Charting a Future for Sequencing RNA and Its Modifications: *A New Era for Biology and Medicine*

Taekjip Ha and Brenda Bass, Study Co-chairs

Report Release Webinar | March 21, 2024

Our New Report

Toward Sequencing and Mapping of RNA Modifications Committee

Sponsors:

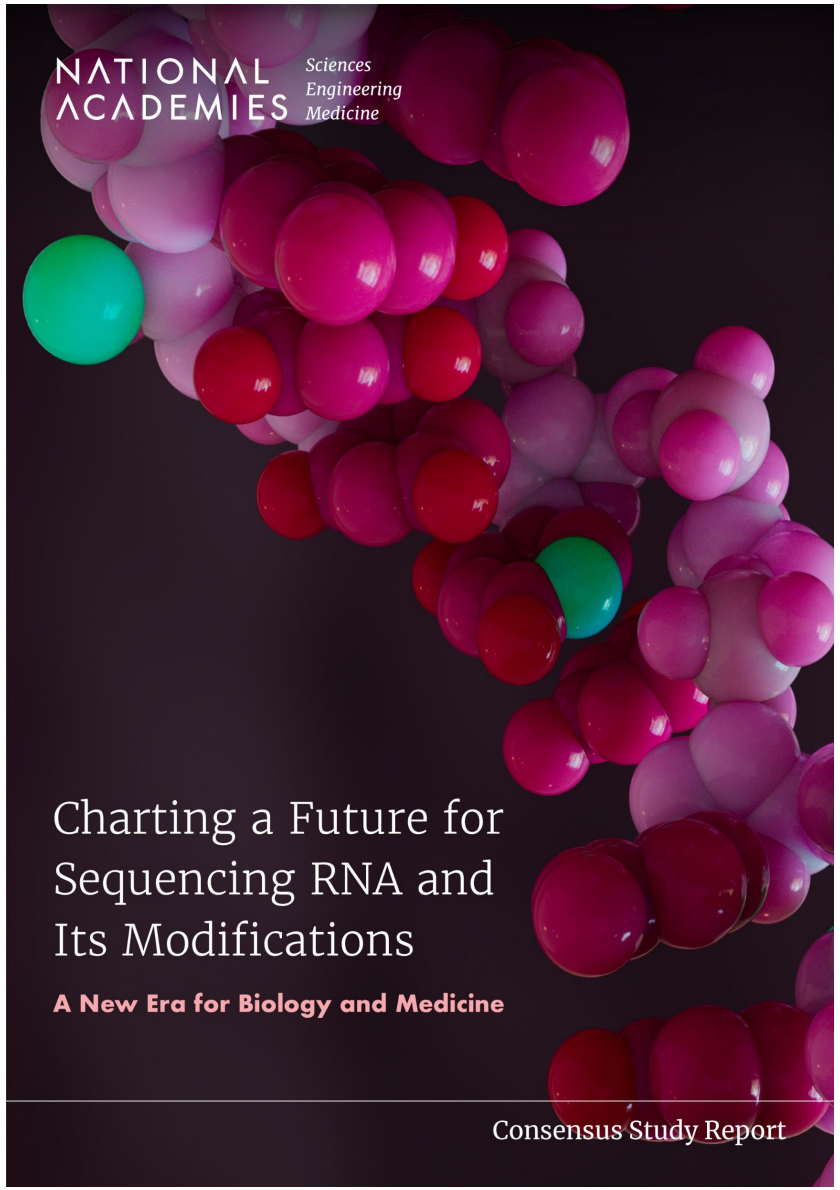
The Warren Alpert Foundation

National Human Genome Research Institute (NHGRI)

National Institute of Environmental Health Sciences (NIEHS)

Board on Life Sciences

Board on Health Sciences Policy



Report available at https://www.nap.edu/catalog/27165

Consensus Study Committee

Brenda L. Bass (Co-chair)
University of Utah School of Medicine

Taekjip Ha (Co-chair)
Harvard Medical School and Boston Children's Hospital

Nick M. Adams
Thermo Fisher Scientific

Juan D. Alfonzo
Brown University

Jeffrey Baker
National Institute for Innovation in Manufacturing and Biopharmaceuticals

Susan Baserga
Yale University and the Yale School of Medicine

Lydia M. Contreras
The University of Texas at Austin

Markus Hafner
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Sarath C. Janga
Indiana University Indianapolis

Patrick A. Limbach
University of Cincinnati

Julius B. Lucks
Northwestern University

Mary A. Majumder
Baylor College of Medicine

Nicole M. Martinez
Stanford University

Kate D. Meyer
Duke University School of Medicine

Keith R. Nykamp
Invitae Corporation

Tao Pan
The University of Chicago

National Academies Staff Team

Trisha Tucholski
Study Director

Steven Moss *(until August 2023)*
Former Study Director

Kathryn Asalone
Associate Program Officer

Kavita Berger
Board on Life Sciences Director

Jessica De Mouy
Research Associate

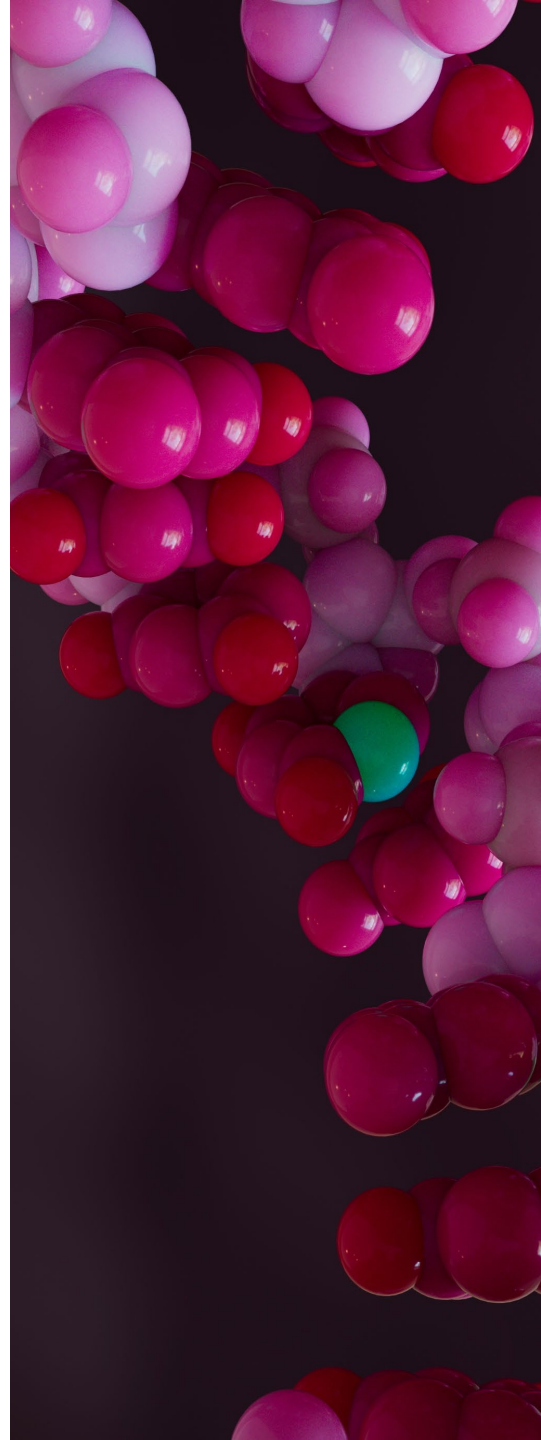
Victoria Hernandez
Mirzayan Fellow

Lyly Luhachack
Program Officer

Nam Vu
Senior Program Assistant

Consultants
Michael Zierler
RedOx Scientific Editing

Special Thanks
Janet Iwasa and Rachel Torrez
University of Utah
For Report figures and Cover image



