Sydney Medical Alumni Association and the University of Sydney School of Medicine magazine Spring 2019

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THE UNIVERSITY OF SYDNEY

Pathogen genomics research transforms disease control 04

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Researcher in a lab at the Marie Bashir Institute.

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Website: sydney.edu.au/medicine/alumni

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Edited by Michael Frommer, Office of the Executive Dean, and Kristen Barnes, Marketing and Communications, Faculty of Medicine and Health

Cover: Researchers from the Marie Bashir Institute conduct vital research in the lab.

Welcome to the Spring issue of *Radius*

As I write this, a distinguished external review panel appointed by the Australian Medical Council (AMC) has just completed its on-site assessment of proposed changes to the University of Sydney's Doctor of Medicine program. If approved, these changes will take effect for students commencing their first year in 2020. Forward-looking and innovative, the 'MD2020' program is designed to give students an easier transition into medicine from their previous studies and a greater range of opportunities to explore their areas of interest, while strengthening their readiness for internships. We hope the revised MD program will serve the needs of our communities and graduates well into the mid-21st century.

While the outcome of the review is not yet known, the panel has generously commented on the commitment and enthusiasm of all those involved in designing the program, their strong spirit of collaboration, and the educational creativity evident in the changes.

Similar commitment, collaboration and creativity characterise Sydney Medical School's research. In this issue of *Radius*, we report on important research outcomes in the field of biosecurity. Future issues of *Radius* will concentrate on one of the fields of health and medical research in which the University of Sydney has been conspicuously successful.

Awards are another mechanism by which we can recognise and reward excellence in all areas of scholarship, which is why I am privileged to introduce the new Ruthven Blackburn Medal for Distinguished Contribution to Clinical Research.

The medal commemorates the life's work of Professor Charles Ruthven Bickerton Blackburn AC (1913–2016), a pioneer of clinical research. In his roles as Bosch Professor and Head of the Department of Medicine for 21 years, he was committed to linking research to patient outcomes; building clinical research capacity at our teaching hospitals. He also dedicated himself to the development and mentoring of a generation of eminent clinical and research leaders.

The new Ruthven Blackburn Medal for Distinguished Contribution to Clinical Research

Our intention is to award the medal every second year to a senior academic staff member of Sydney Medical School in recognition of a sustained, distinguished and notable contribution to clinical research and a demonstrated commitment to mentoring junior colleagues.

Sydney Medical School is planning to celebrate another great figure in the faculty's history: Sir Thomas Peter Anderson Stuart, Professor of Anatomy and Physiology and Dean of Medicine from 1883 until his death in 1920. We will be inviting readers of *Radius* to celebrate his legacy on 29 February 2020, the centenary of his death.

This is my last contribution to *Radius* in my current role because I will be stepping down on 30 September 2019. I would like to thank our readers for their support of *Radius* and continuing support of the University of Sydney and its Medical School.

Professor Arthur Conigrave BSc(Med) '79 MBBS '82 MSc '83 PhD '92 MD '08
Head of School and Dean of Sydney Medical School

New options to study surgery

In 2020, Sydney Medical School will introduce a new postgraduate degree program in surgery.

Students will now have the option to take a Master of Surgery, Graduate Certificate or Graduate Diploma in Surgery, or a Graduate Certificate in Surgical Sciences.

The graduate certificate, graduate diploma and master's degree are intended for medical graduates, and were designed to enhance students' understanding of evidence-based medicine and improve their clinical decision making. With a new compulsory capstone unit, the Master of Surgery will also help participants gain non-technical skills in leadership and professionalism.

Given the wide choice of units, students will also be able to tailor their studies to match their stage in surgical training while still developing their sub-speciality interests in areas like vascular surgery, urology, endoscopy and microsurgery.

The Graduate Certificate in Surgical Sciences is also open to medical students who may enrol in their final year of a medical degree to advance their preparation for training positions in surgery.

Surgical sciences units of study across the program have been revised, and are specifically intended to prepare candidates for the Generic Surgical Sciences Examination conducted by the Royal Australasian College of Surgeons (RACS).

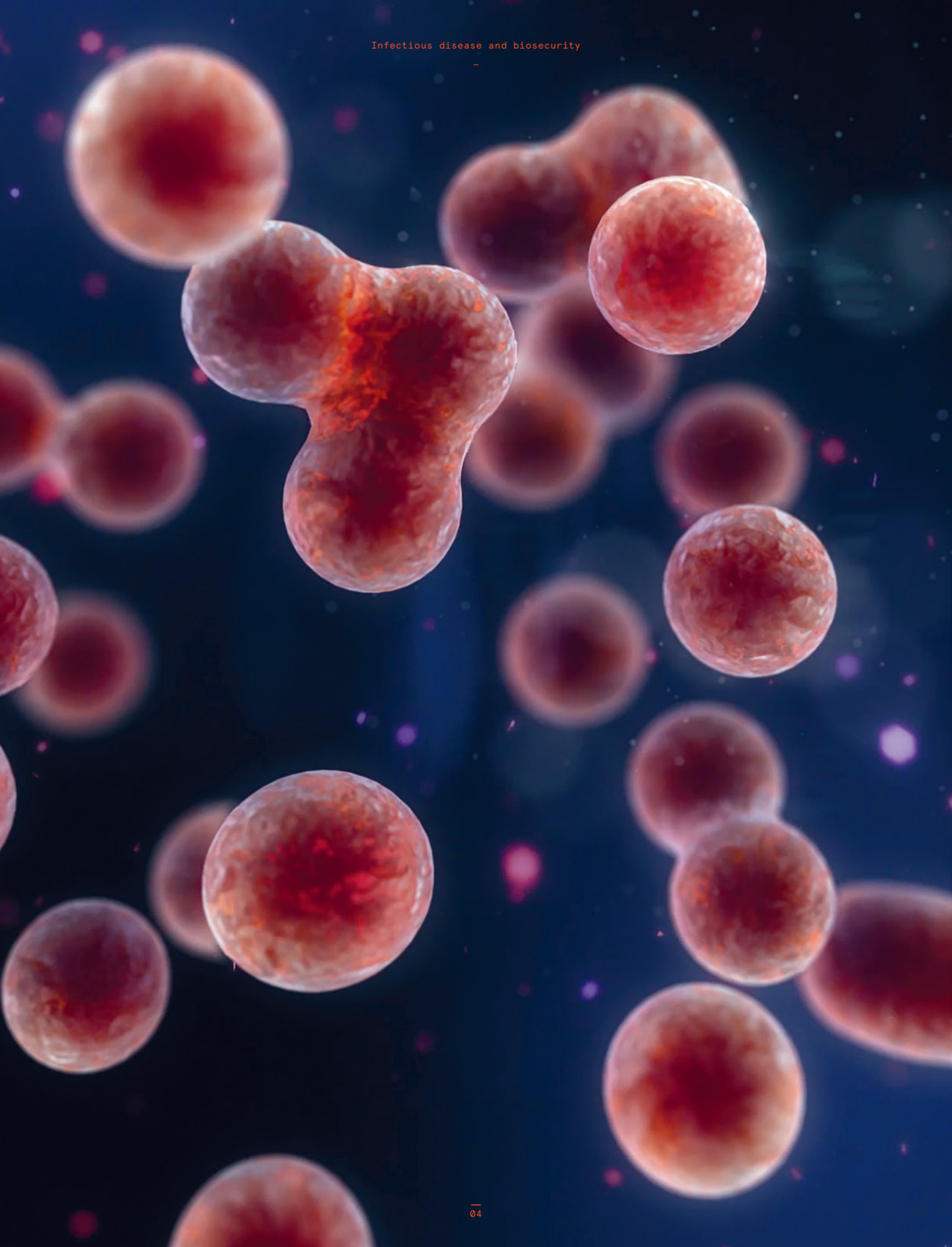
Participants in any of the courses can upgrade (for example, from a Graduate Diploma to a Master of Surgery) or downgrade, offering greater flexibility than ever before.

