EMBL Australia Partner Laboratory Network

2020 Highlights

EMBL Australia

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Foreword by EMBL Director General

The recent pandemic has revealed how imperative it is that countries share knowledge, pool resources, collaborate and align their strategic directions in order to deliver research that is relevant to pressing societal challenges.

Professor Edith Heard

I am very proud that EMBL has been able to provide many of the tools and approaches with which this pandemic is being fought around the world. Foundational scientific contributions by EMBL, such as cryo-EM, genomics, and open data infrastructures, have been critical in addressing the COVID-19 pandemic. You can read more about EMBL's efforts to fight the pandemic further in the report.

EMBL has also acted as a nexus for scientific cooperation that enables the fundamental research that is important to address the worldwide health emergency that we are facing.

This pandemic has highlighted our interconnectedness and our relationship to our planet in other ways too, including climate change, pollution and the catastrophic loss of biodiversity. Some of the next big challenges for human health, including the spread of antimicrobial resistance and the emergence of new pathogens, are linked to some of these planetary changes.

Like other parts of the world, Australia faces environmental emergencies and there is a pressing need for science that shapes effective policy. EMBL is meeting that challenge with new multidisciplinary research and services, as well as world-class technology and diverse training opportunities.

The study of life in context is at the core of EMBL's new programme, *Molecules to Ecosystems*, and is highly relevant to Australian science. In November 2020, EMBL member states unanimously endorsed this 2022-2026 scientific programme, which will leverage EMBL's scientific strengths while adding a strong societally relevant dimension. The new programme focuses particularly on an ecosystem-driven approach towards biological research that can explore matters of planetary and environmental importance, such as marine health and biodiversity, as well as human health. This approach allows for more holistic research.

It also continues EMBL's expertise in developing novel technology, advancing data science and theory, and training the next generation of interdisciplinary scientists.

Foreword by EMBL Director General (cont.)

The benefits of Australia's Associate Membership

Australia has been an extremely engaged and supportive associate member state of EMBL since 2008.

In the past years, EMBL's links to Australia have deepened and expanded. EMBL supports the growing network of Partner Laboratory research groups distributed across Australia, which are modelled on EMBL and continue to deliver excellent results. Through this network, as well as through various exchanges, joint workshops, meetings and use of services and facilities, EMBL has been in a position to contribute to the advancement of Australia's national priorities, such as internationalisation of research, increasing big data capacity, imaging and the development of ambitious research projects in various areas related to life sciences research.

Through the associate membership, Australian delegates can share their country's perspective on the EMBL Council, an important international forum where top scientists and science policymakers strategically discuss breakthrough science with broader societal impacts.

The Australian research community can access and contribute to a large number of EMBL activities, benefit from EMBL's state-of-the-art research facilities and services, and help create next-level science, training, and research. Please see a comprehensive list of EMBL services available to the Australian life science community here, with links to specific facilities and capabilities, including the new EMBL Imaging Centre due to open later in 2021.

A selection of recent stellar research collaborations between EMBL and Australian researchers can be found on page 18 of the report.

Looking to the future, I believe that EMBL's new scientific programme will expand numerous opportunities for cooperation and engagement, as it increases Australia's access to services, facilities, and training.

Several new research areas of EMBL's next programme, such as Human Ecosystems, Microbial Ecosystems, Planetary Biology, Infection Biology, and Data Science, are particularly relevant and align with Australia's national priorities, which should result in ever closer collaborations and new, ambitious directions.

Moreover, the type of research that EMBL will do now will decisively contribute to economic recovery and growth. This is the type of science that the new programme will strongly support.

EMBL's relationship with Australia, and specifically the Australian science community, remains important to increasing the quality and impact of global collaborative research, especially as we move forward with EMBL's new programme.

I look forward to our way ahead, addressing big research questions that benefit society and help us mitigate the effect of this pandemic, together.

Report of EMBL Australia Scientific Head

Without a doubt, 2020 was the most challenging and disruptive year the global community has faced for more than a generation.

Professor
James Whisstock

Whilst Australia has, to date, escaped the worst ravages of the SARS-CoV-2/COVID-19 pandemic, our scientific community has nevertheless faced the challenges of lockdowns, reagent and equipment shortages, and having to rapidly change our laboratory practices.

In response to COVID-19, members of the EMBL Australia Partner Laboratory Network (PLN) have, like the scientific community more broadly, brought their research skills to bear on understanding and combating the infection and disease caused by the SARS-CoV-2 virus (more on page 8). In particular, our scientists have contributed to vaccine trials, developed new computational approaches to track the spread of the virus, and contributed greatly to our understanding of how the immune system responds (and sometimes over-responds) to SARS-CoV-2. The latter research has been performed both in the context of humans and with regards to animals, such as bats, that carry the virus.

Throughout what has been an extremely difficult year, I am also very pleased that the PLN has continued to expand – with Senthil Arumugam establishing his laboratory at Monash University, and Vaishnavi Ananthanarayanan moving to Australia (via hotel quarantine) and establishing her laboratory at UNSW Sydney.

As the sun set on 2020, the first vaccination programs against COVID-19 were commencing – less than a year since the publication of the SARS-CoV-2 genome. As we reflect on this extraordinary effort, it is worth considering how and why the global scientific community was able to respond so fast to a novel disease. In short, basic research and the application of state-of-the-art infrastructure has proven critical – particularly in the context of viral immunology and the structural biology of the SARS-CoV-2 spike protein. In respect to the latter research, the advent of atomic resolution cryo-electron microscopy, developed in part in the 1980s by the then EMBL group leader and Nobel Laureate Jacques Dubochet, has proven particularly critical.

By establishing and supporting outstanding and driven young group leaders, the PLN aims to ensure that Australia remains at the forefront of biomedical research, particularly in the context of the application and development of new technology and infrastructure. Without exception, our group leaders are closely engaged with a diverse array of NCRIS-supported research infrastructure platforms.

Indeed, many of our scientists are directly engaged in the development of new instrumentation that will enable them to address key research questions, as well as contributing more broadly to the wider national and international life-science community.

It is enormously exciting that, in the midst of the pandemic, 2020 saw the launch of several new microscopy technologies and informatic tools from the EMBL Australia PLN in the context of super-resolution microscopy and cryo-electron microscopy. Additionally, many of these ongoing initiatives involve collaborative engagement across multiple NCRIS-supported platforms, including Microscopy Australia and Bioplatforms Australia.

I hope you enjoy this report of our highlights, and wish you all a safe a productive 2021.

About EMBL Australia

EMBL Australia is a life science network that supports ambitious research projects and provides access to infrastructure and training to early-career Australian scientists.

