Ramaciotti Centre for Genomics

Annual Report 2020/21

UNSW SYDNEY

Next generation science.
Working for you.

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Acknowledgement of Traditional Owners
We would like to acknowledge the Bedegal people that are the Traditional Custodians of the land on which the Ramaciotti Centre for Genomics is located. We pay our respects to the elders, past, present, and future, and recognise their continuing connection and contribution to this land.

Design
Slingshot Design

About Us

The Ramaciotti Centre for Genomics is Australia's leading genomics research and resource centre with the capabilities to deliver data, analysis, guidance and advice of the highest quality. It is a national infrastructure facility and a focus for the development and application of genomics in Australia. It was established in 1999 and is the largest genomics facility at any Australian University. It is comprehensively equipped with the latest next-generation sequencing technology, with single cell genomics platforms and with high throughput microarray systems.

Our Mission

Is to deliver internationally competitive genomic services of the highest quality using leading edge technology.

Our Objectives

- To provide our users with access to enabling technology and services, facilitating internationally competitive research.
- To provide genomics and related services of the highest possible quality.
- To provide support for bespoke and niche projects.
- To provide services at competitive rates.
- To build the genomics community in the state of NSW and beyond.

Our Values

- Excellence
- Collaboration
- Innovation
- Diversity
- Respect

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Contents

Director's Report 2020 and 2021

It's been a very busy two years for the Centre, and this biennial report contains many stories and details of the Centre's ongoing success. Nevertheless, 2020 and 2021 did bring some challenges. The arrival of SARS-CoV-2, COVID-19 and the associated lockdowns were unprecedented. The Centre had to find a way to maintain its operations, and to support a research community which was in need of data to keep science moving. Through incredible dedication from its staff, and support from the University of New South Wales, the Centre was able to complete a stunning number and variety of projects. This was done in the face of considerable uncertainty, the challenges of working in PPE at the workplace, supply chain issues and the unavailability of vendor technical support; and all this amongst the complexities of home schooling and other caring responsibilities. UNSW campus was a ghostly-quiet place for many months, but the Centre staff were there. I thank all the team for their professionalism, dedication and their fortitude and I admire the way that they cared and supported each other through the last two years. The Centre staff were recognized in 2020 with the Dean of Science Staff Excellence Award for their service to the community under such trying circumstances.

The Centre has also undergone a number of changes. After 16 years at the Ramaciotti Centre for Genomics, Dr Helen Speirs – the Centre's Deputy Director and Manager – took a new role in industry. We were very excited for Helen but were extremely sad that she was to leave us. Helen had been with the Centre since it was just a service for microarrays, and had been central to its success. She had seen the team change from just a few people to a team of more than 20, and had nurtured and led this team to become the largest genomics facility at any Australian University. We will miss Helen's outstanding strategic planning, business nous, her management skills and her amazing capacity to get things done. We will also miss her warmth, humour, energy and of course the occasional Scottish word! Later in 2021 we were delighted to appoint Dr Helena Mangs as the first Chief Operating Officer for the Centre, and the Centre's new Deputy Director. Helena has been with the Centre since 2011, and as Illumina Service Manager has been responsible for the operations and incredible growth of much of the Centre's short read activities. We look forward to seeing even more of Helena's leadership, enthusiasm, scientific expertise, business wisdom, and her building of teams and team culture in future years.

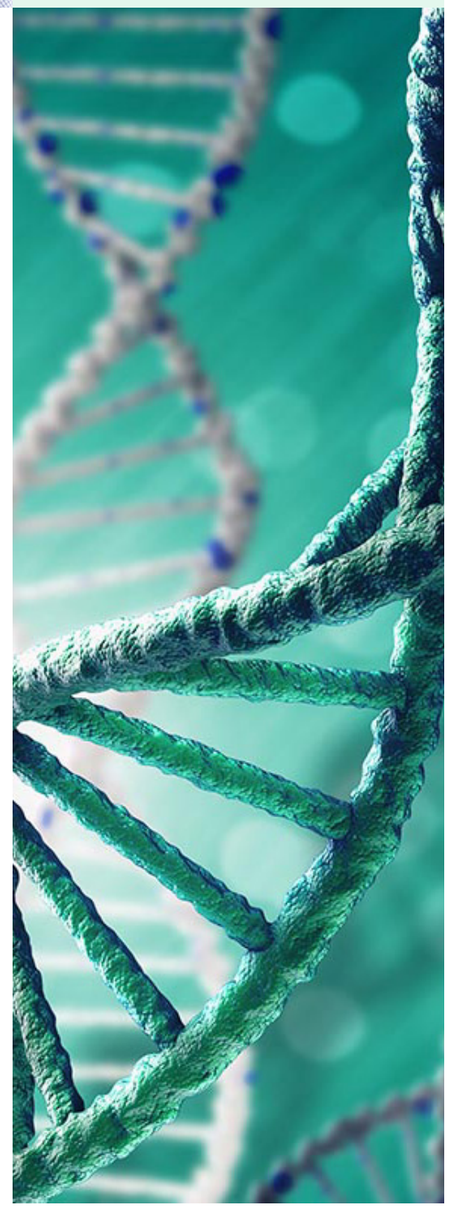
Despite the complexities of 2020 and 2021, the Centre successfully acquired new technology and developed or integrated these into successful services. In 2020, as part of a successful ARC LIEF grant, the Centre acquired an Oxford Nanopore GridION long-read sequencer. This follows on from the PacBio RSII and then Sequel sequencers that it has had to date. The GridION has already been used in a range of fascinating projects. In 2021, the Centre replaced its Sanger sequencer with a new Thermo 3730xl DNA Analyzer. This instrument has greater throughput and flexibility compared to the now (very) old ABI 3730, and we will sequence tens of thousands of PCR products and plasmids per year on this new platform.

Financially, the Centre remains in a strong position, despite a decrease in some types of sample analyses in 2020 and 2021. Our substantial fee-for-service income, support from Bioplatforms Australia (NCRIS) and from UNSW will ensure we can continue to support our team, to acquire exciting new technology and thus comprehensively serve the research community. We have participated in the national NCRIS roadmap process, the draft of which continues to acknowledge the importance of critical mass in genomics capacity and capabilities. We will work with our stakeholders in 2022 to secure support in the next round of NCRIS.

Last of all, we're happy to report some key milestones worth celebrating. We have now passed our 20th year as a Centre, and so are well into our adulthood. We're also delighted to report that some time in 2021, we analysed our 1,000,000th sample for one lucky researcher. We're not quite sure who that was, but we're happy to have had the privilege to do so. Our wonderful staff and steering committee have enjoyed these significant milestones and we warmly thank all in the research community for their ongoing support. COVID-19 has prevented us from having a big party to date, but we will do that in due course. We look forward to working with everyone in genomics in 2022.