Medical students enrolled in the Graduate Certificate in Surgical Sciences can also upgrade to the Graduate Diploma in Surgery or the Master of Surgery on completion of the requirements.

The Graduate Certificate in Advanced Clinical Skills (Surgical Anatomy) will continue to be offered as a separate course in whole-body cadaver dissection.

All coursework units of study in the Master of Surgery are accredited by the RACS. The majority of units of study are taught entirely online, with the exception of anatomy and microsurgery, which are taught face-to-face. Some units require attendance at specified workshops.

For more information, visit:
- sydney.edu.au/medicine-health/surgery



Pathogen genomics research transforms disease control

Research linking public health and genomics has led to game-changing approaches to the control and prevention of communicable disease outbreaks.

Written by Professor Vitali Sintchenko
Institute of Clinical Pathology and Medical Research, Westmead Hospital

For many years, communicable disease outbreaks have been managed using a number of time-consuming investigative tactics. Tracing the cause of the epidemic involved investigating the characteristics of the people affected, doing detective work to identify the causative pathogen, working out the mechanics of the spread and then introducing control measures.

Researchers at the University of Sydney and Westmead Hospital recently developed a faster, more accurate and potentially more economical approach to disease control by studying the genome of affected people using body fluid samples, such as blood or respiratory secretions.

Following this breakthrough, NSW Health Pathology officially launched a state-wide public health pathogen genomics service designed to assist communicable disease control. This service will be offered at the Institute of Clinical Pathology and Medical Research (ICPMR) at Westmead Hospital where a new unit has been formed.

Established in July 2019, this landmark development is the culmination of a decade of translational research led by Professor Lyn Gilbert AO and Professor Tania Sorrell AM.

The research brought together microbiologists from the University of Sydney School of Medicine, as well as specialists in public health, epidemiology, microbiology and genomics.

More specifically, it was a long-term collaboration between clinicians and scientists from the Centre for Infectious Diseases and Microbiology-Public Health (CIDM-PH) at Westmead Hospital, NSW Health Pathology-ICPMR, the Westmead Institute for Medical Research and Westmead Clinical School.

The team recognised that next-generation sequencing technology enabled high-resolution, genome-wide examination of pathogens unequalled by other contemporary methods using gene-by-gene comparisons. They also realised the significance of applying this genomic technology to public health laboratory surveillance and outbreak detection.

In addition, they realised that for genomics to be truly transformational, it must generate the diagnostic data sufficiently and rapidly to support public health action, so a capacity for rapid sequencing and analysis of pathogens was required.

The work began in 2011 when a next-generation benchtop gene sequencer was procured as a result of a generous donation from the Raymond E Purves Foundation. This enabled researchers, for the first time, to develop and evaluate testing and analysis pipelines where all pre-analytical, sequencing and post-analytical steps were controlled and adjusted to maximise the clinical and public health value of results.

We now understand that transmission is an evolutionary event that can have a major effect on the extent and structure of genetic diversity as it flows through the population.

This new capability supported several successful National Health and Medical Research Council (NHMRC) grants and was utilised by three NHMRC Centres of Research Excellence (CREs): the CRE for Critical Infectious Diseases (led by Professor Jonathan Iredell at Westmead), the CRE for Tuberculosis Control and Prevention (Professor Warwick Britton AO, Royal Prince Alfred Hospital), and the CRE for Emerging Infectious Diseases (Professor Sorrell).

The team of clinicians and researchers involved in applied genomics research grew in numbers and expertise. From the beginning, researchers have recognised the importance of cross-disciplinary engagement to maximise the power of genomics and the critical role of informatics.

This has emerged as a critical element of translational biomedicine due to rapid advances in bacterial genomics, pathology informatics and molecular diagnostics. Epidemiologists from NSW Health Protection have also become essential partners in the research.

The establishment of the Marie Bashir Institute for Infectious Diseases and Biosecurity (MBI) by the University of Sydney in 2013 has provided a powerful boost to the agenda of communicable disease control.

The partnership between MBI, CIDM-Public Health and NSW Health Pathology-ICPMR has led to further enhancements in the pathogen genomics capability across campuses.

The NSW Pathogen Genomic Initiative put forward by this partnership attracted $1 million of infrastructure funding from the NSW Ministry of Health.

This enabled the upgrade of next-generation sequencing equipment and led to multiple collaborative projects with staff from Royal Prince Alfred Hospital, the Woolcock Institute of Medical Research, St Vincent's Hospital, the Prince of Wales Hospital and the University of New South Wales.

Activities of MBI and CIDM-PH have provided evidence and examples which led to the recognition of pathogen genomics in the NSW Health Genomics Strategy as an important case study for implementation.

The appointment of Professor Edward Holmes as Professor of Evolutionary Biology in the University's School of Life and Environmental Sciences has broadened the scope of research and facilitated evolutionary approaches to the analysis of microbial genomes.

This has demonstrated that ongoing genomic surveillance can identify determinants of transmission, monitor pathogen evolution and adaptation, ensure the accurate diagnosis of infections with epidemic potential, and refine strategies for their control. Critically, the evolutionary analysis of pathogen genome sequence data allowed epidemiological hypotheses to be tested, often in real time.

The real milestone in the transition of pathogen genomics from bench to practice was the award of the NSW Health Translational Research grant in 2016, aimed at translating pathogen genomics into improved public health outcomes.

The grant was led by Professor Jonathan Iredell and myself. The findings provided justification for the establishment of the NSW state-wide public health pathogen genomics service, which is a node of the Communicable Disease Genomics Network.

The research has helped the NSW Health Protection, Food Authority and OzFoodNet to identify the point sources of transmission sooner and with greater precision than before, and to determine the magnitude of outbreaks.

We have applied genomics approaches to the analysis of strains, allowing us to separate clusters of infections transmitted locally from multiple independent importations of drug-resistant strains from overseas.

Exterior view of Westmead Hospital where the new state-wide public health pathogen genomics service was launched.

In addition, researchers have played a key role in the development and implementation of standard operating procedures and laboratory protocols for bacterial genome sequencing and staff training, leading to accreditation of the ICPMR laboratory for genomics surveillance and drug resistance testing by the National Association of Testing Laboratories.

An example of the application of pathogen genomics is the tularaemia bacterium, which was first identified at the Westmead laboratory as the cause of ulcerative human skin infections in Tasmania. The infections were found to have been acquired through close contact with ringtail possums that carried the same strain.

Genomics also enabled researchers to find missing links in a chain of person-to-person tuberculosis transmission in NSW, finding individuals who were 'silent' transmitters and helping to stamp out the infection.

Experience of pathogen genomics research has confirmed the wisdom of "looking within for value and beyond for perspective". Pathogen genomics has not only improved public health response to disease outbreaks, but has also revolutionised our understanding of the mechanisms of disease transmission.

It has moved from the simplistic view that the spread of diseases is determined mainly by the mechanics of human contact or of contact between a sick animal and a human body. Rather, we now understand that transmission is an evolutionary event that can have a major effect on the extent and structure of genetic diversity as it flows through the population.

Overall, it is clear that the insights provided by pathogen genomics have fundamentally changed our collective understanding of the long-term global and short-term local spread of communicable diseases.

New approaches to the treatment of severe malaria

University of Sydney medical science researchers are investigating novel treatment methods to increase survival rates of severe malaria, combining specific immune-modifying therapies and anti-malarial drugs.

Written by Professor Nicholas King

Malaria is caused by several species of the *Plasmodium* parasite and is spread by mosquitoes, principally in Africa and Asia. In 2015, the World Health Organization (WHO) estimated the number of global malaria cases to be in excess of 200 million.