Australia is an associate member of the European Molecular Biology Laboratory (EMBL) – Europe's flagship life sciences institution.

The associate membership gives Australia the opportunity to internationalise our life sciences research, introduce the world's best young researchers to new networks and tools here in Australia, and develop highly competitive research teams networked across the nation, with Europe and Asia.

Supported by the National Collaborative Research Infrastructure Strategy (NCRIS) program, an Australian Government initiative, EMBL Australia is at the cutting edge of life sciences research in Australia. EMBL Australia has:

- a **Partner Laboratory Network** (PLN) consisting of 16 research groups led by outstanding early-career researchers at nodes in Victoria, South Australia, New South Wales, Queensland and the ACT
- a nationwide reach through **student training programs**, including a PhD course, postgraduate symposium, travel grants and PhD program
- access to **international linkages** through EMBL and the European Bioinformatics Institute (EMBL-EBI).

Australia became the first associate member of the EMBL in early 2008. Launched in 2010, the EMBL Australia Partner Laboratory Network set out to take full advantage of this unique affiliation, with the goal of strengthening the nation's global position in life sciences research.

The EMBL Australia PLN is hosted at the South Australian Health and Medical Research Institute (SAHMRI), University of New South Wales (UNSW), Australian National University (ANU), the Garvan Institute of Medical Research, QIMR Berghofer Medical Research Institute (QIMR Berghofer) and Monash University (Monash).

The EMBL Australia Secretariat is hosted by the Monash Biomedicine Discovery Institute.

The EMBL Australia Council oversees and guides the activities of EMBL Australia.

The Partner Laboratory Network also has a Steering Committee, which is composed of senior representatives of each institution that form part of the network and is chaired by EMBL Australia's Scientific Head, Professor James Whisstock.

An international approach to bioinformatics

The EMBL Australia Bioinformatics Resource (EMBL-ABR) was formed in 2016 in collaboration with EMBL-EBI and has been a significant initiative under Australia's associate membership to EMBL. Evolving from the learnings from EMBL-ABR and significant national consultations and pathfinder activities, the Australian BioCommons was established in October 2019.

In 2020, ELIXIR – an intergovernmental consortium bringing together national life science data infrastructure resources in Europe – launched a three-year collaboration strategy with the Australian BioCommons research infrastructure, seeking to create a cooperative plan to exploit international synergies between the two research infrastructures. Australian BioCommons will be actively involved in many of the activities related to the European life science infrastructures.

The mutually beneficial alliance will enhance the complementary areas of both infrastructures and is based on common areas of alignment, ranging from international adoption of standards, such as the Global Alliance for Genomics and Health (GA4GH), to international training activities.

Research Groups

In 2020, EMBL Australia consisted of 16 research groups at six institutes across Australia.

With the freedom to drive their own ambitious research projects, EMBL Australia group leaders are exceptional and innovative researchers who apply novel approaches and techniques to complex scientific problems.

They ask challenging research questions and publish in high-impact journals.

$29M+

External funding grants*

16

Group leaders

06

Research institutions

62

Researchers

71

Students (PhD, Master & Hons)

* Includes the entire amount of individual and collaborating grants for projects active in 2020

Partner Laboratory Network

Brisbane

QIMR Berghofer Medical Research Institute

Michelle Boyle
Malaria mechanisms

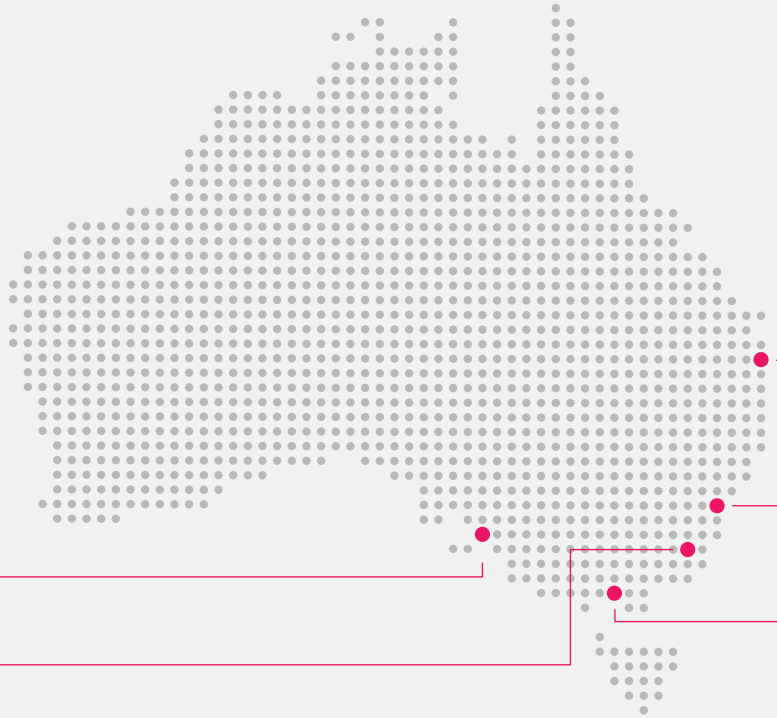
Adelaide

SAHMRI South Australian Health & Medical Research Institute

David Lynn
Immunity and genomics

Ville-Petteri Mäkinen
Systems epidemiology

Pirjo Apaja
Organelles and trafficking



Sydney

UNSW THE UNIVERSITY OF NEW SOUTH WALES

Yann Gambin
Single molecule science

Maté Biro
Immune response

Richard Morris
Systems theory

Vaishnavi Ananthanarayanan
Cytoskeleton and molecular motors

Garvan Institute of Medical Research

Robert Weatheritt
RNA biology

Canberra

Australian National University

Barry Thompson
Epithelial biology

Eduardo Eyras
Computational RNA biology

Melbourne

MONASH University

Prof James Whisstock
Scientific Head

Max Cryle
Antibiotics and bacterial infections

Chen Davidovich
Chromatin biology

Senthil Arumugam
Cellular physiology

Mikaël Martino
Bone regeneration

Harald Janovjak
Synthetic biology

COVID-19 Research

In 2020, the international research community collaborated on a scale and at a speed never seen before to battle the global coronavirus pandemic.

While the pandemic and associated restrictions in various Australian states posed significant challenges to the way research laboratories operate, many EMBL Australia group leaders admirably joined other basic researchers in answering the urgent call to arms, placing their planned research on hold to focus on the fight against COVID-19.