NATIONAL ACADEMIES Sciences Engineering Medicine

Report Reviewers

William Bonvillian
Massachusetts Institute of Technology

Cynthia Burrows
University of Utah

Vivian Cheung
University of Michigan

Robert Cook-Deegan
Arizona State University

Chuan He
The University of Chicago

Mark Helm
Johannes Gutenberg University Mainz

Tracy Johnson
University of California, Los Angeles

Todd Lowe
University of California, Santa Cruz

Intawat Nookaew
University of Arkansas for Medical Sciences

Samuel Schaffter
National Institute of Standards and Technology

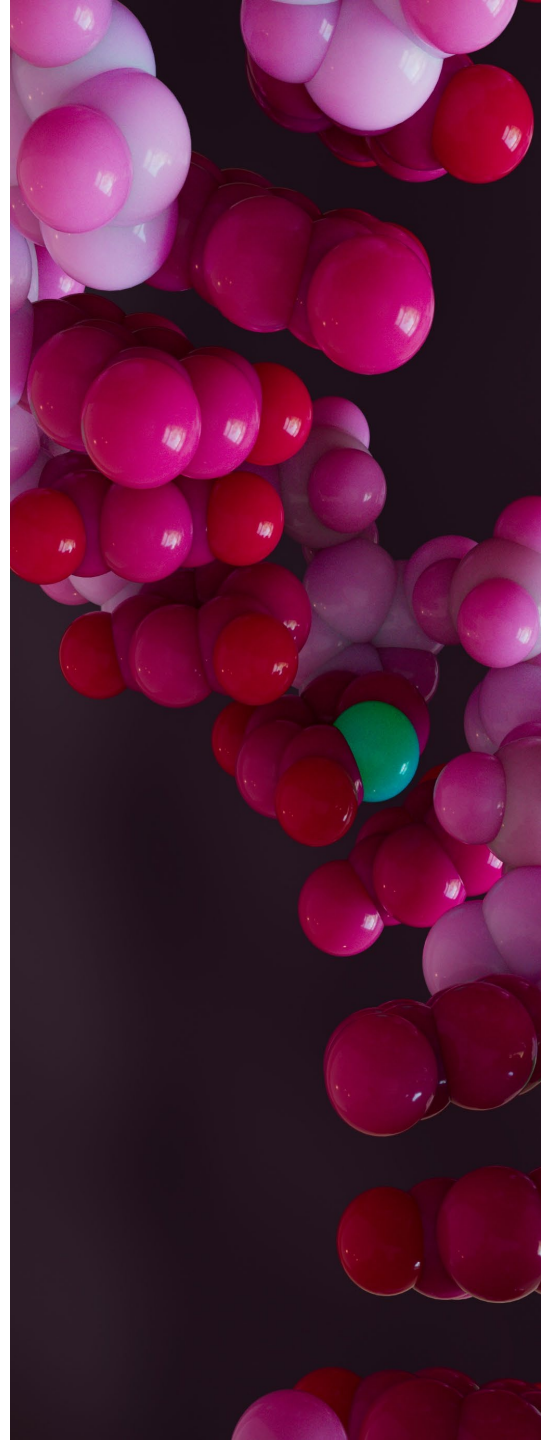
Elizabeth A. Snell
Oxford Nanopore Technologies

James Williamson
Scripps Research

NATIONAL ACADEMIES Sciences Engineering Medicine

Paul Ahlquist (Coordinator)
University of Wisconsin-Madison

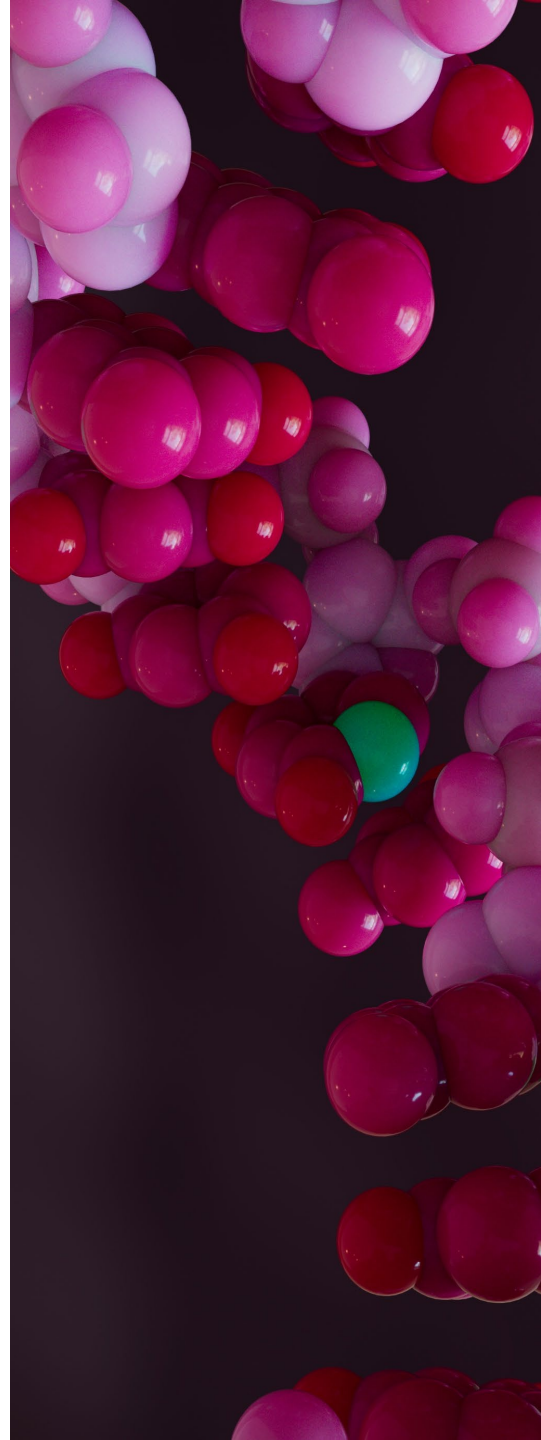
Dan Blazer (Monitor)
Duke University School of Medicine