More than 400,000 of these cases resulted in death due to complications of severe malaria, with children under five accounting for more than 70% of deaths. Of these, 99% were infected with *P. falciparum*.

In severe malaria, infection of the red cells by the malaria parasite makes them stick to the blood vessel wall in the brain and lungs. White blood cells accumulate around the sticky red cells, gradually blocking the flow of blood to these organs, causing seizures, respiratory distress, coma and death.

The WHO recommends parenteral artesunate for 24 hours to treat severe malaria, followed by two days of artemisinin-based combination therapy with quinine-based drugs.

Despite the use of this medication, overall mortality is still 10 to 20 percent, because this treatment does not reduce the accumulation of cells.

With increasing resistance to recommended malaria medications and no current new anti-malarial drug or vaccine candidates, adjunctive therapies, such as immune-modifying therapy, combined with anti-malarial drugs, offer a novel potential avenue to reduce mortality.

To investigate potential approaches, we first used high parameter flow cytometry to characterise in detail the white blood cell accumulation in the brain and lung in a mouse model of severe malaria using *P. berghei* ANKA (PbA), which replicates more than 25 features of the human disease.

Using clustering analysis, we uncovered a specific population of monocytes, Ly6C^{lo}, present in much higher numbers than any other cell type. Previously thought to be the housekeeping cells of the blood vessels, Ly6C^{lo} are actually a major contributor to the accumulating cells in both brain and lung and therefore a potential target for therapeutic intervention.

This unprecedented discovery was enabled using the cutting-edge equipment and analysis techniques available in Sydney Cytometry, a core facility of the University of Sydney.

Under homeostatic conditions, Ly6C^{lo} monocytes originate in the bone marrow, their precursors emigrating in a constant trickle into the blood stream as inflammatory monocytes expressing high levels of Ly6C, which are quickly down-regulated as they become homeostatic monocytes.

In response to acute inflammatory stimuli, however, Ly6C^{hi} inflammatory monocytes start to emigrate from the bone marrow in large numbers within a few days. Their increased manufacture here displaces that of B cells and neutrophils.

Homing via the blood to inflammatory foci, the presence of large numbers of inflammatory monocytes is a hallmark of many diseases caused by infection, autoimmunity and tissue damage. Indeed, these cells are responsible in large part for the associated morbidity and mortality.

We have previously shown that intravenous administration of negatively-charged, immune-modifying particles (IMP) reduce inflammatory monocyte infiltration, markedly increasing survival and improving recovery in a range of monocyte-mediated inflammatory disease models.

To confirm that the Ly6C^{lo} monocytes in the cellular accumulations in the brain and lung could arise from Ly6C^{hi} monocytes, we intravenously transferred pure, marked populations of Ly6C^{hi} monocytes isolated from the bone marrow into PbA-infected mice 24 hours before the onset of cerebral malaria (CM).

Within this period, transferred cells had homed to the brain and lung and down-regulated their Ly6C expression, consistent with our hypothesis that bone marrow-derived inflammatory monocytes were the likely precursors of the accumulating Ly6C^{lo} cells in CM and acute respiratory distress syndrome (ARDS).

To show further proof-of-principle, we then infused IMP on day 4 post infection, the timepoint at which monocytes first begin to accumulate in the brain as Ly6C^{hi} monocytes, well before the appearance of disease signs, to see if we could prevent the onset of CM.

In these experiments, some 50% of the mice survived an otherwise 100% lethal infection, with reduced monocyte numbers in the brain and lungs and reduced clinical disease scores. Not surprisingly, however, as IMP have no anti-malarial action; survivors subsequently showed an increasing concentration of parasites in their blood, which we abolished with quinine treatment.

Since patients do not usually present in advance of disease signs or symptoms, we treated infected animals at the onset of CM signs with artesunate in accordance with WHO protocol, combining it with IMP.

Strikingly, survival in mice treated with combination therapy was almost 90%, while in mice treated with artesunate or IMP alone, survival was 56% and 10% respectively.

Survival statistics were reflected in the clinical scores in each group, but more importantly, the markedly reduced vascular occlusion and interstitial infiltration respectively, in the brain and lung, further borne out by significantly reduced Ly6C^{lo} monocyte numbers in both organs.

Notably, the combination of IMP and chloroquine (quinine-based) also gave this result. This is interesting, as chloroquine alone is much less effective at this late stage than artesunate alone. More interestingly, on a PbA re-challenge, all survivors quickly cleared the parasite without CM signs, suggesting a robust anti-malarial immunity not previously seen in this model.

We have yet to fully understand the mechanism of action of this combination treatment. For example, since IMP act by sequestering Ly6C^{hi} cells in the spleen, we do not understand how artesunate enables IMP to effectively clear Ly6C^{lo}monocytes already occluding the cerebral blood vessels at the onset of CM, when IMP alone are minimally effective.

Nor do we understand how protective anti-malarial immunity is enabled or what elements are involved.

Nevertheless, these results are a first in any pre-clinical CM or ARDS model. They emphasise the immunopathological nature of monocyte accumulation in severe malaria and are proof-of-principle of the potential efficacy of combining specific immune-modifying and anti-malarial therapy, which almost doubled the survival seen with artesunate treatment alone.

This approach could markedly improve human recovery as well as potentially curbing the spread of drug resistance.

This article is based on a collaboration between Nicholas King and Georges Grau. For the full report with sources, refer to: Niewold P, Cohen A, van Vreden C, Getts DR, Grau GE, King NJC. Experimental severe malaria is resolved by targeting newly-identified monocyte subsets using immune-modifying particles combined with artesunate. *Communications Biology* 1:227. (2018)

Research insights: Marie Bashir Institute

In the seven years since the inception of the Marie Bashir Institute, a significant amount of multidisciplinary research has taken place across the Asia-Pacific region to advance our understanding of infectious diseases.

Written by Kristen Barnes

The Marie Bashir Institute for Infectious Diseases and Biosecurity (MBI) was first conceptualised by the then Dean of Medicine, Professor Bruce Robinson AM, while he was travelling through Indonesia in 2009.

"Witnessing a bird flu outbreak firsthand, he realised that collaboration would be required from many disciplines to control the rapid spread of infectious diseases like influenza," explains Professor Tania Sorrell AM, MBI Co-Director and Professor of Clinical Infectious Diseases at the University of Sydney.

On his return to Australia, Professor Robinson coordinated a meeting of 30+ staff from various faculties to establish an infectious disease and biosecurity network led by Professor Sorrell. The network would later be known as the Marie Bashir Institute, named after the Hon. Professor Dame Marie Bashir AD CVO, former Governor of New South Wales, Chancellor of the University, and a psychiatrist committed to helping the marginalised.

MBI's objectives and vision have remained consistent since the network's establishment. "Our goal is to reduce the health and socioeconomic consequences of emerging infectious diseases, particularly in the Asia-Pacific region," says Professor Sorrell.

Professor Tania Sorrell

"We hope to achieve this through research, education, capacity-building and advocacy work with government and professional societies, and through communication with the public. Essentially we want to answer questions surrounding the control and containment of infections and antimicrobial resistance."