Here is how some of the PLN group leaders are contributing to the global efforts to research, understand and conquer COVID-19:

Leading the SA arm of international trial for protective vaccine

Professor David Lynn is leading the South Australian arm of the BRACE trial, one of the largest vaccine trials underway against COVID-19.

The international trial tests whether the Bacillus Calmette-Guerin (BCG) vaccine – originally developed for protection against tuberculosis – can protect healthcare workers who contract COVID-19 from developing severe symptoms.

Led by Professor Nigel Curtis at the Murdoch Children's Research Institute, the trial was expanded in May 2020 following a $10 million grant from the Bill & Melinda Gates Foundation.

Prof Lynn said the study would also have significant implications for our understanding of how important BCG is from a global health perspective, unrelated to COVID-19. "If we can demonstrate that it can provide non-specific protection against COVID-19, then it can potentially be used in many other settings," he said.

The trial is continuing, with international participants being recruited.

Artificial intelligence tool to detect viral co-infections in COVID-19 patients

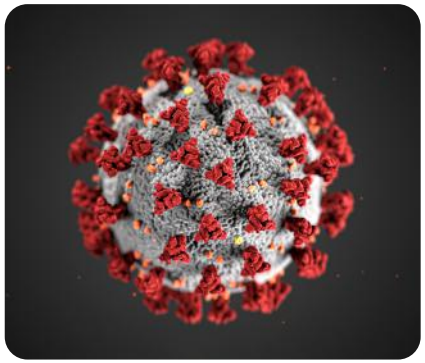
Professor Eduardo Eyras and his collaborators developed a tool to detect viral co-infections in COVID-19 patients to help develop informed strategies for antiviral treatment, vaccination and epidemiological control in the COVID-19 pandemic.

Studies reported that around 20 percent of SARS-CoV-2-positive individuals had a co-infection with other respiratory viruses, which increased the severity of the disease.

Prof Eyras said identifying those co-infections was relevant for treatment and prognostic purposes, but the standard of viral detection was based on PCR assays directed to SARS-CoV-2 only, missing possible co-infecting viruses.

He contributed to the development of PACIFIC – a new computational tool, based on artificial intelligence for natural language processing, which can identify SARS-CoV-2 and 361 other viruses at a sample concentration as low as 0.03%, with high specificity, using high-throughput sequencing.

"With PACIFIC, we were trying to provide a fast and easy-to-use, end-to-end tool that would enable researchers to monitor viral infections and co-infections to help manage the global COVID-19 pandemic," Prof Eyras said.



COVID-19 Research (cont.)

Researching animal models and hyper-inflammation

Dr Yann Gambin and his team researched why the coronavirus affects only some animals – like minks, cats and tigers – but not others, and the molecular mechanism for hyper-inflammation.

The research, published in *Emerging Microbes and Infections*, aimed to help inform new antiviral strategies and enable the development of more effective animal models for COVID-19.

The study also showed that one species of bat presents high similarities with humans and would have enabled the coronavirus to gain pathogenicity. Dr Gambin and his colleagues followed these fascinating new leads, which included comparing the immune response of humans and bats to understand how bats can tolerate coronavirus.

The Gambin Group is now comparing the protease activity of SARS-CoV-2, SARS and MERS and has found exciting differences in selectivity and efficiency. These differences could not be predicted from the consensus cleavage sequence and show that MERS more aggressively attacks our immune system; the mortality rate of MERS is 34%, compared to 11% for SARS and 3-4% for SARS-CoV-2.

Visualising the Australian coronavirus genome

Associate Professor Ville-Petteri Mäkinen visualised the 29,893 base pairs that comprise the SARS-CoV-2 genetic sequence collected from the first Australian person with COVID-19 in January 2020, calling it "among the most influential compact pieces of text ever to emerge".

National COVID-19 artificial intelligence research platform

A team co-led by Associate Professor Ville-Petteri Mäkinen finished the first screening of COVID-19 artificial intelligence literature towards a new evaluation framework for healthcare.

A/Prof Mäkinen co-leads the Algorithm Team within the Australian Alliance for Artificial Intelligence in Healthcare (AAAiH), which created a national COVID-19 artificial intelligence research platform to aggregate available information about COVID-19 and match skilled researchers with COVID-19 projects.

In the Media

Professor David Lynn's work on a COVID-19 vaccine trial received media coverage in various publications and Professor James Whisstock had an opinion piece calling for greater government investment in scientific research published in the *Herald Sun*, the largest Australian newspaper by circulation.

COVID-19 Research (cont.)

Case study: Overcoming the challenges imposed by strict COVID-19 lockdowns

Dr Arumugam began establishing his lab at the Monash Biomedicine Discovery Institute after commencing as an EMBL Australia Group Leader in October 2019, bringing much of his former lab from UNSW.

Microscopy is a central part of the work of the Arumugam Group – which aims to understand the organisational principles of endosomal trafficking – and the lockdowns in Melbourne imposed due to COVID-19 led to delays in the transporting and setting up of his microscopes.

Dr Arumugam told the *Journal of Cell Biology* he was forced to restrategise: "To restart the lab with a dedicated microscope to train students, and to be able to perform some experiments, I scavenged through old microscope parts at our imaging facility and various other storages and put together a wide-field microscope to perform live-cell studies."

He said various departments at Monash University helped provide access to other specialist microscopes with COVID-safe protocols in place, allowing his team to complete impending experiments for the revision of a manuscript.

"Post-acquisition movie-making and analysis of large datasets kept us busy under lockdown," Dr Arumugam said.

"We also moved our analysis computers home, allowing us to work remotely. We managed to parse through various other datasets that we had acquired at UNSW but were awaiting analysis, figures, movie making, et cetera – allowing us to move forward with collaborative projects and our own pending stories."

Dr Arumugam said he was lucky to lead a very adaptable and persistent team of researchers, who made moving forward with experiments while strict restrictions were in place look easier than it was.

Dr Senthil Arumugam (third from right) and his dedicated team persisted through strict Victorian lockdown restrictions.

An EMBL-led international response to COVID-19

The fundamental advances in molecular biology made by EMBL have played a pivotal role in delivering new treatments or vaccines against SARS-CoV-2.

During the pandemic, EMBL actively contributed to discovery research of SARS-CoV-2 and provided its experimental and data infrastructures to the scientific-user community, including in collaboration with institutes in member states.

Over the past months, EMBL has re-purposed its facilities and has started several coronavirus-related projects across all EMBL sites. The European COVID-19 Data Platform was promptly set up: a collaborative space for the rapid sharing and analysis of COVID-19-related data. A significant component of the platform is the COVID-19 Data Portal that, in 2020, recorded over 3.6 million web requests by users from more than 175 countries. Close to 550 institutions from 49 countries have deposited data, and the portal currently offers open access to more than half a million data records.

