



Australian Academy
of Health and
Medical Sciences

Understanding our RNA potential

RESPONSE BY THE AUSTRALIAN ACADEMY OF
HEALTH AND MEDICAL SCIENCES

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The Australian Academy of Health and Medical Sciences

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1. Introduction

The Australian Academy of Health and Medical Sciences (AAHMS, the Academy) welcomes the Department of Industry, Science and Resources (the Department) consultation to better understand the opportunities and challenges for developing Australia's RNA sector. We strongly support the Department's efforts to unleash the nation's RNA potential and to bring together a clearer picture of the technologies and approaches currently under development across the country – and the associated opportunities.

AAHMS is Australia's Learned Academy for health and medicine – the impartial, authoritative, cross-sector voice. We advance research and innovation in Australia to improve everyone's health.

We are an independent, interdisciplinary body of Fellows – elected by peers for outstanding achievements and exceptional contributions to health and medical sciences in Australia. Collectively, AAHMS Fellows are a representative and independent voice, through which we engage with the community, industry and governments.

Through the Academy's Fellows, Associate Members and networks, we hold deep knowledge across numerous disciplines and sectors relevant to RNA research, innovation, translation and application. We are particularly well placed to deliver expert advice on how research and innovation can be translated efficiently and effectively to reach patients and the community.

On 29 September 2023, AAHMS held a roundtable meeting to inform this consultation. The purpose of the roundtable was to convene experts with clinical and translational expertise to explore areas including:

- Australia's local and regional patient population needs in RNA.
- How we can build on our strengths and prioritise our efforts to ensure maximum impact of RNA technologies and research.
- What we need to better translate our RNA research into practice.
- The infrastructure and skills required to develop and use RNA technologies in health.

The roundtable was attended by 17 leading experts from the RNA sector including clinicians, researchers, policymakers and industry experts, and was chaired by Professor Maria Kavallaris AM FAHMS. Professor Kavallaris is Founding Director of the Australian Centre for NanoMedicine at the University of New South Wales and Head of the Translational Cancer Nanomedicine Theme at the Children's Cancer Institute.

This discussion focused on the overarching opportunities and challenges for our RNA sector from a clinical and translational perspective. We examined Australia's capability and capacity for RNA research translation and application, exploring how a clinical perspective might inform Australia's ability to ensure its RNA sector can have maximum impact. We also looked at the international landscape and Australia's comparative advantage. More about the roundtable aims and questions can be found in Appendix A.

This submission has been informed by input from the roundtable and we thank the Department consultation team for the opportunity to provide continued feedback throughout the consultation process.

2. Key focus areas for maximum impact in human health

The potential applications for RNA technologies to improve human health are significant – both in terms of the potential scale of impact and breadth of application. However, given our size, it is not feasible to expect that Australia’s RNA sector can specialise in everything. Australia must be strategic in how it invests in, conducts research into, and develops and translates RNA technologies. A key factor to inform this strategic approach will be to consider local, regional and global population health needs and to examine where Australia’s RNA sector could have the greatest impact.

The following areas were identified at our roundtable as holding promising opportunities to improve human health. We suggest these could be used as a starting point to inform further analyses of the gaps and opportunities to develop Australia’s RNA capability and capacity, and to assist the Department with prioritisation in the short, medium and long term.

Short to medium term

The examples below are those that have the potential to make an impact in the short to medium term (over approximately the next six years) because the research is more advanced and/or the mechanisms for translation of research into practice are better established.

Vaccines for infectious diseases

Research and innovation on how RNA could be delivered into cells has been ongoing for decades. The COVID-19 mRNA vaccines are an excellent example of what long-term, sustainable investment in research and innovation across the full pipeline can achieve. Although much of this research happened internationally, we have seen a rapid and successful increase in research and development of RNA vaccines worldwide. Australia is one country that has strong and relevant expertise in this area making it ripe for strategic growth that can lead to meaningful impact.

Researchers and industry are developing RNA vaccines to protect against many diseases and Australia is at the forefront of much of this progress. Examples of specific areas that could be advanced in the short to medium term include:

- Severe acute respiratory syndrome
- Middle East respiratory syndrome
- Future coronavirus-induced diseases
- Epstein Barr virus
- Human T Cell Leukaemia.