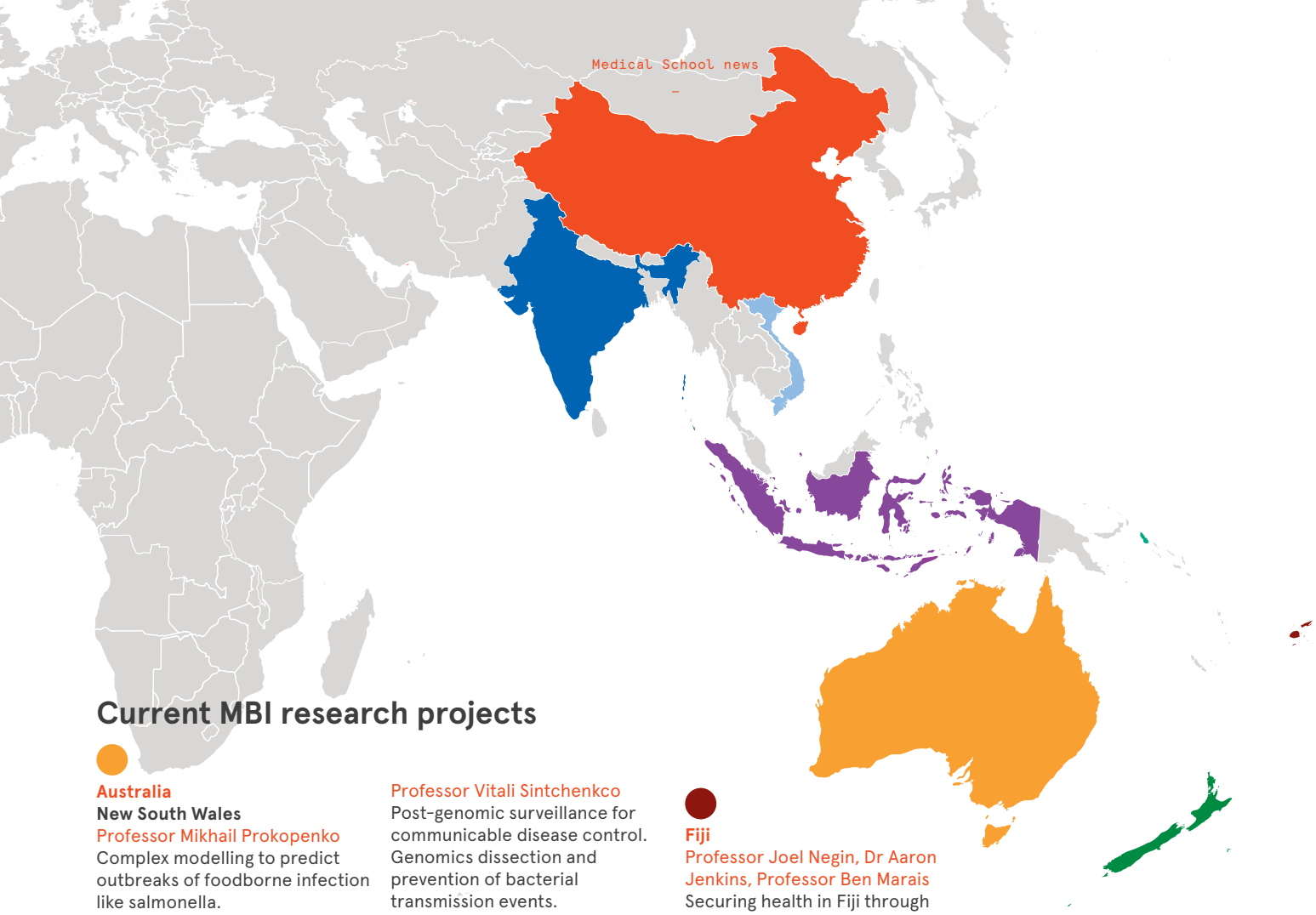
MBI is a virtual institute operating across three main campuses – Camperdown, Westmead and Camden. The internal framework was developed around research themes (or nodes) involving at least three disciplines or schools, to promote multidisciplinary collaborations.

The institute has now grown to 160 members, many of whom are established research leaders who have obtained grants to pursue projects with international collaborators all over the world.

"We've been extraordinarily successful," says Professor Sorrell. "Our return on investment is one of the highest at the University – we attract more than $10 million in multidisciplinary competitive research funding as well as other major funds, each year. We've facilitated the recruitment of some high-level academics to the University. We have also previously offered the Master of Health Security degree, and have run a number of workshops in partnership with the World Health Organization relating to emerging diseases."

Professor Sorrell is internationally renowned for her research on cryptococcus and other fungal infections. She has made major contributions towards our understanding of fungal diseases and continues to take part in much of the key research that happens at the Marie Bashir Institute.

Learn more about MBI's projects:
– sydney.edu.au/marie-bashir-institute



Current MBI research projects

Australia

New South Wales

Professor Mikhail Prokopenko
Complex modelling to predict outbreaks of foodborne infection like salmonella.

Dr Philip Britton
Discovering the infectious causes of unknown encephalitis cases using genomic approaches.

Northern Australia

Professor Tania Sorrell
Improving health outcomes in the tropical north.

Remote Australia

Associate Professor Tess Lea
Housing for health: fixing infrastructure and housing policy in Indigenous Australia and beyond.

Australia – general

Professor Tania Sorrell, Professor Vitali Sintchenko, et al.
Protecting the public from emerging infectious diseases.

Professor Tania Sorrell, Professor Angus Dawson, Professor Lyn Gilbert
An Australian partnership for preparedness research on infectious disease emergencies.

Professor Sarah Palmer
Addressing the major challenges in HIV vaccine and cure research.

Professor Vitali Sintchenkco
Post-genomic surveillance for communicable disease control. Genomics dissection and prevention of bacterial transmission events.

Professor Edward Holmes
Redefining virus ecology and evolution. Using metagenomics to determine the causative agent(s) of tick-borne disease in Australia.

Professor Jonathan Iredell
Tackling antimicrobial resistance as a public health problem using non-antibiotic approaches. High-throughput technology targeting antimicrobial resistance in animals.

Bougainville Island, Papua New Guinea

Professor David Guest, Professor Merrilyn Walton
Sustainability and profitability of cocoa-based farming systems on Bougainville Island and Indonesia.

China

Professor Edward Holmes
Investigating viruses and the use of metagenomics for identification of respiratory infections.

Fiji

Professor Joel Negin, Dr Aaron Jenkins, Professor Ben Marais
Securing health in Fiji through strengthened health systems and integrated water management to tackle the three plagues: typhoid, dengue and leptospirosis.

India

Dr Michael Walsh
The elephant livestock interface in forest fringe areas to the risk of anthrax outbreaks in India.

Associate Professor Adam Kamradt-Scott
International health regulation compliance in India: the politics of global health security.

Indonesia

Professor Merrilyn Walton
Piloting an empowerment program for cocoa farmers in West Sulawesi.

New Zealand

Professor Merrilyn Walton
A One Health collaboration investigating animal and human health interfaces.

Vietnam

Associate Professor Greg Fox, Professor Ben Marais
Prevention of multi-drug-resistant tuberculosis in a high prevalence setting in Vietnam.

Associate Professor Greg Fox, Professor Joel Negin et al.
Combating the emergence and spread of antimicrobial-resistant infectious diseases in Vietnam.

Associate Professor Greg Fox, Professor Joel Negin
An integrated health sector strategy to combat chronic obstructive pulmonary disease (COPD) and asthma in Vietnam.

Associate Professor Adam Kamradt-Scott
Civil and military connections to health outbreak responses in resource-poor settings, particularly in the lower Mekong Delta region.

The University of Sydney introduces professional certificates in medicine and health

New short courses enable postgraduate study for practitioners.

Written by Kristen Barnes

In 2020, a series of professional certificates, each comprising two units of study will be introduced by the Faculty of Medicine and Health. Many of these micro-credentials will come from the University of Sydney School of Medicine – the leading provider of postgraduate vocational coursework for clinicians in Australasia.

These carefully curated postgraduate medicine micro-credentials are the first of many professional certificates that will be available across the University in years to come. Designed to deliver specialised opportunities for lifelong learning to clinicians and healthcare professionals, medicine micro-credentials will help participants stay up to date with the latest technologies, treatments and techniques.

"Once you finish University, the responsibility for learning falls on the individual," says Associate Professor Annette Katelaris, Director of Professional Medical Education at the Sydney Medical School.

