Australian Academy of Science

Australian & New Zealand RNA Production Consortium

PROCEEDINGS OF THE NATIONAL RNA SCIENCE AND TECHNOLOGY ROUNDTABLE

AUSTRALIAN ACADEMY OF SCIENCE
29 JULY 2021

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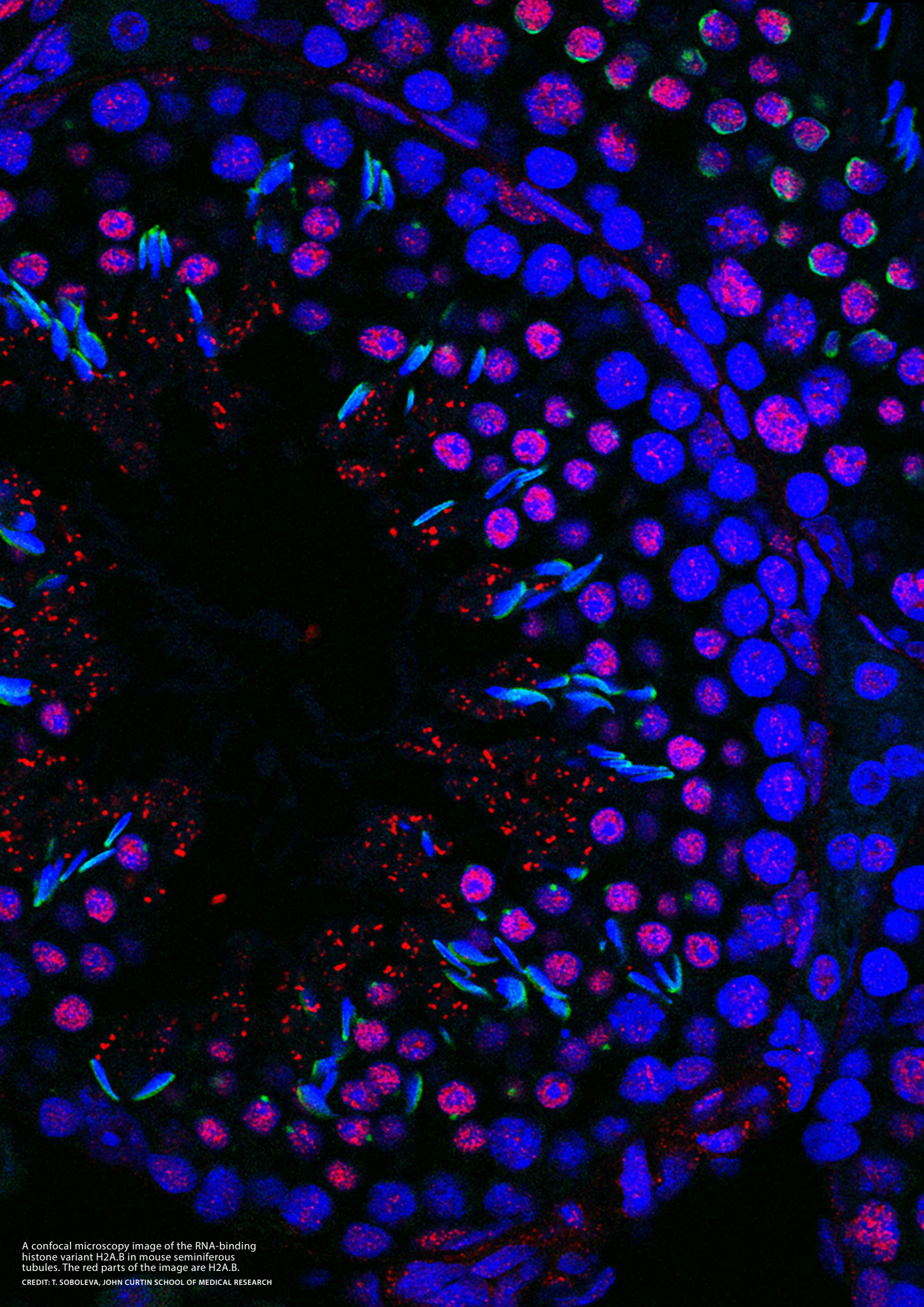


A confocal microscopy image of the RNA-binding histone variant H2A.B in mouse seminiferous tubules. The red parts of the image are H2A.B.

CREDIT: T. SOBOLEVA, JOHN CURTIN SCHOOL OF MEDICAL RESEARCH

FOREWORD

PROFESSOR JOHN SHINE

President, Australian Academy of Science

The Australian Academy of Science is dedicated to the excellence of Australian science, including providing independent, authoritative and influential scientific advice. The Academy's independence and convening power made us the ideal host for the National RNA Science and Technology Roundtable, and we are pleased to have been able to bring together representatives from research, industry and government for this purpose.

The importance of science to society has never been more evident than today. Again and again, it has been basic research, primarily undertaken for new knowledge and understanding and not for a clear applied outcome, that has been the critical seed for breakthroughs that have led to significant improvements in humanity's wellbeing. For example, in response to the COVID-19 pandemic, fundamental research in molecular biology and virology over decades positioned us well to quickly rise to the challenge to sequence the viral genome, make accurate diagnostics and then create vaccines.

The Academy is pleased that the Australian Government has taken up the call to invest in sovereign RNA capability. Such a capability includes not only manufacturing but everything from fundamental research to commercialisation and the creation of companies and jobs. This roundtable was a step forward in presenting a united voice on RNA science and technology in Australia: what we are capable of and what we have the potential to achieve.

I want to thank the roundtable chairs, Professor John Mattick, Associate Professor Archa Fox and Professor Trent Munro, for their leadership and hard work contributing to this project. I would also like to thank Professor Thomas Preiss and the Australian and New Zealand RNA Production Consortium for their work on this project. Finally, I would like to express our gratitude for the support of our partners—the universities and research institutes that sponsored the roundtable. Without them, this work would not be possible.

INTRODUCTION

RNA, or ribonucleic acid, exists in various forms that play a central role in the function of genes and the regulation of gene expression. RNA controls development in plants and animals, influencing areas as diverse as crop yields in agriculture and brain function in humans. There has long been considerable potential for RNA-based products. However, the success of RNA-based technology in the rapid development of safe and effective vaccines for COVID-19 has drawn sustained public interest in the technology. It has also triggered public and private investment to establish capabilities from fundamental scientific research through to process development for clinical and commercial onshore mRNA (messenger RNA) manufacturing.

Pfizer/BioNTech and Moderna mRNA vaccines have been successfully used against COVID-19 and can potentially be reformulated rapidly to counter new strains of viruses. RNA technology has also been shown to have the potential to inoculate against many other infectious diseases such as respiratory syncytial virus, influenza and malaria, as well as retune the immune system to alleviate autoimmune disorders, such as arthritis, which comprise a large part of the disease burden in the population. Applications of mRNA and other forms of RNA, such as siRNA, miRNA, gRNA and dsRNA[1], have potential in medicine beyond vaccines and, more broadly, in the biotechnology and agricultural sectors.

Given the efficacy and flexibility of mRNA-based vaccines, Australia is now working towards developing a sovereign capability to deal with the ongoing COVID-19 crisis and future pandemics. Australia is well placed with many world-leading experts in RNA science, biomaterials and biotechnology located within our universities and research institutes. Through the adoption of policies and strategic investments, opportunities exist to become a leader in RNA science and technology from knowledge creation to translation and manufacturing.

The Australian Academy of Science (the Academy) and the Australian and New Zealand RNA Production Consortium (ANZRPC) hosted a roundtable on Thursday 29 July 2021 to bring together experts in RNA science and technology from academia and industry to:

- identify Australia's RNA research strengths
- define research priorities and provide guidance on how to build a national RNA science and technologies ecosystem
- discuss how to build a framework that will create a pipeline from discovery to translation, leading to clinical stage and commercial RNA manufacturing in Australia.

1 Small interfering RNA (siRNA), microRNA (miRNA), guide RNA (gRNA) and double-stranded RNA (dsRNA).

ROUNDTABLE PROCEEDINGS

WELCOME AND CONTEXT SETTING

Professor John Shine AC PresAA FAHMS(Hon) FRS, President of the Australian Academy of Science, welcomed participants on behalf of the Academy. Shine highlighted that the Academy's independence and convening power made it the ideal host for the roundtable. They also acknowledged that the global success and acclaim of mRNA vaccines has raised the awareness of the possibilities of RNA technologies.

