NSW GOVERNMENT | Health Pathology

Research Activity Report 2019

for all of us

www.pathology.health.nsw.gov.au

Pictured: *Jeremy Watherston, FASS (page 18 'student and supervisor in focus (Forensic & Analytical Science Service, FASS')*

NSW Health Pathology (NSWHP) recognises the right of Aboriginal and Torres Strait Islander Peoples to be engaged in any processes, projects and activities that may impact on them.

We also acknowledge that Aboriginal and Torres Strait Islander Peoples have the right to control and maintain their culture and heritage, and that means benefiting from research undertaken by, with and about them.

The Lowitja Institute, Australia's national institute for Aboriginal and Torres Strait Islander health research, has developed two guides in response to a growing need for resources in this area.

Supporting Indigenous Researchers:
A practical guide for supervisors
A guide to help researchers and research supervisors who are working in Aboriginal and Torres Strait Islander settings.

Researching Indigenous Health:
A practical guide for researchers
A guide including the history, context, values and change priorities of Indigenous health research in Australia and the planning and management of Indigenous health research projects.

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Tracey McCosker PSM
Chief Executive

Robert Lindeman
Director,
Clinical Operations

Welcome

We are thrilled to welcome you to NSW Health Pathology's third Research Activity Report.

We are incredibly proud and impressed by the breadth and diversity of research taking place within NSW Health Pathology. This 2019 report is reflective of the collective efforts and achievements of our research community, our contribution to the national and international research knowledge base and the incredible impact that research translation has on our communities.

2019 was an extremely productive year for research at NSW Health Pathology. This year we:

- continued to implement our Research Strategy
- grew collaborations and partnerships with health services and researchers across NSW
- launched in NSW Health's REGIS system
- employed a Research Project Officer to oversee key initiatives
- continued to build a standardised statewide service for research
- linked our services for research with the NSW Health Statewide Biobank for an all-encompassing end to end service

Research is an investment in the future health of our NSW community. It's one of the most important investments that we as a public health service can make and we want to once again reaffirm our commitment to supporting and fostering high-quality, innovative research.

To our NSW Health Pathology researchers, thank you again for the vital work you do – for all of us.

I encourage all our researchers to continue submitting to the register so that we can track our impact and continue to celebrate your incredible achievements in future reports.

Paul Dunn
Director, Finance and
Corporate Services

Sustainability

In our Strategic Plan – Toward 2025, NSWHP committed to delivering future focused infrastructure and strategic commissioning and to leading the implementation of eco-friendly, sustainable services and workplaces.

In line with our sustainability commitments, I'm proud to announce that our 2019 Research Activity Report has gone green.

This impressive report is specifically designed to be viewed online. Throughout its pages, you will find clickable links that will take you straight to the pages you wish to read about or direct you to even more great research achievements, articles and resources.

You can even click the 'home' button at the top of each page to return to the contents page.

The health of people and communities across our state goes hand in hand with the health of our planet. Let's continue to work together to create real and lasting change, for all of us.

for all of sustainable

02

Our research impact and achievements

Research impact

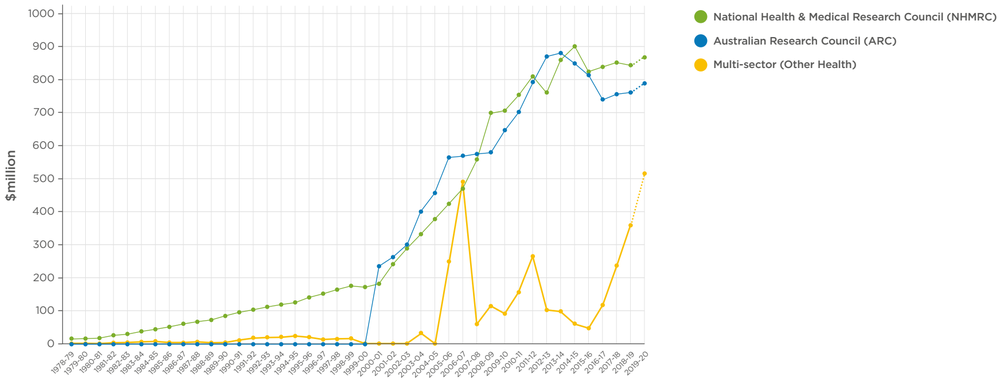
NSW Health Pathology (NSWHP) takes part in research that creates better health and justice systems, every day.

High quality research advances our understanding of the world around us, delivers real change and ultimately improves the lives of the people of NSW.

A look at our current research climate (2019 – 20FY)

- $1.4B in funding toward research and development (R&D) across the health sector
  - National Health and Medical Research >$860M in research
  - Medical Research Future Fund >$390M in research
  - Biomedical Translation Fund >$45M
  - $98M across 29 research programs including Australian Genomic Cancer Medicine Program ($10M), Cancer Clinical Trials ($6.2M), Collaborative Cancer Research ($4.5M) and Lowitja Institute (*Aboriginal and Torres Strait Islander research*) ($4M).
- >$5M in funding towards criminology research via the Australian Institute of Criminology. This included dedicated programs in the areas of serious and organised crime research, child exploitation and drug and law enforcement research.
- $3.6B in funding towards research across industry, innovation and science sectors including; $840M funding towards CSIRO and $185M funding towards Cooperative Research Centres Program. Note: remaining funding was associated with engineering, environment, marine, geoscience and quantum science.

Australian Government investment in R&D by sector and/or subsector, 1978-79 to 2019-20



Australian Government's Science, Research and Innovation Budget Table.
https://www.industry.gov.au/data-and-publications/science-research-and-innovation-sri-budget-tables.
(Note: Multisector (Other Health) includes MRFF funding).

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Research program achievements

Building on the great work carried out across 2018, NSWHP continues to progress the Research Strategy. More than 46% of the Strategy's initiatives have been delivered under careful guidance from the NSW Health Pathology Research and Innovation Advisory Committee.

2019 saw us focus on strengthening the research and innovation agenda through investing in partnerships, networking and processes, and through resource accountability.