"Professional certificates will change the way that medical practitioners engage in continuing education, by providing structured programs in compact packages."

These new programs complement, but are different from, pre-existing postgraduate degree courses within the School of Medicine given their highly targeted course content and short duration.

They are best suited to time-poor advanced practitioners who may have identified a knowledge gap or who want to pursue a subspecialty while maintaining all of their existing commitments.

"If you're a GP and the vast complexity of diabetes management has got away from you, you can come and learn in a case-based environment how to manage complex diabetic patients," says Associate Professor Katelaris.

"Likewise, if you're an anaesthetist and you want to master intraoperative neuromonitoring (IONM), you can come back and do a structured course in this area.

"There has also been rapid progress in many other fields of medicine. For example, traditionally breast surgeons would treat the cancer and the plastic surgeon would reconstruct the breast. Now there's a change in practice so that both procedures occur in the same operation. To respond to this development, we're offering study in oncoplastic breast reconstruction for breast surgeons," she adds.

These new programs provide the opportunity for established practitioners to undertake only the areas of study of their choosing, rather than completing a whole postgraduate degree. The coursework is delivered online and some units have one or two practical day workshops for skills training.

Dr Adam Hastings, University of Sydney Program Director for postgraduate courses in clinical neurophysiology in the operating theatre.

If students wish to pursue further study in a particular field, a corresponding degree program is available and completed units of study can be credited to a degree, provided the relevant requirements are met.

Embracing a new educational trend to provide specialised study opportunities in a shorter format, the University believes micro-credentials will make postgraduate coursework more accessible to a wider range of people.

“Usually in medicine, after completion of training, practitioners use journals, conferences and seminars to stay up-to-date. While these are essential, there remains a role for curated and assessed learning so that content is studied systematically and the learner receives feedback on what they know and their gaps in knowledge.

“Professional certificates will help health professionals to identify what they really need to know and it will help them to assess whether they have mastered important knowledge and skills,” explains Associate Professor Katelaris.

We offer Sydney Professional Certificates in the following specialities:

- Commercialisation of Pharmaceutical and Medical Devices
- Complementary Medicines Regulation
- Diabetes Management
- Diagnostic Electroencephalography (EEG)
- Fundamentals of Immunotherapy
- Intensive Care Medicine
- Intraoperative Neuromonitoring
- Metabolic Health
- Metabolic Management
- Neurological Electrodiagnosis
- Oncoplastic Breast Surgery
- Orofacial Pain Science
- Psychology of Pain
- Retrieval Medicine

Learn more:
- sydney.edu.au/medicine-health/professional-certificates

University of Sydney trade booth at the Sydney Convention and Exhibition Centre for the Global Health Security conference.

World-first gathering showcases health security's past and future

Sydney demonstrates its global leadership in health security.

Written by Jennifer Peterson-Ward

More than 900 members of the global health security community gathered in Sydney recently to participate in the first international scientific conference on global health security. The event was organised by Associate Professor Adam Kamradt-Scott from the University of Sydney Centre for International Security Studies and Associate Professor Rebecca Katz from Georgetown University in the United States.

Participants came from more than 65 countries, representing academia, local, national and international

Associate Professor Adam Kamradt-Scott stands with Professor Rebecca Katz in front of the Sydney Statement on Global Health Security board.

governmental and non-governmental organisations, public and animal health and security professionals, and the private sector, all committed to advancing global health security.

High-profile speakers included Australia's Federal Minister for Health, the Hon. Greg Hunt MP, and representatives from the NSW Government, Peter Sands from the Global Fund for HIV/AIDS, TB and Malaria , the Assistant Director-General and Regional Directors from the World Health Organization, and leaders from the US Centers for Disease Control and Prevention, Médecins Sans Frontières, the Bill and Melinda Gates Foundation and many more.

As well as highlighting research, policies and best practice from around the world, the conference also provided a platform to establish a health security 'community of practice'.

At the conference, members of the global health security community endorsed a guiding set of principles to address global health security threats – from disease outbreaks to biological warfare.

The Sydney Statement for Global Health Security describes the numerous challenges that pose significant risk to global health and involves seven primary principles to guide and inform addressing future threats.

"In the wake of the 2014 West African Ebola outbreak, the international spread of the Zika virus, the ongoing transmission of antimicrobial resistance, and the ever-present threat of another influenza pandemic, global health security has taken on a new level of importance," Associate Professor Kamradt-Scott says.

"Whether they begin in humans or animals, these infectious diseases and public health emergencies cause not only loss of human life, but also massive social, economic and even political change.

"Achieving global health security requires collaboration across disciplines, industries and seniority, and Professor Katz and I are thrilled that our conference was able to bring together members of the global health security community for the first time to measure progress, determine gaps, and identify new opportunities to enhance national, regional and global health security."

The Global Health Security 2019 Conference was sponsored by the University of Sydney.

Prior to the official start of the conference, the University also hosted a two-day Military Health Security Summit, jointly sponsored by the US military and Australian Defence Force to discuss the role of militaries in global health.

The event involved 170 participants from the Indo-Pacific region and was the first meeting of its kind.

Participants discussed a range of topics extending from humanitarian assistance and disaster relief, research and development, and civil-military coordination.

Mycobacterium tuberculosis

Improving TB detection in Vietnam

Leading large clinical trials in Vietnam, Associate Professor Greg Fox is addressing the problem of tuberculosis (TB) case detection in endemic settings using active screening and a modern new molecular test.

Written by Kristen Barnes

Affecting 10.4 million people each year, TB is the leading infectious cause of death worldwide. In 2017, almost two million people died from this illness, most in low and middle-income countries.

TB is a treatable respiratory disease and, if detected early, can usually be completely cured with antibiotics. Despite this, morbidity and mortality rates remain high because of under-diagnosis. According to the World Health Organization, one third of people with TB are never diagnosed.

To tackle this case detection gap, Associate Professor Greg Fox has been evaluating the effectiveness of active screening in Vietnam. His work aligns with the WHO End TB Strategy, which aims to eliminate TB by the middle of the century and reduce TB deaths by 95 percent before 2035.

More than 35,000 people across Vietnam participated in ACT2, the initial randomised controlled trial conducted by Associate Professor Fox and his team. Their findings have the potential to transform global TB control efforts.

“A key driver of the high mortality and continuing transmission of TB is the substantial gap between the number of people with the disease

and the number who are detected," Associate Professor Fox explains.

"Our research tested the effect of new active screening strategies on TB detection and risk of death. In the two years after participation in our study, the number of cases that were detected more than doubled in the active screening intervention group. The study also showed that screening for TB reduced the risk of death."

The second trial, led by Professor Guy Marks and Associate Professor Fox (ACT3), evaluated the effectiveness of a new molecular diagnostic test called GeneXpert in diagnosing TB, requiring sputum specimen from 23,000 people.

"We found that the GeneXpert test was substantially more accurate than previously recognised," says Associate Professor Fox. "The specificity of GeneXpert was at least 99.78%, with a positive predictive value of at least 61%.

"These findings show, for the first time, that molecular methods are highly accurate when used as screening assays for TB, and are suitable for community-wide screening. This novel approach may transform active case finding for TB in moderate risk populations."

The two trials have had major implications for global TB reduction efforts. The results provide the evidence required to justify the expansion of programs to screen household contacts of TB patients to high-burden settings.

Associate Professor Fox developed an interest in international health through short placements in Malawi and Timor-Leste during his medical training. He later completed a Master of International Public Health degree at the University of Sydney before pursuing a research pathway.

Associate Professor Greg Fox attends a meeting in Hanoi in 2018 for the VRESIST study.

Professor Guy Marks, Associate Professor Greg Fox and Dr Nguyen Thu Anh receiving a national award from the Ministry of Health in 2019.