On behalf of the Australian and New Zealand RNA Production Consortium (ANZRPC), **Professor Thomas Preiss,** Professor at the John Curtin School of Medical Research, the Australian National University, described the history and goals of the ANZRPC. The ANZRPC is an informal group of academics from universities around Australia and New Zealand that formed in mid-2020 to provide a constructive voice working towards strategies to help end the pandemic. The group focuses on the solutions that RNA science and technology has to offer and how Australia and New Zealand can emerge from the pandemic with stronger R&D ecosystems and biotech industries.

To frame the roundtable, **Mr David Luchetti,** General Manager at the Department of Industry, Science, Energy and Resources, gave an overview of the Australian Government's approach to vaccine manufacturing. The government undertook an audit in August 2020 to understand vaccine manufacturing capability in Australia, in which it identified a strong national capability.

The government started looking at a business case to set up mRNA manufacturing capability in Australia from 2020. In the May 2021 budget, the government announced a decision to run an approach to market with three main objectives: priority access to vaccines for Australians; security of vaccine supply chains for future health emergencies; and strengthening the Australian biopharma sector by augmenting translation and commercialisation paths for research and development.

Current events have raised the profile of this technology in government, and mRNA manufacturing complements other government priorities such as the University Research and Commercialisation Scheme and the Australian Government's manufacturing strategy.

Professor John Mattick AO FAA FTSE FAHMS HonFRCPA, Professor at the School of Biotechnology and Biomolecular Sciences, UNSW Sydney, provided a short overview of the background and context for the roundtable. The context revolved mainly around the COVID-19 pandemic. The subsequent development of mRNA vaccines has brought RNA into the public consciousness and the potential of Australia to be at the leading edge of RNA science and technology.

The roundtable was called to scope out Australia's future potential in RNA science and technology and determine how to develop Australia's RNA research and translation capabilities.

GLOBAL EMERGING AREAS IN RNA SCIENCE AND TECHNOLOGY

Led by Professor John Mattick

The first session focused on emerging research in RNA science and technology. Mattick noted that RNA science had for years been considered just the intermediate between genes and proteins, overlooking its major roles in gene regulation and developmental biology. RNA is also an excellent way to deliver instructions to make a protein antigen to create an immune response. The rapid and successful development of RNA vaccines may change vaccinology forever. RNA vaccines can be created quickly, and production can be scaled rapidly and changed readily to adapt to new viral strains.

The potential of RNA-based therapeutics is significant. For example, they could be used to treat autoimmune disorders, such as diabetes, arthritis and multiple sclerosis, which are a major health burden. The real potential of RNA therapeutics will be achieved by better understanding the role of RNA in normal and abnormal biology and with the development of improved delivery mechanisms so they can be delivered to any target tissue.

THE POTENTIAL OF RNA SCIENCE AND TECHNOLOGY

When reflecting on the potential for RNA science and technology, participants were encouraged to think creatively about future breakthroughs in the discipline.

> **Now is the time for us to be bold.**
>
> **Associate Professor Archa Fox**

In the RNAi (RNA interference, i.e. with the aim of reducing levels of an RNA target) field, there have been several new therapeutics approved by the US FDA, as well as some therapeutics approved in Europe, with an explosion of products now in clinical development. These new therapeutics have been largely made possible due to advances in second generation chemistry, leading to more stable RNA formulations and the use of lipid nanoparticles for delivery. **Professor Peter Leedman**, Harry Perkins Institute of Medical Research, argued that if Australia is going to be competitive we need to work more on ways to improve delivery, especially targeting to affected tissues.

Associate Professor Tim Mercer, Australian Institute for Bioengineering and Nanotechnology, University of Queensland, noted that while mRNA vaccines received a surge of attention, the potential of RNA is reaching into other fields. An example is combining therapies with what has been achieved in synthetic biology by hijacking gene expression and alternative splicing for anti-inflammatory conditions, COVID-19, ageing and diabetes.

There remains a need to better understand which forms of RNA exist in cells in order to either target these or copy them (e.g. understanding how RNA interacts with proteins through secondary structures). **Dr Minni Änkö**, Hudson Institute of Medical Research, highlighted that this is an emerging and interesting idea to develop therapeutics by potentially influencing interactions within the cell. By altering these interactions, complex diseases like neurological diseases may be able to be treated.

Success in RNA science and technology depends on interactions across multiple fields, but the ways this can be encouraged on multiple levels in Australia remains to be seen. Some opportunities are obvious. For example, translation into medical applications requires cooperation from medicine, biology, chemistry, physics and engineering. Preiss stressed that researchers in fields covering all domains of life (including plants, prokaryotes, animals etc.) should be encouraged to come out of their silos and work together to help realise the full potential of RNA.

Internationally, researchers use small molecule drugs to target RNA structures, and various start-up companies exist in this area. **Professor Pall Thordarson**, School of Chemistry, UNSW Sydney, recognised that the chemistry community in Australia is strong in this field. There may be potential to control RNA function and activity in the future, but this will require a better understanding of how RNA affects cellular biology.

Associate Professor Chen Davidovich, Monash University, suggested that molecules used to make RNA today come from organisms familiar to molecular biology, but these may not necessarily be the best model organisms for exploring the potential of RNA therapies in the future. Mattick agreed that researchers can benefit from looking at the chemical diversity of life to inspire innovation. The community needs to be receptive to outlier organisms that can greatly influence understanding and technology. **Professor Damien Purcell**, The Peter Doherty Institute for Infection and Immunity, University of Melbourne, agreed and noted that researchers must think about data differently to look for novel intellectual property.

Dr Martine Keenan, Epichem, noted that novel research platforms can impact the speed of translation. Enabling efficient translation of discoveries is an aspect that should be considered and supported.

Associate Professor Archa Fox, University of Western Australia, noted that beyond the science and technology, there is also an opportunity for Australia to achieve breakthroughs in RNA production. The cost of making large amounts of RNA needs to come down significantly to be viable for use in crops and agriculture. There is great potential for innovation in biomanufacturing.

Professor Anton Middelberg FTSE, University of Adelaide, highlighted the need for a facility to make Good Manufacturing Practice (GMP) material for projects to avoid the valley of death. There is also a need to biomanufacture at scale, possibly different to GMP facilities.

Professor Kevin Morris, School of Medical Sciencesgmp Griffith University, said that centralising manufacturing should be the first thing established, allowing basic research to trickle up. Australian scientists currently don't have access to manufacturing and are required to develop this overseas. If you build it, they will come. Morris also noted that a centralised structure that researchers can all use collaboratively instead of competing would be a good path forward.

Associate Professor Charlotte Conn, RMIT University, noted that there is strong lipid nanoparticle research in Australia, and formulations of COVID-19 vaccines are similar in terms of lipids they use. An opportunity exists for high throughput screening of lipids to stabilise RNA and in organ-specific delivery. Middleberg said there were opportunities to better connect chemistry and nanoscience networks in order to understand the structures being created with lipids and how it interacts

with RNA. Australia has a history of leadership in understanding lipid structures encapsulating RNA and how it interacts with RNA to create the biological outcomes you want. If we find a mechanism to connect disciplines towards this opportunity, Australia can position itself to be at the cutting edge.

Professor Carl Walkley, St Vincent's Institute of Medical Research, discussed the perspective of modifying RNA in the cell by modifying enzymes and drug targets that modify RNA. There are opportunities to engage with international development in this area. Understanding what RNA modification does in the context of diseases will assist in developing novel therapeutic approaches. Mattick agreed, noting that understanding structure–function relationships allows these to be manipulated for therapeutic outcomes.

Mattick also noted that it is now clear that there are many epigenetic transitions in cancer, which may be good targets for drugs. The persistent problem of using mRNA in cancer is finding a good target and targeting the cancer cells. RNA can be used to change targets, and potentially change the epigenetic state of cancer cells to reverse tumorigenicity.

FACILITATION FOR COLLABORATION

Professor Andrew Hill, La Trobe Institute for Molecular Science, La Trobe University, highlighted the National Institute of Health funded consortium of extracellular RNA experts that developed bioinformatics and mapping tools. Hill presented this as an example of consolidating an RNA research community's expertise to generate and advance science in a new area.

Professor Greg Goodall FAA FAHMS, Centre for Cancer Biology, an alliance of SA Pathology and University of South Australia, agreed that there is an existing need to connect people working at different levels in Australia and highlighted the need for proposals that bring those people together, to break down silos and join in with the full pipeline. Goodall suggested a conference within Australia to promote these interactions and collaborations, the first of which, Australasian RNA Biology and Biotechnology Conference (A-RNA) is planned for November this year. Goodall also noted that funding mechanisms should support this interaction rather than drive competition (e.g. hybrid between Medical Research Future Fund and Cooperative Research Centres), by calling for specific area of research with a long lead time and significant funding for people to seek out partners at various levels of the process.

