



RNA Canada ARN

WHITE PAPER FOR

RNA CANADA ARN

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SUMMARY

As recently demonstrated by mRNA vaccines for SARS-CoV-2, RNA technologies are transforming many aspects of Canadian life. RNA-driven applications in agriculture and medicine are poised to bring innovative solutions to emerging infectious diseases, non-communicable diseases, antibiotic resistance, climate change and environmental hazards. This progress is rooted in the knowledge and technologies developed in part by Canadian scientists (a). Given the potential of RNA research, it is imperative for Canada to build on its RNA expertise to produce a coherent strategy that will harness the strength and diversity of Canadian RNA-based research and discoveries for the well-being of Canadians. To meet this challenge, more than 300 leading Canadian RNA scientists in academia and industry have come together to create **RNA CANADA ARN**. The objective of **RNA CANADA ARN** is to provide a framework that will accelerate RNA-based discoveries and stimulate their development into applications. The goal of making RNA research and innovation a national priority will be tightly integrated with multidisciplinary training programs that will produce and sustain the next generation of RNA scientists. Informing the Canadian public on the importance of RNA in life processes as well as in its potential in the future economy will also be prioritized. With the cooperation of academic institutions, governments and the private sector, **RNA CANADA ARN** will coordinate, stimulate and transform RNA research to ensure that Canada remains a world leader in RNA-based discoveries.

The fundamental importance of RNA research

Recent progress has shown that RNA is an exquisitely versatile and powerful tool to develop a drug or a vaccine. Most impressive was the rapidity with which mRNA vaccines were developed in response to the COVID-19 crisis. This exceptional breakthrough was made possible by decades of fundamental research in various disciplines, including RNA sequencing to reveal targets, RNA chemistry to improve the stability of RNA, and an advanced understanding of the biochemistry needed to manufacture and deliver RNA. Because RNA is remarkably versatile and performs a variety of functions, from encoding every protein in the cell to regulating nearly every cellular process, RNA-based technologies are also being applied against a variety of diseases and emerging threats. For example, RNA is used both as a drug (antisense) and as a target to correct human hereditary diseases such as spinal muscular atrophy (ref. 1). Similar strategies have been approved to treat Familial Amyloid Polyneuropathy and Duchenne Muscular Dystrophy. Other RNA molecules such as small interfering RNAs (siRNAs) and aptamers are currently used against other diseases such as macular degeneration. The mRNA delivery approach that has led to vaccines against COVID-19 is now being applied to other viruses (e.g., HIV, CMV, Influenza, Zika) as well as a whole series of human diseases that include cancer and microbial infections. In addition, RNA-based biosensors are being used to detect harmful

bacteria in the water supply (2). RNA can also be used to provide crop tolerance to natural stresses such as climate change (3). RNA-based drugs and drugs that target RNAs are perceived as our next chance to fight antibiotic resistance (4). Technological breakthroughs, such as RNA-guided CRISPR/Cas genome editing, RNA interference, antisense-based technology and small molecules targeting RNA are demonstrating the awesome power of RNA-based approaches (5a,b). Moreover, hundreds of proteins that specialize in recognizing, modifying or degrading RNA to modulate biological processes represent a large untapped reservoir of targets and tools for biomedical and agricultural applications (6).

The emerging RNA revolution is promoting the rapid development of a new class of versatile and relatively inexpensive new drugs against diseases that were previously considered difficult to treat pharmacologically. A concerted strategy to discover, exploit, leverage and apply RNA-based discoveries will therefore be highly impactful and of tremendous benefit to Canadians.

Globally, RNA science is expected to have a significant economic impact. It is estimated that the global market for RNA vaccines will double to reach 100 billion US dollars by 2026 (7). In the next 10 years, the RNA biosensors, RNA therapeutics and RNA diagnostics sectors are expected to contribute another \$65 billion US dollars (8). It is crucial for Canada to play a leadership role in this global endeavor. While the opening of a *Moderna* branch in Quebec is a step in this direction (9), emerging opportunities are not restricted to biomedical applications. Indeed, the leadership of Canada in agriculture is associated with new challenges in food security and crop resilience to pests and climate change (10). RNA-based discoveries by Canadian scientists in this sector are already being implemented to rise to agricultural challenges.

Why is RNA science important for Canada?