His interest in research stems from a commitment to improving the health care of disadvantaged communities in low and middle-income countries.

He was awarded the University of Sydney Cornforth Medal for PhD achievement in 2013 after completing extensive research on TB which was later published in the *New England Journal of Medicine*.

In the years since the initial studies were completed, he has worked with collaborators from the Vietnam National TB Program to determine ways to increase case detection. This included the completion of ACT4, a six-country randomised controlled trial conducted in partnership with McGill University in Canada, which has provided evidence that will help countries to scale up screening and treatment for latent TB infection.

"Thanks to the commitment of our Vietnamese colleagues, contact investigation has been implemented routinely throughout the two provinces of Vietnam participating in the ACT4 study, and it will be implemented nationally over the coming years," says Associate Professor Fox.

Influential alumnus makes impact on medical community

The University of Sydney School of Medicine alumnus and philanthropist, Dr Barry Catchlove AM, led an extraordinary career in healthcare management. He has also made a significant contribution at the University, generously supporting young researchers.

Written by Kristen Barnes

Dr Barry Catchlove AM graduated from Sydney Medical School in 1966. When he started the program at the age of 16, his cohort of 800 was the largest of its size since the influx of students following the Second World War. At the time, the University of Sydney was the only medical school in New South Wales.

After completing his medical studies and training as a physician at Royal Prince Alfred Hospital, Dr Catchlove pursued an impressive career in healthcare management spanning five decades. He took on a number of varied roles in operations and management, leading reform in public and private hospitals across Australia.

Dr Catchlove's journey in the medical community came full circle in the '90s when he was approached by Sydney Medical School to lead another kind of reform – to continue to engage alumni through a variety of initiatives, initially as President of the Medical Alumni Association and then President of the University's Alumni Council. This led to six years representing alumni on the Senate of the University.

"When I was a student, I was involved with a wide range of projects like the yearbook and the Lambie-Dew Oration, so I had a big group of contacts," explains Dr Catchlove.

He felt that volunteering for the University was a good way to give back to the community.

"I'd been approached by a lot of fundraising institutes over the years and everyone wanted money. I came back to the University so I could contribute by doing the helping bit first until I could afford to start donating."

During his tenure as a volunteer with the Medical Alumni Association and the Alumni Council, Dr Catchlove focused on reconnecting with alumni through events and reunions to build a sense of community. When the time was right, he also became philanthropically involved, initially in a small way, supporting students within the faculty.

"When I had surplus income, I decided that I really liked the work that the Charles Perkins Centre did – I liked the model and the multidisciplinary nature of the work there."

Since 2016, Dr Catchlove has donated to the Charles Perkins Centre in support of early career researchers investigating diabetes, cardiovascular disease and obesity through the Nicholas Catchlove Early Career Researcher Development Fund, honouring the memory of his late son, Nick.

"There are usually adequate funds available to support PhD students and established researchers, however postdoctorate students are often competing with thousands of others for a grant that they desperately need to get off the ground," he says.

Dr Catchlove and Dr Melkam, inaugural Nicholas Catchlove fellowship recipient, in the labs at the Charles Perkins Centre.

"By giving something now while you're alive, you can see where the money goes and you can get involved in the relevant societies and activities available, and that's rewarding."

As part of the fund, Dr Catchlove supports Dr Melkam Kebede – the inaugural and current holder of the Nicholas Catchlove fellowship, valued at $20,000 per annum.

Dr Kebede's research investigates the prevention and treatment of the progression of type 2 diabetes, through developing our understanding of the role of pancreatic beta cells.

Speaking about her work, Dr Kebede says, "The diabetic patients I have met through my community work inspire me. Their questions and encouragements are my constant source of inspiration to continue waging war on diabetes. They remind me of the real-world impact of what we do here."

Dr Catchlove has also established a biennial lecture. The Nicholas Catchlove Lecture educates and informs the wider community about global health issues, developments and discoveries. Open to the public, the event highlights a guest lecturer who is an eminent Australian or overseas expert in their field.

An enduring member of the community, Dr Catchlove has now expanded these activities to a bequest. He hopes his donations will continue to help young scientists advance their understanding of pressing health concerns so that as a community we can create inroads into some of the public health issues faced in Australia and worldwide.

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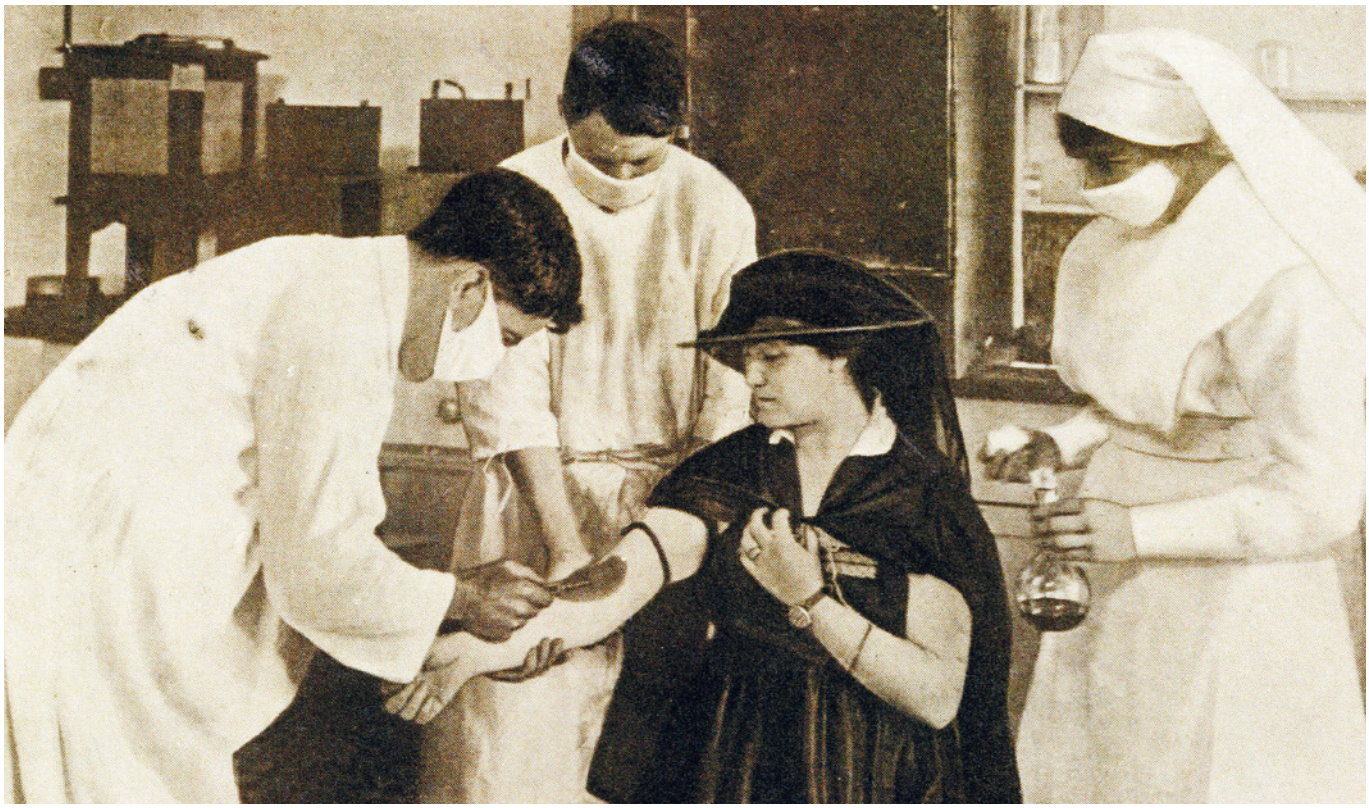


Dr Burton Bradley takes blood from a volunteer to manufacture vaccine (Annual report, RNSH 1920)