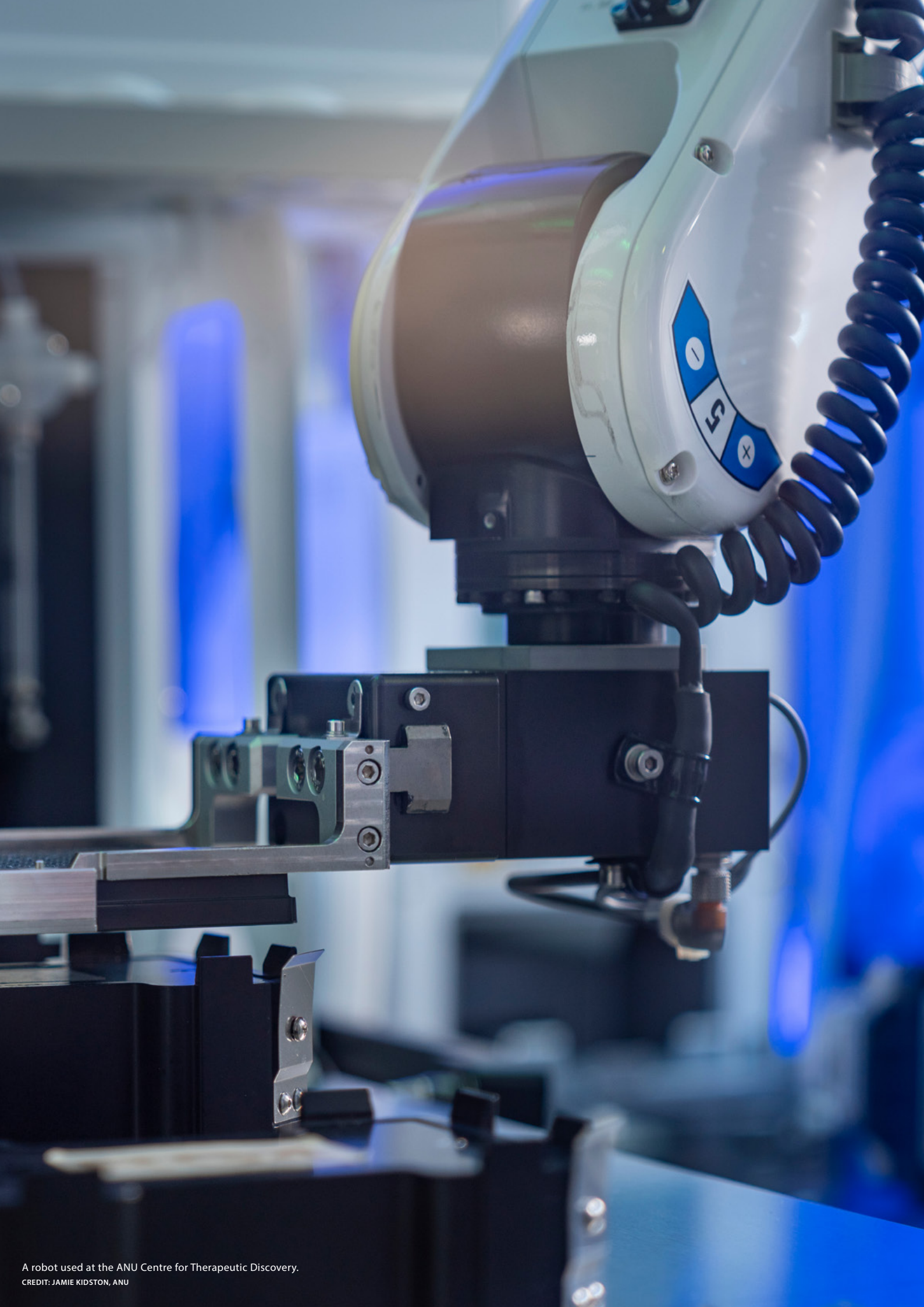
Professor Karlheinz Peter, Baker Heart and Diabetes Institute, presented that another emerging area internationally continues to be nanomedicine, combining chemistry and biology, which is essential for mRNA. Fox also noted that the discussion had not yet touched on RNA detection. However, this will be a large area in developing specific tools to detect RNAs, including biosecurity.

Professor Pall Thordarson CChem FRACI FRSC, School of Chemistry, University of Sydney, noted that manufacturing processes needed to be streamlined and RNA manufacturing democratised and upscaled to contribute on an international level. This may include observing and learning from successes and failures in other countries.

Associate Professor Simon Conn, Flinders Health and Medical Research Institute, agreed that the research community need to play to their strengths, academic skills and knowledge. These include circular RNAs, cap-independent translation, and stability of circularised RNA molecules. People working in this space are seeing good immune responses and producing more stable molecules.

Associate Professor Traude Beilharz, Monash University, noted that the interface between metabolism and RNA biology is an emerging area, as cell metabolism is key to RNA therapy. Small molecule RNA interactions are also an emerging field open for a huge amount of innovation. Mattick noted the interaction of RNA with central metabolism and signalling proteins is particularly interesting.

Researcher setting up cancer cells for high-throughput treatment analyses.
CREDIT: CHILDREN'S CANCER INSTITUTE



A robot used at the ANU Centre for Therapeutic Discovery.
CREDIT: JAMIE KIDSTON, ANU

AUSTRALIA'S RESEARCH STRENGTHS AND OPPORTUNITIES IN RNA SCIENCE

Led by Associate Professor Archa Fox

In the second session, participants considered Australia's strengths and opportunities in RNA research. Australia has contributed to significant breakthroughs in RNA science and technology in the past and can be a leader in the field in the future if certain barriers can be overcome.

AUSTRALIA HAS A HISTORY OF CONTRIBUTING TO ADVANCES IN RNA SCIENCE

To open the session, Fox asked participants to share their favourite Australian RNA breakthrough. The most popular Australian discovery listed by participants was RNAi in plants by Peter Waterhouse/CSIRO, with around half of the responses referencing this discovery in some way. Other popular discoveries included the Shine-Dalgarno sequence and that non-coding RNAs have broad functions in plant and animal development, as well as in the brain.

> **We must not fall into the trap of shifting funding to the front of the pipeline, translation, only to decrease funding for basic science.**
>
> **Associate Professor Archa Fox**

AUSTRALIA IS STRONG IN BASIC RESEARCH, BUT WE NEED TO WORK TOGETHER TO IMPROVE COMMERCIALISATION AND TRANSLATION

One of Australia's strengths is great basic science. **Professor Nigel McMillan**, Menzies Health Institute Queensland, Griffith University, noted that the range of exciting work on RNA technology in Australia reflects the funding that has gone into basic research. However, McMillan also commented that Australia has not invested in translation to take the next step of turning discoveries into something with commercial and therapeutic success. Purcell observed that while Australia is excellent at making 'widgets', we don't necessarily assemble them into a complete, cohesive product. Purcell also suggested that Australia must bring different disciplines together, be courageous and have clear objectives.

Fox remarked that when investing in translation, Australia must also continue to fund basic research, stating that Australia needs to fund the whole research, development and commercialisation pipeline. They also observed that many discoveries come from basic research but that it can be hard to identify a patentable product at the basic research stage. Supporting Fox's comments, Thordarson observed that basic research keeps the engine going on the translational front.

Keenan noted that translation work would identify issues that need to be solved by more basic research and thus direct research to solve relevant problems for translation. However, Davidovich highlighted that we also need decent funding for blue sky research without thinking about what the application will be.

Änkö noted Australia's broad coverage across many research areas but highlighted that Australia needs to build depth. They observed that it would be challenging to form a critical mass when our efforts are spread around Australia.

> **There are things coming that we can't imagine because they are so innovative.**
>
> **Associate Professor Chen Davidovich**

A key theme of discussions during this session was how to work together to support translation. Keenan suggested that multidisciplinary research consortia are the way forward in research translation. **Professor Steve Wilton,** Murdoch University and the Perron Institute University of Western Australia, commented that consortia should be international. Änkö noted that such consortia could attract significant funding, help bridge the gap from discovery to translation and bring together experts in different fields.

> **Collaborations and competition were the springboard for RNAi.**
>
> **Professor Peter Waterhouse**

While reflecting on the breakthrough to commercialisation in relation to the discovery of RNAi, **Professor Peter Waterhouse FAA,** Queensland University of Technology, highlighted the importance of bringing people together and noted the role a key conference of 20–30 people from a range of areas of expertise played in the research taking off. They also emphasised that a rapid influx of money from the medical area accelerated the work.