Key achievements include:

Research Activity Report – the very first report was published (2017)

Research & Innovation Support Project Officers – two new team members were employed to assist in the implementation of the Resesarch and Innovation Framework

Acknowledgement Policy – was rolled out across the organisation

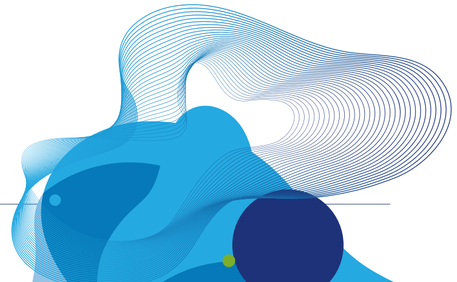
Research services – were promoted to our research partners across NSW

Research governance – we streamlined our processes to ensure high quality research following regulations, legislation and laws related to research

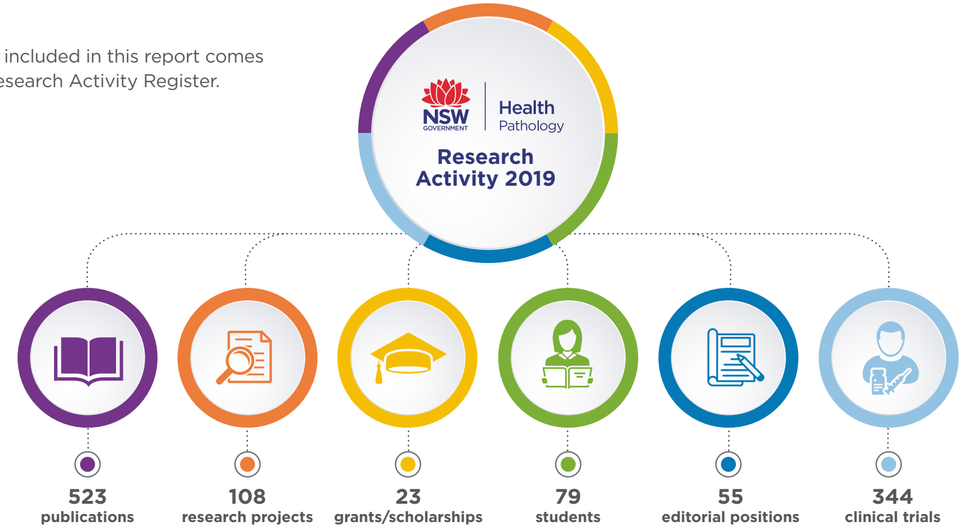
Round 1 Biospecimen Collection Grant – was launched through the NSW Health Statewide Biobank

Intellectual Property (IP) Framework – was released to establish a system for effectively managing the creation, use, sharing, protection and commercialisation of IP

Research support website – was developed to show our research partners that we have established a dedicated research strategy and research governance advisory committee



All research activity included in this report comes from the NSWHP Research Activity Register.



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Publication overview

Unrestricted, free online access to scholarly articles through open access has revolutionised medical communications. In 2019, NSW Health Pathology staff registered 523 research publications in our Research Activity Register. We also recognise that unregistered publications are likely to exist.

Publication types ranged from original peer reviewed articles, review articles, editorials or commentary, reports and guidelines, book chapters and original non-peer reviewed articles.

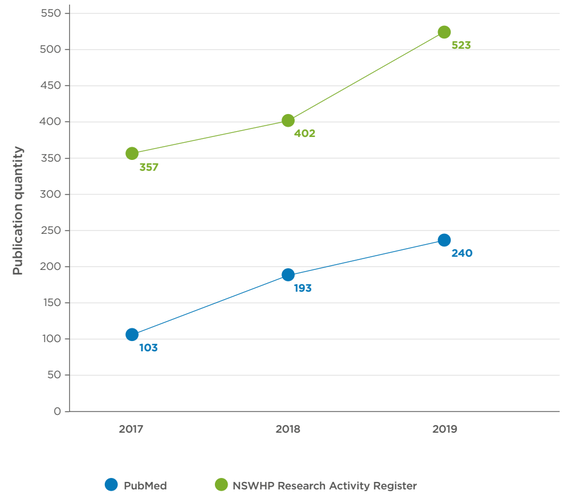
Registered in our NSWHP Research Activity Register for 2019

360 original peer reviewed articles	**35** review articles	**9** book chapters
45 reports and guidelines	**52** editorials and commentary	**22** original non-peer reviewed articles

NSW Health Pathology's peer-reviewed publication impact has increased progressively since 2011.

This graph displays publication growth for NSWHP from 2017 to 2019 using data from PubMed (green) using search terms like NSW Health Pathology, New South Wales Health Pathology, NSW Pathology and New South Wales Pathology, compared to data in our Research Activity Register.

To make your publication count, please read our **Authorship, Affiliation and Acknowledgment Policy**.



02

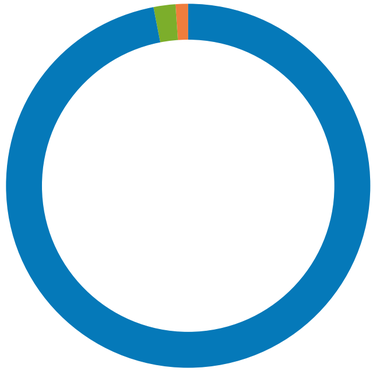
Grants

NSW Health Pathology staff attract many research grants (as chief and/or associate investigators) and we are excited to highlight our grant successes and achievements.

2019 saw 24 grants registered in our NSWHP Research Activity Register, totalling $18,502,973.00.

Funding bodies included NHMRC, MRFF JDRF, ARC, Cancer Council NSW, Tour de Cure and many more.

This level of achievement would not have been possible without the collaborative partnerships between our NSWHP staff and colleagues in Local Health Districts (LHDs), universities, research institutions and other external partners.



Proportion of funding type

Research	97%
Infrastructure	2%
Fellowship	1%

The proportion of funding types registered in the NSWHP Research Activity Register for 2019.

02

Grants in focus

Grant title	**Dissecting the structural and functional heterogeneity of terminal effector CD8+T cells from MGUS and newly diagnosed MM patients, in order to identify therapeutic targets and unlock their anti-myeloma potential**
Funded Institute	International Myeloma Foundation
Funding type	Brian D. Novis Research Grants – funding promising myeloma research
Junior grant recipient	**Christian Edward Bryant, BsC(med), MBBS, PhD**
Funding amount	$73,489.00
Funding period	2019

Study outcome and impact

A type of T cells named terminal effector CD8+T cells are responsible for keeping Myeloma in an asymptomatic pre-cancerous stage for many years, and when they fail the disease progresses. In this study we use cutting edge technologies to discover changes in genes and proteins in these cells during disease progression. These changes describe structural and functional disturbances in these T cells caused by the malignant cells, potentially identifying therapeutic targets and suggesting ways to improve their capacity to eliminate myeloma.

Grant title	**c-FIND: CRISPR Frontier Infection Diagnostics to Detect Infection**
Funded Institute	Medical Research Future Fund (MRFF)
Funding type	MRFF Frontier Health & Medical Research Fund
Grant recipient	Pellegrini M; **Sintchenko V, Chen S** and many more
Funding amount	$1,000,000.00
Funding period	2019 – 2020

Study outcome and impact

c-FIND is designed for diagnostic results to inform optimal patient care. It was created by Mark Pellegrini and colleagues as part of an inter-institutional collaboration that involves 5 clinical trials arms.

CRISPR has the capacity to offer rapid POC tests that can be updated in real time. CRISPR-Cas is a bacteria's defence against viruses and can be adapted as a diagnostic (pathogen specific sequences). CRISPR-Cas combined with conventional PCR has exquisite sensitivity and specificity.

NSW Health Pathology's Sharon Chen, is involved in clinical trial arm 3: infections in infants and children, while Vitali Sintchenko is involved in clinical trial arm 4: spread of imported undiagnosed Tuberculosis disease in adults and children.