Professor Marc Wilkins, Director

"We have now passed our 20th year as a Centre, and so are well into our adulthood. We're also delighted to report that some time in 2021, we analysed our 1,000,000th sample for one lucky researcher."



Steering Committee

The Ramaciotti Centre for Genomics is affiliated with other universities and medical research centres in the Sydney region.

These include the University of Sydney, Macquarie University, the University of Technology Sydney, the University of Newcastle, the Victor Chang Cardiac Research Institute and the Garvan Institute of Medical Research. Representatives from each sit on the Centre's scientific advisory committee. The committee help guide the Centre's strategic direction and objectives. We thank all current committee members for their contribution.

At the close of 2021 the committee consisted of:

Emeritus Professor Ian Dawes (Chair)
UNSW Sydney

Professor Marc Wilkins (Director)
UNSW Sydney

Dr Helena Mangs (Deputy Director)
UNSW Sydney

Professor Paul Munroe (Deputy Dean Faculty of Science) – UNSW Sydney

Professor Katherine Belov
University of Sydney

A/Professor Mark Cowley
Children's Cancer Institute, Sydney

Professor Garry Myers
University of Technology

A/Professor Sarah Kummerfeld
Garvan Institute of Medical Research

Professor Ian Paulsen – Macquarie University

Professor Brett Neilan – University of Newcastle

Alternates

Dr Amy Cain – Macquarie University
Professor Steven Djordevic – University of Technology, Sydney
Dr Carolyn Hogg – University of Sydney

Professor Aaron Darling from UTS stepped down from the committee in 2021. We thank him for his service and contributions to the Centre.

Our People

2020–2021 was a challenging year due to the COVID-19 pandemic. Our dedicated team allowed the Centre to continue operations. We thank them all for their hard work during what was a very difficult two years. We're especially in debt to many of our laboratory-based staff, who at times formed the only team onsite in UNSW biosciences during the lockdown periods. We're also very grateful to our staff who worked so effectively off site, in many cases juggling their role with schooling and caring responsibilities.

In 2021 we farewelled our Deputy Director and Centre Manager Dr Helen Speirs, who after 16 years at the Centre pursued a role with Illumina. We were delighted to appoint Dr Helena Mangs as the first Chief Operating Officer for the Centre, and the Centre's new Deputy Director. Helena been with the Centre since 2011 and has been responsible for the operations and successful growth of much of the Centre's Illumina-based services in that time.

The Centre also farewelled Dr Kristin North, Lisa Phan and Dr Eurwin Suryana in 2020, as well as Dr Gurjeet Kohli and Stefano Vecchiarelli in 2021. Kristin and Stefano joined Qiagen, Gurjeet joined Thermo Fisher Scientific, Lisa joined Vow Food, and Eurwin joined Neuroscience Research Australia. We welcomed five new members to our laboratory team, Dr Christie Foster, Dr Chathurika Daulagala, Ani Lack, Jane Phan Au and Steven Chan. We also welcomed Sarah Wilkinson stepping into the role of Administration Officer, covering for Abigail Teo who went on maternity leave in 2021.

At the close of 2021 our team included:

Centre Director
Professor Marc Wilkins

Deputy Director & Chief Operating Officer
Dr. Helena Mangs

Quality Manager
Keren Natalia

Research Manager
Jason Koval

Senior Research Officers
Dr. Jackie Chan
Tonia Russell

Research Officers
Dr. Erika Becker
Dr. Angela Chilton
Dr. Christie Foster
Scott Genner
Dr. Jessica Gurr
Dr. Caitriona Murray
Dr Kerry Nutt
Dr. Darshi Ramesh

Research Assistants
Jane-Phan Au
Steven Chan
Crystal Cui
Dr Chathurika Daulagala
Ani Lack
Rhys Stark

Administrative Officer
Abigail Teo (Maternity Leave)
Sarah Wilkinson

IT Infrastructure
Robin Heron

"We've had a real culture of excellence in the Centre, and it's been a privilege to work with our staff members, academia and industry"

Farewell Helen Speirs

Helen joined the Centre in August 2005 as Centre Manager and was appointed to the position of Deputy Director in 2016. Her leadership and operational expertise were instrumental in transitioning the Centre from a manufacturer of printed microarrays to that of a national facility delivering services using cutting edge genomic technologies. Those included next generation sequencing, high-throughput microarrays and single cell platforms. As each new technology came online it demanded a growth in staff numbers and a steady increase in the number of services offered, projects completed, and samples processed. Helen skillfully managed the increase in the size of the Centre and its operations throughout unprecedented growth. Helen also designed the floorplan and operational flow for the new laboratories built for the Centre in Biosciences E26. She then oversaw the complex move in 2017 whilst ensuring seamless operation.

She also initiated and championed the Centre's successful transition to an ISO accredited facility in 2018, and secured NATA accreditation for its operations. Helen said "When I joined the Ramaciotti Centre, it was a very small operation consisting of two staff printing microarrays for local research groups. I am immensely proud of how the Centre has grown and matured to where it is now, a leading genomics service provider that serves researchers Australia-wide and overseas. It was a privilege to work with so many talented staff over the years and see a culture of excellence develop within the team." Helen's legacy is a strong management and technical team, which ensured a seamless handover to Helena Mangs when she moved to her new role. Helen is enjoying her role in Illumina's APJ Large Genomics Initiative Team, which sees her working with multiple stakeholders across ANZ to deliver projects at scale.

Research Collaboration Highlights

Koala Genome Project: 450 new genomes to help koala conservation

Centre staff have joined with researchers at the University of Sydney to sequence, assemble, and publish the genomes of 450 Australian koalas as part of a world-first genomic sequencing program.

The Koala Genome Project was established by a consortium of 54 scientists from seven countries, with the goal to double koala numbers by 2050. The first koala genome was sequenced using PacBio long read sequencing technology at the Ramaciotti Centre for Genomics in 2018 (Johnson et al. (2018) Nature Genetics 50, 1102–1111). This story made headlines around the world, receiving media coverage from *CNN*, *National Geographic*, *New Scientist*, the ABC, and *The Australian*.

Having completed a reference koala genome, the project received more than $1 million in combined funding from the New South Wales and Australian Governments to map the genomes of 450 new koalas from across the entire species range.

This work has been led by Dr Carolyn Hogg (*pictured at right*), a Senior Research Manager and population biologist from the University of Sydney. Hogg and her team use genomic data to gain important insights into the unique biology of some of Australia's most vulnerable species, such as the koala.