- **RNA science is relevant to multiple areas critical to the Canadian economy (health, agriculture, forestry)**
- **The current successes of RNA-based technologies warrant their use against future threats to global health: pandemics and infectious diseases, antimicrobial resistance, non-communicable diseases, impact of climate change on health and agriculture**
- **RNA research is bursting with innovative translational applications whose economic impact is expected to grow exponentially**

A vibrant community of Canadian RNA scientists

The Canadian RNA community consists of more than 300 self-identified RNA research laboratories spread across Canada. The fraction of RNA researchers amongst all researchers is lower in Canada than in other G7 countries, hence there is room for expansion and growth. Several countries have already prioritized RNA science and have created their own RNA organizations (e.g., Switzerland and Japan) (11,12). Moreover, other countries are prioritizing investments in RNA research (e.g., Australia, UK and the European Union, refs. 13,14,15).

Canada is recognized internationally for the quality and innovation of its RNA research community. Key findings and accomplishments of the Canadian RNA community include the discovery of important regulatory features of mRNA splicing and translation; artificial intelligence tools to predict RNA structure and function; the role of defective translation and splicing in cancer and autism; as well as the crucial function and medical relevance of a multitude of RNA binding proteins. Innovative RNA-based technologies have also been developed, such as RNA biosensors, antisense-based approaches, RNA emulsification technologies that led to mRNA vaccines, new rapid detection methods for SARS-CoV-2, as well as novel ways to target this and other RNA viruses. A broad collection of national, provincial and institutional platforms is providing RNA-tailored services to the scientific community including next-generation sequencing of transcriptomes, ribosome profiling, single RNA molecule sequencing, and spatial RNA localization and sequencing.

Canadian RNA laboratories are grouped together in multiple forums, several of which have established partnerships. For example, the RiboClub Sherbrooke (founded in 1998, ref 16) and RiboWest Lethbridge (founded in 2005, ref 17) have affiliated in order to facilitate exchanges of knowledge and ideas. More recently established groupings include the Toronto RNA Club (18), which is comprised of academic institutions in the Greater Toronto Area, and the Montreal RNA Salon (19), with 11 affiliated institutions in Montreal. These organizations hold annual meetings that bring together RNA researchers from across Canada and internationally. The Toronto RNA Club hosts the annual Toronto RNA Enthusiasts Day (TRENd) and RiboWest and RiboClub hold annual meetings. The latter celebrated its 20th anniversary in 2019 with presentations by four Nobel laureates. Of note, 33 Nobel prizes have been awarded for pioneering discoveries in RNA biology (20). These meetings, and a variety of local RNA salons, are supported by the international RNA Society, the Genetics Society of America, and multiple biotech companies, and testify to the vigor of the Canadian RNA community. In addition, the RiboClub hosts a pan-Canadian monthly seminar video session of scientific presentations on RNA by students and trainees. Collaborative efforts between the University of Lethbridge and the Université de Sherbrooke led to the first specialized RNA training curriculum, supported by a NSERC-CREATE program.

These established collaborative endeavors form the springboard from which launched RNA CANADA ARN. While these initiatives do not currently possess the financial resources to generate a national research and training program, they are key foundational investments that can be leveraged to achieve long-term goals.

In 2018, the Canadian life sciences and biotechnology sector generated \$54 billion in annual revenues, across nearly 8,000 companies with more than 190,000 employees and 52,300 students (21). In 2020, biotech and life-sciences companies raised more than \$1 billion in venture capital. RNA technologies are intrinsically associated with the science of a significant fraction of these companies. Other companies are recognizing the power of RNA science and are planning its integration in their R&D portfolios.

Overall, the Canadian RNA ecosystem is ideally suited to embark on a concerted effort to maximize the outcome of RNA science. In comparison to the USA for example, the large but manageable number of RNA groups in Canada offers a wide diversity of approaches and expertise that is compatible with greater accountability, autonomy, and flexibility, both in terms of scheduling- and idea-based changes. Our interactive RNA community is ideally sized to foster trust among members, improving communication and stimulating innovation.

The strength of RNA science in Canada

- **Strong community of interactive RNA scientists**
- **High-quality science, important discoveries and innovative programs**
- **Dynamic biotechnology environment**

Gaps, Challenges and Opportunities facing RNA Science in Canada

1. Basic and translational RNA research

The RNA field is still expanding and is generating fundamental discoveries that improve our understanding of biological processes and offer innovative avenues that feed the pipeline of potential applications. Basic RNA research in Canada is dispersed across many disciplines and is supported by a variety of funding agencies. Since there is no specific program in Canada that directly funds RNA research, RNA researchers must identify programs that are most likely to acknowledge fit, with the caveat that RNA expertise may often be lacking in review panels. It is essential that funding for basic RNA research grows and remains a national priority to ensure that the pipeline of discoveries that has led to current advances in RNA science does not run dry.

