily for foot disease. 'From these findings we were the first to estimate an annual incidence of foot disease hospitalisations of 290 per 100 000 people at an annual cost to Australia of up to $3.8 billion.

'The findings indicate foot disease imposes a much larger burden on the Australian hospital system than we assumed. There is a need to more accurately identify potential predictors for all people with foot disease, not just those with diabetes, that may assist in targeting interventions to minimise future burden.

'With the world's population ageing and affected by chronic conditions for longer, it is important we properly investigate and understand the foot disease hospitalisation burden to inform health service planning – not just in Australia, but globally.'

Dr Lazzarini's fellowship involves analysing data from sources including the Australian Bureau of Statistics, the National Hospital Morbidity Database and the National Death Index, along with Queensland Foot Disease registries.

He will consider patient factors as potential predictors such as age, gender and socio-economic status; additional diseases, known as co-morbidities; existing foot conditions and past foot treatment; and history of hospitalisations.

'We hope the findings will enable clinicians managing patients with foot disease to better identify which of their patients, both living in the community and in hospital, need immediate and intensive care to prevent future hospital admission, amputation and death.

'It will also enable governments to directly compare the morbidity and mortality of foot disease with other diseases, such as heart, kidney and eye disease.'

The collaboration involves La Trobe University's Professor Hylton Menz, a global expert in the epidemiology of foot conditions; and Associate Professor Jaap van Netten, a joint QUT and University of Amsterdam appointment, a global expert in diabetic foot disease research.

IHBI Associate Professor Steven McPhail brings to the collaboration extensive epidemiology experience in analysing large datasets to inform and improve health service planning.

Dr Lazzarini is co-chair of Diabetic Foot Australia, a national peak body for diabetic foot disease with the goal of ending avoidable amputations within a generation in Australia.

FOOT DISEASE

Defined as ulcers, infection and ischaemia (poor blood supply) below the ankle.

THE FOOT'S ROLE IN DISEASE DETECTION

The foot is often the first place diseases, or symptoms of disease, are detected because the foot is the most distant part of the body from the brain and heart and its tissue's unique exposure to pressures from the ground when walking.

Dr Nathalie Bock

Laboratory modelling points way to personalised cancer care

Cancer is a complex disease that requires researchers to take into account the ability of cells to adapt, build therapeutic resistance and metastasise.

The challenges make it vital for researchers to work towards personalised medicine approaches, with treatment regimens and use of therapeutics tailored to individual patients.

IHBI's Dr Nathalie Bock is working on 3D models that mimic the human tissue microenvironment to enable studies of cancer development, progression and metastasis in the laboratory – and also test therapeutics for efficacy. Importantly, the models have the potential to one day replace testing conducted on animals.

Dr Bock is a Postdoctoral Research Fellow at the Centre for Regenerative Medicine at the Australian Research Council (ARC) Training Centre in Additive Biomanufacturing at IHBI and the Australian Prostate Cancer Research Centre – Queensland (APCRC-Q), based at the Translational Research Centre (TRI).

THE LUSH PRIZE

- **A joint project between Lush Cosmetics and the Ethical Consumer Research Association.**
- **Founded in 2012 to support initiatives to replace the use of animals in toxicology research.**
- **Open to scientists up to 35 years at the time of application.**
- **Up to 15 young researchers awarded each year.**

THE AUSTRALIAN PROSTATE CANCER RESEARCH CENTRE – QUEENSLAND

Aims to improve the clinical management of prostate cancer by developing better diagnosis and treatment strategies.

Spans the full spectrum of prostate cancer research, including discovery, diagnostic and therapeutic development, and health services.

The mission is to drive the development and translation of new therapeutics and biomarkers for prostate cancer through integrated and consolidated resources and expertise, national and international partnerships, and leveraged funding.

'I focus on recreating bone metastasis, when cancer has disseminated to the bones,' Dr Bock says. 'At that stage, present therapies are only effective in the short term and are likely to trigger cancer adaptation and resistance, processes that research fails to understand.

'It is essential to recreate the *human* bone tumour microenvironment in order to understand the mechanisms behind the adaptation so that efficient therapeutic strategies can be developed.'

Using human cells will overcome failures that result from testing conducted on animals, given the biological and physical differences and difficulties that flow from using results to predict human disease states.

'What works in animals may not working in humans.'

Dr Bock's work has been recognised with a 2017 Lush Prize, provided to support initiatives to replace the use of animals in toxicology research. She received the prize from Lush Cosmetics and the Ethical Consumer Research Association in London in November, as part of a schedule that involved networking with campaigners, lobbyists and scientists from around the world.

Associated funding will enable Dr Bock to improve her cancer models with the addition of bone-degrading cells called osteoclasts. The cells are known to play a key role in bone remodelling and metastasis.

Her models already contain bone-forming cells called osteoblasts and fat cells from patient-derived tissue.

Collaboration with Technical University Munich in Germany will enable Dr Bock to use an established protocol for generating osteoclasts from a patient's blood by spontaneous addition to her present osteoblast 3D model.