According to Hogg, sequencing the genomes of a wider group of koalas from across Australia will be informative for conservation decisions and policy. "We wanted to generate a genomic database for the species' entire range, which could be used to inform a range of koala management questions. Which populations have the greatest adaptive potential? How will koalas respond to a changing climate? Is there a genetic basis for disease resistance?"

"A single reference genome is the puzzle box lid to which we refer all the other re-sequenced genomes: the 450 new koalas will provide us with information on genetic variation across the species range."

Whole genome sequencing of koala DNA samples was performed at the Ramaciotti Centre for Genomics using the Illumina NovaSeq 6000 platform. It was the Centre's largest genome sequencing project in a non-human species to date.

Centre staff from the next generation sequencing (NGS) team worked on the koala project under the direction of NGS Research Officer, Dr Jessica Gurr. Gurr has a background in conservation biology that helped her to effectively manage a wildlife sequencing project of this scale.

"A single reference genome is the puzzle box lid to which we refer all the other re-sequenced genomes: the 450 new koalas will provide us with information on genetic variation across the species range."

"Working with wildlife species is exciting but can be challenging as samples are often collected using various methods and from various sources. Coming from a conservation background gave me an awareness of the potential difficulties when working with wildlife samples."

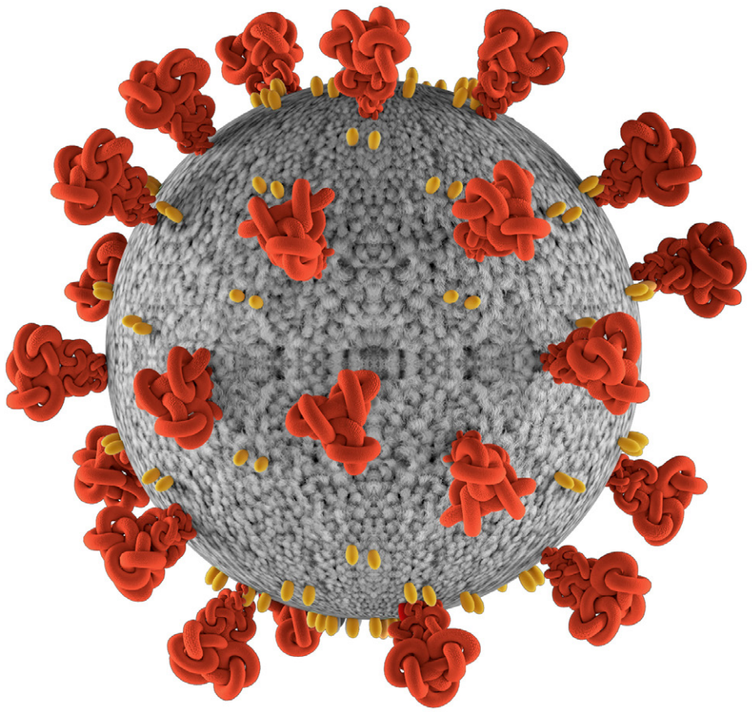
Gurr credits the combined knowledge and technical experience within her team for the completion of this challenging project. "The Ramaciotti team has extensive experience working with diverse sample types, and we understand the precious and often irreplaceable nature of samples derived from a threatened species. This project was truly a group effort and involved contributions from many different members of our team."

The new koala genomes have been made publicly available as part of the Amazon Web Services (AWS) Open Data Sponsorship Program, which covers the cost of data storage and transfer for datasets of high value to the scientific community. This allows researchers from around the world to access and analyse the genome sequences in the cloud.

Hogg believes that mining these koala genomes may hold the key to their long-term conservation. "Knowledge is power, and genomic data can be highly informative for conservation managers and their decision making. Maintaining a species' adaptive potential is important for their survival, and NGS allows us to develop tools to maintain genome-wide diversity."

The importance of genomics for preserving threatened species is echoed by Gurr. "NGS is a crucial part of the conservation toolkit when managing small and vulnerable populations, and can inform captive breeding recommendations, translocations, and target priority areas for habitat preservation."

"The Ramaciotti Centre is equipped with the latest NGS technology – we are dedicated to always delivering the highest quality advice and data to our clients and strive to make genomics accessible to all Australian researchers, including those working in the conservation space."