Diseases affecting the liver

RNA technologies for diseases affecting the liver hold great promise for improving human health. There are already RNA therapeutics on the market that are successful and accessible, and new RNA therapies are being approved for clinical practice.

There is significant potential in this area as research is advancing to develop therapeutics for increasingly complex conditions. The mechanisms by which these RNA therapies work mean they can be used to control a range of liver activities. Consequently, they can be targeted to treat many different diseases related to the liver – accelerating our ability to improve health outcomes for some diseases causing the greatest burden in Australia. Additionally, the nation

has a strong skills base for this type of research which can underpin our capacity to become global leaders.

Examples of conditions which are seeing positive advances from RNA therapies targeting the liver include:

- Hypertension
- Hyperlipidaemia
- Rare liver diseases
- Liver cancer
- Chronic liver disease

Rare diseases

Around 8% of Australians (2 million people) live with a rare disease and around 80% of rare diseases are genetic.¹ Rare diseases affect millions of people worldwide. Such conditions can impair quality of life and can lead to premature death. RNA therapies currently provide some of the best opportunities to treat rare diseases and improve health outcomes.

Australian research in this area is advancing and is globally competitive. This is partly because of our capacity to do phase to clinical trials, which can help to shorten the timeline for evaluation and approval. Australian researchers also work well together across, and within, many rare disease areas and this contributes to greater collective benefits.

Examples of rare diseases that are seeing positive advances from RNA therapies include:

- Paediatric epilepsies
- Childhood dementia
- Neuromuscular diseases such as Duchenne muscular dystrophy and familial amyloid polyneuropathy.

Cancers

The global prevalence rate of cancer is increasing, and the number of people dying from cancer is also rising each year.² There are decades of science behind the development of personalised cancer vaccines with the most recent successes occurring in phase 2 trials. These vaccines provide a potent approach to trigger a broad-based antitumour response that is both beneficial and relevant to individual cancer patients. Australian research is already contributing to the knowledge base here, and developments in RNA therapies for cancer will continue. There is important research ongoing, including in children's cancer, melanoma, and head and neck, prostate, pancreatic cancers.

But there is room for growth. Business, particularly those in the pharmaceutical industry, are investing heavily in RNA science for cancer, expanding potential avenues for sustained investment. There may be value in Australia taking advantage of this opportunity given the significant impact it could have on health outcomes locally and globally.

¹ Australian Government Department of Health and Aged Care. What we're doing about rare diseases. Published 2022. Accessed October 7, 2023. <https://www.health.gov.au/topics/chronic-conditions/what-were-doing-about-chronic-conditions/what-were-doing-about-rare-diseases>

² World Cancer Research Fund International. Worldwide cancer data. Accessed October 7, 2023. <https://www.wcrf.org/cancer-trends/worldwide-cancer-data/>

Long term

Investment in research which has the potential to deliver benefits in the longer term (beyond 6 years) will also be critical to Australia taking a truly strategic approach to developing our RNA sector. There are many promising areas the Department should consider for this future focused investment including RNA vaccines and therapeutics for:

- Tuberculosis
- Malaria
- Autoimmune diseases
- Haemophilia
- Atherosclerosis.

Another key consideration will be to advance research and innovation that combines different RNA technologies. These emerging combined technologies are starting to show great potential, but further investment and research is needed to fully understand where Australia might see impact. While this is less well known, Australia must be at the forefront if we want sustainable progress over the long term.

3. Opportunities and challenges for advancing RNA research and technologies to benefit human health

Australian research has been an important contributor to RNA science that has impacted human health. However, our RNA ecosystem is not set up as well as it could be to enable these breakthroughs to be efficiently and effectively translated into clinical care. Australia's RNA ecosystem must evolve quickly to make the most of the excellent research and innovation that is taking place in this country.

There are fundamental barriers and challenges that cut across the full RNA pipeline, independent of discipline or disease area. Here, we focus on some key examples of issues that we heard at our roundtable are preventing Australia from maximising the value and outcomes of the RNA research in which it invests, and those that are affecting our ability to get RNA technologies to patients and the community. If we can overcome these barriers, we will be in a stronger position to harness the opportunities for Australia's RNA sector to play a leading role in the global ecosystem of RNA science – bringing substantial health, societal and economic benefits.