It is crucially important that we now develop and expand tools that promote the translation of Canada's innovative knowledge and discoveries in RNA science, in part by bolstering institutional and government commitment and planning.

The recent surge in RNA discoveries and the speed with which the RNA discovery pipeline can lead to tangible translational and clinical advances is generating significant interest from the private sector. This refocusing on RNA in the biotechnology industry is exciting, but it is also prudent to examine whether there are gaps to fill in the efficiency with which these innovative findings are translated into real-world applications. Several on-going academia-industry funding opportunities dealing with RNA are expected to multiply in the very near future. Moreover, the current boom of interest in RNA technologies is now percolating into targeted initiatives to facilitate translation of RNA discoveries. As an example, the Canada Biomedical Research Fund (CBRF) and Biosciences Research Infrastructure Fund (BRIF) will be investing \$750M over the next 4 years to support the creation of hubs that will enhance Canada's foundational biomanufacturing excellence and pandemic readiness. RNA science should be a fundamental part of that effort across Canada. Additional funding opportunities at the federal (e.g., Genome Canada) or provincial (e.g., AQRIA in Quebec, ref 23) levels are expected.

Overall, there is a growing excitement that forthcoming programs will recognize and stimulate Canadian RNA research and that these activities will impact positively the economical and health sectors in the upcoming years.

2. People drive RNA science

Given the strength, excellence and collaborative nature of the Canadian RNA community, the foundation is already in place to build a framework at the national level that stimulates basic RNA research and optimizes its translation into applications. Indeed, such a strategy is essential to ensuring Canada's autonomy and its future leadership in RNA-based biotechnology. On the other hand, the upcoming burst in funding and new opportunities will require a corresponding increase in the workforce qualified to perform RNA science in various disciplines. Indeed, although financial resources in the biotech sector are available and growing, Canada lacks the infrastructure to develop, recruit and retain enough senior talent to leverage these new investments (21). It is estimated that Canada's bioeconomy will need an additional 65,000 workers by 2029 (22). Given the potential contributions of RNA technologies, in the biomanufacturing of mRNA drugs for example, Canada needs to identify, recruit and train a new generation of RNA scientists who can accelerate the growth of promising startups into global powerhouses.

Last but not least, there is a responsibility of the RNA community to educate non-experts in RNA-related biology and its opportunities. A better understanding by Canadians of the concepts and challenges of RNA science is expected to feedback positively on those in leadership and policymaking roles who can ensure that RNA research remains a priority for Canada.

GAPs in the Canadian RNA sector

- **Difficulty for basic RNA researchers to access funding and translational research initiatives, and to link with biotech companies**
- **Lack of training programs that prepare the next generation of RNA scientists for industrial needs**
- **Need to inform non-experts and political leaders on RNA technologies and its potential**
- **Lack of a national RNA innovation and application strategy**

CHALLENGES ahead

Develop a national RNA research strategy for Canada that will

- **ensure control over the development of future medicines and biotechnology products**
- **reduce Canada's dependency on foreign technologies to increase the biosecurity of Canadians**
- **facilitate the growth of Canada-based RNA research and technologies**
- **maintain Canadian expertise and stimulate job creation in the RNA sector**

The Promise: Coordinating, Stimulating and Transforming RNA science in Canada

To sustain world-class innovation in the RNA sector, **RNA CANADA ARN** plans to act as a conduit to **protect, stimulate** and **transform** RNA research in Canada. **RNA CANADA ARN** will become a repository of national expertise on RNA. This consortium of RNA experts will play a key role of coordination:

- to maximize concerted interactions and collaborations among groups implicated in various research programs,

- to facilitate the dissemination of results and the development of partnerships with the commercial sector,
- to encourage the recruitment and training of highly qualified personnel (HQP),
- to improve public awareness of RNA technologies,
- to articulate our goals to public office holders to influence policy.

The potential and need for coordination are likely to grow at a rapid pace in the following months/years based on the current evolution of new national and provincial initiatives that will integrate RNA science (e.g., CBRF/BRIF funding for pandemic readiness). The expertise of RNA CANADA ARN will play a decisive role in fostering interactions among groups associated with these initiatives. Likewise, RNA CANADA ARN will help trigger and coordinate international collaborations to benefit our national goals or fill identified gaps in specific technologies or expertise in the commercialization pipeline.