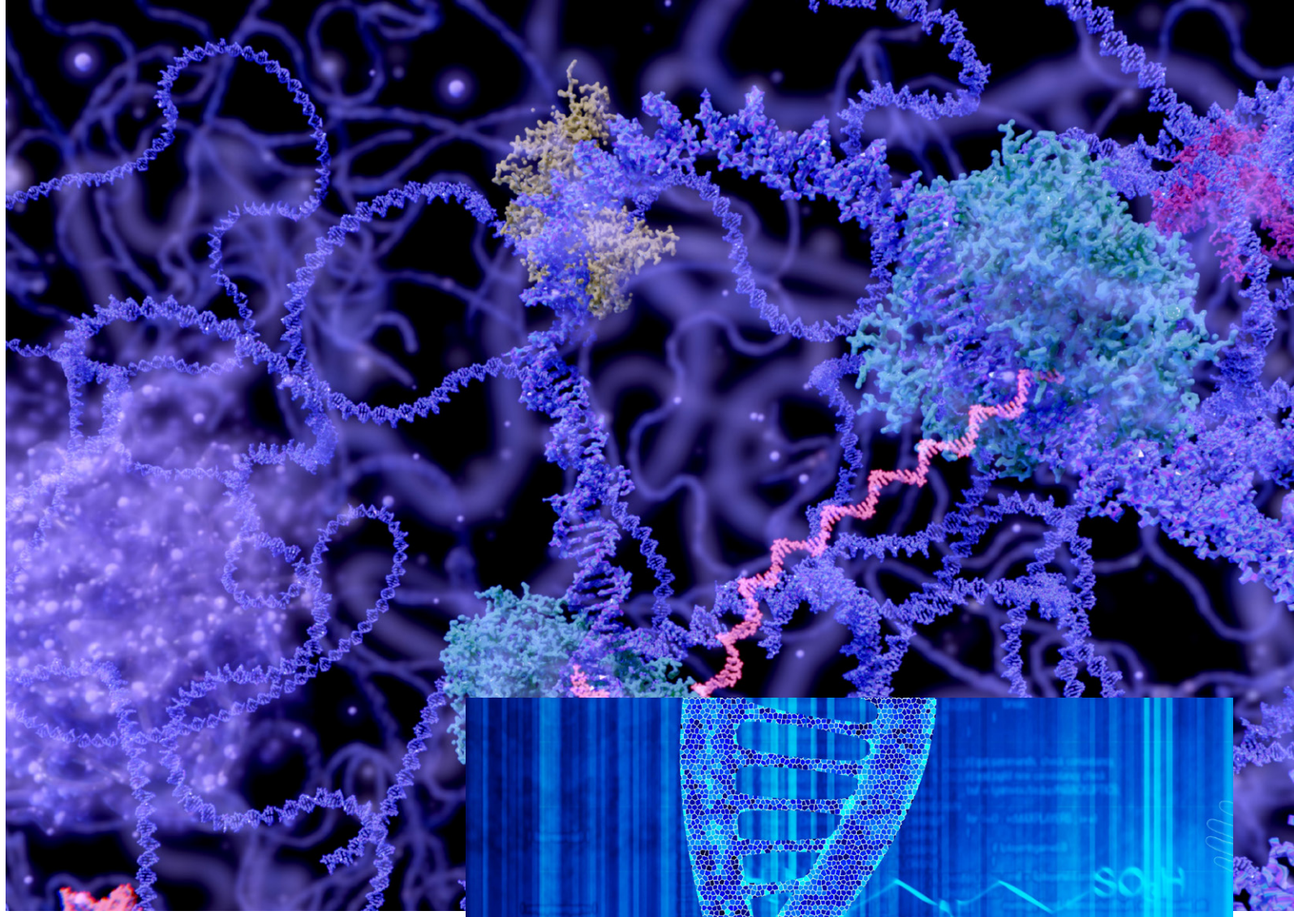


Are patients with serious COVID-19 co-infected with multiple viruses?

In patients with serious COVID-19, a pressing question is whether they are also infected with another respiratory virus. Professor Bill Rawlinson and team, from NSW Health Pathology and the Prince of Wales Hospital, investigated this question through analysis of the virome of 92 SARS CoV-2 patients. The Twist respiratory virus panel was used for this, along with short read sequencing, generating near-complete sequencing of the SARS CoV-2 virus in almost all patients. Use of that panel also revealed that 8% of patients were co-infected with either a rhinovirus or, less commonly, influenza virus. The study is important as it developed an effective method to determine the degree of co-infection and showed that in most of the patients sampled, that they were infected only with the SARS CoV-2 virus. The study was published in 2021, in the journal Scientific Reports (Kim et al. 2021 Feb 16;11(1):3934).

Multi-omics of disease progression in the oesophagus

Associate Professor Nadeem Kaakoush, from the School of Medical Sciences at the University of New South Wales, reported a multi-omics analysis of the oesophagus in Deshpande et al. (2021) Genome Medicine 13: 133. His team analysed biopsy samples from normal oesophagus and that affected by gastro-oesophageal reflux or metaplasia. To do this, they studied the transcriptome of the host cells by RNA-seq and the microbiome of the mucosa by 16S rRNA amplicon sequencing. Subsequently, the genomes of 11 disease-relevant strains of *Campylobacter concisus* were sequenced with PacBio and short-read methods. The study discovered dramatic changes in host transcriptome in metaplasia and reported five biomarker genes that change during progression. It also reported, for the first time, that the esophageal microbiome is distinct from the salivary microbiome and the enrichment of Campylobacter species is a signature of oesophageal disease.



The RNA Atlas project – a new resource for the human transcriptome

UNSW researcher Dr Ashwin Unnukrishnan, and Ramaciotti Centre staff Dr Nandan Deshpande and Professor Marc Wilkins, were members of a consortium that published a new human RNA atlas in Nature Biotechnology in 2021 (Lorenzi et al. 2021 39:1453-1465). The project analysed the total transcriptome of some 300 different human cell types, tissues and cell lines, with ultra-deep Illumina sequencing of ~150 million reads per sample. In itself, this is a unique resource that provides unprecedented depth and detail of the human transcriptome. Some of the most striking observations were the identification of a suite of novel non-coding RNAs – with 316 new microRNAs and 3,310 new long non-coding RNAs. The latter were confirmed through the mining of Oxford Nanopore long-read data. Functionally, the non-coding RNAs showed evidence of regulating protein-coding genes and pathways.

How do fruit flies change their response to attractants?

The Queensland fruit fly is a massive pest in the Australian fruit and grape industry, causing ~$1.3 billion of loss each year. Dr. Olivia Reynolds and team at the NSW Department of Primary Industries worked with the Ramaciotti Centre for Genomics to investigate how the fruit flies changed their response to attractants, after having been exposed to an attractant during development. RNA-seq analysis of the heads of flies, involving de novo assembly of the transcriptome and differential gene expression analysis, showed that the flies that did not respond to attractants expressed different chemoreceptor genes than those that did not. These were likely changing in the antennae of the flies, which then affected fly behaviour. The work was published in Scientific Reports (Khan et al. 2021 11(1):17632).

2020/2021 Updates

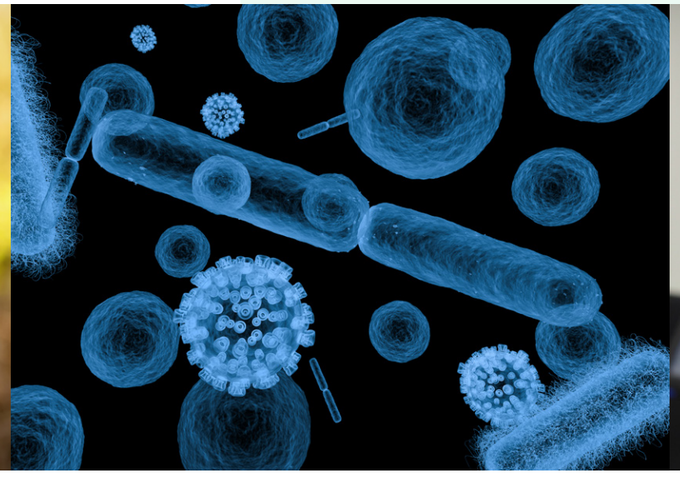
The Centre remained operational during the Covid-19 pandemic. We supported non-COVID-19 as well as COVID-19 research, with expedited turn-around times for time-sensitive research projects.