Content adopted from: https://cancerandinfections.org/s/Marc-Pellegrini.pdf

02

Students and supervisors in focus

Forensic & Analytical Science Service, FASS

PhD student	Jeremy Watherston
Supervisors	Professor Dennis McNevin (University of Technology Sydney), Associate Professor Jodie Ward (University of Technology Sydney) and **Dr David Bruce (FASS)**
Project title	Optimisation of DNA profiling from compromised human remains

Project outcome and impact

Jeremy's PhD project focused on the recovery of DNA from compromised human remains for DNA-based disaster victim identification (DVI).

By considering sample selection, collection, preservation, preparation, novel profiling approaches and the application of rapid DNA instruments, he developed rapid approaches for the genetic identification of compromised post-mortem (PM) samples and DVI, focused on minimally-invasive sampling. These rapid methods mean sample collection, preparation and testing can occur simply, with faster turnaround times and with simple tools suitable for in-field application. They are also compatible with current DNA testing kits and high-throughput, automated backend DNA testing.

The impact of increased speed of DNA analysis in forensic casework:

- provides informative results for forensic decision-making
- streamlines the investigation process by providing preliminary leads during the early crucial stages of an investigation.

Jeremy's work will inform further research to develop and optimise rapid protocols for future field deployment for identifying deceased individuals in mass casualty, counter terrorism and humanitarian forensic operations.

Jeremy's work has already made impact on his field, with three published book chapters (Forensic genetic approaches for the identification of human skeletal remains: Challenges, best practices, and emerging technologies, New York: Elsevier Academic Press 2021), as well as two published and one submitted journal article.

In collaboration with the Australian Facility for Taphonomic Experimental Research.

Jeremy Watherston and Dr David Bruce

Student – Jeremy Watherston

While working full time and doing my PhD part time has been challenging, it has also been a very rewarding experience. I am so grateful to have worked with world leaders in genetic identification whilst developing our methods.

Working with supervisors from UTS and NSWHP FASS, we have been able to conduct this research in the very nexus of research and professional practice. As Senior Forensic Biologist reporting extensively on the identification of human remains, I have been able to draw on my experience to help shape our approaches, fully aware of the reporting implications for the coronial and/or criminal process. I am excited to see our work developed, optimised and implemented into identification cases in the future, and know our work has helped provide answers to families sooner and directed investigators in a criminal investigation.

Supervisor – Dr David Bruce

It is a great privilege to supervise a post graduate student. We are fortunate to have intelligent and motivated individuals like Jeremy, who are willing to undertake the significant challenge and additional work of a post graduate degree on top of their substantive roles at NSWHP. Research projects are crucial in developing the collegial relationships between NSWHP and universities. Likewise, a reputation for good research is important in establishing the national and international reputation of FASS as a centre for excellence in forensic science.

The outcome of this applied research project in the area of victim identification not only informs our practice and improves our forensic science testing protocols but assists us in providing the best scientific advice to our stakeholders in the police and judiciary. It will ultimately lead to better justice outcomes and possible closure for the families of victims.

02

Students and supervisors in focus

NSW Health Statewide Biobank (NSWHSB)

PhD Student	Amanda Rush
Supervisor	**Professor Jennifer Byrne** and a multi-disciplinary team of co-supervisors
Project title	A health economics analysis of cancer biobank costs and outputs in NSW

Project outcome and impact

Amanda's thesis comprised a series of three studies, which aimed to:

- investigate the current approach to discussing and reporting on biobank outputs,
- determine the costs and publication outputs that result from the provision of biospecimens and data from NSW cancer biobank operations, and
- determine the needs and experiences of Australian biospecimen users.

Together, the studies contributed to the body of knowledge on operational and financial sustainability of biobanks, where sustainability has been a longstanding challenge for biobanks across the world. An evidence-based approach to biobank business planning, costs and outputs data, and information on the needs and experiences of researchers, contributed to improving the capacity of human biobanks to facilitate health and medical research.

Amanda Rush and Professor Jennifer Byrne

Student – Amanda Rush

My PhD began in late 2009 when I met Jennifer (Jenny) Byrne, who was head of the Children's Cancer Research Unit at The Children's Hospital at Westmead. During my time at the Tumour Bank, Jenny gently encouraged me to pursue an emerging passion for research. With her guidance, I was successful in getting awarded one of the scholarships from the inaugural round of PhD scholarships to develop researcher skills in under-represented areas offerd by the NSW Ministry of Health in 2017.

Jenny's leadership, high research standards and encouragement transferred easily from our working to supervisory arrangements. With great accuracy, Jenny was able to identify my strengths and weaknesses, tailoring my studies to something that I could capably undertake. My PhD encompassed a multi-disciplinary approach, lending itself to a large co-supervisory team with varying ideas and approaches for me to reconcile.

In addition to developing a strong knowledge base on all things biobanking, I acquired a set of broader research skills such as literature searches, data analysis, writing for varied audiences and presenting research outputs. Beyond this, I further developed my 'soft skills': independence, communication, negotiation, collaboration, perseverance and resilience.

Supervisor – Professor Jennifer Byrne

Supervising Amanda's PhD as part of a broader team was a joy and privilege from start to end. Amanda was the 11th PhD student that I've supervised to completion as a primary supervisor, yet every PhD student is different and represents a learning opportunity for the supervisor. Before commencing her PhD, Amanda was already working as if she had one - she just needed the title. In that sense, Amanda was more like a colleague than a student, and she supported me as much as I supported her.

Amanda's leadership and research have provided gifts to biobanking that will continue to pay forward in years to come, in terms of evidence for the need for a national biobanking framework for Australia, and the need to position biobanking upon an evidence base to more effectively partner with health and medical research. Perhaps the best part is having also made a lifelong colleague and friend, who is now just across the road from the NSWHSB on the University of Sydney campus.

> ***My advice to future PhD students?***
> ***Follow your passion, but also choose a supportive supervisor who'll be there for you in both the good and the not-so-good times. And like any major life decision, it can pay to shop around.***

03

Our clinical streams and services

Clinical streams

Scott Jansson
Clinical Streams Coordinator

NSW Health Pathology has six **clinical streams**.

- Anatomical pathology
- Chemical pathology
- Haematology
- Immunology
- Microbiology
- Transfusion

The clinical streams were established to improve the quality, safety and efficiency of public pathology services, and promote collaboration among clinicians, scientists and other staff across pathology disciplines. They are charged with developing strategies that will improve the outcome and value for patients, clinicians, customers and stakeholders through the equitable, safe and efficient delivery of pathology services across NSW and to all patients.

They provide expert advice and undertake tasks to achieve NSWHP's strategic initiatives.

The purpose of our clinical streams is to:

- provide leadership in shaping the statewide direction for clinical services
- develop recommendations for innovative models of service delivery to patients and customers
- set best practice clinical standards and policy for services at a statewide level, and
- provide clinical advice on emerging issues and areas of risk to help ensure NSWHP provides high quality, safe clinical services to the NSW Health system.

> ***"The clinical streams actively support research in medical and scientific areas relevant to public pathology through their respective clinical disciplines."***
> ***Scott Jansson, Clinical Streams Coordinator***

Clinical services

Dr Stephen Braye
Chief Medical Information Officer, Director of Clinical Services

NSW Health Pathology has four statewide clinical services.