Basic Research • RNA CANADA ARN wishes to unite the strong Canadian fundamental research expertise on RNA and proposes to work towards this goal by:

- improving communication between RNA labs,
- providing a platform to help coordinate research groups that require RNA expertise to increase cross-disciplinary collaborations

Several strategies will be implemented to stimulate RNA research and strengthen communications between members such as to:

- advocate for the establishment of new dedicated funding programs to support multidisciplinary, innovative and collaborative approaches (21),
- advocate for an increase in funding for scientific research grants so that researchers at the graduate, post-graduate and professional levels are paid a competitive living wage,
- facilitate access to technology platforms and support updates of infrastructure that ensure competitiveness and drive innovation,
- maintain and expand national RNA meetings and opportunities for presentations by members,
- encourage meeting events with multidisciplinary themes,
- organize meetings designed to attract media coverage and engage the public,
- inform members about RNA CANADA ARN's accomplishments and survey members about ways to build content that members can utilize to support the development of RNA research in Canada,
- create a web site that describes the expertise and research interests of its members, and that includes a public outreach section,
- establish a social media presence to be used for timely announcements, quarterly newsletters, links to national and international RNA meetings, RNA Clubs and Salons; promote the science of members; and highlight RNA research, jobs, scholarships and funding opportunities,

Translational Research • RNA CANADA ARN's objective is to become a one-stop shop for RNA based solutions for future pandemics, human and animal diseases and other challenges such as crop resistance to cold or the protection of Canadian forests. To achieve this goal, **RNA CANADA ARN** plans to create a framework that will accelerate the development of candidate biologics from the academic sector and foster national partnerships between industry and academia. By establishing a network of private collaborators and institutional experts with an interest in RNA technologies, **RNA CANADA ARN** will endeavor to optimize existing Canadian academia-industry partnerships, catalyze new partnerships and address technological gaps in the innovation chain. To achieve these goals, **RNA CANADA ARN** will:

- identify contacts in Canadian companies with an interest in RNA research,
- identify the needs of the Canadian RNA biotechnology sector in terms of consulting expertise, specific technologies and highly qualified personnel (HQP),
- integrate Canadian RNA biotechs in setting up, promoting and supporting **RNA CANADA ARN** activities (e.g., meetings, training, funding),
- identify ways to facilitate collaborative research with the private sector,
- use the expertise of our consortium to support the creation of start-ups

Training • RNA CANADA ARN envisions the creation of programs that will attract the brightest students as trainees for the next generation of RNA scientists. The burgeoning interest in RNA science demonstrated by the private sector, as well as the anticipated growth of its partnership with academia will require an increase in the workforce including highly qualified personnel (HQP) at the postdoctoral, graduate and undergraduate levels, as well as skilled technicians. Graduate students have typically been forced to work at below minimum wage and live below the poverty line. To be attractive, such programs must offer competitive salaries and packages, and implement best practices in equity, diversity and inclusion (EDI). Several members of RNA CANADA ARN have already created a national specialized RNA training curriculum supported by NSERC-CREATE. RNA CANADA ARN will build on this success and will accelerate training for the next generation of Canadian RNA researchers in industry and academia by promoting programs that will:

- support and accelerate the development of strong and relevant expertise in various aspects of RNA biology, chemistry and manufacturing,
- facilitate trainee collaboration and transfer of technical skills among RNA CANADA ARN-affiliated labs and with the private sector,
- offer multidisciplinary training, for example through programs that integrate artificial intelligence and scientific communication,
- organize courses and workshops dedicated to career development and the networking of trainees,
- interact with colleges and universities to integrate RNA science in their training portfolios,

- establish links with philanthropic foundations with the goal to create Research Chairs in RNA Science.

Policymaking • RNA CANADA ARN will aim to establish a communication network with elected or appointed government officials and policymakers to develop programs that will support the growth of RNA science and technologies. RNA CANADA ARN will also mount a concerted effort to inform non-experts about the new discoveries, challenges and potential of RNA science. Public participation in consortium activities will be promoted as part of an open-science policy. As provincial efforts aimed at consolidating RNA science are also likely to emerge, RNA CANADA ARN will endeavor to establish productive interactions with these initiatives to prevent duplications and optimize efficiency.