Overview of Statement of Task

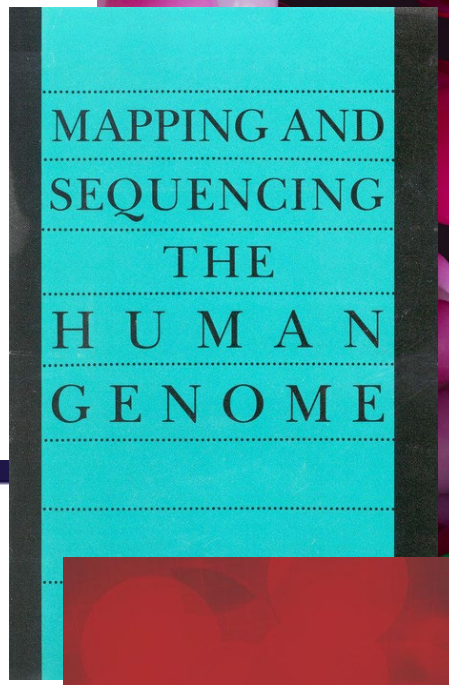
The committee will develop a roadmap for achieving sequencing of any RNA, including its modifications. The committee will examine:

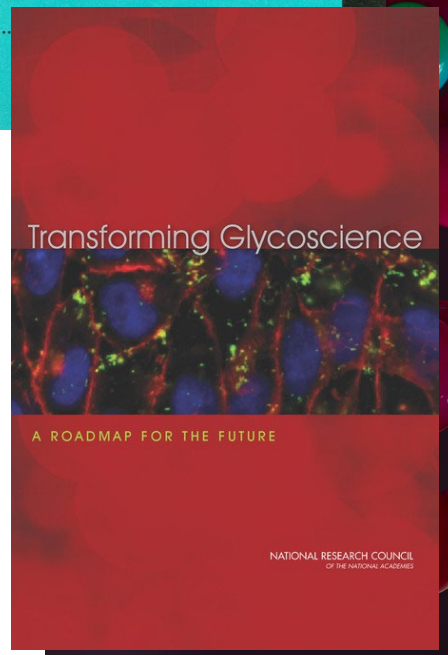
- Scientific needs
- Current methodologies and their limitations
- The state of current RNA databases
- Challenges related to using information for scientific, clinical, and public health analysis needs
- Computational and analytical needs
- Data ecosystems
- Policy, workforce, and infrastructure needs
- Potential new technologies



Committee's Approach

- NIEHS/NHGRI workshop – May 2022
- NASEM Workshop – March 2023
- Information gathering sessions
- Meetings of experts
- Ideation challenge – June 2023
- Commissioned papers

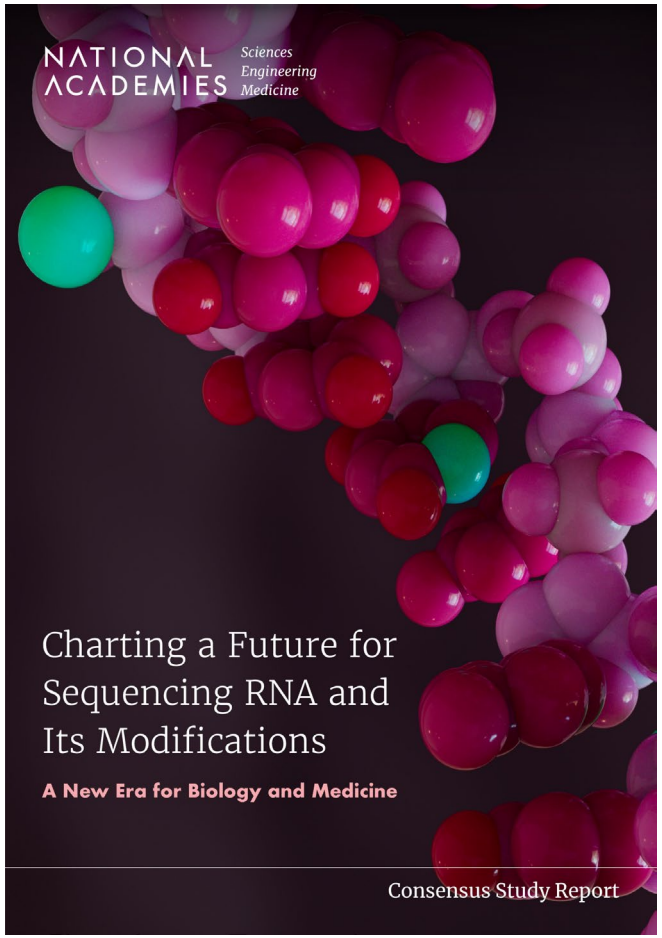




- Other National Academies reports:
  - Mapping and Sequencing the Human Genome (1988)
  - Transforming Glycoscience: A Roadmap for the Future (2012)