Point of Care Testing (PoCT)
NSWHP has the world's largest managed PoCT network delivering diagnostic services to NSW, with more than 680 devices and over 26,000 users.

Genomics
NSWHP has three streams consisting of pathogen genomics, cancer genomics, and rare disease genomics. We are developing a genomics cloud reporting framework through the Privacy and Security Accreditation Framework of eHealth NSW.

Public Health Pathology
NSWHP is actively participating in the establishment of the expanded pathogen genomics service. We are undertaking a comprehensive review of testing for notifiable diseases in the NSWHP laboratory network, identifying what, where and how testing is undertaken for organisms of public health significance.

Perinatal Postmortem Service
NSWHP provides compassionate and dignified care, consulting with relevant healthcare professionals to help families find the answers they need. We manage all non-coronial perinatal postmortem needs, providing timely, reliable results with expert examination using the highest ethical standards of care.

The clinical services were established to provide leadership, develop innovative models of care, set best practice and provide clinical advice. In some cases, the clinical services also provide operational oversight. They work closely with clinical streams, operations groups and local health district partners to develop effective services for patients and NSWHP clients.

The Statewide Clinical Services also participate in service development and instrument design across national and international realms. They are exploring relationships with tertiary institutions for scientific research, higher degree opportunities, as well as engaging with ICT faculties to develop artificial intelligence in clinical systems.

04

Our research streams

Anatomical Pathology

deals with the tissue diagnosis of disease using a broad-based knowledge and understanding of the pathological and clinical aspects of many diseases (using tissue from living patients).

Chemical Pathology

encompasses detecting changes in a wide range of substances in blood and body fluids (electrolytes, enzymes, proteins, tumour markers, hormones, poisons and both therapeutic and illicit drugs).

Haematology

is a rapidly developing discipline which deals with many aspects of those diseases which affect the blood such as anaemia, leukemia, lymphoma, and clotting or bleeding disorders.

Immunology

involves both laboratory medicine (the testing of specimens collected from patients related to the immune system) and clinical practice (interviewing, examining and advising patients about clinical problems).

Microbiology

deals with diseases caused by infectious agents such as bacteria, viruses, fungi and parasites. Clinical aspects involve control of outbreaks of infectious disease and dealing with the problems of infections caused by antibiotic-resistant bacteria.

Genomics

We have created a statewide genomics service which pools the expertise that exists across our laboratories into a coordinated service dedicated to delivering state-of-the-art diagnostics and care for patients with cancer, heart disease, developmental delay in children and other diseases.

Public Health

is a key part of the value we bring to the health system and includes experts across a range of areas including; disease outbreaks, laboratory investigations for notifiable diseases, responses to emerging diseases, monitoring public health trends, public health research and education, and supporting emergency preparedness.

Forensic & Analytical Science Service

provides expert scientific and forensic pathology services to the NSW criminal and coronial justice system, NSW Police, NSW Health and other key partner agencies to find answers for grieving families and the community throughout NSW.

NSW Health Statewide Biobank

exists to support and enable world-class health and medical research in NSW and is providing a pathway to better research that leads to better treatment for patients.

04

Anatomical Pathology

Research activity summary

177 Publications
- 139 Original Peer Reviewed
- 14 Review Articles
- 4 Reports/Guidelines
- 9 Books/Book Chapters
- 10 Editorials/Commentary
- 1 Original non-Peer Reviewed

6 Grants

36 Research projects

29 Students

23 Editorial positions

Publications

Other Research Activity

Publication in focus

Journal citation	Nature Communications 2019 Sep 2;10(1):3935 **https://pubmed.ncbi.nlm.nih.gov/31477716/**
Title	**The molecular origin and taxonomy of mucinous ovarian carcinoma**
Authors	Dane Cheasley, Matthew J Wakefield, Georgina L Ryland, Prue E Allan, Kathryn Alsop, Kaushalya C Amarasinghe, Sumitra Ananda, Michael S Anglesio, George Au-Yeung, Maret Böhm, David D L Bowtell, Alison Brand, Georgia Chenevix-Trench, Michael Christie, Yoke-Eng Chiew, Michael Churchman, Anna DeFazio, Renee Demeo, Rhiannon Dudley, Nicole Fairweather, Clare G Fedele, Sian Fereday, Stephen B Fox, C Blake Gilks, Charlie Gourley, Neville F Hacker, Alison M Hadley, Joy Hendley, Gwo-Yaw Ho, Siobhan Hughes, David G Hunstman, Sally M Hunter, Tom W Jobling, Kimberly R Kalli, Scott H Kaufmann, Catherine J Kennedy, Martin Köbel, Cecile Le Page, Jason Li, Richard Lupat, Orla M McNally, Jessica N McAlpine , Anne-Marie Mes-Masson, Linda Mileshkin, Diane M Provencher, Jan Pyman, Kurosh Rahimi , Simone M Rowley, Carolina Salazar, Goli Samimi, Hugo Saunders, Timothy Semple, **Ragwha Sharma**, Alice J Sharpe, Andrew N Stephens, Niko Thio, Michelle C Torres, Nadia Traficante, Zhongyue Xing, Magnus Zethoven, Yoland C Antill, Clare L Scott, Ian G Campbell and Kylie L Gorringe.

Partnership with Peter MacCallum Cancer Centre (Melbourne) and many more

Study outcome and impact

Mucinous ovarian carcinoma (MOC) is a unique subtype of ovarian cancer with an uncertain cause, and no certainty about whether it genuinely arises at the ovary or is metastatic disease from other organs. In addition, the molecular drivers of invasive progression, high-grade and metastatic disease are poorly defined.

Genetic analysis of MOC across all histological grades was performed, including benign and borderline mucinous ovarian tumors, and these were compared to tumors from other potential extra-ovarian sites of origin. Ragwha Sharma was involved in pathology review of cases. The exome and RNA sequencing data have been deposited in the European Genome-phenome database.

The publication shows that MOC is distinct from tumors from other sites and supports a progressive model of evolution from borderline precursors to high-grade invasive MOC. Key drivers of progression identified are TP53 mutation and copy number aberrations, including a notable amplicon on 9p13. High copy number aberration burden is associated with worse prognosis in MOC.

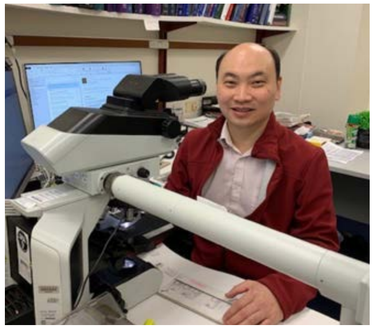
The data presented conclusively demonstrate that MOC arise from benign and borderline precursors at the ovary and are not extra-ovarian metastases.