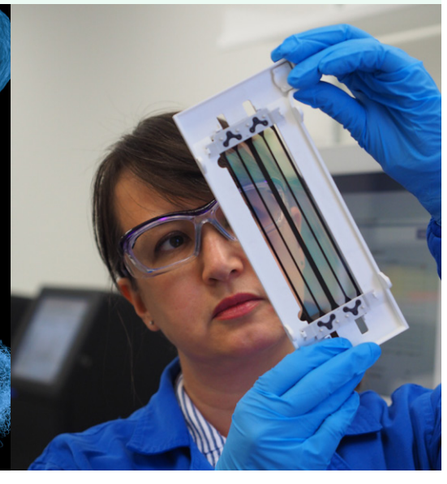
COVID-19-related projects included whole-genome sequencing of the SARS CoV-2 virus, investigation of the immune response to COVID-19, and detection of viral co-infections. In Feb 2020, we worked as usual but with social distancing restrictions, and by mid-year a proportion of staff were mandated to work from home. Staff with children were at times juggling home schooling with work, and training was interrupted for new staff. Despite shutdowns, Centre throughput remained strong in 2020. However, in 2021 the pandemic had a wider impact, with a year-on reduction in samples of 23%. This reduction in activity is of no lasting consequence for the Centre or its sustainability, and we are confident that sample numbers will recover in 2022 once shutdowns are minimized.

National Framework Dataset Programs

The Centre continues to work on several Bioplatforms Australia-funded framework dataset projects. These projects aim to build biomolecular datasets that have impact on problems of importance to Australia. The Centre has played a key role in providing expertise and generating data for the following projects:

- **Australian Microbiome (AM):** microbial diversity profiling across geographically expansive and diverse areas of Australian terrestrial and aquatic ecosystems (amplicon and metagenome sequencing).
- **The Amphibian and Reptile Genome Initiative (AusARG):** evolution and conservation of Australia's unique amphibians and reptiles that are under threat from climate, disease or habitat modification (RNA and DNA-seq).
- **Genomics for Australian Plants (GAP):** developing genomic resources to enhance our understanding of the evolution and conservation of the unique Australian flora (HiC/DNA-seq).
- **Oz Mammals Genomics:** building a foundation of genomic data for Australia's mammals, to support studies of evolution and conservation of the Australian mammal fauna (RNA and DNA-seq)
- **Threatened Species Initiative (TSI):** Improving conservation practices in wildlife recovery programs, using genomic technology and advanced computational biology (RNA and DNA-seq).





Quality system

The Centre was audited by National Association of Testing Authorities (NATA) in August 2020, the first official surveillance audit since acquiring NATA accreditation in early 2019. Accredited workflows are next generation sequencing of client prepared libraries and genotyping by microarray, but all other services offered by the Centre are run under the same quality management system in the same laboratories. This ensures an ongoing and consistent standard of service. Nine staff members received official internal audit training from NATA, and fourteen internal audits were performed in 2020 and 2021. Regular audits are important for continuous improvements to ensure we can deliver the quality customers expect from a service provider.

In 2021, with the support of UNSW office of the Pro-Vice-Chancellor (Research Infrastructure), the Centre procured a cloud-based quality management system software, Qualtrax. Qualtrax will house and manage our quality documents and provide automation on key processes, which will increase efficiency and reduce processing time as well as providing visibility and insight into performance. It will also allow us to make training and onboarding easier and faster through automatic reminders and role-based training assignment.

NATA
WORLD RECOGNISED ACCREDITATION

Partnership with the UNSW Cellular Genomics Futures Institute

The UNSW Cellular Genomics Futures Institute was founded in 2019 by UNSW and the Garvan Institute of Medical Research. It works in collaboration with the Ramaciotti Centre and the Garvan-Weizmann Centre for Cellular Genomics, bringing the power of genomics to study life at the level of the single cell.

The Ramaciotti Centre is a key provider of sequencing technology and expertise in the Institute, which in 2021 supported 96 research groups in 243 researcher-initiated projects. Single cell sequencing was undertaken on more than 66 million individual cells, generating approximately 400 billion total sequence reads. This made the Futures Institute the world's 3rd largest generator of cellular genomics data, only behind the Broad Institute at Harvard / MIT and the Sanger Institute at Cambridge University.

The long-term strategy of the Institute is to focus its resources and research on immunogenomics, especially to advance translation into clinical practice. This will be for the treatment of cancer and of autoimmune disorders. The Ramaciotti Centre will continue to be a core part of the integrated workflow of the Institute, in the realisation of this vision.

Technology and Analysis Highlights

Investigating 3D conformation; HiC
HiC, a genome-wide chromatin conformation capture method, is used to detect chromatin interactions in the nucleus. Crosslinking of genomic regions in close spatial proximity is followed by next-generation sequencing. The sequence data can be used to scaffold genomic assemblies, detect structural variation and provide 3D genome conformation information. The Ramaciotti Centre offers a HiC service using Phase Genomics or Dovetail kits. Tonia Russell, who manages the service, said "We handle a wide range of species and sample types. HiC requires a customized approach and careful consideration about the collection and types of samples used. I work closely with customers to ensure a successful outcome." The Centre recently contributed to the assembly of the New South Wales Waratah (Telopea speciosissima) and the Bilby (Macrotis lagotis) genome using HiC.

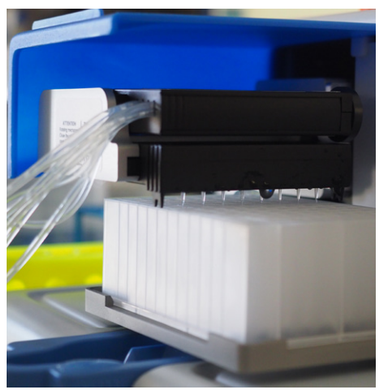
Client-prepared library service
The Centre offers a NATA-accredited client-prepared library (CPL) sequencing service, using Illumina's iSeq 100, MiSeq, NextSeq 500 and NovaSeq 6000. We have processed over 320 submissions under the CPL umbrella over the last 3 years. Submissions vary from whole-genome libraries, epigenetic studies, single-cell projects, transcriptomic and targeted amplicon or exome projects. The expertise accumulated over 12 years in NGS service provision means that our customers can be assured that we find the right solution for each project and ensure that the data produced exceeds manufacturer's specification. Dr Darshi Ramesh, who coordinates CPL submissions in the Centre, said "I really enjoy working with our clients and learning about their projects. We perform many different library prep types in-house but working with clients submitting client-prepared libraries means we are exposed to a larger range. We have learnt even more about how different library types behave, through this service." We work with vendors as well as our clients to ensure we offer a fast turn-around time for projects. Research Manager Jason Koval said "The majority of our customers are skilled in library construction, but we also get submissions from researchers that need extra assistance. We are always happy to provide guidance as needed".