Up until now, Australia's national RNA strategy has been limited and our system has not kept up with the rapid growth of RNA science. We welcome the Department's efforts to address this gap. To stimulate and nurture a successful and accessible RNA system, we need future-focused strategic investments and policies that play to our strengths and comparative advantages. We suggest that the Department undertake a thorough gap and expertise analysis – the following areas could provide a starting point to guide this strategic development.

Making research and innovation more efficient and affordable

Access to, and affordability of materials

RNA science is expensive – for governments, researchers, industry and others involved in the development and translation of RNA technologies. While there have been advances in certain areas, if Australia is to grow our system successfully, we must find ways to improve the overall cost and efficiency of undertaking RNA science and translation on our shores.

At present, there are limited and inadequate funding sources and policies to stimulate cost effective and efficient research activities throughout the full pipeline. This has created a high level of competition in the field, which can disincentivise collaboration and stifle progress.

For instance, researchers face challenges obtaining materials for lab testing and human trials. Lipid nanoparticle formulations and RNA capping materials remain some of the most costly but critical parts of the RNA research and production process. They are not only expensive to procure, but Australian researchers face challenges around obtaining and retaining patents, competing with international counterparts and working within our limited sovereign manufacturing capability and commercial landscape.

The Government could see broad impact if it can help make fundamental components for research cheaper, more accessible, and available in the quantities needed to scale up research and development. One option to help achieve this would be to improve Australia's sovereign capability to produce and patent some of these materials. The Government could explore setting up a platform where Australian researchers have shared access to relevant research

information and materials at a better cost, and where researchers can get government support to patent and develop their ideas. This could then be used across the sector to advance Australia's overarching RNA goals. A platform like this would make the Australian RNA system more efficient and could also help researchers take on more risk and test more ideas. Additionally, IP Australia are investigating ways to create co-design opportunities that produce high quality and timely patents and leverage new technologies – making the process easier and cheaper for their customers.³ The Department could look at opportunities to feed into that process to ensure any outcomes can benefit the country's RNA sector.

Governance

Efficiency could also be enhanced by improving governance and regulation processes, which at present, can be slow and costly. One example of this is the ethics approvals process. Ethics committees are an essential step as part of any human research and an important mechanism for ensuring patient safety, but assessment of these applications often moves slowly when compared internationally – impacting our ability to be globally competitive and to conduct cutting-edge research.

With the rate and scale of new emerging technologies and advancing RNA research, ethics committees cannot be expected to keep up in a timely manner. Consequently, Australia could benefit from improving mechanisms for expert input. For instance, finding ways for specialised and independent RNA expertise to be fed directly into existing ethics committees to assist with, and speed up, approvals processes. One option might be to set up RNA advisory groups that connect directly with ethics committees and can help review incoming research and protocols. It will also be important to continue educating existing ethics committees to remain competent to assess these types of applications efficiently.

From our roundtable, we heard that there is also some confusion in the sector around how the Office of the Gene Technology Regulator interprets RNA technologies and what we consider to be a genetically modified organism in Australia. This can impact the efficiency of approvals processes. The Department could explore whether the current legislation is promoting a safe, quality and efficient research environment for the development and translation of RNA technology.

Clinical trials

Australia has a highly active and proficient clinical trials community and as a nation, we have the components in place to be a go-to destination for clinical trials. In developing our RNA sector, it will be important to build on these strengths to facilitate an efficient research pipeline. However, we must improve certain aspects of our clinical trial landscape to be globally competitive, including in the RNA sector.

When it comes to translation and the clinical setting, one of the most challenging bottlenecks occurs at the stage between pre-clinical and clinical trials. From our roundtable, we heard a perception that Australia can have limited appetite for risk when it comes to moving RNA technology into a phase 1 trial – although these trials are at the tipping point to determine if RNA technologies could be successful, and therefore potentially beneficial in humans. Governance processes, costs and workforce could be adjusted so that they better incentivise a system that enables phase 1 trials, managing the potential risks.

³ IP Australia. Patents initiatives. <https://www.ipaustralia.gov.au/about-us/our-agency/our-research/patents-initiatives>

Phase 4 trials are also crucial to understanding whether treatments are working out in the community and for identifying any potential issues. This is a critical component of research and development and should be incentivised and enabled in all areas including RNA.