The issue of patents and IP were also discussed. **Professor Fiona Cameron,** Australian National University, observed that IP is critical to translation and doesn't need to hold back research if appropriately managed. Wilton also noted that patents protect efforts and costs.

DRUG DISCOVERY AND DELIVERY IS AN AUSTRALIAN STRENGTH

Thordarson highlighted delivery as a strength in Australia and proposed that Australia could capitalise on this and target high-value targets such as the blood–brain barrier (e.g. for brain cancer and neurodegenerative diseases). **Professor Colin Pouton,** Monash University, also commented on Australia's strong background in drug discovery and delivery and suggested that it could be leveraged to collaborate on designing drugs for modulation of RNA biology. Pouton made this comment via Slido[2] and eight other participants upvoted it.

RNA PROVIDES MANY EXCITING OPPORTUNITIES IN MEDICINE AND BEYOND

Shifting the discussion to consider future opportunities for Australia, Fox asked participants to share what headline discovery, or product, they would like to see emerge from Australian RNA via an open poll. Most of the responses fell into one of three key themes: therapeutics, delivery technologies and manufacturing.

Participants highlighted a range of future research and development opportunities. Fox reflected that there is an opportunity to make much more sophisticated products such as long non-coding RNA, and noted their excitement about combining lipid nanoparticles with lncRNAs and mRNAs. **Professor Maria Kavallaris AM FAHMS FRSN,** Children's Cancer Institute, UNSW Sydney, commented that designing a

2 Slido is a live polling and interactive engagement website to support running virtual events. Users are able vote on the comments submitted by others.

modular RNA therapeutics platform that can respond rapidly to emerging threats or diseases would be very useful. Wilton noted opportunities to combine different RNA technologies and asked whether there is potential to attack viruses directly with RNA.

Purcell noted the opportunity to make RNA vaccines, highlighting that this is where the investment is right now. They remarked that Australia has research strengths in immunology and virology, particularly in companies like CSL. Australia should meet the opportunities that exist now in virology and immunology. Morris commented that Australia should build manufacturing for RNA vaccines, observing that it is something Australia needs. There are also companies in the United States waiting for manufacturing opportunities that would come here. If Australia builds the infrastructure, there will be a flow on to other benefits. Further, Morris and Fox both noted that a strength for Australia is the value of our dollar.

Several participants highlighted opportunities for RNA science and technology beyond clinical applications. Preiss emphasised the role RNA can play in sensing and diagnostics and the opportunity for Australia to innovate and expand into these areas. Fox noted that another area to consider is biotechnology. For example, there are considerable needs in areas such as improving agricultural yields and adapting to climate change.

END-USER NEEDS MUST BE CONSIDERED

S. Conn commented that cost should be considered when looking at treatment options, noting that some strategies are more affordable. Wilton noted that the cost of personalised medicines will be a challenge unless there is a common platform and that the cost of a treatment does not just reflect the cost of production but also the cost of many years of research. Fox observed that projects creating RNA based products for large numbers of recipients could be used to subsidise personalised, niche products for individuals, or rare diseases.

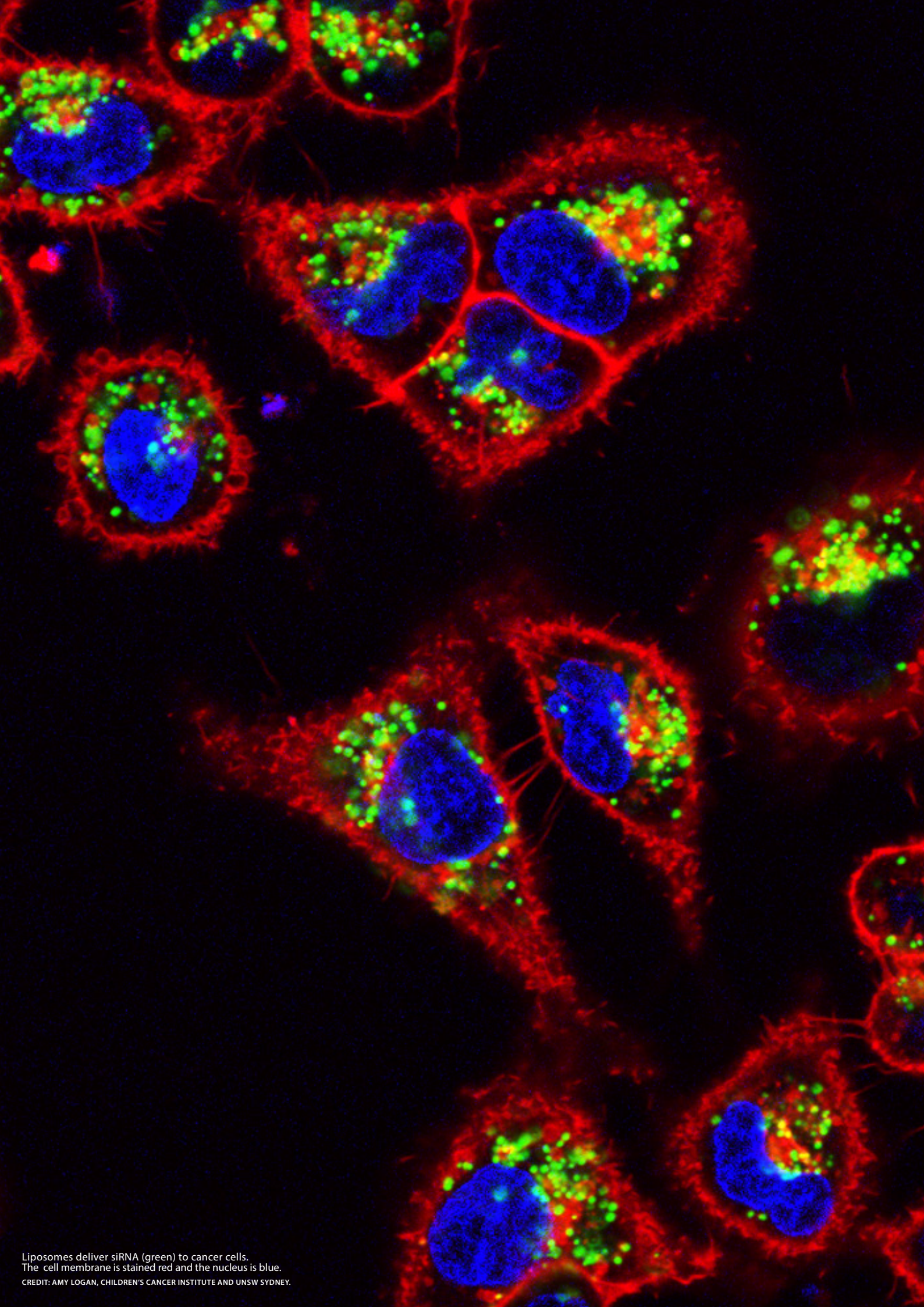
Änkö noted that safety testing for products should be considered, observing that we have seen that Australians are sceptical of new products during the COVID vaccine program. We need to be able to test safety to give people the confidence to trust Australian made products. Änkö also suggested that there is potential for Australia to develop expertise in this area and share it with other countries.

ACCESS TO MATERIALS AND AFFORDABLE MANUFACTURING IS LACKING IN AUSTRALIA

Fox noted that a bottleneck preventing development is not getting enough material for lab testing or clinical trials. The inability to produce enough material to experiment with is a critical barrier for Australia. Fox also commented that future Australian RNA-based biotechnology and biopharmaceutical companies are going to need a pipeline of products for the system to be viable.

Pouton noted that Australia needs affordable GMP manufacturing for Phase 1 trials; if it is too expensive it won't be accessible to academic researchers using grant funding. They emphasised the need to keep an eye on this so that researchers can do proof of concept research in animals and commence clinical trials without needing millions of dollars. McMillan noted that there would be interest in doing trials on shore in Australia if it was accessible, but it is currently too expensive. Middelberg remarked that the model the government chooses is critical and needs to support investment in the research community to enable the maximum translation of basic research.

Comments received by Slido were incorporated into the summary of this session.



Liposomes deliver siRNA (green) to cancer cells.
The cell membrane is stained red and the nucleus is blue.

CREDIT: AMY LOGAN, CHILDREN'S CANCER INSTITUTE AND UNSW SYDNEY.