Clinicians from the Princess Alexandra Hospital will also have a collaborative role in Dr Bock's research, providing prostate cancer tissue recovered from radical prostatectomies. Upon isolation of cancerous cells, they will be introduced to her 3D models to recreate a metastatic bone tumour microenvironment for studying interactions between bone and tumour cells.

'Using the models will enable a deeper level of experimental manipulation,' Dr Bock says.

The 3D models will also enable screening of therapeutics such as anti-androgen treatments, bisphosphonates and repurposed medicines, testing for efficacy without having to be prescribed to patients – potentially saving them from receiving a cocktail of ineffective drugs.

'The platform is directly relevant because it uses human cells and tissue,' Dr Bock says. 'It provides more relevance to human disease than animal models.

'My ultimate goal is to offer clinicians a versatile platform for personalised medicine for any bone-metastasising cancer. By providing a human and patient-specific platform to clinicians, a variety of therapeutic options can be quickly tested and personalised treatments administered.'

Poorly understood infection the focus of infertility research

Chlamydia trachomatis is the most common sexually transmitted infection worldwide. The consequences on women are well established, including infertility and ectopic pregnancy, in which a fertilised egg implants outside the uterus. Consequences in men are largely ignored and underestimated.

Professor Ken Beagley

IHBI Professor Ken Beagley says men with *Chlamydia trachomatis* (Ctr) represent a major challenge, with figures showing that in 25 to 50 per cent of couples with fertility issues, the problem is with the male partner.

He also says up to 50 per cent of male infections are asymptomatic, or lacking in obvious symptoms, resulting in cases being untreated and allowing infection to spread to new sexual partners.

Funding from the National Health and Medical Research Council (NHMRC) is enabling Professor Beagley to conduct research that aims to investigate the role of particular cells in spreading Ctr, affecting male infertility and evading the immune system.

CHLAMYDIA TRACHOMATIS

The most common sexually transmitted bacterial infection worldwide.

Incidence of infection increasing in all countries.

Consequences in women include pelvic inflammatory disease, tubal factor infertility and ectopic pregnancy.

Undetected in most men. Standard urine test used clinically will not detect infection in the testis.

Possible cause of inflammation of the urethra, epididymis, prostate and testis in men.

The cells that the research focuses on are macrophages, responsible for detecting, engulfing and destroying pathogens such as Ctr.

Biological studies have already shown that within days of an initial Ctr infection at the penile urethra, *Chlamydia*-infected macrophages are readily detected in blood, enabling infection of the testis and disrupting the production of sperm.

Professor Beagley aims to study the role of *Chlamydia*-infected macrophages in transferring infection and their resistance to antibiotics.

'Our studies show that the levels of the antibiotic needed to clear *Chlamydia* growing in macrophages is up to 10 times higher than the dose needed to clear infected epithelial cells that line the male and female genital tract,' he says.

'It is possible that *Chlamydia* in macrophages will persist even after standard antibiotic treatment.'

Research from Professor Beagley's laboratory has provided ground-breaking evidence that *Chlamydia* infects three key cells in the testis, resulting in damage to sperm DNA. It reduces sperm motility, the ability to move spontaneously and actively; and the capacity to fuse with specific cells of the membrane, required before penetrating and fertilising the female egg.

'What this means is that chlamydial infection has long-term effects on sperm quality and has the potential to significantly impact male fertility,' Professor Beagley says.

Infected human macrophages will be used in his research to investigate the efficacy of antibiotic-loaded nanoparticles to clear *Chlamydia* from the testis, overcoming the limitations of normal antibiotic treatment.

IHBI Associate Professor Tim Dargaville has previously shown that the nanoparticles, made from a synthetic material, harmless to the body, that encapsulates antibiotics, increased the effective concentration of a therapeutic in specific tumour cells.

'We will determine if the nanoparticles are taken up by the macrophages,' Professor Beagley says, 'and how effectively the encapsulated antibiotics clear the infection.'

Figures show that 131 million new Ctr infections are reported each year. The Australian healthcare systems spends up to $160 million annually treating the infections, with the highest costs associated with infertility.

Between 70 million and 80 million couples around the world have infertility issues, including 1 in 6 Australian couples. Assisted reproductive technologies cost Australian couples more than $300 million each year.


Dr Johanna Kenyon

Harnessing bacteria to develop key pharmaceutical component

Research is contributing to a greater understanding of biological mechanisms and determining how they can be exploited to advance the field of medicine and industrial applications. One IHBI researcher aims to better understand bacterial glycans.

IHBI's Dr Johanna Kenyon is part of a collaboration involving researchers from Brisbane, Sydney and Russia looking at the synthesis, or development, of bacterial sugar structures with potential use in several industries.

The research involves glycans, one of the four fundamental classes of macromolecules that comprise living systems, along with nucleic acids, proteins and lipids. They are made up of individual sugar units linked to one another in a multitude of ways. The researchers aim to study the construction of bacterial glycans to pave the way for the creation of synthetic tailor-made structures with potent properties, called 'glycans-by-design'.

GLYCANS
Cell surface molecules attached to specific locations on many proteins, modulating aspects of their biological activity.