To see success, Australia must have the underpinning infrastructure and resourcing to grow the clinical trials phase of the research pipeline. One opportunity is in patient recruitment, for instance, recruiting patients with rare diseases for studies and trials associated with RNA technologies. There are many challenges associated with this type of recruitment that could be addressed to ensure everyone can participate in and benefit from research.

Access for certain groups to become part of research is also a big challenge, particularly for rural and remote communities who face many barriers preventing them from participating in trials. Culturally and linguistically diverse groups are also underrepresented in clinical trials, creating a lack of equity and diversity.

Skills and workforce development

Australia has highly skilled researchers within our RNA sector. However, we need sustained investment and policies to attract and retain talent. Any barrier to optimising this sector also acts as a disincentive to growing and nurturing our RNA workforce. Additionally, Australian research, industry and healthcare are not sufficiently connected, limiting our ability to deliver and develop quality RNA science throughout the entire pipeline – and ultimately improve human health.

The Department should conduct a thorough expertise analysis to ensure it has a thorough understanding of current and future skills gaps in the Australian RNA workforce. Some gaps to consider are in the preclinical development phase. Australia should grow expertise in the proof of principle and drug development areas.

We should also develop stronger pathways and programs that incentivise and support clinicians to become involved in RNA research. Clinician researchers (who combine clinical and academic roles) are central to a workforce that can embed research and innovation in the health system. This will be a key mechanism through which Australia can apply RNA technologies in practice. At present, clinician researchers have no clear training pathway and face many barriers in pursuing this career path. The Academy published a report in 2022 highlighting these issues and we called on the Australian Government to develop a strategy and implementation plan for how Australia can build a world-class clinician researcher workforce.⁴ The Department should collaborate with other Government departments to ensure this can happen. International evidence shows that research-rich health systems are better at taking up new innovations and cutting-edge treatments. A health system in which research and innovation are embedded will therefore be better placed to embrace RNA technologies and ensure these reach patients and the community.

Public awareness and education

Global awareness of RNA technologies has grown substantially, primarily because of the mRNA vaccines that were developed to tackle the COVID-19 pandemic. But alongside this public awareness, we have seen the spread of mis- and dis-information, and challenges to

⁴ The Australian Academy of Health and Medical Sciences. *Research and Innovation as Core Functions in Transforming the Health System: A Vision for the Future of Health in Australia*. 2022. <https://aahms.org/wp-content/uploads/2022/10/AAHMS-Vision-Report.pdf>

public trust in science. Public buy-in will be critical to ensuring that RNA technologies can be applied and deployed for community benefit.

A national strategic approach to grow public awareness around RNA science is needed. The Government should lead this endeavour but will need to work in partnership and collaborate with trusted scientific and health institutions, as well as local groups and trusted community leaders. An important part of this strategy will be an assessment of the risks around mis- and dis-information in this space, which can be used to inform work to share facts and accurate information with the community. A public that is engaged in, confident about and excited by RNA science will contribute substantially to an optimised RNA sector.

It will also be essential to support the healthcare workforce – to ensure it is equipped with the knowledge and skills to underpin a system in which RNA technologies can be used. This is a long-term endeavour that should be approached strategically to ensure healthcare professionals can be educated and become champions for RNA technologies and their applications in practice. This can start in medical schools and the Department should collaborate with other government departments to ensure consistent messaging to build trust within and across these groups.

Collaboration

A thriving RNA sector will depend heavily on strong links within the RNA community, across disciplines and between sectors. RNA research is competitive, but the Government could promote a 'Team Australia' approach to advance our overarching goals for national RNA capability and capacity – and to ensure RNA developments can be translated equitably to the whole community. Information sharing, collaborations and partnerships will be critical to achieve this.

Collaborations should be incentivised and as part of this, the Government could use its platform to make a strong case for Australia's RNA system that can attract international partners to our shores and retain local collaborators. A health economics perspective could be useful here to demonstrate the value of our opportunities.

RNA science and application crosses many sectors; therefore, the Department should also work closely with other government departments and state and territory governments to ensure all areas of the RNA pipeline are supported. From a health translation and clinical perspective, the Department could foster strong links with the Department of Health and Aged Care to enable coordinated policy development and funding practices that can influence healthcare through RNA research.