INTERNATIONAL RNA SCIENCE AND TECHNOLOGY LANDSCAPE, AND THE OPPORTUNITIES FOR COOPERATION

Led by Associate Professor Archa Fox

In Session 3, participants discussed the international RNA science and technology landscape, and opportunities for and barriers to international cooperation. Throughout the session there was general agreement that we should establish Australia as a leader in RNA science and technology. However, participants also noted several barriers to achieving this, including an overall lack of funding in Australia and structural funding barriers for multidisciplinary research.

A LACK OF FUNDING IS A BARRIER TO AUSTRALIA CONNECTING INTERNATIONALLY

Fox began the session by asking participants to respond to a multiple-choice poll asking, 'What holds us back in connecting internationally in RNA science and technology?'. Participants identified two main factors holding Australia back from connecting internationally on RNA science and technology: lack of funding in Australia for RNA science and technology (72% of respondents) and lack of facilitation for developing international grants and programs (25% of respondents).

THE AUSTRALIAN RNA COMMUNITY SHOULD WORK TOGETHER TO TAKE ADVANTAGE OF INTERNATIONAL OPPORTUNITIES

Fox asked participants to consider how the Australian RNA science and technology community can link with other efforts around the world, such as Wellcome Leap R3 and the NIH RNA biology subdiscipline. Fox also mentioned that there are a range of international funding groups and opportunities and asked for input on how Australia can connect to these. On this, Keenan observed that many countries have published healthcare missions and priorities and that the Australian RNA science and technology community should be ready to take advantage of funding opportunities and calls for ideas. Keenan suggested forming a group that addresses problems that have been highlighted internationally so that the community can get on the front foot and be prepared for calls by having thought about them already.

> **We should establish Australia as a leader not a follower.**
>
> **Professor Thomas Preiss**

AUSTRALIA HAS THE POTENTIAL TO BE A REGIONAL AND GLOBAL LEADER IN RNA SCIENCE AND TECHNOLOGY

Thordarson suggested Australia could lead something internationally, perhaps leveraging on the work of Australia's development program. For example, Thordarson noted that Australia could lead something in our region, focusing on agriculture or tropical diseases as both issues are relevant to nearby countries and could contribute to stability in our region. Cameron noted that tropical diseases will be an increasing problem for Australia and our neighbours in a warming climate and that there are few, if any, good vaccines available. Preiss, **Professor Gyorgy Hutvagner,** University of Technology Sydney, and Beilharz endorsed Thordarson's suggestion. Preiss commented that it is better for a small player like Australia to be a leader and disruptor rather than simply following a model that has worked elsewhere.

Mattick observed that RNA science is poorly developed around the world and that the lack of appreciation for the potential of RNA is widespread. For example, there are only about six institutes in the United States that focus on RNA. Mattick suggested that Australia could become an international centre for RNA research if we look at what Australia can be good at and how we can be particularly useful in our region. Preiss endorsed Mattick's suggestion, noting that Australia could be a leader in this disruptive industry with courageous leadership from the government.

TO BECOME AN INTERNATIONAL LEADER IN RNA SCIENCE AND TECHNOLOGY, AUSTRALIA NEEDS TO FIX STRUCTURAL FUNDING PROBLEMS FOR MULTIDISCIPLINARY RESEARCH

Participants in this session highlighted the importance of collaboration and multidisciplinary work in the RNA field. RNA science and technology requires interconnectivity between chemistry, biology and health, and engineering and nanotechnology. For Australia to become a leader in this field, we will need to fix structural funding problems for multidisciplinary research.

> **We are big enough and small enough to do it well.**
>
> **Professor John Mattick**

Noting earlier discussions about the interconnectivity between fields in RNA research, Middleberg suggested that Australia has the breadth of research capacity to come together around grand challenges and generate national wealth and health for Australians. Further, they observed that other countries don't have the framework to build the collaborative structures but we do, and that this should be the focus of Australia's platform. However, they also noted that to achieve this, Australia will need to fundamentally fix structural funding problems so that different disciplines can work together. An example would be opening the MRFF to greater strategic investment in emerging areas of great future potential in medicine, including in the physical sciences.

Thordarson commented that artificial barriers in funding schemes make it harder to do work and suggested that Australia needs to think differently and break down barriers in funding systems. For example, they noted that the NHMRC doesn't have the breadth to support fundamental science that doesn't look immediately medical. Middelberg noted that the classification of funding schemes is not a unique problem to Australia and that there are globally recognised ways to fund multidisciplinary initiatives. They also noted when considering changes to funding schemes, we should be mindful of unintended consequences like the ARC simply becoming another health funding agency.

Kavallaris noted that there is a precedent for ARC and NHMRC to co-fund projects and that there are also opportunities to have multidisciplinary teams on NHMRC grants. They also highlighted the need to be creative and take opportunities to lobby and advocate to the government to help advance the field. Cameron noted that the ARC ITRP scheme allows medical research focused on industrial transformation.

Closing the session, Fox reemphasised the opportunity for Australia to be a leader in this field in the Australasian region and globally, and called on the ARC, NHMRC and other observers to take note of this chance to do something different.

Comments received by Slido were incorporated into the summary of this session.

STRENGTHS AND WEAKNESSES IN THE AUSTRALIAN RESEARCH, DEVELOPMENT, AND COMMERCIALISATION PIPELINE

Led by Professor Trent Munro

The focus of session 4 was strengths and weaknesses in the Australian research, development and commercialisation pipeline.

THE DRUG DEVELOPMENT LANDSCAPE IS CHANGING, AND WE CAN NO LONGER RELY ON THE US TO FUND INNOVATION FOR THE REST OF THE WORLD

Professor Trent Munro, Australian Institute for Bioengineering and Nanotechnology, University of Queensland, introduced the session with an overview of current trends in drug development. Technology cycles are long and unpredictable, and the cost barrier to moving into production is not unique to RNA. A challenge the whole sector faces is the cost of bringing a product to market; it is impossible without someone willing to fund it and take on risk. The cost is not just the cost of production but also the investment in the research leading to its development. In the past, the US has funded innovation for the rest of the world, but how we think about funding and risk in commercialisation is changing.

LACK OF CAPITAL, INFRASTRUCTURE AND EXPERTISE ARE BARRIERS TO RESEARCH TRANSLATION AND COMMERCIALISATION IN AUSTRALIA

Based on the pre-event survey, Munro shared that some of the issues Australia faces are a lack of expertise, a lack of scale, a lack of funding and a lack of biotech sector involvement. To expand on this, Munro asked the participants to share their challenges and barriers to research translation via two live polls to begin to answer the broader question of what is holding Australia back from commercialising the research and ideas we have. In the first poll, Munro asked what holds them back from rapid translation or commercialisation of their research. Access to capital and access to infrastructure were the two main barriers identified. The second poll asked, 'If you had a start-up company for a new RNA technology what would be your biggest concern about keeping operations in Australia?'. Nearly 50% of respondents selected lack of expertise.

On expertise, **Professor Sue Fletcher,** Murdoch University and PYC Therapeutics, remarked that Australia lacks translational expertise and capability. Fox asked whether solving the lack of expertise is more about training or attracting expertise from overseas. **Associate Professor Jingxiu Bi,** University of Adelaide, suggested that engineering training and education for biomanufacturing in Australia may be one of the solutions for the long term. Hill noted that it would be important to embed entrepreneurship training in the next generation of scientists. Cameron observed that consistent support for good and experienced business development personnel in universities is patchy, noting the importance of integrating this expertise within research teams.

AUSTRALIA NEEDS TO INVEST IN MANUFACTURING CAPABILITY STRATEGICALLY

McMillan observed that the Australian RNA ecosystem needs the whole gambit of GMP manufacturing capability and asked what investments can be made to benefit everyone across the country. Munro suggested that investment in translational

biomanufacturing needs to be strategically linked. **Professor Susie Nilsson,** CSIRO, noted that it is costly to make something at GMP standard. Building and maintaining the necessary infrastructure itself is costly, let alone creating product.

Dr Andrew Nash, CSL, noted that it is crucial to have processes in place to transfer research into manufacturing facilities. There is a lack of experience to do this in research organisations. Further, they observed that accessing the level of money required for the clinical and manufacturing stage is very hard in the Australian academic environment. Nilsson remarked that money would be needed for ideas to come out of academia and create products.

WE NEED TO RECOGNISE THAT IT IS OKAY TO FAIL AND THAT IT IS BETTER TO FAIL FAST

Kavallaris asked how we change the culture in Australia to see failing as okay, noting that the funding and university system is not very forgiving. Munro commented that we should accept risk and failure and embrace an entrepreneurial spirit. Middelberg observed that we need an ecosystem like a funnel to speed through early stages, noting that it is better to fail fast. Further, they also observed that Australia hadn't invested heavily in this area and that manufacturing at scale is challenging. Ultimately, Australian researchers and innovators must access international expertise and value chains, but we should support them to do this later in the process. Ideally, researchers need to be able to go from labs to clinical trials in Australia and need funding to bridge the translation gap before going to contract development and manufacturing organisations or big pharma. Nilsson noted that the manufacturability of products must be considered earlier as this is critical when moving from Phase 1 trials and beyond.