GLYCOSCIENCE
A transdisciplinary field aiming to better understand the structures and functions of glycans and how they can be used.

BIOLOGICAL PATHWAY
A series of actions among molecules in a cell that leads to a certain product or a change in the cell. Such a pathway can trigger the assembly of new molecules, such as a fat or protein.

SYNTHESIS
The execution of chemical reactions to form a more complex molecule from chemical precursors

BIOSYNTHESIS
The creation of an organic compound in a living organism, usually aided by enzymes.

All living cells are coated on their membranes with glycans or include glycan structures as integral components of their cell walls. They play diverse roles, including critical functions in cell signalling, a communication process that governs cell activities; molecular recognition, the interaction between molecules through bonding; immunity; and inflammation.

Recent advances have led to a greater understanding of many basic biological mechanisms, yet relatively little research has focused on glycans. Because glycans are made of different types of individual sugar units linked in multiple ways, large numbers of different glycan structures can be created from the same carbohydrate molecules.

Dr Kenyon will work with the bacterial species *Acinetobacter baumannii*, known to produce five of six specific types of carbon acidic sugars. The species forms the largest known reservoir of these unique biological sugar substances, two of which Dr Kenyon only recently discovered in *A. baumannii*.

'Our research will investigate the biosynthesis pathways of the acidic sugars produced,' Dr Kenyon says. 'That means looking at the way the compound is created in a living organism – in this instance, in the bacterial species.'

Dr Kenyon says a better understanding will open the door to enable tailoring of the acidic sugars that are produced. 'There is the potential to exploit the bacteria as high-throughput "eco-friendly factories" to produce complex glycans with properties that make them suitable for specific purposes such as pharmaceuticals.'

The glycans also have the potential to be used for new vaccines, enhanced cosmetic formulations and even for bioremediation of oil spills.

Dr Kenyon has the support of an Australian Research Council Discovery Early Career Researcher Award to undertake the work. It involves collaborating with Associate Professor Milton Kiefel, an organic chemist at Griffith University; Professor Ruth Hall, who investigates the mobility of DNA in bacteria at the University of Sydney; and the Russian Academy of Science.

She is part of IHBI's infectious disease research, with expertise in the genetics, biosynthesis and structure of surface carbohydrates from clinically important bacteria. Among her research interests is gaining an understanding of how the surface carbohydrates contribute to the survival of pathogens that cause hospital-acquired infections.

Glycans are an important part of the research, given their role in molecular recognition. One example is their role in the movement of white blood cells through the body to a site of infection, enabling the immune system to respond where needed.

Understanding glycans and applying the knowledge can help find solutions to a diverse set of challenges, including early detection through identification of biomarkers that point to the presence of disease. Protection against infectious diseases such as influenza has the potential to flow through increased understanding of the role of glycans in interactions and the immune response.

EXECUTIVE DIRECTOR'S REPORT

It is natural for people in the community to make the connection between medical research and improvements in their healthcare. What may not be immediately obvious is the work that goes on behind the scenes that evaluates technology, public policy and even ethics to ensure a seamless translation of research from the laboratory to the clinic.

One example is the research **Professor Andry Rakotonirainy** is leading in collaboration with industry, government and research partners to investigate the use of technology such as connected cars to improve road safety. The trial involves fitting technologies to about 500 cars to alert drivers to dangers such as red lights, road works, changing speed limits, traffic queues and hazards.

IHBI and QUT are contributing 12 researchers to the collaboration, enabling consideration of aspects including planning and design of future transport networks and services; driver behaviour and responses to the technology; and strategies for enhancing driver adoption.

Similarly, **Associate Professor Wenbiao Hu** is conducting research that will inform public health policies to improve health education; mosquito control and surveillance; and ultimately reduce the incidence of dengue virus. The scope is wide, involving government departments in six countries and insights into weather, mosquito densities and control programs, population growth, urban development and vegetation.

Dr Peter Lazzarini is widening the scope of understanding of foot disease, using technology to develop a model capable of predicting which people are at risk of hospitalisation, amputation or even death. It aims to help clinicians, researchers and government agencies measure, predict and take action to prevent hospital admissions.

Dr Johanna Kenyon is also aiming for better understanding, with a focus on biological mechanisms so they can be exploited to advance the field of medicine. She will work with a specific bacterial species to create a compound that can be used in a new generation of pharmaceuticals.

Bridging a similar knowledge gap is the research of **Professor Ken Beagley**. He is using nanoparticles to test their efficacy in clearing *Chlamydia* and overcoming the limitations of normal antibiotic treatment.

Ethics is a consideration in **Dr Nathalie Bock**'s research into cancer development, progression and metastasis. She is working on 3D models that mimic the human tissue microenvironment in a laboratory, enabling the screening of therapeutics without having to be prescribed to patients. Importantly, the models have the potential to one day replace testing conducted on animals.

The research aims to clear hurdles so treatments, therapeutics, education and public policies can be easily and effectively introduced for the improvement of healthcare. It may not be front of mind when the average person thinks of medical research, but it plays a major role in bringing about better health in our lifetime.

Professor Lyn Griffiths
Executive Director, IHBI

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