Reports freely available at nap.nationalacademies.org

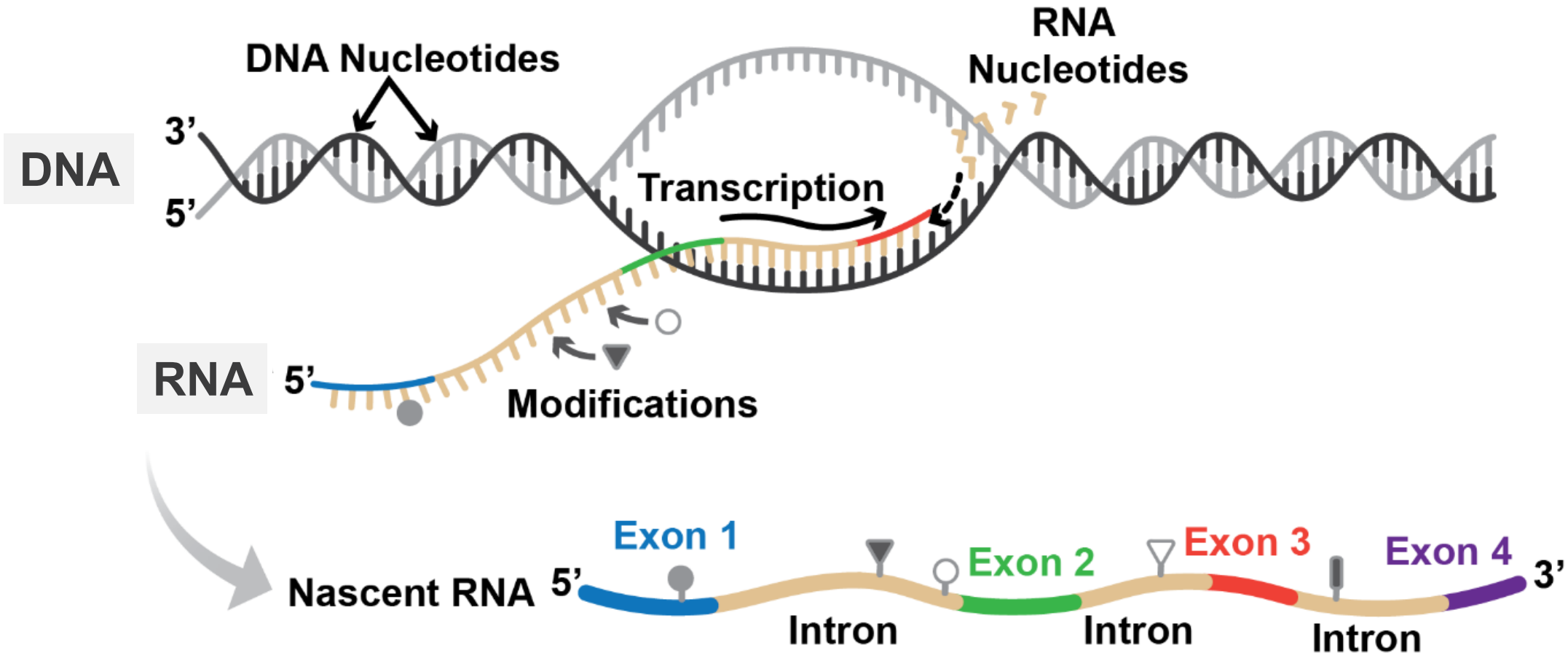
Organization of the Report



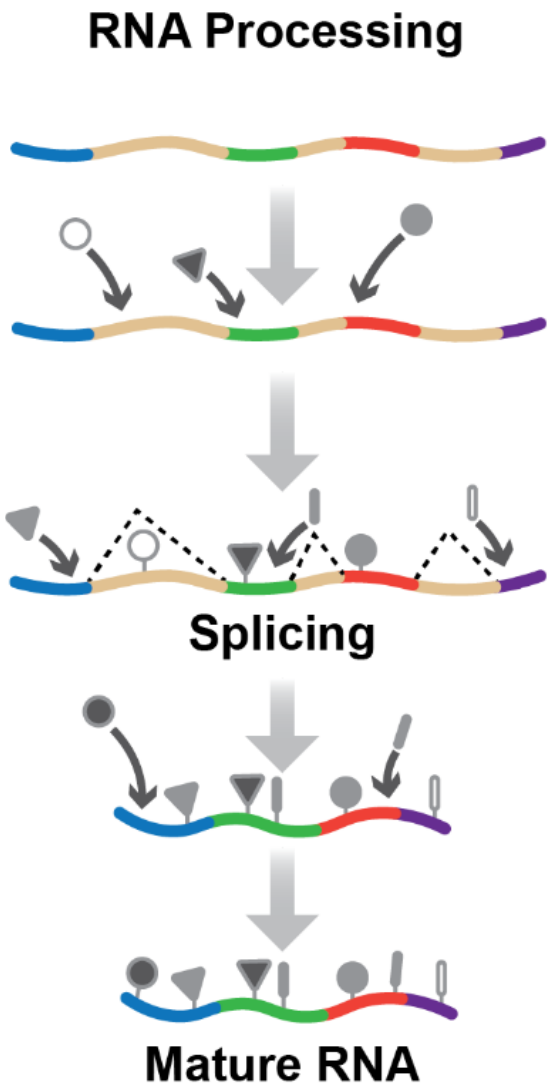
- **Summary**
- **Chapter 1:** Introduction and Committee's Approach
- **Chapter 2:** Importance and Impacts of RNA Modifications
- **Chapter 3:** Tools and Technology
- **Chapter 4:** Standards and Databases
- **Chapter 5:** Drivers of Innovation
- **Chapter 6:** Conclusions, Recommendations, and Roadmaps
- **Appendices**

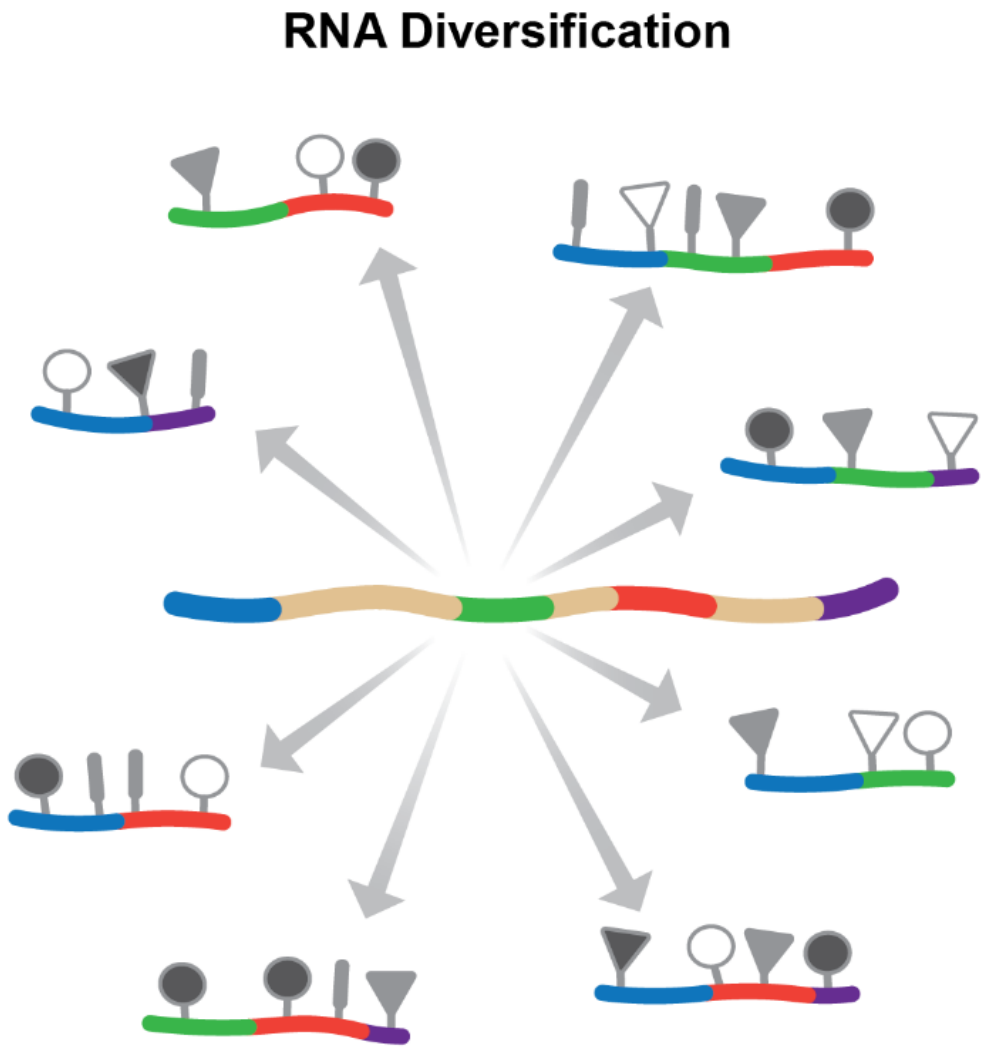
This presentation only includes *selected* highlights and recommendations from the full report.