In addition, the COVID-19 Data Platform as a whole enables the mobilisation and coordination of viral genome sequence data across Europe and globally via the International Nucleotide Sequence Database Collaboration. A specific feature offered to EMBL's member states is the provision of support for setting up Data Hubs where viral genome sequence data can be coordinated (e.g. from a particular nation) with controlled public release.

By the end of 2020, the Data Portal had been accessed more than 20,000 times by Australian visitors. The Australian scientific community had by then deposited close to seven per cent of all the viral sequences that are available through the Data Portal.

Alongside many other COVID-19 research topics, EMBL scientists have been involved in understanding the structure and function of components of the SARS-CoV-2 virus, the genomic epidemiology of the faster-transmitting B.1.1.7 strain (the 'UK variant') and the EMBL Hamburg SAXS beamline has been used for research by companies who develop mRNA vaccine technologies. A periodic update of EMBL's efforts was regularly provided to the Australian Council delegates.

Various EMBL research groups and scientific service facility teams have joined forces with external colleagues – locally, nationally, across member states and beyond. These close collaborations have been very fruitful, led to important insights into SARS-CoV-2 biology, and contributed to the development of new detection methods, mRNA vaccines, and the identification of potential COVID-19 treatments.

To exchange valuable know-how, learn from experience and identify best practices relating to the handling of SARS-CoV-2, on 3 July 2020, EMBL hosted a conference bringing together experts in various disciplines. The speakers presented latest findings from their research on SARS-CoV-2 and other viruses, showed first epidemiologic data on the ongoing pandemic, and addressed current limitations in our scientific understanding of emerging pathogens. They highlighted the importance of fundamental research, collaboration and data-sharing in containing the SARS-CoV-2 pandemic, and discussed opportunities to improve the response to pandemics in future.

The quick and easy international sharing of SARS-CoV-2 data, particularly sequence data, is helping researchers to understand the virus and the disease, monitor its spread and develop treatments and vaccines.

In January 2021, EMBL-EBI initiated an open letter in the hope to galvanise the international scientific community to show support for open sharing of SARS-CoV-2 data. The open letter, hosted on the COVID-19 Data Portal website, has already been signed by hundreds of researchers.

In September 2020, EMBL Deputy Director General and Joint EMBL-EBI Director Prof Ewan Birney – who was a participant in the Oxford trial for a COVID-19 vaccine – shared his views on the global coronavirus pandemic in the EMBL Australia newsletter.

Enhancing Australia's Research Infrastructure

Australia's associate membership to EMBL provides Australian researchers with access to EMBL's world-leading facilities, and the ability to directly enhance Australia's research infrastructure.

EMBL's scientific services encompass more than 40 bioinformatics and data resources* and more than 20 experimental services in the fields of structural biology, imaging, genomics, proteomics, metabolomics, in vivo gene editing, and chemical biology.

Beyond the facilities that exist overseas, EMBL Australia also directly contributes to the development of Australia's own research capabilities – for example, by leading the development of a national-scale data asset to integrate molecular imaging with bio-analytics.

However, EMBL Australia's biggest contribution to enhancing Australia's research infrastructure is the world-leading early-career researchers that form the Partner Laboratory Network. Inspired by EMBL, EMBL Australia adopted a research model unique to Australia that focuses on recruiting and nurturing the brightest and most ambitious early-career researchers and building a national network to best utilise Australia's scientific infrastructure. EMBL Australia group leaders are connected to key NCRIS platforms and have access to infrastructure and expertise to maximise the nation's technology investment.

Most importantly, EMBL Australia group leaders – via their cutting-edge research and expertise in specialised and innovative areas – are helping to build new and ground-breaking life sciences infrastructure and enhance the reputation of leading institutes and universities across Australia.

* In 2019 alone, bioinformatics databases at EMBL-EBI registered 144,959,023 web requests and 833,371 unique hosts from Australia. These resources, provided and maintained by EMBL, are free of charge to Australian scientists. According to a 2015 Beagrie EMBL-EBI economic impact study, the average value for an annual subscription for access to these services that users would theoretically pay was €1,845; Australia's user numbers would translate into €1.5 billion saved in 2019 (833,317 users x €1,845).

NCRIS cross-facility national-scale data asset to integrate molecular imaging with bio-analytics

EMBL Australia Scientific Head Professor James Whisstock is leading the development of an integrated microscopy and proteomics resource that will enable Australian researchers to understand the precise molecular makeup of the intracellular environment.

Electron microscopy has advanced to the point where it is possible to determine the 3D structure of individual proteins in situ. However, a fundamental limitation of this technique is that the identification of proteins in the region of interest is exceptionally challenging and relies on exhaustive comparative experiments.

Professor Whisstock said the aim of this project was to develop a new resource to organise and navigate multidimensional data and drive connectivity between molecular imaging and proteomic datasets. "The Integrated Microscopy and Proteomics project will enable a new, publicly accessible, national-scale data asset to underpin the integration of molecular imaging with bio-analytics, driving discovery research across the whole of the life sciences," Prof Whisstock said.

It will use artificial intelligence bioinformatics approaches to seamlessly integrate and interrogate high-resolution imaging data (derived from optical and electron microscopy and X-ray crystallography) with proteomic/genomic data and gene ontology/protein interaction network data.

Currently, this information is distributed across numerous disparate databases, precluding the ready interpretation and analysis of imaging data.

The online platform will host the final, released and annotated datasets and permit presentation of the data, which will have immediate application in fields such as drug discovery, infectious diseases and molecular diagnostics.

The Australian Research Data Commons (ARDC) is co-investing $400,000 in the project under their Cross-NCRIS initiative. EMBL Australia, Microscopy Australia, Bioplatforms Australia and the Multi-modal Australian Sciences Imaging and Visualisation Environment (MASSIVE) are also funding the million-dollar project.

Enhancing Australia's Research Infrastructure (cont.)

Building genomics and bioinformatics platforms in South Australia

EMBL Australia group leader Professor David Lynn is the Scientific Director of a new $7 million state-of-the-art centre for genomics in South Australia that he played a vital role in championing.

The South Australian Genomics Centre (SAGC) was established in July 2020 as a state-wide genomics facility to support research in Australia and internationally. Prof Lynn and Adelaide BioMed City general manager Yvette Van Eenennaam advocated for the state-wide collaboration, the establishment of which took more than a year of planning and millions of dollars in funding – including $2 million from Bioplatforms Australia through NCRIS.