> **We need to encourage an active and vibrant biotech start up environment, while also ensuring a fail fast or pivot early strategy for future success.**
>
> Professor Trent Munro

Munro observed that the problem is that MRFF funding for trials programs have a Clinical Trial Notification (CTN) pathway, and this may encourage people to do things as cheaply as possible and may not stack up to scrutiny internationally. However, **Professor Peter Leedman,** Harry Perkins Institute of Medical Research, noted that the CTN path is rapid and less complex than the US path. The data is very well accepted by the pharmaceutical industry, making Australia a good place for early clinical trials. Instead, the issue is how to get out of academia into phase 1 trials—universities do not have the resources to do this, nor does the MRFF or NHMRC. Leedman remarked that we need to foster a culture in which failure is okay and find people who are happy to invest in bridging the gap from preclinical to phase 1 trials.

Middelberg recognised that Australia is fortunate to have NCRIS collaborative facilities rather than building 'white elephants'. Nilsson also noted that NCRIS has been hugely valuable and that research has benefitted but asked how we can keep growing it.

Keenan observed that partnerships are a great way of moving things forward, observing that spin-out companies will attract investment. However, Munro noted that university commercialisation focuses on licensing rather than spinouts.

Several participants noted overseas examples. Leedman commented that US and Israeli technology transfer offices are skilled. Pouton compared the Australian environment to the US, Germany and the UK, noting that investment is completely different here and that in Australia we are scrambling.

ACCESS TO TALENT AND ZOMBIE START-UPS ARE CHALLENGES IN THE AUSTRALIAN ENTREPRENEURIAL ECOSYSTEM

Keenan noted that the skills gap is a big problem. While there is lots of talent out there, we need to capture and recruit them. Munro commented that we need to kill zombie companies (companies that neither fail, nor flourish, leading to low growth potential and becoming unattractive to investors) when start-ups don't work, to get our talent back.

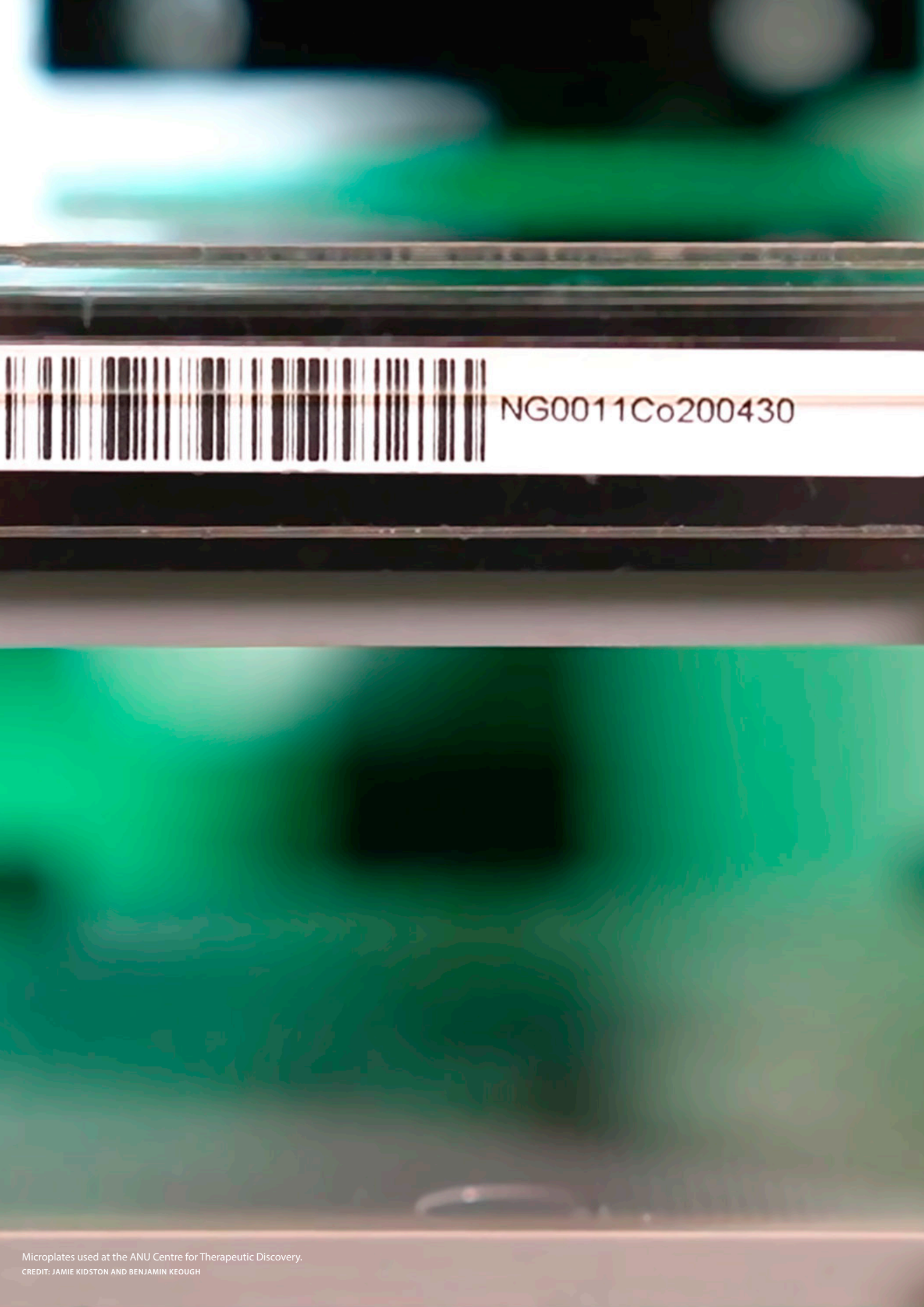
Middelberg remarked that government policies could encourage universities to see how they can contribute to the innovation and start-up ecosystem, noting that universities have a greater focus on commercialisation and engagement and those policy settings will drive connectivity. However, Purcell noted that incentivisation at the academic coalface to translate is not optimal, observing that providing opportunities to develop expertise is not rewarded and not a readily countable metric when seeking further funding.

RNA IS A PLATFORM TECHNOLOGY

> **RNA's beauty is it is a platform technology.**
>
> **Associate Profesor Archa Fox**

Fox reflected on the nature of RNA as a platform technology, noting that once you have the production platform, some issues are eliminated. For example, the manufacturability issue could be the same for any sequence, so it just needs to be solved once. Munro commented that platforms offer a streamlined approach for manufacturing and allow for the coordination of research costs.

Comments received by Slido were incorporated into the summary of this session.



Microplates used at the ANU Centre for Therapeutic Discovery.
CREDIT: JAMIE KIDSTON AND BENJAMIN KEOUGH

NATIONAL RNA RESEARCH AND TRANSLATION PRIORITIES

Led by Professor Ian Chubb AC FAA FTSE FACE FRSN

Following a short lunch break, participants reconvened for the final roundtable session. They considered the conclusions from the earlier sessions and discussed proposed recommendations to be published as concrete outcomes of the roundtable.

Professor Ian Chubb AC FAA FTSE, Secretary Science Policy, Australian Academy of Science, began the session by summarising the key conclusions from the earlier sessions.

Australia can create an innovative RNA research and development 'ecosystem' and become a strong global player in this disruptive industry, creating and manufacturing high-value RNA-based products for local use and exporting them to the world. However, becoming a world leader in RNA science and technology will only be possible if the investment is made to build and support the pipeline with sustained funding from fundamental research to translation and manufacturing.

> **Australia has the capacity and history. We're not doing this because it's trendy, but because we have a historical place in RNA research.**
>
> **Professor Ian Chubb**

The Australian way all too often results in short-term funding, but RNA science and technology needs to be a long-term initiative. Talented staff, financial support, capital and infrastructure are indispensable. We need to make the case that benefits flow from leadership and sustained funding. It is not enough to go to government and say these are the same problems we have been facing for the last 20 years. We need to highlight what the country can be, what the best ways are to translate this research into products and how it will benefit the users and the economy. Examples include sovereign risk mitigation and issues RNA can help solve in agriculture, tropical diseases and biosecurity. Australia also has a role to play as global citizen, such as on issues like the spread of diseases in our near neighbours. We can produce science and technology for the good of people in our region and ourselves.