Propel Axiom genotyping
In 2020 the Centre expanded its Thermo Fisher Axiom genotyping throughput by adding the Propel workflow to this service. Chemistry improvements include a faster amplification time as well as a new Fast Wash protocol, saving significant processing time. The Propel workflow includes Multidrop cassettes to dispense solutions, negating the need for single-use pipette tips. The Ramaciotti Centre is constantly looking for ways to minimize plastic waste and reduce environmental impact, and the multidrops are vital to achieving this goal. The Propel format is available in 96 and 384-sample formats and increases processing speed by 2–3 times. The genotyping team process samples from all areas of life sciences,

The Centre recently contributed to the assembly of the New South Wales Waratah (*Telopea speciosissima*) and the Bilby (Macrotis lagotis) genome using HiC.

but majority of samples have been from aquaculture or population genomic studies. Dr Helena Mangs, Deputy Director of the Centre, said "the Propel workflow is a massive improvement to the genotyping landscape. Not only does it mean we can process thousands of samples per week, but it is also a fantastic cost saving for the customer. It is a win-win for all". The Axiom service acquired NATA accreditation in 2019 and the Propel workflow has been validated and added to this list.

Long read sequencing
In 2020 we added GridION to our list of sequencing platforms. The GridION, from Oxford Nanopore Technologies, is a compact sequencer able to sequence and analyze up to five MinION flowcells per run. The flowcells can run independently or at the same time, ensuring flexibility. The GridION generates up to 50Gb of data per flow cell. For projects that require a larger amount of data, we collaborate with the Garvan Institute of Medical Research team to offer PromethION sequencing. Applications available include genome assembly, scRNA-seq, RNA isoform detection and targeted assays including adaptive sampling and Cas9 approaches. Long read sequencing improves de novo assemblies, mapping certainty, transcript isoform identification, and detection of structural variants. In addition, amplification-free kits allow direct, long-read sequencing of DNA and RNA while preserving base modifications. Since adoption of this technology, the Centre has sequenced fungal, microbal, plant and human DNA samples using ONT, and have lately implemented adaptive sampling. Adaptive sampling, or "read until" technology, is an advancement where the sequencer can be programed to reject or accept DNA strands based on specific sequences defined by the user.



Sanger sequencing
The ABI 3730 DNA Analyzer reached end-of-life in 2021 and we thus replaced it with the 3730xl DNA Analyzer. Sanger sequencing is still needed for many projects, including confirmation of plasmid or PCR sequences. It is a useful tool in confirming variants identified by NGS and to patch regions that are poorly covered by NGS. The Sanger team offers a wide range of services, from core prep to fragment analysis and variations of user prep. Ongoing studies performed at the Centre also include environmental metabarcoding, for quick and reliable species identification.

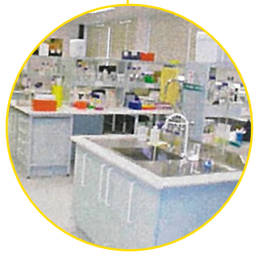
NanoString technologies
Since 2016 the Centre has used the NanoString nCounter FLEX and prepstations at the Faculty of Medicine to offer a gene expression profiling service. In early 2020 the machines were relocated to the Centre, to allow increased usage and access. NanoString technologies offer single-molecule detection with no amplification, suitable for gene expression profiling as well as gene fusion and CNV analysis. The system targets fragments as small as 100bp and can also capture miRNA. Low input requirements make it suitable for a range of sample types, total RNA, plasma, serum, PBMC, FFPE and cell lysates. Multiple panels are available for gene expression profiling, in oncology, immunology and neurology. The ease of use of this platform, and the streamlined data analysis, make it a useful tool for both standard and challenging FFPE samples.

20 years of genomics

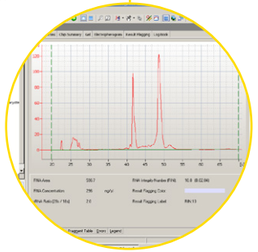
1999
Millennium Award from the Clive and Vera Ramaciotti Foundations and a Research Infrastructure Grant from ARC to support infrastructure in genomics

2001
Official opening of Centre wet lab facility, Sydney Microarray user group formed to share expertise, meeting monthly.

1 August 2000
The Clive and Vera Ramaciotti Centre for Gene Function Analysis formally established at the University of New South Wales. Printed microarrays for human, mouse and yeast genomic sequences. Expertise input to viral and custom human array work. 240sqm laboratory in the Life Sciences Building at UNSW.



2002
Expertise: DNA microarrays, robotics (genomics and proteomics), high-capacity PCR, and gene knockout technology including a large collection of yeast gene knockout mutants. Close relationship with the DNA sequencing facility (Sanger).
4 staff plus Director Ian W Dawes.



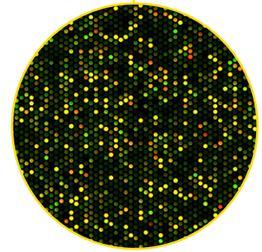
2003
A new microarray system acquired, to run boutique arrays and protein arrays. Total number of array systems now three. Additional servers installed, with additional expertise in bioinformatics added. Rat arrays offered.

2004
Cattle and sheep arrays added to the repertoire. Additional QC equipment installed.

2005
Affymetrix GeneChip system installed, providing a full service for users.

2006
Human and murine GeneChip arrays processed with robotics; 568 arrays in total (all species, expression and genotyping).
Sale of printed arrays; 385 in total. 48 publications arising from work performed or acknowledging the Centre.

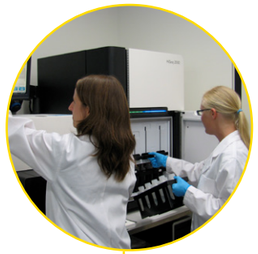
2007
Centre merges with the UNSW DNA Sequencing Facility.



2008
Name officially changed to "The Ramaciotti Centre for Gene Function Analysis". Agilent microarray and Bioanalyzer service set up. 6 staff members.

2009

Two next generation sequencers installed: Illumina GAIIx and Roche GS FLX platforms.



2010

Gene Titan installed, to automate Affymetrix array processing. Refurbishment of laboratory. Professor Ian Dawes stepped down from Director role late 2010.

2011

Illumina HiSeq 2000 sequencer, Illumina BeadArray reader and Covaris shearing machine installed. Professor Marc Wilkins appointed to the Director role.

2012

Illumina MiSeq and a second HiSeq 2000 acquired. 50 human genomes sequenced, as part of the Melanoma project (70X/50X coverage).

2013

Fluidigm Biomark and C1 single cell system installed, alongside a second MiSeq sequencer. Staff receive UNSW Faculty of Science Excellence Award in Professional and Technical Services. Name change to Ramaciotti Centre for Genomics.

2014

Illumina's NextSeq 500 sequencer installed. Collaboration with the Kinghorn Centre for Clinical Genomics to offer low-cost human whole genome sequencing on the HiSeq XTen platform. 11 staff members.