The SAGC's six founding partners – SAHMRI, the University of Adelaide, the University of South Australia, Flinders University, the Australian Wine Research Institute and the Australian Genome Research Facility – collectively invested funding, equipment and staff totalling more than $5.6 million.

The SAGC provides a broad range of services (including RNA sequencing, small RNA sequencing, exome and genome sequencing, epigenomics, metagenomics, single cell genomics and a range of custom methods), supported by a dedicated bioinformatics platform.

Prof Lynn also runs a multi-disciplinary research group at SAHMRI that is equally divided between computational systems biology and experimental immunology. The group investigates the interplay between the microbiome, vaccines and the immune system and develops novel computational analysis tools to facilitate this research, including new network analysis and visualisation tools.

He also co-led the establishment of a germ-free mouse facility in South Australia, one of only three such facilities in Australia.

SAHMRI, where the SAGC's central hub is located. Image via Twitter/@DrSarahBray

Invigorating long-read genomics in Australia

Computational biology and bioinformatics are central to advances in genomics and precision medicine.

EMBL Australia group leader Professor Eduardo Eyras' research is devoted to the development of new computational algorithms and software tools that leverage new sequencing technologies to address a broad range of biological questions.

Prof Eyras' research has contributed to key advances in genomics and transcriptomics, from the annotation of the human genome, to the large-scale analysis of cancer patients. This, in turn, has facilitated the identification of disease mechanisms and strategies to target them therapeutically.

The Eyras Group is currently working closely with the sequencing and bioinformatics core facilities at the John Curtin School of Medical Research (JCSMR) to enable the efficient use and interpretation of the new long-read sequencing platform.

To this end, the group works closely with the experts running these facilities to develop new computational tools and experimental protocols for long-read sequencing data analysis to address open questions in biomedical research.

In this regard, the group is aiming at a model in which research drives the development of new computational and experimental approaches that can be made available to other researchers in Australia and the world via the JCSMR facilities.

Additionally, through Prof Eyras' national and international collaborations in the application of long-read sequencing to a broad range of biological systems and clinical questions, he aims to invigorate long-read genomics in Australia, and strengthen its position in this area in the world.

Enhancing Australia's Research Infrastructure (cont.)

Animal model platforms and biomedical engineering approaches at ARMI

EMBL Australia group leader Associate Professor Mikaël Martino is one of the only researchers in the field of regenerative medicine that has expertise in a multitude of pre-clinical models of tissue repair and regeneration – such as diabetic wound healing, musculoskeletal regeneration, therapeutic angiogenesis, and heart repair following ischemia-reperfusion injury.

Pre-clinical models are essential for the discovery and the development of novel therapeutics for regenerative medicine applications and, as a regenerative medicine institute, the Australian Regenerative Medicine Institute (ARMI) needed to build up its expertise and capability to run the important animal models used in regenerative medicine research.

A/Prof Martino brought his animal model platform and expertise to ARMI, which aspires to be a leader in the discovery of new regenerative therapeutics. His expertise and pre-clinical models are now not only used across ARMI, but also across different faculties at Monash University, including Medicine and Engineering.

In addition, A/Prof Martino is an expert in cell delivery systems and in rational protein engineering for therapeutics based on biologics (e.g. recombinant cytokines and growth factors). This expertise is essential for the development of the next generation of regenerative strategies, which will rely heavily on these biomedical engineering approaches.

A/Prof Martino brought this expertise and his connections to world-leaders in the field of biomedical and molecular engineering to Australia, with the aim of expanding the biomedical engineering landscape in the country.

Bringing first-of-its-kind optogenetic equipment to Australia

Optogenetics is an emerging research technology that has been applied to answer fundamental and previously unresolvable questions in bacteria, animals and plants.

Despite its young age, the impact of optogenetics is widely recognised (e.g. optogenetics was highlighted as a Top 10 Emerging Technology at the World Economic Forum 2016). However, in Australia, researchers lacked the ability to remain internationally competitive in this field because the technological capacity to perform sophisticated and high-throughput optogenetic experiments was not available.

This was addressed by EMBL Australia group leader Dr Harald Janovjak (based at ARMI) establishing, developing and sharing first-of-its-kind, state-of-the-art optogenetic equipment as a research platform for training and collaboration. This includes high-throughput multi-colour optogenetics in bacteria, plant and animal cells, as well as wireless multi-colour optogenetics in tissues of freely-behaving mammals.

Dr Janovjak has also established Optogenetics Australia, a research network of Australian researchers interested in optogenetics, chemogenetics and optical control. The recent 2nd annual Optogenetics Australia workshop was a virtual event with more than 100 participants and lectures and practical modules from 10 leaders in the field.

Collectively, new equipment and new networks provide unprecedented research, collaboration and training opportunities for the Australian scientific community.

Unique microscopy capabilities in super-resolution and single-molecule imaging

UNSW's Single Molecule Science initiative focuses on transforming medicine by providing a molecular perspective on complex biological systems and processes, encompassing biophysics, biochemistry and cell biology, as well as nanotechnology and nanofabrication. This work is underpinned by the new imaging and analysis technologies that were developed by the teams led by the late Professor Katharina Gaus, Australian EMBL Partnership Lab Head at UNSW and Deputy Director of the ARC Centre of Excellence in Advanced Molecular Imaging.

Under Prof Gaus' leadership, the Single Molecule Science node – including EMBL Australia group leaders Yann Gambin, Maté Biro, Richard Morris and Vaishnavi Ananthanarayanan – developed unique microscopy capabilities in super-resolution and single-molecule imaging and contributed to: nanofabrication at the Australian National Fabrication Facility; drug development at the Australian Cancer Research Foundation Drug Discovery Centre; genomics at the Ramaciotti Centre; proteomics at the Bioanalytical Mass Spectrometry Facility; animal models from Australian BioResources; and the Mark Wainwright Analytical Centre.

Research Excellence Snapshot

70

Publications by group leaders in 2020, including journal articles, reports, reviews, letters and book chapters.

View all 2020 publications

Enabling the early diagnosis of Parkinson's disease

A new detection method co-developed by Dr Yann Gambin could enable the early and accurate detection of Parkinson's disease, vastly improving patient outcomes.

Dr Gambin, Dr Emma Sierecki and their team at UNSW Sydney created the new diagnostic method by combining a single-molecule counting technique (a compact and powerful 3D-printed microscope) they developed in 2019 with a rapid amplification assay to detect alpha-synuclein – a promising biomarker for the disease.

Published online in *Angewandte Chemie International Edition*, the new diagnostic strategy enables the analysis of protein aggregates in cerebrospinal fluid to detect alpha-synuclein, and discriminate between Parkinson's disease and other neurodegenerative diseases.