> **We need to be bold. If ever there was a time, it is now.**
>
> **Professor Ian Chubb**

We need 'outside the square' thinking about getting translation to commercial product. Fundamentally, success here needs cultural change and there is a rare opportunity to initiate that process through the focus on RNA technologies. Part of the cultural change needed is to move away from intrinsic risk aversion. Support is needed to encourage taking calculated risks.

Each of the three chairs commented on the conclusions, highlighting different aspects of the discussion. Mattick emphasised the importance of thinking about a constructive, compelling and actional way forward and providing an acceptable roadmap to key agencies, including strategic funding and shared objectives. At the same time, Fox reflected on the importance of working together synergistically without individual motivation and preparing for uncertainty and

rapid responses. Finally, Munro highlighted that the most significant challenge is the breadth of the field. The opportunities for advancement in the field sit at the interface between chemistry, biology and nanoscience.

DRAFT RECOMMENDATIONS

Based on the conclusions from the earlier sessions, Chubb proposed four recommendations to support RNA science and technology in Australia for the participants to consider and discuss:

1. A single RNA manufacturing facility in Australia that is well-maintained and has a sustainable funding source
2. A mechanism to encourage and support interdisciplinary work
3. Sustainable funding for the research, development, and commercialisation pipeline to attract, retain and maintain skills
4. A targeted mobility program between staff and students, research and industry

DISCUSSION OF MANUFACTURING RECOMMENDATION

To ensure all participants had the opportunity to contribute to the manufacturing discussion in the limited time available, they were asked to respond to the question 'What does the ideal RNA manufacturing capability in Australia look like?' via an open text poll in Slido. Key themes from the responses were:

- a mixed manufacturing ecosystem with end-to-end capability and a range of facilities including GMP and pilot facilities (8)
- accessibility, sustainability, flexibility and scalability (7)
- a coordinated platform with multiple expertise hubs/facilities located in different places (6)
- links with and support for academic, translation, and commercial capabilities and expertise (4)
- investment by companies/industry (3)
- an NCRIS-like facility (2).

Chubb asked the participants whether there should be a single manufacturing facility in the country for products to be used in research and eventually trials and market. Chubb noted that it would need to be maintained with sustainable funding.

In response, Kavallaris noted that Pfizer used many companies to manufacture what was needed for their mRNA COVID-19 vaccine and questioned whether Australia would be able to get one site to do everything. They suggested multiple sites would be better as RNA manufacturing is more complicated than what can be provided with just one facility. Thordarson also commented that it might not be possible to have everything together as there are competing technologies and projects.

Chubb agreed that this approach seemed sensible but noted the importance of having a string around it to ensure collaboration and avoid disparate facilities. Mattick reinforced this noting the risk of never-ending dispersion. Mattick recommended that we need to think about what capabilities are needed.

Pouton remarked that further clarification was needed regarding a manufacturing centre, including considerations like what scale, whether it is a GMP facility, and whether it is for early clinical trials or the population response to the pandemic.

These are different facilities. One might be publicly funded, and the other most certainly wouldn't be. Pouton suggested that a GMP facility can be centralised for emerging therapeutic applications to be produced for clinical trials. Others would be needed for low-cost production for proof-of-concept products and for large scale GMP for full production.

Preiss noted that it is vital to have a coherent, coordinated strategy but observed that different manufacturing steps don't necessarily need to be in one place. They noted that it would be good to illustrate examples when making the recommendations from this roundtable. Examples could include that CSL started as a government organisation and is now the biggest Australian company on the stock exchange, and that Australian discoveries, such as the Shine-Dalgarno sequence and RNAi, have changed the world. .

Professor Bernard Carroll, University of Queensland, commented that for agriculture and environment applications, the production of double-stranded RNA should be included as a priority for a national RNA manufacturing facility.

S. Conn commented that, ideally, we need to ensure we can generate the base reagents (lipids, nucleotides etc.) for these facilities within Australia (or have an uninterrupted supply).

DISCUSSION OF OTHER RECOMMENDATIONS

Purcell noted that it is difficult as an academic to understand what genuine IP is and that universities don't have the resource to support IP on ideas. They suggested a centralised location for looking at what could be IP. Chubb suggested including a comment on the patent box in the final report from the roundtable. Chubb also commented that we have not managed IP well in the country.

Änkö remarked that fundamental research is Australia's strength and should be supported.

Fletcher noted that the R&D rebate is an incentive for investment, but it is not as widely publicised or understood as it should be. The rebate gives companies a runway in drug development. Fletcher also observed that Australia lacks translational capability, noting that this is a major challenge for small biotechnology companies wanting to translate research. While we can work with overseas contract research organisations, they don't understand the Australian R&D environment. Fletcher also noted that industry experience programs for research students would help build capability and expertise in this area.

Chubb remarked that Australia needs a mechanism to encourage interdisciplinary work, noting that the challenges to getting interdisciplinary work funded means funding often goes to an expert here and there rather than supporting work that truly draws on multiple disciplines.

Chubb commented that the pipeline needs to be funded on a sustainable basis to attract, retain and train talent. They suggested recommending a targeted mobility program between staff and students in research and industry. A targeted mobility program supporting cross-disciplinary work could be a way to bridge gaps in understanding between different cultures. Mattick remarked that we should think about practical and effective ways to sustain the sector in Australia. They suggested that the ARC and NHMRC could partition some funding into NIH-style

strategic funding initiatives. The MRFF has the flexibility to be extended to other areas of biology. McMillan proposed that there should be an RNA future mission, like the genomics one.

Fox reflected that for the ANZRPC, connections to industry were an issue. At the start, the ANZRPC struggled to identify who the industry partners were, but they are now at a point with good industry links. They noted that formalising something to create a sector could be significant and suggested that a body charged with doing this could be created.

On how Australia can encourage the biotech industry, Chubb suggested looking at the R&D tax incentive and considering how to use it to encourage research-linked SMEs, noting that there is lots of development in Australia from SMEs. **Professor Ian Small FAA,** University of Western Australia, noted that biotech start-ups generally sell products and services to established biotech companies, so we need to attract multinationals here to have a target market. Keenan commented that the initiative should support a start-up culture to attract external funding.

FINAL RECOMMENDATIONS

Based on this session's discussions and input from participants via Slido, a final set of recommendations was developed and published in a statement the day after the roundtable. The agreed recommendations from the roundtable are to advance opportunities towards:

- a national mission for the whole RNA science and technology pipeline in Australia, driven by strategic investment and prioritisation across funding schemes
  - the national mission should provide sustainable, long-term funding for projects from fundamental research to translation
- a local mixed RNA manufacturing ecosystem, including pilot facilities to enable new Australian products to be translated, production of pre-clinical trial components and GMP sovereign manufacturing capability to support clinical trials
- the formalisation of cross-disciplinary coordination to:
  - develop a roadmap for a national RNA science and technology mission
  - holistically nurture the entire research to translation pipeline
  - connect the research community to each other and industry
- the facilitation of commercialisation and establishment of a self-sustaining RNA biotechnology industry through new and existing mechanisms, including incentivising the capture of new intellectual property, the R&D tax incentive and proposed patent box initiative
- schemes to build capacity in entrepreneurial and translation expertise, including facilitating greater mobility between research and industry.

CONCLUSION AND NEXT STEPS

Led by Professor Trent Munro

Munro concluded the roundtable by providing an outline of the next steps: the publication of a statement the day after the roundtable (see Appendix 1) and the publication of a final report (this report) within two months of the roundtable.

ROUNDTABLE STRUCTURE

The virtual roundtable was held via Zoom webinar from 10 am to 2:30 pm AEST, 29 July 2021. The event included five main sessions covering key topics, as well as short introductory and concluding sessions.

AGENDA

Timing	Item	Chair/speaker
10.00am	Welcome	Prof John Shine Prof Thomas Preiss
10.10am	Address regarding Australian Government investment in RNA manufacturing capability	Mr David Luchetti
10.15am	Background and context setting	Prof John Mattick
10.25am	Overview of roundtable agenda and tools	Dr Hayley Teasdale
10.30am	**Session 1 –** Global emerging areas in RNA Science and Technology	Prof John Mattick
11.15am	**Session 2 –** Australia's research strengths and opportunities	A/Prof Archa Fox
12.00pm	**Session 3 –** International landscape and opportunities for cooperation	A/Prof Archa Fox
12.20pm	**Session 4 –** Strengths and weaknesses in the Australian research, development and commercialisation pipeline	Prof Trent Munro
1.00-1.30pm	Lunch break	
1.30pm	**Session 5 –** National RNA research and translation priorities	Prof Ian Chubb
2.20pm	Conclusion and next steps	Prof Trent Munro
2.30pm	**Event concludes**	**All**

Robotics that dispense small volumes of reagents for high-throughput therapeutic screening.