Funding for research

For Australia to become a world leader in RNA science, we must deliver sustained funding in research and innovation across the full pipeline. Short term or ad hoc funding will not be sufficient if these are our ambitions, and we must be strategic with our investment to meet our national goals for RNA science.

Funding for RNA research at the translational and clinical end of the pipeline remains limited. The Medical Research Future Fund does not include the full scope of RNA translational research and there is no specific funding to enrich this end of the pipeline for new RNA projects. This does not mean we should shift funding from basic science to translation, but we could be more strategic in how we coordinate and fund research to improve translation, commercialisation and application of RNA technologies.

The Department of Health and Aged Care (DoHAC) is currently reviewing Australia's health and medical research landscape, including its funding through the MRFF and the National Health and Medical Research Council. As part of this, DoHAC are developing a national health and medical research strategy. We would urge the Department to engage with this process to ensure funding throughout the health and medical research and innovation pipeline is coordinated and delivered strategically for maximum impact.

4. Australia's comparative advantage and international opportunities

Australia has the potential to be a regional and global leader in RNA science. We are already in a strong position to advance certain opportunities that will grow our international contributions and improve health, particularly in the Asia-Pacific region, and we should approach these opportunities strategically. We can no longer rely on countries like the US, UK and other European nations to fund and deliver research and innovation for the rest of the world. Australia is already a regional leader, and we have a comparative advantage that should be built upon to grow our success.

Australia has numerous characteristics that make it an attractive place to conduct and invest in research and innovation for regional and global health impacts including that:

- We are aligned linguistically with many countries that have the most money to invest.
- We have a multicultural community, which strengthens our ability to conduct research with people from diverse backgrounds. This could increase the applicability of our research in the region.
- We have a strong regulatory environment when compared to other countries in the region.
- We are a trusted scientific nation.
- We have established relationships with many other countries in the region.

These and other factors make us uniquely qualified to work closely with industry counterparts who are keen to invest and regional countries who could benefit from Australian RNA research and technologies.

It will be important for the Government to develop a strong case to promote Australian RNA science and develop partnerships with countries in the Asia Pacific to ensure we can identify areas to be advanced collaboratively. Successful collaborations and partnerships take time, and we must build and sustain critical relationships over the long term to see true societal, health and economic benefits. Opportunities could be leveraged in areas such as infectious diseases, cardiovascular diseases, respiratory diseases, cancer and diabetes. Australia is also a trusted source for advanced technologies in medical sciences and this is an area in which there is less regional competition.

To be competitive on the world stage we should also assess the opportunities to attract new investors to our shores. Part of this will be considering how to increase venture capital funding and optimise R&D tax incentives. We acknowledge the Government is working to improve Australia's capacity in this space. The Department could consider ways to shift our research and innovation culture to ensure investors and researchers are encouraged to take more risks.

Appendix A: About the roundtable

The aims of the roundtable were to:

- Explore the potential applications and population health needs for RNA that would have the greatest impact in practice.
- Consider pathways for RNA research to be translated into practice and scaled up, including infrastructure for clinical trials, workforce and collaborations.
- Identify key opportunities and priority actions for better application and uptake of RNA research in the short, medium and long term.

Roundtable participants were asked to consider seven key questions, which were used to guide the discussion:

1. In the short (under 2 years), medium (2-6 years), or long term (7 years or more), which two disease states or disease areas are most likely to be advanced with RNA technologies and why?
2. What are the key opportunities for advancing the RNA technologies identified in the last question and when might Australia see the benefits of advancing these technologies?
3. What are the current barriers and challenges for translation of RNA research into practice?
4. What should the Australian Government do to ensure RNA technologies can reach patients and the community?
5. Is Australia attractive to international counterparts for collaboration? If so, in what areas should we focus our attention? If not, how can we resolve this?
6. Do we have a unique value proposition in the Asia-Pacific region and if so, what is it?
7. Where are the bottlenecks that could prevent optimal uptake of future RNA technologies?

We are grateful to the Fellows and other experts who contributed to this response. For questions about this submission, or to arrange a consultation with Fellows and Associate Members of the Academy, please contact Lanika Mylvaganam, Head of Policy (lanik.mylvaganam@aahms.org) at the Australian Academy of Health and Medical Sciences.

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