This technique, which takes a little over five hours, will allow clinicians to detect Parkinson's disease at early stages before the onset of clinical signs, allowing for earlier therapeutic intervention.

Presently, the only definite way to diagnose Parkinson's disease is at autopsy.

Keratins determine cell fate in early mammalian development

Research by EMBL Australia alumnus Dr Nico Plachta and group leader Dr Maté Biro, and published in *Nature*, led to a fundamental discovery that advances our understanding of how mammals develop in the earliest stages after fertilisation.

The international study uncovered the surprising role of the protein keratin – best known as the main structural component of hair and nails – in determining cell fate.

"It has long been known that keratins show some heterogeneity in these early embryos but no one knew why, so we followed that up and found out that they are actually determining the eventual fate of cells," Dr Biro said.

Gene research could lead to cancer breakthrough

Professor Eduardo Eyras developed a general-purpose tool to study how cells function in glioma – the most prevalent type of brain tumour – but that could also be applied to other tumours and diseases.

The research by Prof Eyras and his colleagues at the Australian National University (ANU), published in *Nature Communications*, will help us better understand rare forms of cancer.

"The more we understand about how the cells transform during the development of glioma, the more options we could eventually have when it comes to developing new ways to treat this devastating disease," Prof Eyras said.

The researchers discovered a new alteration in genes that affect the production of proteins in brain cancer.

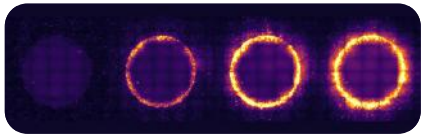
Research Excellence Snapshot (cont.)

Cancer-killing T cells 'swarm' to tumours, attracting others to the fight

Immune T cells swarm to tumours to help subdue the threat by following a chemical gradient left by other cancer-killing T cells, a pre-clinical study by Dr Maté Biro and his team showed.

The discovery of this swarming behaviour, published in *eLife*, could help scientists develop new cancer therapies that boost the immune system.

This is particularly important for solid tumours, which so far have been less responsive to current immunotherapies than cancers affecting blood cells.



When immune system T cells find and recognise a target, they release chemicals to attract more T cells which then swarm to help subdue the threat. Image supplied.

Leap forward in antibiotics to fight 'superbugs'

Associate Professor Max Cryle has provided a new understanding of glycopeptide antibiotics (GPAs) biosynthesis that allows new GPAs to be made and tested in the laboratory – a vital step in the quest to develop new antibiotics to keep pace with the ever-evolving 'superbugs' that threaten global public health.

Building on their earlier studies, A/Prof Cryle and his team showed, for the first time, how a wide range of new GPAs can be made by combining the natural biosynthesis machinery and chemical modifications.

These findings – published in *Angewandte Chemie International Edition* – will enable the discovery and development of new antibiotics for clinical use and is an avenue being rapidly pursued.

Major cell network mapping reveals extensive rewiring in colorectal cancer

An international consortium of researchers, co-led by Professor David Lynn, has painstakingly mapped an intracellular network that could open the door to discovering new targeted treatments for colorectal cancer.

The team of researchers from Australia, Ireland, the UK, Europe and Canada focused on interactions between proteins along the epidermal growth factor receptor (EGFR) network – the key cellular pathway that controls how cancer cells survive and grow in colorectal cancer.

"Our team was particularly interested in how this network is rewired within particularly nasty colorectal cancer cells that contain a mutated protein called KRAS," Prof Lynn said.

The research, published in *Nature Communications*, indicates the web of interactions is substantially altered within those cells.

They performed more than 1100 analyses and mapped more than 6000 protein interactions.

Novel method of enhancing regenerative activity

Associate Professor Mikaël Martino and Dr Ziad Julier spearheaded a novel method of enhancing regenerative activity, with clinical implications on improving the effectiveness of growth factor-based therapies.

Published in *Science Advances*, the work explored how proinflammatory signals impact growth factor-mediated regenerative potential.

A/Prof Martino said the efficacy of growth factor therapies – which currently had limited clinical use due to several issues, including suboptimal delivery systems – could be enhanced by dampening local proinflammatory signalling.

"This work presents an argument for integrating immunomodulation when designing growth factor-based therapeutic protocols," A/Prof Martino said.

"The key to improving the safety and efficacy, and thereby realising the potential of growth factor-based therapies, is understanding the complex interplay between growth factors, their targets and their environment."

Research Excellence Snapshot (cont.)

Fish school by randomly copying each other

An interdisciplinary team of researchers co-led by Dr Richard Morris has revealed the mechanisms behind fish schooling and presented the first experimental evidence of noise-induced ordering, which previously only existed as a theoretical possibility.

The study, published in *Nature Physics*, found that fish school by copying each other and changing directions randomly, rather than calculating and adapting to an average direction of the group.

The research has shed light on the behavioural dynamics that govern alignment, or collective motion, of cichlid fish – offering new insights into the dynamics of schooling, and potentially the coordinated behaviour of other animals.

"In the fish that we have studied, schooling turns out to be noise-induced. It's not what anyone traditionally thought it was," said Dr Richard Morris. "Noise, in this setting, is simply the randomness arising from interactions between individual fish."

Targeting the protein that empowers cancer cells could kickstart new therapies

Dr Maté Biro has contributed to an unexpected discovery about cancer cells.

New research, published in *Nature Cell Biology*, shows a protein called actin allows cancer cells to repair their DNA and even helps them to resist chemotherapy.

The finding in cell lines and animal models will spark efforts to produce new tailored therapies to kill cancer cells.

"Understanding that actin assembled within the nucleus helps overcome malfunctions in DNA replication opens the door to the development of new and more precisely targeted therapeutics that stop cancer cells from dividing," said Dr Biro.

Framework for analysing complex population-based datasets

Associate Professor Ville-Petteri Mäkinen and his team continued to develop and maintain the statistical R package 'Numero' – a statistical framework to define multivariate subgroups in complex population-based datasets, which has multiple applications in systems epidemiology.

The Mäkinen Group, in collaboration with the Australian Centre for Precision Medicine, also completed the first large-scale analysis of metabolic phenotypes in the UK Biobank.

Giving back to the research community

Many EMBL Australia group leaders continued to invest their expertise, time and energies into developing learning and training opportunities for other early-career researchers in 2020.

The Optogenetics Australia research network – initiated by Dr Harald Janovjak to foster collaboration between researchers in the rapidly growing field of optogenetics – held its inaugural two-day workshop, which brought together some of Australia's leading scientists from various research areas who utilise optogenetics in their work.