2015

PacBio RSII arrived, launch of the Koala genome project in association with the Australian Museum, the University of Sydney and University of Sunshine Coast. NGS Express and Zephyr robotics platforms installed. Rollout of a laboratory information management system (Clarity LIMS).

2017

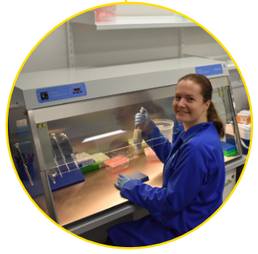
The Illumina NovaSeq 6000 and the PacBio Sequel acquired. Labarchives e-notebook implemented for record keeping and metadata management, replacing paper copies. The Centre moved into new custom-built 496 sqm facilities in the Biosciences building.

2016

10X Genomics Chromium single cell system installed, NanoString service implemented in conjunction with UNSW School of Women's and Children's Health.

2018

Landmark aspirin trial ASPREE, initiated to genotype 15,000 individuals using Axiom arrays. The UNSW Cellular Genomics Futures Institute launched, a collaboration between UNSW Sydney and the Garvan Institute of Medical Research. Illumina iSeq 100 and a third MiSeq added to Centre's extensive sequencing suite.



2019

The Centre acquired ISO/IEC 17025 accreditation by the National Association of Testing Authorities (NATA). Microsoft Dynamics 365, a customer relationship management (CRM) system, implemented to manage project enquiries. An MGI sequencer (G400) and further robotics systems installed.

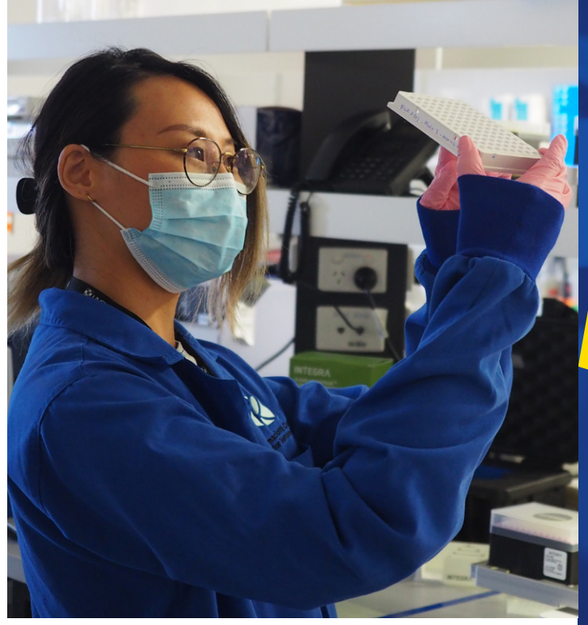
2020

Oxford Nanopore Technology GridION acquired, Propel implemented for Axiom High-throughput arrays. >88,000 samples analysed by the Centre. Staff receive the UNSW Dean of Science Staff Excellence Award.

2021

A Sanger 3730xl DNA Analyzer installed, replacing the ABI 3730. Over 1M samples processed by the Centre over the years. 22 staff members.

Operational Report



The Centre has a comprehensive technology portfolio that supports a wide range of genomic services. It is the largest genomics Centre at any Australian university. The Centre's technology suite includes long- and short-read next-generation sequencing, gene expression, microarrays and capillary sequencing. It works in association with the UNSW Cellular Genomics Futures Institute for the provision of analysis in single cell genomics.

Short Read Next Generation Sequencing
- Illumina NovaSeq 6000
- Illumina NextSeq 500
- Illumina MiSeq
- Illumina iSeq 100
- MGI DNBSEQ-G400

Long Read Next Generation Sequencing
- Oxford Nanopore Technology GridION

Sanger Sequencing
- AB3730xl

Gene Expression & Genotyping
- Thermo Fisher Scientific GeneTitan
- Fluidigm BioMark
- NanoStrin g nCounter

Single Cell Genomics
- 10X Genomics Chromium (machine located at Garvan-Weizmann Centre for Cellular Genomics, GWCCG)

Services Offered

The Ramaciotti Centre offers a wide range of genomic, transcriptomic and epigenomic services. All genomic analyses performed by the Ramaciotti Centre are carried out in our ISO/IEC 17025 accredited laboratories. Services offered to the research community include:

Next Generation Sequencing
Whole Genome
Exome, targeted and panel
Epigenome
RNA sequencing
Single cell sequencing (through UNSW Cellular Genomics Futures Institute, at GWCCG)
Microbiome and amplicon
Metagenome

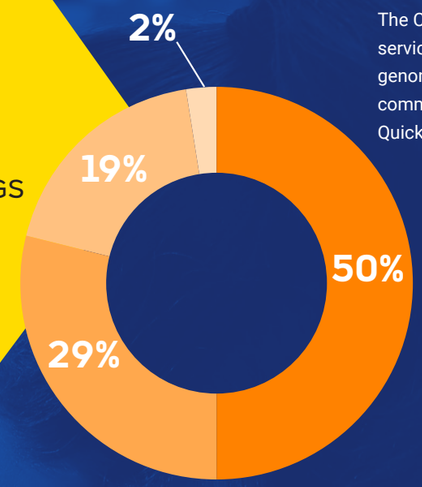
Sanger Sequencing
Core and user prep
Fragment analysis
Custom design & validation

Microarray
Genotyping
Gene expression
Transcriptome

Other Services
Gene expression by qPCR
Gene expression by NanoString
Genotyping by qPCR

2020

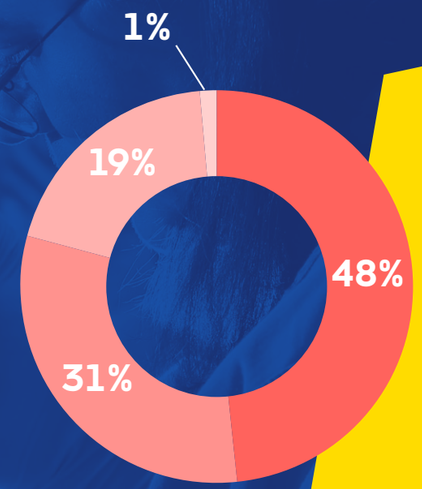
889 projects
88,645 samples
652 next generation sequencing runs
145Tbp of data produced NGS



Services Provided

The Centre has an outstanding track record in service provision, consistently delivering high quality genomic and transcriptomic services to the research community and to industry.
Quick stats by year:

44,472 samples sequenced by Next Generation sequencing
25,672 samples sequenced by Sanger sequencing
16,444 samples analysed by Microarray
2057 samples analysed using other genomic technologies