04

Publication in focus

Journal citation	Transplant Direct 2019 Nov; 5(11): e502 **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6831120/**
Title	**Brief Normothermic Machine Perfusion Rejuvenates Discarded Human Kidneys**
Authors	Ahmer M. Hameed, David B. Lu, Ellis Patrick, Bo Xu, Min Hu, Yi Vee Chew, Karen Keung, **Chow H. P'ng**, Renan Gaspi, Chris Zhang, Paul Robertson, Stephen Alexander, Gordon Thomas, Jerome Laurence, Ronald De Roo, Germaine Wong, Ray Miraziz, Greg O'Grady, Lawrence Yuen, Wayne J. Hawthorne, Natasha M. Rogers and Henry C. Pleass.

Partnership with WSLHD, USYD, Industry and University of Auckland



Chow H. P'ng in the laboratory

Study outcome and impact

This study was wholly reliant upon the provision of discarded and/or non-utilised deceased donor human kidneys provided by NSW Organ and Tissue Donation Service. NSWHP's involvement was from our senior staff specialist Chow H. P'ng, who provided pathological analysis towards this study.

Normothermic machine perfusion (NMP) may allow resuscitation and improved assessment of kidneys before transplantation. The study showed that the method completely resolved nonperfused regions in discarded donation after cuculatiory death in kidneys and demonstrated some significant mechanistic benefits in comparison to cold static storage (CS) alone. NMP was directly compared with CS in paired donor kidneys using simulated transplantation.

NMP may have the potential to reduce organ discards and enhance early graft function in donor kidneys.

Pathology input, from both diagnostic and research perspectives, are essential to the renal transplantation service at Westmead Hospital, one of the largest in the country. This study is just one of many which highlights the importance of collaboration between pathologists and medical and surgical colleagues to provide the best possible service.

04

Chemical Pathology

Research activity summary

16 Publications
- 8 Original peer-reviewed articles
- 1 Review article
- 7 Original non-peer reviewed articles

1 Research project

Publications

Other Research Activity

Publication in focus

Journal citation	Ann Clin Biochem 2019 Sep; 56(5):527-535 **https://pubmed.ncbi.nlm.nih.gov/30987429/**
Title	**Setting clinical performance specifications to develop and evaluate biomarkers for clinical use.**
Authors	Lord SJ, St John A, Bossuyt PM, Sandberg S, Monaghan PJ, O'Kane M, Cobbaert CM, Röddiger R, Lennartz L, Gelfi C, **Horvath AR** for the Test Evaluation Working Group of the European Federation of Clinical Chemistry and Laboratory Medicine.

Partnership with European Collaborators

Study outcome and impact

This is the fifth paper in a series of publications on how a newly developed biomarker should be evaluated before it can become a clinically useful test. The first four publications were:

- "From biomarkers to medical tests: The changing landscape of test evaluation" (2013)
- "Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine" (2015)
- "Setting analytical performance specifications based on outcome studies - Is it possible?" (2015)
- "Biomarker development targeting unmet clinical needs" (2016)

The work discusses the clinical performance element of a test evaluation framework published by an international team set up by Andrea Rita Horvath when she was president of the European Federation of Clinical Chemistry and Laboratory Medicine. Rita is very proud of this interdisciplinary group of leading experts in epidemiology, evidence-based diagnostics, chemical pathology, clinical biochemistry and representatives of the IVD industry which is providing ongoing guidance and practical tools as well as education in the field of test evaluation.

The article describes biomarker discovery studies that often claim 'promising' findings, motivating further studies and marketing as medical tests. Unfortunately, the patient benefits promised and the exact role of the new biomarker in the clinical pathway are often inadequately explained to guide further evaluation, so few biomarkers have translated to improved patient care.

The article offers a practical guide for setting minimum clinical performance specifications to strengthen clinical performance study design and interpretation. This great tool classifies the proposed patient benefits of a new test into three broad groups and describes how to set minimum clinical performance requirements at the level where the potential harms of false-positive and false-negative results do not outweigh the benefits. It is an approach that requires early collaboration and crosstalk between biomarker discovery researchers, clinicians, laboratory professionals, the IVD industry, as well as patients and health policy makers.

04

Haematology

Research activity summary

79 Publications
- 51 Original peer-reviewed articles
- 3 Reports and guidelines
- 15 Review articles
- 10 Editorials and commentary

3 Grants/scholarships

10 Research projects

9 Students

10 Editorial positions

Publications

Other Research Activity

Publication in focus

Journal citation	Nature Communications 2019 Mar 21;10(1):1322. **https://pubmed.ncbi.nlm.nih.gov/30899022/** Web of Science: "Highly Cited Paper", top 1% in the field of clinical medicine in the publication year
Title	**Neutrophil activation and NETosis are the major drivers of thrombosis in heparin-induced thrombocytopenia**
Authors	José Perdomo, Halina H L Leung, Zohra Ahmadi, Feng Yan, James J H Chong, Freda H Passam and **Beng H Chong**.

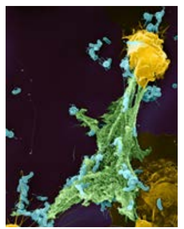
Partnership with UNSW, USYD, WIMR, WSLHD and Victor Chang Cardiac Research Institute

Study outcome and impact

The conventional concept is that activation of platelets and blood coagulation are essential for clot formation.

This paper shows strong scientific evidence that clot formation in heparin-induced thrombocytompenia (HIT) is driven by activated neutrophils and the resultant release of Neutrophil Extracellular Trap (NET), which activates blood coagulation and platelets. NET is a net-like DNA structure that forms the framework of thrombus formation. This process is called NETosis (a new 'hot' topic in thrombosis). It also shows that thrombosis can occur in the absence of platelets - a very surprising and unexpected finding. NETosis also plays an important role in clot formation in stroke, heart attack (acute myocardial infarction) and venous thromboembolism.

Additionally, the study discovered potential new therapies for HIT for which conventional anticoagulants have not been very efficacious.



Neutrophil Extracellular Trap (NET). Image adopted from Thâlin C et al. Arterioscler Thromb Vasc Biol. 2019 Sep;39(9):1724-1738.

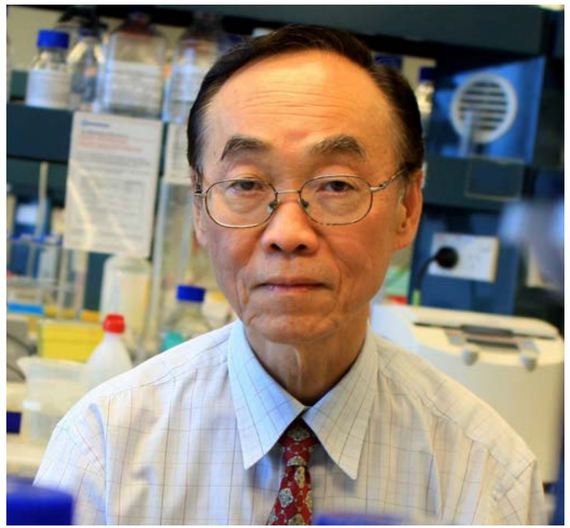
> ***This paper has significantly changed our understanding of the mechanisms that drive thrombosis in general, and pathogenesis of HIT (heparin-induced thrombocytopenia) in particular.***

"Recently HIT has attracted worldwide attention because a HIT-like rare severe clotting disorder, called vaccine-induced thrombocytopenia and thrombosis (VITT) has been reported in people after vaccination with AstraZenica and Johnson & Johnson vaccines.