From DNA “blueprint” to RNA



RNA and the complexity of life

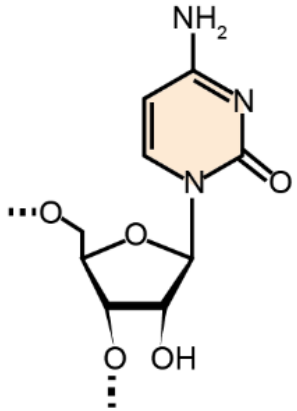




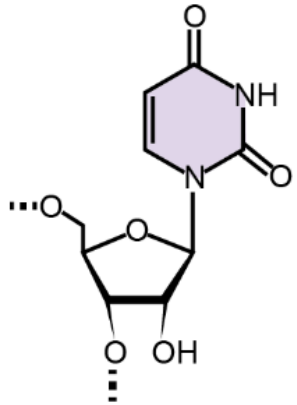
Many distinct RNA molecules derive from *each* gene!

What exactly are “RNA modifications”?

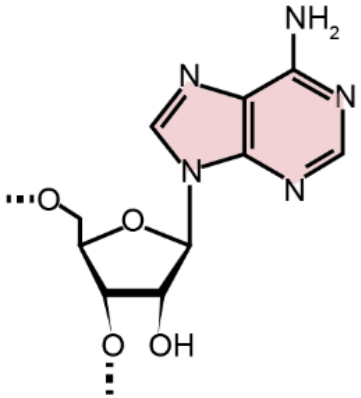
Nucleosides



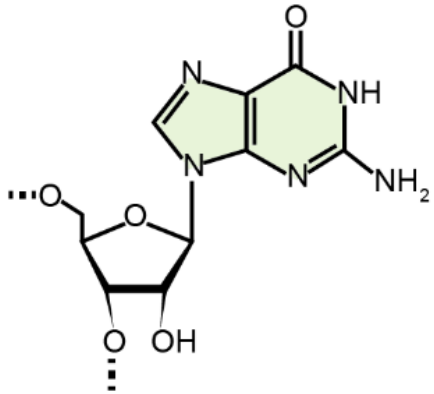
Cytidine (C)



Uridine (U)

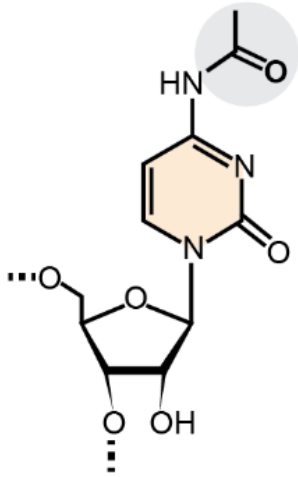


Adenosine (A)

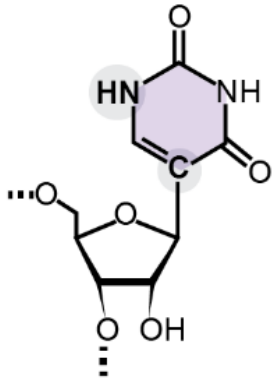


Guanosine (G)

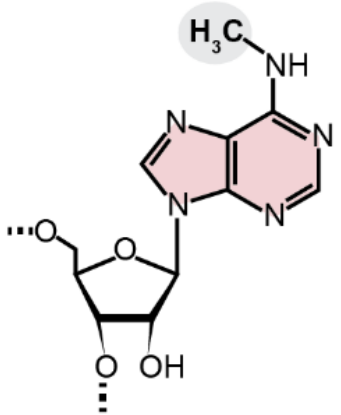
Modified Nucleosides (4 of ~170 known)



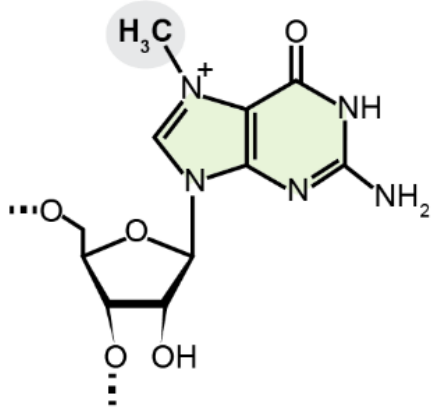
***N*^{4}-acetylcytidine (ac^{4}C)**



Pseudouridine (Ψ)



***N*^{6}-methyladenosine (m^{6}A)**

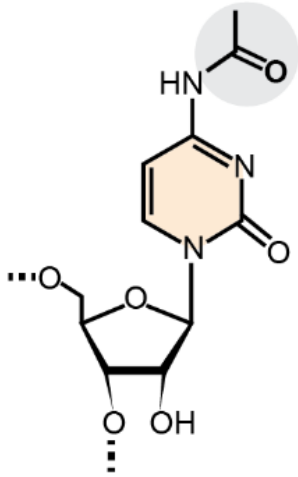


***N*^{7}-methylguanosine (m^{7}G)**

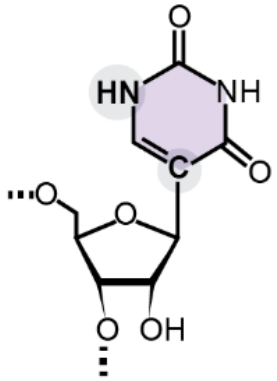
NATIONAL ACADEMIES Sciences Engineering Medicine

RNA modifications can:

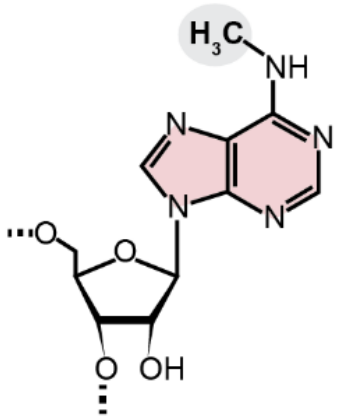
Modified Nucleosides (4 of ~170 known)



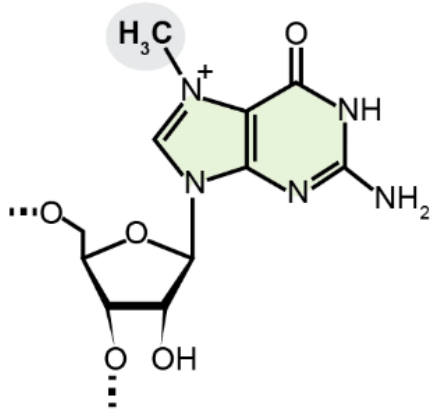
***N*⁴-acetylcytidine (ac⁴C)**



Pseudouridine (Ψ)



***N*⁶-methyladenosine (m⁶A)**



***N*⁷-methylguanosine (m⁷G)**

NATIONAL ACADEMIES Sciences Engineering Medicine

Why are RNA modifications so important?