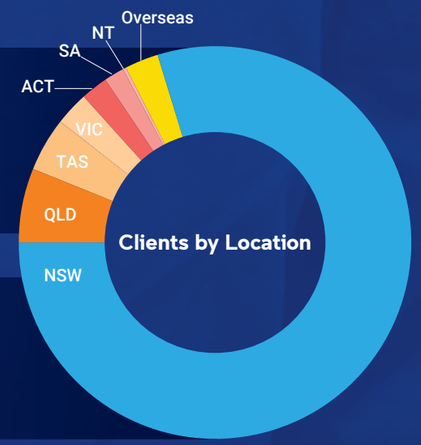
31,925 samples sequenced by Next Generation sequencing
12,693 samples analysed by Microarray
20,480 samples sequenced by Sanger sequencing
879 samples analysed using other genomic technologies

2021

861 projects
65,977 samples
549 next generation sequencing runs
223Tbp of data produced NGS

Client Profile

The Centre has a client base of over 500 research groups representing over 1,000 individual researchers from academia and industry. We serve all the leading universities and research institutes in Australia and support a wide range of research covering many disciplines.



Journal article acknowledgments

2020 170
2021 120

Publications

The Centre supports research across all areas of life sciences. In 2020 and 2021 the Centre was acknowledged as a service provider in 170 and 120 peer-reviewed publications, respectively. We thank the authors for their acknowledgement of the Centre's contribution. Below is a snapshot of publications from 2020-2021.

Constitutively bound CTCF sites maintain 3D chromatin architecture and long-range epigenetically regulated domains. Khoury et al. *Nature Communications* (2020). 10.1038/s41467-019-13753-7

Lymphoma driver mutations in the pathogenic evolution of an iconic human autoantibody. Singh et al. *Cell* (2020). 10.1016/j.cell.2020.01.029

Safety of bacteriophage therapy in severe Staphylococcus aureus infection. Fabijan et al. *Nature Microbiology* (2020). 10.1038/s41564-019-0634-z

Comparison of Bacterial DNA Profiles in Mid-Trimester Amniotic Fluid Samples From Preterm and Term Deliveries. Stinson et al. *Frontiers in Microbiology* (2020). 10.3389/fmicb.2020.00415

Lifting the veil on arid-to-hyperarid Antarctic soil microbiomes: a tale of two oases. Zhang et al. *Microbiome* (2020) 10.1186/s40168-020-00809-w

Heat-evolved microalgal symbionts increase coral bleaching tolerance. Buerger et al. *Sciences Advances* (2020). 10.1126/sciadv.aba2498

Ubiquitin chromatin remodelling after DNA damage is associated with the expression of key cancer genes and pathways. Cole et al. *Cellular and Molecular Life Sciences* (2020). 10.1007/s00018-020-03552-5

Genetic variation in PEAR1, cardiovascular outcomes and effects of aspirin in a healthy elderly population. Lewis et al. *Clinical Pharmacology & Therapeutics* (2020). 10.1002/cpt.1959

Eosinophil function in adipose tissue is regulated by Krüppel-like factor 3 (KLF3). Knights et al. *Nature Communications* (2020). 10.1038/s41467-020-16758-9

MicroRNA dynamics during hibernation of the Australian central bearded dragon (Pogona vitticeps) Capraro et al. *Scientific Reports* (2020). 10.1038/s41598-020-73706-9

Respiratory microbiota of humpback whales may be reduced in diversity and richness the longer they fast. Vendl et al. *Scientific Reports* (2020) 10.1038/s41598-020-69602-x

Intratumoral Copper Modulates PD-L1 Expression and Influences Tumor Immune Evasion. Voli et al. *Cancer Research* (2020). 10.1158/0008-5472.CAN-20-0471

Gut microbiota impact on the peripheral immune response in non-alcoholic fatty liver disease related hepatocellular carcinoma. Behary et al. *Nature Communications* (2021). 10.1038/s41467-020-20422-7

Application of environmental DNA for assessment of contamination downstream of a legacy base metal mine. Kavehei et al. *Journal of Hazardous Materials* (2021). 10.1016/j.jhazmat.2021.125794

Transcriptomic signature of early life stress in male rat prefrontal cortex. Green et al. *Neurobiology of Stress* (2021). 10.1016/j.ynstr.2021.100316

Using RNA-seq to characterize pollen–stigma interactions for pollination studies. Lobaton et al. *Scientific Reports* (2021). 10.1038/s41598-021-85887-y

Australian bush medicines harbour diverse microbial endophytes with broad-spectrum antibacterial activity. Ingrey et al. Journal of *Applied Microbiology* (2021). 10.1111/jam.15122

Combination efficacy of ruxolitinib with standard-of-care drugs in CRLF2-rearranged Ph-like acute lymphoblastic leukemia. Bohm et al. *Leukemia* (2021). 10.1038/s41375-021-01248-8

Characterization of beta-lactam-resistant Escherichia coli from Australian fruit bats indicates anthropogenic origins. McDougall et al. *Microbial Genomics* (2021). 10.1099/mgen.0.000571

Reduced adult neurogenesis is associated with increased macrophages in the subependymal zone in schizophrenia. Weissleder et al. *Molecular Psychiatry* (2021). 10.1038/s41380-021-01149-3

Temporal Comparison of Microbial Community Structure in an Australian Winery. Varela et al. *Fermentation* (2021). 10.3390/fermentation7030134

Improved high-throughput MHC typing for non-model species using long-read sequencing. Cheng et al. *Molecular Ecology Resources* (2021). 10.1111/1755-0998.13511

Microbiomes of an oyster are shaped by metabolism and environment. Scanes et al. *Scientific Reports* (2021). 10.1038/s41598-021-00590-2

Personal Network Inference Unveils Heterogeneous Immune Response Patterns to Viral Infection in Children with Acute Wheezing. Coleman et al. *Journal of Personalized Medicine* (2021). 10.3390/jpm11121293

Events and Engagement

The Centre is involved in events throughout the year to support the genomics community. This includes hosting seminars, holding educational tours and seminars, and exhibiting at national conferences. In 2020 and 2021, most of these were online due to Covid-19. Activities included:

6 educational seminars (online, and/or in person)

5 technology-specific seminars hosted (online)

2 educational virtual tours

2 promotional videos
https://www.youtube.com/watch?v=rA8MUR4pqNE
https://www.youtube.com/watch?v=5sRVUwSu7CE

8 conferences supported (exhibitor online, and/or in person)

2 student grants supported

Acknowledgements

The work that we do would not be possible without the support from our partners. The Ramaciotti Centre gratefully acknowledges the support it receives from NCRIS and the co-contributions made by the University of New South Wales

UNSW SYDNEY

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