VITT is very similar to HIT – both are immune reactions (the former trigger by a vaccine, the latter by heparin), occurring 4 – 20 days after the triggering event. Clinically both have severe thromboses often at rare sites, an accompanying thrombocytopenia and a PF4 (platelet Factor 4)-dependent platelet activating IgG antibody.

Both are diagnosed by the same ELISA and functional laboratory tests and treated by non-heparin anticoagulants plus/minus IVIg." Beng Chong.

Past research in HIT (to which Professor Chong has contributed for the past 30 years) has enabled rapid understanding of the pathogenesis of VITT, the quick establishment of diagnostic tests and immediate availability of appropriate treatment of this new disorder when it suddenly emerged.



Professor Beng Chong, Haematologist, St George Hospital.

04

Immunology

Research activity summary

- **8 Publications**
  8 Original peer-reviewed articles
- **1 Grants/scholarship**
- **5 Research projects**
- **3 Students**
- **2 Editorial positions**

Publications

Other Research Activity

Publication in focus

Journal citation	Dev Med Child Neurol. 2019 May; 61(5):610-614 https://pubmed.ncbi.nlm.nih.gov/30221764/
Title	**Isolated seizures during the first episode of relapsing myelin oligodendrocyte glycoprotein antibody-associated demyelination in children**
Authors	Sudarshini Ramanathan, Gina L O'grady, Stephen Malone, Claire G Spooner, **David A Brown**, Deepak Gill, Fabienne Brilot and Russell C Dale.

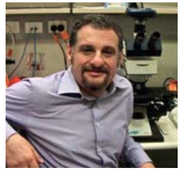
Partnership with WSLHD, USYD and national and international collaborators

Study outcome and impact

Recent reports suggest that seizures and encephalopathy may occur in children and adults with Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease. We describe the clinical, laboratory, and radiological course of four MOG antibody-positive children who first presented with isolated seizures without fulfilling clinical or radiological criteria for acute disseminated encephalomyelitis (ADEM) or other central nervous system demyelination syndromes, who months to years later developed more typical demyelination.

This study is an example of the continued collaboration between NSW Health Pathology and basic researchers. In this case, NSWHP's Immunopathology at Westmead Hospital (ICPMR) has had extensive collaboration with A/Prof Fabienne Brilot-Turville and Professor Russell Dale of the Sydney Children's Health Network.

Aside from this paper, there are have been several others that have been published, the latest in PLoS Medicine. This suite of studies has allowed NSWHP to fulfil its goals of translating bench to bedside research, supporting innovation and ensuring the availability of the best possible testing for our customers.



Professor David A Brown

04

Microbiology

Research activity summary

166 Publications
- 92 Original peer-reviewed articles
- 29 Reports and guidelines
- 3 Review articles
- 28 Editorials and commentary
- 14 Original non-peer reviewed articles

11 Grants/scholarship

31 Research projects

19 Students

12 Editorial positions

Publications

Other Research Activity

Publication in focus

Journal citation	BMC Infect Dis 2019 Jun 3;19(1): 491 **https://pubmed.ncbi.nlm.nih.gov/31159777/**
Title	**Contamination by respiratory viruses on outer surface of medical masks used by hospital healthcare workers.**
Authors	Abrar Ahmad Chughtai, Sacha Stelzer-Braid, **William Rawlinson**, Giulietta Pontivivo, Quanyi Wang, Yang Pan, Daitao Zhang, Yi Zhang, Lili Li and C Raina MacIntyre.

Partnership with UNSW, SESLHD, Kirby Institute and international collaborators in China and USA

Study outcome and impact

Who would have thought that this article would be so timely when it was written? The amount of online attention this article has had speaks for itself, with over 62k views at the time this report was produced.

The main aim of this study was to study the presence of viruses on the surface of medical masks. William Rawlinson assisted in data/sample collection and lab testing for pilot studies in Australia. Two pilot studies in laboratory and clinical settings were carried out to determine the areas of masks likely to contain maximum viral particles. A laboratory study using a mannequin and fluorescent spray showed maximum particles concentrated on upper right, middle and left sections of the medical masks.

Overall virus positivity rate was 10.1%. Respiratory pathogens on the outer surface of the used medical masks may result in self-contamination and virus positivity was significantly higher in masks samples worn for > 6 h and in samples used by participants who examined > 25 patients per day.

To maintain the functionality and capacity of the health care workforce during outbreaks or pandemics of emerging infections, they need to be protected. This study provides new data, which will help in developing policies for safe workplace environments.

Professor William (Bill) Rawlinson

04

Publication in focus

Journal citation	Australian Entomology 2019 Nov;58(4) **https://doi.org/10.1111/aen.12420**
Title	**Topical and spatial repellent bioassays agains the Australian paralysis tick, Izxodes holocyclus (Acari: Ixodidae)**
Authors	Chutipong Sukkanon, Theeraphap Chareonviriyaphap and **Stephen L Doggett**.

Partnership with Kasesart University, Bangkok

Stephen L. Doggett

Study outcome and impact

The Australian paralysis tick, Ixodes holocyclus, is the cause of significant human morbidity. Bites from the tick may result in paralysis and allergic reactions can include anaphylaxis and death, mammalian meat allergies and the transmission of infectious agents. This study focused on the personal protection options (repellents) to prevent a bite from the species.

Five personal repellents were tested along with coconut oil, and a citronella patch and wristband. These were all tested for repellency in a laboratory assay over the time intervals of 15 min, 1, 2, 3 and 4 h post application. For the personal repellents at 4 h, there was no statistical difference in repellency between the formulations of picaridin, DEET and lemon eucalyptus, with over 84% repellency recorded for all. Thus, these would be the personal repellents recommended for preventing tick bites. The citronella patch produced 100% repellency over 4 h; however, as this type of product is known to only provide protection close to the patch, it is not recommended for routine use.

Two spatial repellents were also tested in the laboratory for repellency and toxicity against I. holocyclus and tested for toxicity in the field. For the spatial repellents, both produced significant repellency and toxicity in the laboratory, but failed to produce any tick mortality in the field, and their use cannot be recommended.

This is the first published study investigating personal and spatial repellents for the prevention of tick bite from I. holocyclus.

04

Genomics

Research activity summary

54 Publications
- 50 Original peer-reviewed articles
- 1 Reports and guidelines
- 2 Review articles
- 1 Editorials and commentary

8 Students

6 Editorial positions

Publications

Other Research Activity

Publication in focus

Journal citation	Am J Med Genet A 2019 Oct;179(10):2152-2157 **https://pubmed.ncbi.nlm.nih.gov/31321886/**
Title	**Fetal diagnosis of Mowat-Wilson syndrome by whole exome sequencing**
Authors	Carey-Anne Evans, Jason Pinner, **Cheng Y Chan**, Lucy Bowyer, David Mowat, **Michael F Buckley** and **Tony Roscioli**.