The Theory of Living Systems webcast seminar series – co-organised by Dr Richard Morris – has attracted a list of high-profile international speakers and covered a wide range of topics where high-end theory and/or computation has been used to further experimental research in the life sciences. Some seminars have attracted more than 100 participants from Australia, New Zealand, Japan, the United States and India.

Prof Eduardo Eyras was the chair of the organising committee for the ABACBS 2020 Conference, the annual conference of the Australian Bioinformatics and Computational Biology Society. The conference was successfully held virtually in 2020, with 370 participants, 18 invited speakers (eight from international institutions), 146 recorded talks and 70 live presentations.

EMBL and Australian research collaboration highlights

Human Pangenome Reference Consortium collaboration:

One of several ongoing collaborations between EMBL-EBI Senior Scientist and Associate Director of EMBL-EBI Services Paul Flicek and colleagues in Australia is in the context of the Human Pangenome Reference Consortium, an international effort focused on developing an inclusive collection of human reference genomes that represent human haplotype diversity and the tool ecosystem needed to fully utilise this resource.

Paul Flicek has been engaging with the researchers at the ANU National Centre for Indigenous Genomics to determine how it may be possible to ethically include the genomic information from native Australian populations. These issues will be addressed in a white paper published later this year.

Pan-Cancer Analysis of Whole Genomes project:

The Pan-Cancer Analysis of Whole Genomes project is a collaboration involving more than 1300 scientists and clinicians from 37 countries, including Australia. The project, initiated and co-led by EMBL Head of Data Science Jan Korbel, involved analysis of more than 2600 genomes of 38 different tumour types, creating a huge resource of primary cancer genomes. From there, 16 working groups studied multiple aspects of cancer development, causation, progression, and classification. Several Australian institutions were involved in the project: Queensland Institute of Medical Research (QIMR), the Sir Peter MacCallum Cancer Centre, the University of Melbourne and the University of Queensland.

A key finding is that it's possible to identify mutations in the genome that occurred years, or even decades, before a tumour appears – theoretically opening a window of opportunity for early cancer detection. The results of the project are published today in more than 20 papers in *Nature* and its affiliated journals.

Grant bringing together EMBL and the EMBL Australia PLN:

The call for a joint research project between EMBL and the EMBL Australia PLN was launched after the scientific symposium at EMBL Heidelberg in September 2018 to encourage new international collaborations between group leaders.

The grant, valued at €75K over 36 months, brought together two group leaders – one based at EMBL, the other at the Monash Biomedicine Discovery Institute and their teams. The joint project utilises methods of genomics and genome editing to manipulate and control histone H3 variants during cell differentiation, combined with methods for the reconstitution and study of chromatin modifier complexes and chromatin.

The project started in April 2019 and, while the pandemic slowed down the interactions, each lab made significant progress in 2020.

Collaboration with EMBL Alumni:

EMBL Heidelberg principal investigator Oliver Stegle has been collaborating with his former postdoctoral student, who has left EMBL to establish his own group researching Bioinformatics & Cellular Genomics at St Vincent's Institute in Melbourne.

The two groups continue to collaborate on methods for assessing human genetic variants using single-cell omics technologies. They have worked together on several joint publications in recent years.

Awards and Achievements

Viertel Fellowship

A/Prof Chen Davidovich

Associate Professor Chen Davidovich was awarded a prestigious Viertel Senior Medical Research Fellowship of $1.25 million to solve a fundamental question about how genes operate.

Margaret Baird Women in Immunology Lectureship Award

Dr Michelle Boyle

Dr Michelle Boyle was awarded the 2020 Margaret Baird Women in Immunology Lectureship Award by the Australia and New Zealand Society for Immunology.

Fellow of the Australian Academy of Science

Prof Peter Currie

Professor Peter Currie was elected by his peers as a Fellow of the Australian Academy of Science. The renowned stem cell biologist is the director of the Australian Regenerative Medicine Institute and an Australian EMBL Partnership Lab Head at Monash University.

Lorne Genome Mid-Career Award

A/Prof Chen Davidovich

Associate Professor Chen Davidovich received the Millenium Mid-Career Award at the 2020 Lorne Genome Conference.

Grant Success for Group Leaders

Dr Maté Biro

University of New South Wales

Awarded a National Health and Medical Research Council (NHMRC) Ideas Grant, with Dr Daryan Kempe and Dr Szun Tay, to harness extracellular matrix remodelling by cancer-associated fibroblasts to increase T Cell infiltration of solid tumours.

Dr Michelle Boyle

QIMR Berghofer

Awarded an NHMRC Ideas Grant of more than $2 million, with A/Prof Bridget Barber, to host targeted adjunctive therapies to boost antimalarial immunity and inform the development of new malaria control tools.

A/Prof Max Cryle

Monash University

Awarded an NHMRC Ideas Grant with Dr Jennifer Payne to create novel antibiotics that harness innate immunity to overcome multi-drug resistant bacteria Staphylococcus aureus (golden staph) by combining existing clinical antibiotics with either a targeted immune response, or by removing the ability of bacteria to hide from our immune system.

Awarded an Australian Research Council (ARC) Discovery Project Grant to expand his research into antimicrobial resistance, specifically to understand peptide bond formation in non-ribosomal peptide biosynthesis.

Professor Eduardo Eyras

Australian National University

Awarded an ARC Discovery Project Grant, together with Prof Thomas Preiss and Dr Rippei Hayashi, to investigate how RNA molecules that carry the genetic code from genomes are biochemically modified and how this impacts their function.

Dr Yann Gambin

University of New South Wales

Awarded a grant from the Michael J. Fox Foundation, allowing him to access samples from Parkinson's disease patients and apply his team's new single molecule technique to detect early protein aggregates in biofluids.

Dr Harald Janovjak

Monash University

Awarded an ARC Future Fellowship to develop novel genetic methods and instrumentation for the local, rapid and reversible activation of genes in cells and mice.

Prof David Lynn

South Australian Health and Medical Research Institute

Awarded funding under a collaborative research agreement with a major international vaccine company to research the influence of microbiota on vaccine responses, as well as two other grants to investigate whether COVID-19 leads to long-lasting perturbations of the immune system and the non-specific effects of the BCG vaccine.

A/Prof Mikaël Martino

Monash University

Awarded, together with Australian EMBL Partnership Lab Head Prof Peter Currie, a grant of more than $820,000 from the Medical Research Future Fund's Stem Cell Therapies Mission to develop new therapies using stem cell and tissue-engineering approaches to treat muscle injury and wasting disorders.