Medical School history

The 1919 influenza pandemic: meeting the challenge at the Royal North Shore Hospital

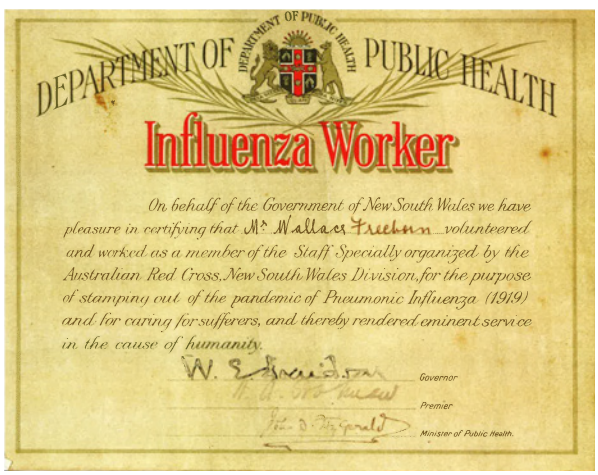
Written by Clinical Associate Professor Catherine Storey OAM, Faculty of Medicine and Health

In 1919, an influenza epidemic swept across the world; a world which was re-emerging after the First World War. An estimated 500 million people were infected worldwide, with over 50 million dead. Australia did not escape through its isolation. Soldiers returning from the battlefields of Europe were particularly at risk.

On the 24 January 1919, a traveller arrived from Melbourne with symptoms of influenza. The Board of Health had been anticipating such an event and quickly mobilised its resources to restrict the spread. Four days later, the Australian Government ordered all places where crowds congregated to close. The closures included "libraries, schools, churches, theatres, public halls, places of indoor resort for public entertainment". By the end of January, all citizens were required to wear masks.

When the University of Sydney suspended lectures and closed schools, medical students and teachers often took on voluntary roles in the hospitals, local relief centres and convalescent units. One such student was Wallace Freeborn (1898–1971) (MM, MB ChM). Freeborn was a 16-year-old high school student when he enlisted in the army in 1915 (he recorded his age as 18 on official records). He served in Egypt and subsequently at Pozières, France, where he was wounded. Following his repatriation in July 1916, he returned to school, matriculated and in 1919, entered the (then) Faculty of Medicine at the University of Sydney.

Within a few weeks, with the school closed, Freeborn volunteered as a Red Cross worker. He went on to become the General Medical Superintendent at Royal North Shore Hospital (RNSH) in 1948,



Top left: Nurses in isolation unit in RNSH during influenza epidemic (Courtesy Archives and Heritage Collection RNSH)

Top right: Vincent Welch (Courtesy of the State Archives)

Left: Volunteer influenza certificate - Wallace Freeborn (Courtesy of Archives and Heritage Collection, RNSH)

the year it became a teaching hospital of the University of Sydney. In 1919, however, the RNSH was a small cottage hospital serving an expanding, but virtually isolated, population on the north shore. On 28 March 1919, a representative of the Board of Health contacted the hospital to request that 65 beds (more than half the hospital complement of 120 beds) be isolated for use by influenza patients. Within a few days, not only had the beds been cleared, but a small wooden building appeared on the hospital grounds to house the 34 nurses who were required to nurse the patients in isolation.

The hospital received 534 influenza patients between 28 March and 31 July; 74 of these patients died. Twenty of the nurses contracted influenza, but fortunately, all recovered. One medical practitioner, Dr St Vincent Welch (1881–1919) (DSO, MB ChM 1906), a veteran of Gallipoli and the Somme, where he too was wounded, tragically died of influenza at RNSH on 21 May 1919.

The pathology department of this small hospital, under the direction of Dr CH Burton Bradley (MB ChM *Sydney* MRCS Eng LRCP DPH *Lond.*), using the blood from volunteer donors, made sufficient vaccine to inoculate 25,000 of the population. In the wake of the influenza outbreak and with recognition that the hospital needed to expand, Dr Emma Buckley (MB ChM 1911) was the successful candidate for the new position of Medical Superintendent and Associate Pathologist, a position she filled until her marriage in 1922.

What an extraordinary commitment from the nurses and doctors at the Royal North Shore Hospital, all early graduates of the Faculty of Medicine at the University of Sydney. These men and women set the hospital on a course towards the teaching hospital that it is today.

Reunion recaps

Class of 1955

Class of 1955
64-year reunion

Dr David Jeremy

It was one of those magical days! Clear and sunny-bright with hardly a breath of wind. Our private dining room opened to a beautiful terrace, lawn and gardens, and was set with four splendid tables each with floral decoration.

This is our 64th year after graduation. Seventeen alumni and a number of guests were greeted by Linda O'Malley from the University of Sydney. After the group photo was taken, we were welcomed, the names of those who had sent apologies were read and we toasted our University.

We all feel a great debt to Linda and her colleagues – Jessica Sullivan, Sally Forbes and Anushri Mitra to name a few. They all work so hard to plan and arrange these reunions. Vera Gallagher and I found liaising with them such a pleasure.

As ever, the Royal Sydney Golf Club treated us proud! Delicious canapés and drinks on arrival and impeccable service throughout. The food was splendid! Sincere thanks go to Hannah Beattie who liaised in the planning. To her and her colleagues at the club, we owe a great debt of thanks.

What was especially notable about this reunion was the high spirits and goodwill throughout. Lots of fun and chatter. Many reaching for the microphone and sharing stories from undergraduate days and after.

Everyone seemed to be having a jolly good time. When having such fun, time passes too quickly and before we knew it, this splendid luncheon was over and we had to say our goodbyes and see you again next year. We really look forward to that!

Dr David Jeremy

Class of 1957

Class of 1969

Class of 1957
62-year reunion

Dr Raymond Hyslop

At high noon on Tuesday 16 April, former students gathered in the Macleay Room at the Australian Club. With accompanying wives, partners and carers, the room soon filled with animated chatter facilitated by drinks and canapés. All were then seated at one long table with some having a magnificent view of the harbour as sliced beef fillet followed by a cheese platter were enjoyed.

To allow the maximum time for conversation there was no guest speaker. The Chairman, Ray Hyslop, spoke of the sadness felt by all at the sudden death of Bill Benz. Bill had always been snapping at the heels of the top people of our year and a golfing devotee. One of the first to book a seat, he had died just before we met. Lorraine Livingstone and Graham Williams, both now living in Molong, were late withdrawals. All too soon, 3pm arrived and all departed wishing to repeat the outing.

Class of 1969
50-year reunion

Susan M Pond AM and Arabella (Ellie) Smith

Our class graduated in the same year that NASA's Apollo 11 mission landed a man on the moon for the very first time. Fifty revolutions by our planet around the sun later, we found 102 classmates from our MBBS 1969 graduating year and 80 guests to gather in the Holme Building at the University of Sydney on Saturday 9 March 2019 to reminisce over lunch.

We recalled many defining moments in Australian and global history since we graduated. We celebrated the prodigious breakthroughs in health care that have benefited our patients. Entire disciplines have been transformed by ingenious technological innovations. We enjoyed seeing photographs of the old and new medical schools in which we spent so many hours, group photographs taken in the Oval No. 1 Grandstand while we were students, and our senior year exam papers.

A smaller but still significant number of us had taken the opportunity the day before to discover changes on campus since our university days by visiting two of the University's exciting multidisciplinary research buildings, the Sydney Nanoscience Hub and the Charles Perkins Centre. The festivities continued on Sunday at a well-attended brunch in Walsh Bay.

Fifty years is a momentous milestone. We knew each other before we became influential in our profession, before we became parents and grandparents. The three days of celebrations provided us with a wonderful opportunity to look back, catch up and look forward.