Partnership with NeuRA, Sydney Children's Hospital and Royal Hospital for Women

Study outcome and impact

Mowat-Wilson syndrome (MWS) is a complex genetic disorder associated with changes in a gene called ZEB2, a gene that provides instructions for making a protein needed for proper formation of many organs and tissues before birth. The syndrome is mainly characterised by moderate-to-severe intellectual disability, facial dysmorphism, epilepsy, and various malformations including Hirschsprung disease, corpus callosum anomalies and congenital heart defects. It is rarely diagnosed before birth and there is limited information available on observable characteristics through ultrasound that are associated with MWS.

The publication reports the detection of a new fault in the ZEB2 gene, before birth, using whole exome sequencing. The fetus displayed microphthalmia (eye abnormality) in addition to heart defects and typical MWS facial dysmorphism. As the prenatal phenotypic spectrum of MWS expands, the routine addition of fetal genomic testing particularly in the presence of multiple malformations will increase both the sensitivity and specificity of prenatal diagnostics.

Genomic testing of rare syndromes gives parents of unborn children knowledge and guidance at what is an incredibly difficult time.

04

Public Health

Research activity summary

- **3 Publications**
  - 3 Original peer-reviewed articles
- **1 Student**
- **1 Research project**

Publications

Other Research Activity

Publication in focus

Journal citation	J Clin Microbiology 2019 Mar 28;57(4): e01727 **https://pubmed.ncbi.nlm.nih.gov/30541934/**
Title	**Impact of Rapid Molecular Diagnostic Testing of Respiratory Viruses on Outcomes of Adults Hospitalized with Respiratory Illness: a Mulitcenter Quasi-Experimental Study**
Authors	Nasir Wabe, Ling Li, **Robert Lindeman**, **Ruth Yimsung**, Maria R Dahm, **Susan McLennan**, Kate Clezy, Johanna I Westbrook and Andrew Georgiou.

Partnership with Macquarie University, University of Sydney and SESLHD

Study outcome and impact

A standard multiplex polymerase chain reaction (PCR), a method widely used to rapidly make millions to billions of codes of a specific DNA sample, offers comprehensive testing for respiratory viruses. However, it has traditionally been performed in a referral laboratory with a lengthy turnaround time, which can reduce patient flow through the hospital.

A controlled quasi-experimental study was conducted across three hospitals in NSW. The introduction of rapid PCR was associated with a non-significant 8.9-h reduction in median length of stay for all patients and a significant 21.5-h reduction in median length of stay among patients with positive test results. Compared with standard PCR testing, rapid PCR use was significantly associated with fewer blood culture, sputum culture, bacterial and viral serology tests, but not with fewer urine culture tests.

The introduction of rapid PCR testing of influenza and respiratory syncytial viruses (RSVs) for hospitalised adults was associated with a significant reduction in hospital length of stay for patients with positive results and a significant reduction in microbiology test use compared with those for patients who received standard multiplex PCR testing. These findings suggest there may be economic and patient outcome benefits from this intervention that should be tested in a future cost-effectiveness study.

04

Forensic & Analytical Science Service (FASS)

Research activity summary

8 Publications
- 5 Original peer-reviewed articles
- 3 Reports and guidelines

9 Students

23 Research projects

Publications

Other Research Activity

Publication in focus

Journal citation	Australian Journal of Forensic Science 2019, 52(6): 618-625 https://www.tandfonline.com/doi/full/10.1080/00450618.2019.1628303
Title	**Amylase testing on intimate samples from pre-pubescent, post-pubescent and post-menopausal females: implications for forensic casework in sexual assult allegations.**
Authors	**Sari D, Hitchcock C, Collins S, Cochrane C and Bruce D.**

Research making a difference

Study outcome and impact

The determination of the biological source of DNA recovered from exhibits in forensic investigations has become crucial information to either support or refute the allegations in a criminal trial.

The presence of amylase is the common method for identifying saliva in samples using antibody based Rapid Stain Identification (RSID) technology. However, amylase is also present in lower amounts in other body fluids e.g. breast milk and vaginal secretions. As NSW Health Pathology's Forensic & Analytical Science Service was validating commercial RSID kits it discovered that positive reactions were obtained with vaginal secretions from post-pubescent females. This has significant implications in the investigation of alleged sexual assaults involving oral contact with the genitalia of females of all ages. However, no empirical data was available as to whether amylase was also present in vaginal secretions of pre-pubescent children or menopausal adult females. Therefore, the main aim of this project was to determine whether there are detectable levels of amylase in female vaginal secretions at different stages of physiological sexual maturity using cohorts from each of these groups.

The results showed that some samples in each of the age cohorts gave positive results, albeit weak reactions, when compared to saliva controls. This illustrated an important limitation of the test in that a positive result obtained from a complainant's intimate swabs or underwear did not necessarily indicate that saliva was present. This has provided crucial information to inform accurate court testimony in cases of sexual assault. The study has also led to a re-validation of the kits using shorter elution times to examine whether weaker reactions from vaginal amylase are still detected and hopefully increase the specificity of the kit for the detection of salivary amylase only.

04

NSW Health Statewide Biobank

Research activity summary

- **12 Publications**
  - 5 Original peer-reviewed articles
  - 4 Review articles
  - 3 Editorials and commentary
- **2 Grants/scholarships**
- **1 Research project**
- **1 Student**
- **2 Editorial positions**

Publications

Other Research Activity

Publication in focus

Journal citation	Value Health 2020 Aug; 23(8):1072-1078 **https://pubmed.ncbi.nlm.nih.gov/32828220/**
Title	**Improving Academic Biobank Value and Sustainability Through an Outputs Focus**
Authors	Amanda Rush, Daniel R Catchpoole, Rod Ling, Andrew Searles, Peter H Watson and **Jennifer A. Byrne**.

Partnership with USYD, The Children's Hospital at Westmead, HMRI

Study outcome and impact

Many biobanks face challenges to remain financially sustainable and relevant. This commentary discusses the potential link between a lack of biobank sustainability and a lack of available data describing the outputs and benefits that are produced by biobanks. We conducted a bibliometric analysis of a comprehensive suite of biobank output terms (such as publications, personalised medicine, collaborations and grants), compared with three common single biobanking terms (processing, consent, and storage) over a defined period of time. Our analysis highlighted an under-representation of publications that enumerate biobank outputs.

Using biobank outputs as a measure of biobank value, we hypothesised that the current lack of information on valuing biobanks by their outputs confers a threat to their sustainability.

Boosting the available information on biobank outputs and utilising a broader range of output metrics would permit economic analyses such as cost-consequence analyses of biobank activity. Output metrics and cost-consequence analyses can allow biobanks to achieve efficiencies, improving the quality and/or quantity of their outputs. Biobank output measures provide all stakeholders with explicit and accountable data on biobank value, contributing to the evolution of biobank operations to best match research needs. Recognising that incorporation of an outputs focus into individual biobank business planning will require a shift from the current predominant focus upon internal biobank activities. Our work calls for a more far-reaching vision that emphasises biobank contributions to health and medical research.