CREDIT: CHILDREN'S CANCER INSTITUTE

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- Australian National University
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- Menzies Health Institute, Griffith University
- University of Western Australia
- University of Queensland
- Monash Institute of Pharmaceutical Sciences, Monash University
- UNSW Sydney.

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METHODOLOGY

The methodology for this roundtable was adapted from the Sutherland methods for 'collaboratively identifying research priorities and emerging issues in science and policy'. The published method includes gathering a large amount of feedback from the community and using breakout groups during the discussion. While these features were not used, the general structure and values of the method were maintained.

SELECTION OF PARTICIPANTS

Thirty-eight experts were selected to bring together a representative group of the nation's most eminent RNA science and technology expertise.

A call for nominations identified these experts to the learned academies, Australia's Chief Scientist, state and territory chief scientists and other relevant peak bodies, including the Association of Australian Medical Research Institutes.

Ninety-three experts were nominated, and the selection of participants was made by the roundtable chairs, considering geographical spread and discipline expertise.

PRE-EVENT SURVEYS

FIRST SURVEY (OPEN RESPONSES)

A survey was distributed to participants to gather information about both Australian and international research priorities. The questions were:

1. What do you believe are the emerging areas in RNA science and technology, globally? Please list a maximum of three.
2. Which areas of RNA science and technology do believe are poised to have the greatest impact on society, globally? Please list a maximum of three.
3. What areas of RNA science and technology particularly require international cooperation or a global mission to progress? Please list a maximum of three.
4. In what areas of RNA science and technology development does Australia have particular strengths? Please list a maximum of three.
5. What are uniquely Australian challenges that RNA science and technology can help solve? Please list a maximum of three.
6. Where do you see the gaps or weaknesses in the research and development pipeline, in Australia? Please list a maximum of three.
7. Is there an area of RNA science and technology where you see Australia as an existing or potential world leader? Please list a maximum of three.

Questions were reviewed by the chairs before distribution to participants, who were given one week to respond to the survey.

SECOND SURVEY (RANKING)

The second survey included the same seven questions from the first but instead asked the participant to select and rank their top five answers from a list. The list of options was generated by summarising the responses to the first survey into categories.

For each question, the online survey tool used assigned each option a score based on the number of times that option was selected and the weighting each participant gave it. These scores were used to determine the rankings.

DISTRIBUTION OF SURVEY RESULTS

The results of the pre-event surveys were distributed to participants before the roundtable. The five highest-ranked options for each question were highlighted as a starting point for the discussion during the roundtable. However, all options were included in the survey summary distributed to participants ahead of the event, and topics were not excluded from the discussion if they were outside the top five.

ROUNDTABLE

The roundtable was held virtually using Zoom Webinar and the live polling tool Slido. Participants could contribute to discussions in each session verbally via a comment tool through Slido and six live polls.

The event was broken into five main sessions as well as short introductory and concluding sessions. The first four sessions covered key topics also covered in the pre-event surveys:

- Global emerging areas in RNA science and technology
- Australia's research strengths and opportunities
- International landscape and opportunities for cooperation
- Strengths and weaknesses in the Australian research, development and commercialisation pipeline.

In the fifth and final session, the conclusions from the earlier sessions were discussed and the recommendations from the roundtable were finalised.

STATEMENT

A statement (Appendix 1) was released the day after the roundtable sharing the key recommendations from the roundtable. The statement was based on the discussions during the roundtable and was reviewed by the chairs, the Academy and ANZRPC.

POST-EVENT SURVEY

After the roundtable, a survey was distributed to both participants and observers to capture their feedback on the topics discussed and the organisation of the event. The survey included the following questions:

1. Which priorities/recommendations did you particularly agree with?
2. Which priorities/recommendations did you particularly disagree with?
3. Was there any topic that wasn't discussed today, that should have been?
4. Do you have any feedback for the organisers?

FINAL REPORT

The input gathered from the participants at each stage of this process is collated and explored in this report.

APPENDIX 1 – STATEMENT

STATEMENT – NATIONAL RNA SCIENCE AND TECHNOLOGY PRIORITIES

A national roundtable to identify Australia's RNA science and technology priorities was held on Thursday, 29 July, hosted by the Australian Academy of Science and the Australia and New Zealand RNA Production Consortium.

The group, comprised of experts in RNA biology and biotechnology from academia and industry, discussed how Australia can play a leading role in the global ecosystem of RNA science and harness the opportunities for Australian industry to develop RNA-based products and services for global markets. The group concluded that a national mission is required to ensure Australia can fulfil this leading global role.

RNA, or ribonucleic acid, exists in various forms that play a central role in the function of genes and the regulation of gene expression. RNA controls development in plants and animals, influencing areas as diverse as crop yields in agriculture, and brain function in humans. There has long been considerable potential for RNA based products. However, the success of RNA based technology in the rapid development of safe and effective vaccines for COVID-19 has drawn sustained public interest in the technology. It has also triggered public and private investment to establish capabilities from fundamental scientific research through to clinical and commercial onshore mRNA manufacturing.

With the first commercially approved mRNA-based vaccines there is considerable potential for developing more advanced uses of RNA therapies and technologies, including the treatment of disorders such as arthritis, cancer and malaria and genetic engineering of plants and animals to improve productivity and reduce environmental pressures. Further, developing products that can accurately detect pathogenic RNA will be essential for biosecurity in Australia and globally.

Considering the uniquely Australian problems that stand to be solved by RNA science, including sensing new biosecurity threats, and supporting climate change adaptation in agriculture, the group determined a list of research priorities by balancing Australia's strengths against emerging global trends. These research priorities are RNA vaccines, including vaccines for people with autoimmune disorders; RNA therapeutics; RNA sensing tools; RNA in plant and animal development; RNA in brain function and disorders; RNA chemistry; Stability and advanced manufacturing of RNA therapeutics; RNA delivery technologies.

The agreed recommendations from the roundtable are to advance opportunities towards:

- A national mission for the whole RNA science and technology pipeline in Australia, driven by strategic investment and prioritisation across funding schemes.
    - The national mission should provide sustainable, long-term funding for projects from fundamental research to translation.
- A local mixed RNA manufacturing ecosystem, including pilot facilities to enable new Australian products to be translated, production of pre-clinical trial components and GMP sovereign manufacturing capability to support clinical trials.

- Formalise cross-disciplinary coordination to:
  - Develop a roadmap for a national RNA science and technology mission.
  - To holistically nurture the entire research to translation pipeline.
  - To connect the research community to each other and industry.
- Facilitate commercialisation and establishment of a self-sustaining RNA biotech industry through new and existing mechanisms, including incentivising the capture of new intellectual property, the R&D tax incentive and proposed patent box initiative.
- Schemes to build capacity in entrepreneurial and translation expertise, including facilitating greater mobility between research and industry.

Australia has an opportunity to create an innovative RNA research and development 'ecosystem' and become a global player in this disruptive industry, creating and manufacturing high-value RNA-based products here, and exporting them to the world.

The Australian Academy of Science will produce a full report of the roundtable for policymakers and science funders in the coming weeks.

WHAT IS RNA SCIENCE?

RNA is one of the three major biological macromolecules essential for all known forms of life, along with DNA and proteins. For decades RNA has been viewed as the intermediate between gene and protein. It is now evident that many RNAs are not translated into proteins, but rather act to control the complex processes of differentiation and development. These RNAs are also subject to modification, particularly in the brain, which connects hardwired genetic information to environmental parameters.

Pfizer/BioNtech and Moderna mRNA vaccines have been successfully used against COVID-19 and can be potentially reformulated rapidly to counter new strains of viruses. They have also been shown to have the potential to inoculate against many diseases such as autoimmune disorders, RSV, influenza and malaria. Applications of mRNA and other forms of RNA, such as siRNA, miRNA, and gRNA, have potential beyond vaccines, including the treatment of neurodegenerative and neuropsychiatric disorders, cancer, and genetic engineering in agriculture.

Australia is well placed with many world-leading experts in RNA science, biomaterials and biotechnology located within our universities and research institutes. Australia is also developing the capability to manufacture RNA on an industrial scale for products, including mRNA vaccines.

Through the adoption of policies and strategic investments, opportunities exist to develop sovereign capability in RNA science and technology from knowledge creation to translation and manufacturing.