Prof Barry Thompson

Australian National University

Awarded an ARC Future Fellowship of more than $1 million over four years to investigate the genetic control of tissue growth in animal

People Highlights

Dr Vaishnavi Ananthanarayanan

New Group Leader

Vaishnavi commenced in November 2020 and established her lab at the University of New South Wales (Single Molecule Science).

The Ananthanarayanan Group is interested in understanding how stochastic and rare events, such as motor protein binding to cytoskeletal tracks or cargo, give rise to complex cellular organisation across scales.

▶ More about Dr Ananthanarayanan

A/Prof Edwina McGlinn

New Alumna

Edwina established the first PLN research group in January 2011 at the Australian Regenerative Medicine Institute at Monash University, where her team focused on elucidating novel gene networks that drive growth and identity in the early embryo. Following EMBL's unique funding model, nine years later her EMBL Australia tenure came to an end.

Edwina made many contributions academically, including developing tools and resources to assist others in advancing broader questions of gene regulation, as well as to the wider scientific community and EMBL Australia network.

▶ More about A/Prof Edwina McGlinn

Prof Ian Smith

New Chair Council

Ian joined the EMBL Australia Council, replacing the outgoing Professor Brandon Wainwright AM as chairperson, in November 2020. Around this time he stepped down from his role as Vice-Provost (Research and Research Infrastructure) at Monash University, where he was responsible for research strategy, infrastructure and alliances, and was appointed as an Emeritus Professor at Monash.

With a background in both industry and research, Professor Smith says he is eager to continue to build and further strengthen the relationship between EMBL and Australia and to help ensure the exciting discoveries made in the laboratory have global impact.

▶ More about Prof Smith

Student Programs

To identify and develop future scientific leaders, EMBL Australia attracts Australia's best students by offering a number of highly sought-after programs.

In 2020, many of our student programs were disrupted by the global pandemic and associated restrictions on travel and gathering.

However, where possible, our agile program organisers found alternative options to allow events to continue – for example, by transforming our traditional in-person student symposium into a virtual event.

Travel grants

Supporting PhD students to take a short course, attend a conference or work collaboratively alongside some of the world's best researchers at EMBL's facilities in Germany, Italy, France, Spain or the UK.

In a normal year, EMBL Australia travel grants afford 20 Australian PhD students the opportunity to train at one of EMBL's six European facilities, go to a conference or take a short course. The $2000 grants usually assist students in attending the 20th EMBL PhD Symposium in Heidelberg, Germany (which was held virtually in 2020), a course or conference run by EMBL, or the opportunity to work with EMBL researchers at one of their European facilities.

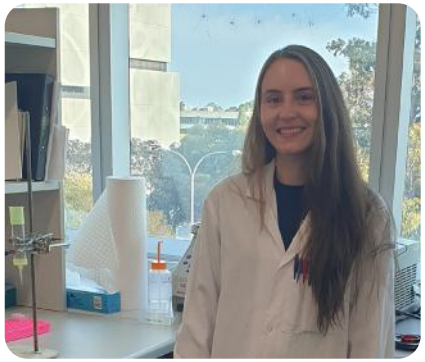
Whilst travel restrictions meant this program was suspended for most of 2020, Brady Owen – a third-year PhD student in the Davidovich Lab at Monash University – was able to use her travel grant to attend the Analysis and Integration of Transcriptome and Proteome Data course at EMBL Heidelberg in early February.

Ms Owen said the skills she gained at the five-day course would be extremely useful in her research, in which she is biochemically determining how the polycomb protein cofactors of PRC2 interact with DNA and developing DNA-binding-deficient mutants.

"I had the opportunity to try some of the analysis tools I would need to use in this project," Ms Owen said.

"By going through the cleaning and analysis process for the sample datasets, I gained a deep understanding of how to generate and identify high-quality data. Having this skill before conducting my first experiment was invaluable to reduce the amount of optimization that was needed."

Ms Owen said attending the course extended the scope of questions she would be able to answer in her research and inspired a new hypothesis to explain the results of an unsuccessful past project, motivating her to reanalyse the data using a new tool.



A $2000 travel grant helped PhD Student Brady Owen fund her travel to Germany, where she was introduced to new tools, experts in the field and fresh ways of looking at her research.

Student Programs (cont.)

2020 EMBL Australia Postgraduate Symposium: 'To Innovation and Beyond'

An annual student-developed symposium for honours, masters and PhD students provides an opportunity for students to learn from world-leading researchers, network and present their work.

Due to the restrictions associated with the pandemic, the 7th annual EMBL Australia Postgraduate Symposium (EAPS) was held virtually from 11 to 13 November.

EAPS 2020 was attended by more than 135 delegates from all around Australia, with 80 poster presentations, 18 selected oral presentations and eight invited plenary presentations given over the course of the three-day symposium.

The meeting's theme was 'To Innovation and Beyond: A new decade for new breakthroughs' and the program covered a variety of topics, including cancer, immunology, regenerative biology, computational biology, molecular cell biology and translating science.

Prominent scientists delivered inspiring presentations – including a keynote address from Professor Mark Post, the scientist behind the world's first slaughter-free hamburger, and a plenary address on COVID-19 by Professor Kanta Subbarao – and delegates enthusiastically participated in online social activities, including competitions and network opportunities.

The conference utilised an award-winning online conference platform (Whova) to deliver oral presentations, view student posters and their accompanying video presentations, and to facilitate the networking, engagement and discussion that attendees typically engage in at traditional conferences.

The EMBL Australia PhD Course

Modelled on EMBL's predoc course, the two-week annual program offers sixty first or second-year PhD students symposium-style presentations and workshops from Australian and international speakers.

Unfortunately, the 2020 course was cancelled due to lockdowns and travel restrictions associated with the coronavirus pandemic. We look forward to bringing the hugely popular annual event back in 2021.

Partnership PhD Program

EMBL Australia group leaders offer scholarships to outstanding students, who receive additional career, research and monetary support during their doctoral studies.

The program was suspended in 2020 due to travel restrictions associated with the coronavirus pandemic.

Stay updated with EMBL Australia's PLN news through:

Our quarterly newsletter: Subscribe here

Online: emblaustralia.org

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EMBL Australia is supported by:

NCRIS National Research Infrastructure for Australia
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EMBL Australia PLN is hosted at the South Australian Health and Medical Research Institute, University of New South Wales, Australian National University, Garvan Institute of Medical Research, QIMR Berghofer Medical Research Institute and Monash University. The EMBL Australia Secretariat is hosted by the Monash Biomedicine Discovery Institute (BDI).

EMBL Australia