- Crucial in nearly every life process!
  - Regulation of metabolism
  - Circadian rhythm
  - Immune system regulation (e.g., differentiation between host and viral RNAs)

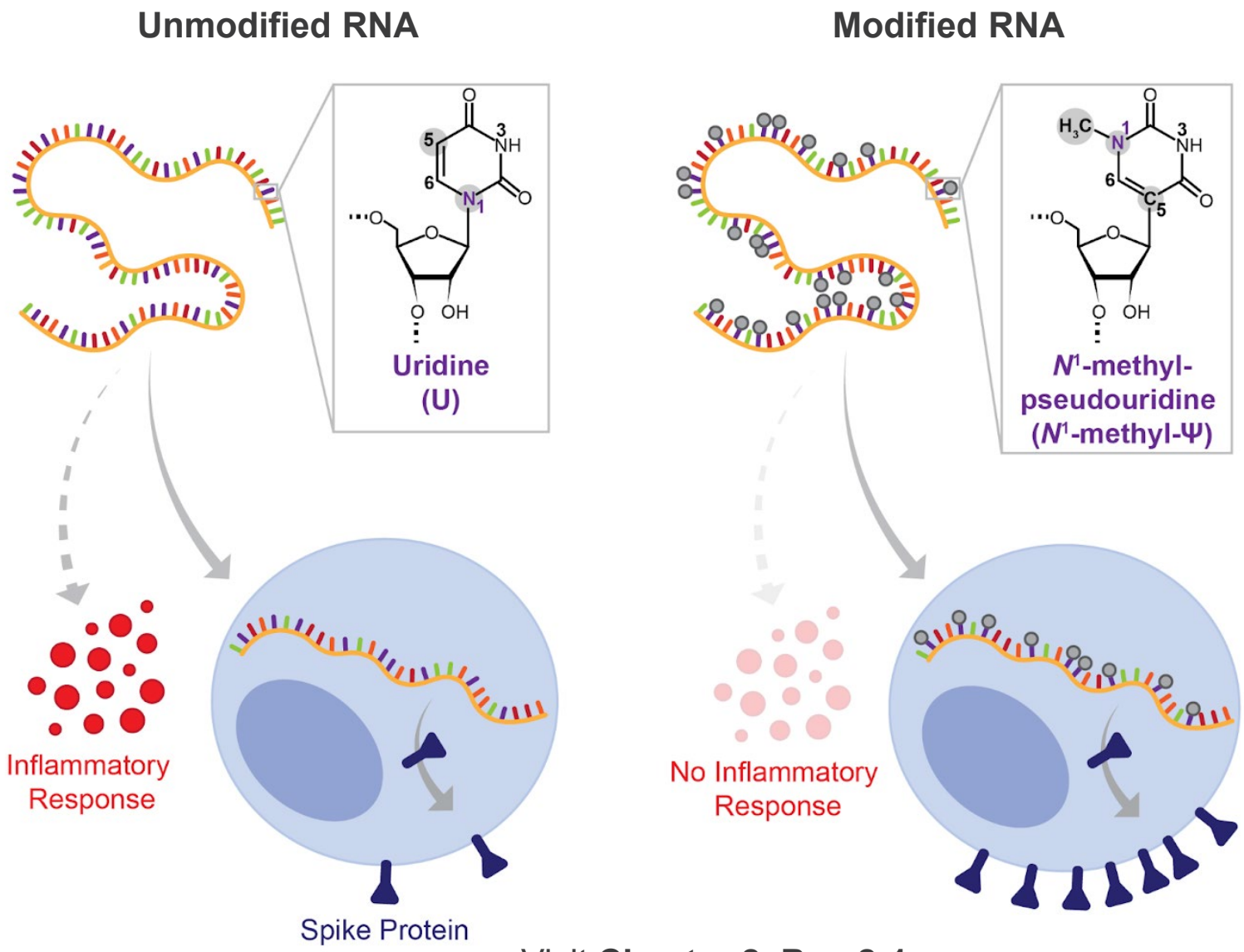
- Implicated in human diseases and disorders
  - Neurological disorders (e.g., intellectual disability, microcephaly)
  - Heart disease (e.g., hypertrophic cardiomyopathy)
  - Cancer (e.g., breast, skin, colorectal, bladder)
  - Diabetes
  - “tRNA modopathies”

Visit **Chapter 2, Table 2-1** for a list of human diseases caused by aberrant tRNA modifications

RNA modifications in vaccines against COVID-19

- Modifications permit the COVID-19 mRNA vaccines to succeed in protecting against infection and serious disease
- Foundational research awarded the 2023 Nobel Prize in Physiology or Medicine

Dr. Katalin Karikó Dr. Drew Weissman



Visit **Chapter 2, Box 2-1**

NATIONAL ACADEMIES Sciences Engineering Medicine

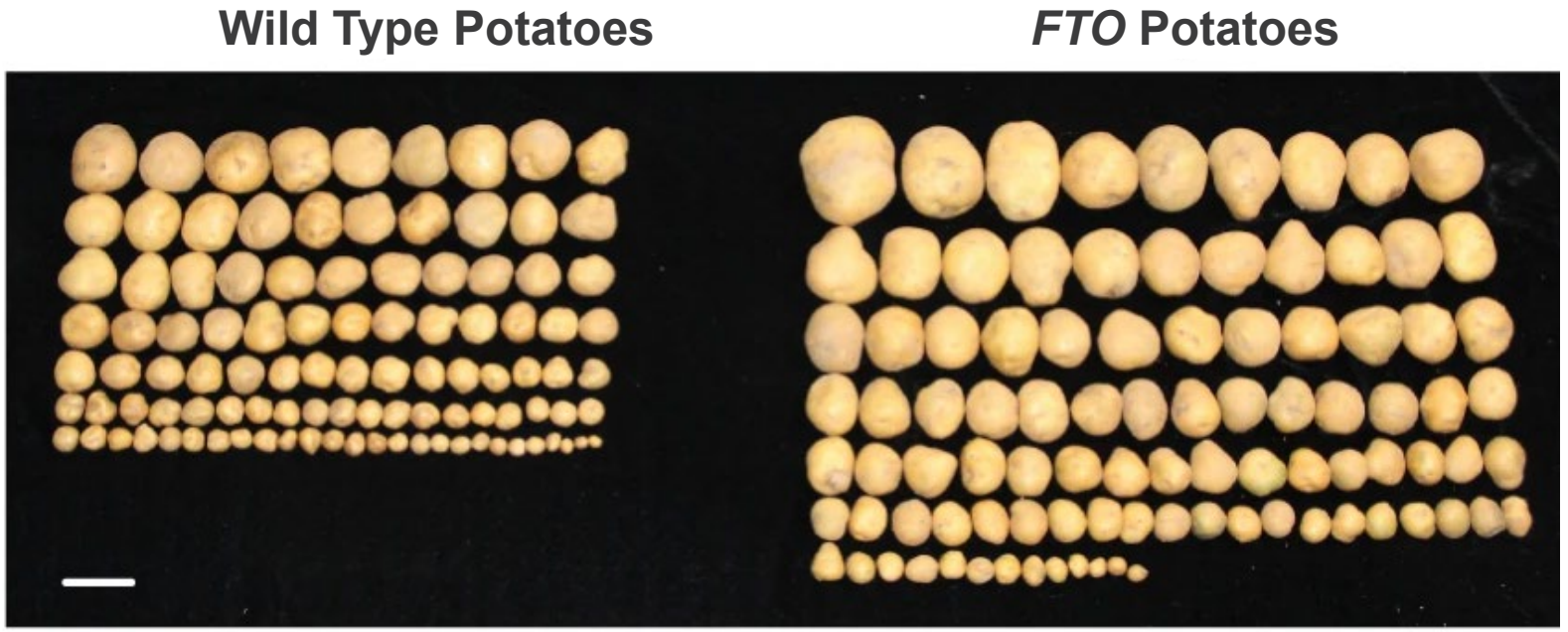
RNA vaccines and medicines

- mRNA vaccines against cancer (in clinical trials)
- mRNA vaccines for other pathogens (e.g., HIV, influenza, bacteria)
- Antivirals and antibiotics
- Therapeutics to treat rare diseases (e.g., spinal muscular atrophy)
- Enhancement to gene-editing, CRISPR, a promising tool for gene therapy