05

Our research services

NSW Health Pathology provides a wide range of research services.

You can find more information on our **website**, including our statwide pricing model.

Toby Baldwin
NSW Health
Statewide Biobank

Hayter Wong
South Eastern
Sydney

Neil Catlett
Rural and
Regional NSW

Marette Dean
Illawarra
Shoalhaven

Catherine Hitchcock
Forensic &
Analytical Science
Service

Karla Jerez
Sydney

Tony Kay
Hunter New England
Central Coast
Mid North Coast
Northern Sydney
Northern NSW

Naheela Lalee
Western Sydney
Nepean
Blue Mountains

Andrew Sargeant
Point of Care
Testing (PoCT)

Zarah Timbol
Western Sydney
Nepean
Blue Mountains

Rina Upadhyay
South Western
Sydney

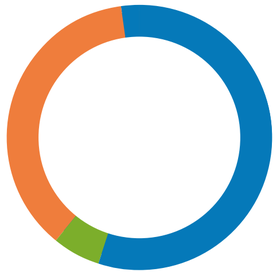
Santiago Vazquez
Forensic &
Analytical Science
Service Clinical
Trials

If you would like to request NSW Health Pathology clinical, forensic or statewide services to support your research project, our Research Coordinators are available to guide you. Contact information can be found **here**.

Clinical trials and research projects

Data from our Research Activity Register shows that NSWHP provided research services to 222 clinical trials registered to commence in 2019. There are a further 593 clinical trials registered as 'ongoing'.

Research services included sample collection and processing, archival (FFPE) tissue block and slide retrieval, tissue assessment of adequacy and processing, data entry, clinical testing and drug toxicology testing.



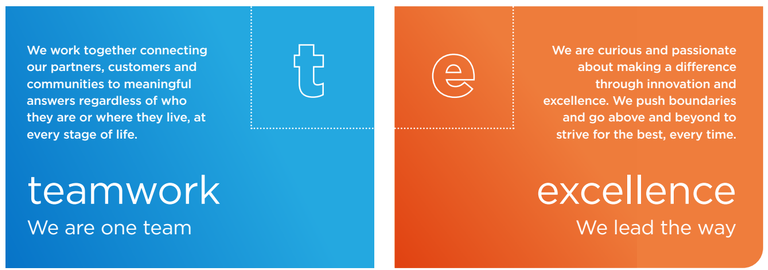
Clinical trials/research projects with start date in 2019

Commercial	129	58%
Cooperative	16	7%
Investigator initiated	77	35%
Total	222	

05

Our values

We always walk our talk by committing to our RITE values and behaviours.



Our structure and research committee

NSW Health Pathology's structure is focused on:

- building closer, more responsive relationships with our customers
- ensuring statewide strategies are more quickly and effectively implemented through a new operations model and stronger governance
- putting a stronger focus on the needs of regional and rural services
- a statewide service with a clear purpose of creating better health and justice systems

Our organisation is led by a Strategic Leadership Team that is responsible for setting and driving the direction of NSW Health Pathology and monitoring performance.

The NSW Health Pathology's **Research Advisory Committee** provides:

- Research leadership: monitor the **Research and Innovation Framework** implementation plan, identify gaps in activity and report back to the NSWHP Strategic Leadership Team
- Research advocacy: facilitate research collaboration, promote partnering opportunities and advocate for the use of NSWHP research policies and procedures
- Research culture: encourage a culture of sharing research activity
- Research advisor: on issues that may impact NSWHP researchers
- Research support: grant applications, business cases and research governance
- Research promotion: gather research material required for annual reports

05

Contacts

Position	Name	Email
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Acknowledgements

- Report development: Dr Bente Talseth-Palmer (Research Program Lead)
- Research Activity Register: Jessica Shephard (ICT Support Officer) and Dr Bente Talseth-Palmer (Research Program Lead)
- Strategic Communications: Renée Mantle (Communications Manager)
- Clinical Stream (Research) Leads: Stephen Adelstein (Immunology), David Sullivan (Clinical Chemistry), Catherine Hitchcock (FASS), James Kench (Anatomical Pathology), Sharon Chen (Microbiology), Emmanuel Favaloro/Leonardo Pasalic (Haematology), Dominic Dwyer (Public Health Pathology)
- Clinical Services Leads: Kristen Palmer (Genomics Project Officer)
- 2019 Clinical Trials (Services data): Tony Kay, Karla Jerez, Hayter Wong, Naheela Lalee, Zarah Timbol and Marette Dean.

Finally, a huge thank you to all the researchers across NSW Health Pathology who have taken the time to enter data into the Research Activity Register.

Your ongoing involvement in leading and supporting research underpins our purpose to 'create better health and justice systems' and is a true reflection of our vision to connect, pioneer and most importantly care.

Home

06

Donate

Research is an investment in the future health of our NSW community. No matter how big or small, a donation to NSW Health Pathology's Research Fund will help us create a better health and justice system.

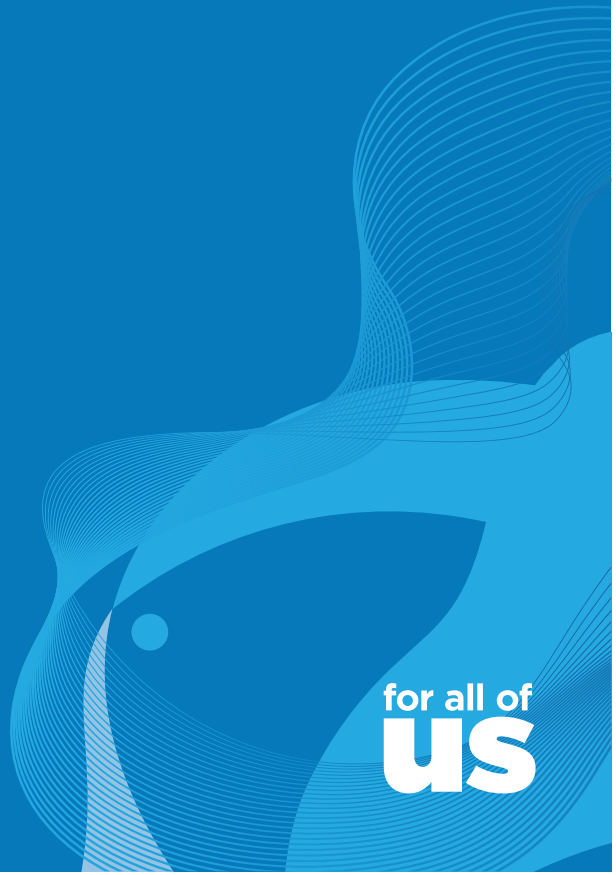
Donations to the NSW Health Pathology Research fund are greatly appreciated and all donations go directly to funding vital research into the causes, prevention or cure of diseases.

Donations over $2 are tax deductible and you will be provided with a receipt that can be used for taxation purposes.

Donate to our research

https://www.pathology.health.nsw.gov.au/research-and-innovation/donate-to-our-research

Leading through research and collaboration to deliver excellence in service and outcomes



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