To become a driving force in the growth of RNA science, **RNA CANADA ARN** must secure its own funding. The **first purpose** is administrative and deals with offering activities that will foster information transfer between members and their potential partners (e.g., national meetings, communications with the private sector and government officials, maintenance of web page, secretarial work), as well as building training programs. Currently, the nine RNA CANADA ARN subcommittees rely on the voluntary contributions of its members to develop the structure and goals of RNA CANADA ARN (Executive, Advocacy, Education, Administration, White Paper, Industry Liaison, EDI, Meeting and Outreach, Funding and Grants). We anticipate that salaries for a Scientific Director, a coordinator and an administrative assistant will be required for this portion of RNA CANADA ARN's activities. The **second purpose** for funding is to create research synergy and for RNA CANADA ARN's activities to become transformative. RNA CANADA ARN must be in a position to count on significant and reliable funding to permit a rapid investment when such a need is identified. Acceleration and innovation in a competitive environment require flexibility and adaptability. Having the capacity to provide rapid support to specific projects will allow RNA CANADA ARN to propel game changing technologies that require transient but immediate support. In addition, the leverage potential of funding will be demonstrated when research programs require partners or, for example, when a contribution is required to create a Research Chair.

The PROMISE

- RNA CANADA ARN will become a **consortium** of national **expertise** on RNA
- RNA CANADA ARN will improve the **coordination** of basic research, and facilitate the development of **partnerships** and links to companies to **synergize** translational opportunities
- RNA CANADA ARN will stimulate **innovation** and the **training** of HQP

- RNA CANADA ARN will **transform** RNA research into an **efficient** and **competitive** pipeline dedicated to **RNA discoveries** and their optimal use for the benefit of Canadians

The strategy expressed above leads us to anticipate that many objectives will have been accomplished by 2030. The leadership of RNA CANADA ARN will ensure increased funding for RNA science. The multiple new interactions created among groups will have triggered several new discoveries whose impact on Canadians will already be in the process of being implemented by the private sector for the benefit of Canadians. Furthermore, the potential for a continuum of discoveries will be secured by programs that recruited and trained the next generation of RNA scientists, with funding to match continuing growth. This transformation of the RNA sector in Canada will be noted worldwide. The success of our national efforts in RNA science will secure the leadership position of Canada and its capacity for innovation.

CONCLUSIONS

RNA science is driving new discoveries in the biomedical and biotechnological sectors. Given its potential for growth and the recognized expertise of Canadian RNA scientists, RNA research must become a sustained national priority. **RNA CANADA ARN** plans to coordinate the creation of an environment that will synergize RNA science locally and nationally by providing opportunities to meet, exchange and develop national networks with specific and multidisciplinary expertise. This academic ecosystem will be networked with government agencies and research foundations to foster discussions with decision makers, and with industry to promote competitive partnerships. In consultation with RNA scientists, this unique approach will maximize the motivation of the community and the return on government investments. **RNA CANADA ARN** will help create programs to train HQP at different levels (college, undergraduate, graduate and post-doctoral) to support growth and provide the next generation of RNA researchers that will continue to drive major advances in academia and industry. **RNA CANADA ARN** therefore plans to become a key player in developing the capacity for RNA research in Canada, and will actively work with research institutions, universities, government agencies, private foundations, and industrial partners to create a roadmap that will transform the RNA research ecosystem in Canada. Overall, this commitment by **RNA CANADA ARN** to administer, coordinate, stimulate and transform RNA research will provide health, social and economic benefits to all Canadians.

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écosystème favorable à l'innovation des technologies ARN et aux investissements du Québec pour une santé inclusive et durable.

Research Centers offering seminar series are listed here: [Alberta RNA Research and Training Institute \(ARRTI\)](#), [Cambridge RNA Club](#), [European Molecular Biology Laboratory \(EMBL\)](#), [Groupe de Recherche RNA](#), [Harvard Medical School Initiative for RNA Medicine](#), [Helmholtz Institute for RNA-based Infection Research](#), [Institute of Molecular Biology \(IMB\)](#), [Istituto Italiano di Tecnologia \(IIT\)](#), [MD Anderson Center for RNA Interference and Non-Coding RNAs](#), [NCI RNA Biology Initiative](#), [NUS-CSI Singapore RNA Biology Center](#), [Penn RNA Group - University of Pennsylvania](#), [RiboClub Sherbrooke](#), [RNA MaxiGroup](#), [University of Wisconsin-Madison](#), [RNA Research Centre in Poznan](#), [Shanghai RNA Club](#), [The Bay Area RNA Club \(BARC\)](#), [The RNA Institute](#), [University At Albany](#), [UCSC Center for Molecular Biology of RNA](#), [USTC RNA Institute](#), [UMass Medical School](#), [RNA Therapeutics Institute](#), [University of Michigan Center for RNA Biomedicine](#), [University of North Carolina RNA Research Group](#), [University of Rochester Center for RNA Biology](#), and [Yale Center for RNA Science and Medicine](#)