Visit **Chapter 2, Table 2-2** for a list of RNA therapeutics approved by U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA)

RNA modifications beyond health and disease

- Agriculture
- Synthetic biology
- Nanotechnology
- Bioeconomy



Visit **Chapter 2, Figure 2-4**

Yu et al., *Nat Biotech* 2021

Conclusion 1: *RNA modifications are a critical, but underexplored area of research*

A more complete understanding of RNA modifications will be important for:

- Significantly advancing the fundamental knowledge of living systems
- Maintaining the health of humans, plants, animals, and the environment
- Preventing and treating disease
- Improving crop yields and resilience
- Stimulating the bioeconomy
- Addressing other issues of societal importance

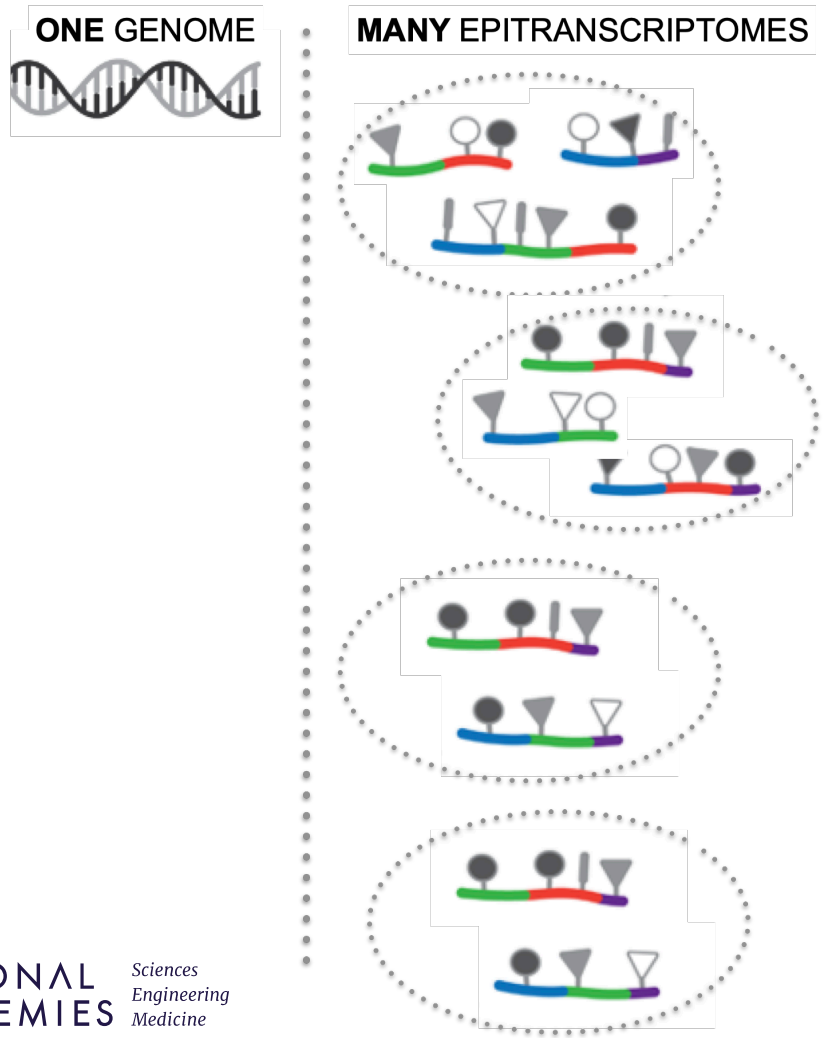
NATIONAL ACADEMIES Sciences Engineering Medicine

Conclusion 2: *Enabling the determination of any epitranscriptome will be the most impactful goal*

- “Epitranscriptome” = the sequences of a set of RNA molecules and their modifications
- Epitranscriptomes vary between cells and tissues, and with age, sex, and environment.

Conclusion 2: *Enabling the determination of any epitranscriptome will be the most impactful goal*

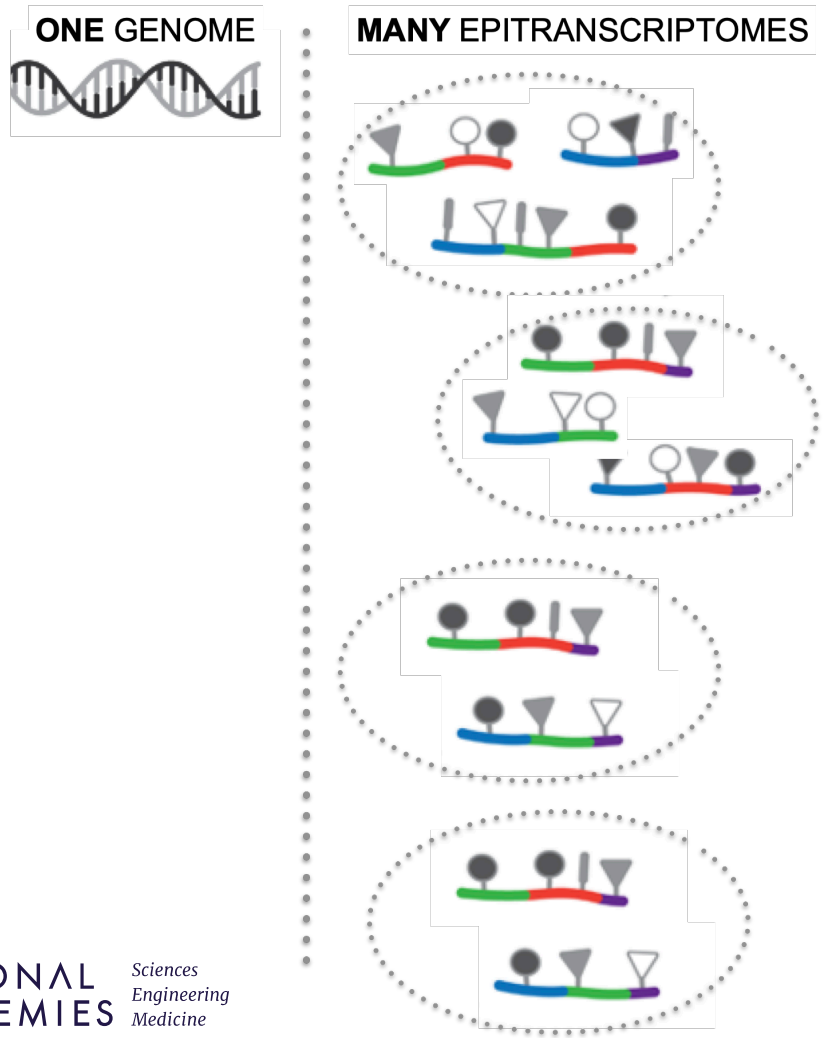
To define an individual requires sequencing:



- "Epitranscriptome" = the sequences of a set of RNA molecules and their modifications
- Epitranscriptomes vary between cells and tissues, and with age, sex, and environment.