The University of Sydney School of Medicine – upcoming reunions

Date	Class of	Milestone	Key organisers	Venue	Time
Friday 18 October 2019	1954	65 years	Dr Ray Hollings AM Dr Mark Killingback	The Royal Sydney Golf Club	12–3pm
Saturday 2 November 2019	1974	45 years	Dr Gregory Don Dr Maureen Palmer	The Sibyl Centre, The Women's College	12–3.30pm
Saturday 9 November 2019	1999	20 years	Dr Paul Nicolarakis Dr Pradnya Dugal Dr Loren Rose Dr Tim Shortus Dr Duc Van Dr Fiona McLean	Anderson Stuart Building	6.30–11.30pm
Wednesday 13 November 2019	1956	63 years	Dr John Alam Dr Michael Owen Dr James Roche	The Sibyl Centre, The Women's College	12–3.30pm
Saturday 15 February 2020	1970	50 years	Dr Stuart Spring Dr Paul Anseline	The Refectory, Holme Building	6–11pm
Sunday 19 April 2020	1960	60 years	Dr Brian Kearney Dr Dick O'Reilly	The Sibyl Centre, The Women's College	12pm

Enquiries and further information

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sydney.edu.au/medicine/alumni

A family of doctors

Written by the descendants of the Mayer sisters

Dr Beris Olwyn Mayer (centre) and Dr Pat McKay (third from left), Conferring of Degree, Faculty of Medicine, the University of Sydney, 27 January 1954.

Three sisters, Jess, Loris and Beris Mayer, graduated from the University of Sydney Faculty of Medicine with MBBS in the 1940s and 50s. Even when Beris, the youngest, graduated, women made up only 10 percent of the class. They juggled families and medical practice while pursuing many other interests.

Jess Mayer: University was very different in Jess's day; the girls wore gloves and all students were assigned seats in the lecture halls. The seats had numbers on them, so if you skipped a lecture, the lecturer had your number – literally! Jess worked in Muswellbrook for 30 years, even delivering the babies of the babies she'd delivered. In rural practice, she could see someone in the surgery in the morning and operate on them in the hospital that afternoon. Her son, Guy, and his cousins, remember waiting for hours while Jess dealt with emergencies at the hospital.

Loris Mayer: Loris was born in 1921. She was awarded a scholarship to study medicine and made close friends with some of the other women in her year. After working for a few years, she took a break to start a family; one of her two daughters went on to graduate from Sydney Medical School. Loris returned to the workforce full-time in 1964 and helped to establish a revolutionary residential cottage unit for asthmatic children in the grounds of the Crippled Children's Hospital at St Ives. During this time, she became very interested in the mental health of her patients. She was indignant when she was refused admission to retrain as a psychoanalyst, on the grounds that, aged 57, she was "too old". Ultimately, she obtained membership of the NSW Institute of Psychotherapy in 1978, was awarded Honorary Life Membership in 1998, and established her own paediatric psychotherapy practice.

Beris Mayer: Beris graduated in January 1954 and practised for 40 years. She was introduced to Ted McIntosh, her future husband during an anatomy lab. Beris and her friend Pat Merrifield (née McKay) perplexed lecturers because they were able to knit and learn medicine simultaneously. The graduation yearbook recorded that she would be "remembered with anguish and affection by her tutors and colleagues". Beris was a resident at St Luke's Hospital in Kings Cross, where she was trusted to suture aortic repairs after the surgeon left – perhaps drawing on her sewing skills. Dr Margaret Mulvey encouraged Beris to become an obstetrician, but she chose the family-friendly option of general practice. She was a formidable homemaker and encourager of education. All four of her sons went into the medical field. Beris maintained her professional standards by working in the practices of other distinguished medical doctors in Sydney. Later in her career, she tutored medical students at St George Hospital and taught English with Ted at the Wuhan Medical University in China in 1988. Beris Olwyn McIntosh (née Mayer) died in Sydney in May 2019, aged 88. She and her sisters are fondly and proudly remembered by their families for their pioneering work as women in medicine, who each achieved an equilibrium between their professional and personal lives.

If you have multi-generational family connections to the University, we'd love to hear from you. To share your family's story or to consider a gift in your will to the University in honour of a family member, please contact:

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Where are they now?

In every edition of *Radius*, we profile Sydney Medical School graduates to see where their studies have taken them. This time we report on **Dr Agus Simahendra**.

Dr Agus Simahendra has travelled the world learning about infectious diseases with the goal of returning home to Indonesia to improve the health outcomes of his people and others in low-income countries.

After graduating at the top of his class from a leading medical school in Indonesia, Dr Simahendra worked in rural villages with populations of less than 50,000 people.

"The first job I took after completing medical school was with the Indonesian Ministry of Health as a General Practitioner in rural Java and North Borneo," says Dr Simahendra.

"I spent approximately two years serving marginalised and poor communities in an extremely resource-limited health setting to educate people and tackle medical issues.

"Most of the people I treated suffered from deadly infectious diseases due to limited access to basic hygienic measures and facilities."

As a result of these experiences, Dr Simahendra developed an interest in infectious diseases and resolved to reduce the number of unnecessary deaths caused by malaria, tuberculosis and many other diseases among young Indonesians.

Dr Simahendra works at the International Medical Centre Hospital in Bali as a medical practitioner.

Infection and immune disorders are the leading cause of death both in low-income areas of Indonesia and around the world. According to the World Health Organization, more than 10 million lives are lost to infectious diseases annually.

"Deeply ingrained habits inimical to health like smoking, overcrowding, nutritional inaccuracies, lack of sanitation, and many other unknown factors need to be identified, challenged and rectified," says Dr Simahendra.

After working for several years at the Bali International Medical Centre Hospital, Dr Simahendra moved to the United States and took up a position in a research university hospital specialising in internal medicine. He wanted to learn more from the experts.

"By serving patients while working with high-calibre, internationally recognised physicians and scientists, I was able to better understand the importance of medical research in developing best practice for patient care," he explains.

Still curious about infectious diseases, and wanting to advance his career further, Dr Simahendra later decided to pursue postgraduate study by moving to Australia to complete a Master of Medicine (Infection and Immunity) at the University of Sydney.

> "Learning medicine is a lifelong process. As a physician-scientist, I see the importance of well-developed channels of knowledge exchange to ensure that breakthroughs in basic science can be rapidly translated into the clinic."

"Throughout the master's program, I was able to practise my clinical judgement skills using state-of-the-art technologies under the mentorship of international leaders in the field. This is something that's not possible in Indonesia.

"It also helped me to leverage my collaborative networks and to build interdisciplinary partnerships with other physicians, researchers, and industry to address health-related discrepancies in Indonesia and the wider Asia-Pacific."

After graduating, Dr Simahendra returned to Indonesia and resumed his work as a medical practitioner in Bali. He is currently placed in an ambulatory care setting and manages the treatment of a variety of infectious diseases and immunological disorders. He was also appointed a clinical trainer to educate other staff.

"My primary role as an educator is to relay the knowledge I learnt while completing my master's degree in Australia. I teach basic techniques in sterilisation, infection control strategies, and proper antibiotic stewardship to prevent antibiotic resistance and to treat commonly encountered infectious diseases," Dr Simahendra explains.

"The knowledge that I acquired during my study can be widely translated into all communities, removing barriers as a result of cultural differences, backgrounds, and any social discrepancies to transform the lives of those affected by these ailments into a better one."

In the future, Dr Simahendra would like to establish a clinical research group in Indonesia with international collaborators he has met throughout his travels. His continued ambition is to minimise the burden of infectious diseases and prevent the hardships associated with illness, which further entrench inequality.

In order to achieve this goal, Dr Simahendra would like to complete a PhD. He intends to move to Germany for this study and for other postdoctoral training to gain the skills required to nurture other researchers who wish to pursue a career in infectious diseases.

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