Conclusion 2: *Enabling the determination of any epitranscriptome will be the most impactful goal*

To define an individual requires sequencing:



- "Epitranscriptome" = the sequences of a set of RNA molecules and their modifications
- Epitranscriptomes vary between cells and tissues, and with age, sex, and environment.
- There are many important epitranscriptomes to determine even for one individual!!
- **Developing technology and infrastructure to enable the sequencing of *any* epitranscriptome will be the most impactful goal**

Key efforts needed to unlock any epitranscriptome

A Path Forward

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Advancing Technology	• Standardize sample isolation, preparation, and handling for global analyses • Refine and optimize existing experimental and computational approaches • Centralize information about available technology, tools, methods, and computational toolkits • Explore novel experimental and computational approaches ✓ **RNA core centers that offer a range of sequencing and computational services and associated expertise in house** ✓ **Maps for abundant RNA types (e.g., tRNAs) for multicellular eukaryotic organisms in single, well-defined states** ✓ **Viral epitranscriptomes (e.g., SARS-CoV-2, HIV, influenza)**	• Establish high-throughput, low-cost, highly sensitive clinical assays for multiple RNA modifications • Facilitate broad access to epitranscriptome sequencing by driving down cost and improving usability • Accurately measure changes in modification stoichiometry across multiple defined cellular conditions for tRNAs • Understand modification cross-talk via modification measurements at the single molecular level for tRNAs ✓ **Epitranscriptomes for cultured cell lines and tissues in single, well-defined states** ✓ **Complete epitranscriptome for simple multicellular eukaryotic organisms (e.g., flies, worms, zebra fish) in single, well-defined state**	• Enable end-to-end sequencing and mapping of all RNA molecules and their modifications • Apply tools and technologies to answer important questions and provide insights into human health and disease

Chapter 3, Figure 3-6
A Roadmap for Advancing Tools and Technology

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Physical Standards	• Establish modified nucleoside standards for 25–30 known modifications • Create 50–100 modified oligonucleotides for use as reference standards ✓ **Commercially available standard kit**	• Synthesize longer modified oligonucleotides and expand repertoire of available modifications • Develop isotopically enriched modified nucleosides for quantification of modification stoichiometry ✓ **Commercial kits with expanded repertoire of available modifications and isotopically labeled oligonucleotide standards**	✓ **Readily available, affordable oligonucleotides of any custom-ordered sequence, length, modification stoichiometry, and structure**
Data and Database Standards	• Establish universal standards for RNA modification nomenclature and common ontologies for use in publications and databases • Establish guidelines and standards for raw data submissions • Require that raw and processed datasets be made publicly available ✓ **A model for RNA modification data resource with guidelines for data inclusion, sharing, and accessibility**	• Put in place a financial mechanism for ensuring the long-term sustainability of critical RNA data resources ✓ **A sustainably funded, stable, integrated, and centrally managed data resource that is a long-lasting and always current source of curated information about modified RNAs**	

Chapter 4, Figure 4-3
A Roadmap for Developing Standards and Databases

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Cultivating the Future Workforce	• Design multidisciplinary modules and training curricula for different educational levels • Develop experiential learning modules for high school and college students • Create learning materials for professional development and retraining programs • Organize courses and workshops that provide hands-on training in wet-lab techniques • Create dedicated conferences and funding mechanisms to convene professionals from different disciplines ✓ **A suite of cross-disciplinary educational resources and training materials well-suited for a variety of levels**	• Include information about the importance and impacts of RNA modifications in high school and college courses • Equip members of the existing workforce to contribute to advancing and applying RNA science through professional development and training programs	✓ **A well-trained, impassioned, diverse U.S. workforce with interdisciplinary expertise that is engaged in advancing and applying RNA biology and epitranscriptomics across the public and private sectors, academia, and industry**

Chapter 5, Figure 5-1
A Roadmap for Cultivating the Future Workforce

A Roadmap for Developing Standards (Figure 4-3)

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Physical Standards	• Establish modified nucleoside standards for 25–30 known modifications • Create 50–100 modified oligonucleotides for use as reference standards ✓ **Commercially available standard kit**	• Synthesize longer modified oligonucleotides and expand repertoire of available modifications • Develop isotopically enriched modified nucleosides for quantification of modification stoichiometry ✓ **Commercial kits with expanded repertoire of available modifications and isotopically labeled oligonucleotide standards**	✓ **Readily available, affordable oligonucleotides of any custom-ordered sequence, length, modification stoichiometry, and structure**

Conclusion 3: *Large-scale, coordinated efforts in the life sciences have been vital in driving science and technology innovation*

- E.g., Human Genome Project, Glycoscience Program, Human Microbiome Project, BRAIN Initiative
- Such efforts hold value in their ability to:
  - Align federal agencies
  - Support public–private partnerships
  - Organize consortia
  - Fund individual laboratories
  - Prioritize closing gaps in technology development, synthesis of standards, infrastructure buildout, workforce training, and public awareness

Conclusion 4: *A large-scale epitranscriptomics effort is needed to accelerate technological innovation and progress in the field*

- We envision it will impact multiple sectors (e.g., health, agriculture)
- Require expertise spanning multiple scientific disciplines (e.g., engineering, computer science, life science, social science)
- Require dedicated funding to key federal entities—such as NSF, NIH, NIST, DOD, and the DOE—to enhance their ability to work with academia, industry, philanthropic organizations, and international partners
- An endeavor of this scale and scope will entail a substantial investment of time and resources

Key Recommendations

Recommendation 1 (abbr.): An **established oversight body**, such as the Office of Science and Technology Policy or a similar entity with appropriate breadth and authority, **should catalyze and coordinate efforts** supporting a large-scale epitranscriptomics initiative

Recommendation 2 (abbr.): Federal funders of research such as NIH, NSF, DOD, and DOE **should invest in and prioritize closing gaps** in the existing tools, exploring new technologies, and centralizing resources for available tools and methods.

Recommendation 3 (abbr.): NIST should **develop, curate, and promote standards** to support the field of epitranscriptomics. Specifically, modified RNA reference materials should be developed with a focus on making them widely available and affordable.

Visit the **Summary** or **Chapter 6** for more details on Recommendations

NATIONAL ACADEMIES Sciences Engineering Medicine

Key Recommendations (cont.)

Recommendation 4 (abbr.): NCBI should establish and **promote standards** for databases, data deposition and exchange, and nomenclature for RNA modifications.

Recommendation 5 (abbr.): NIH should establish and maintain a sustainably funded and centrally **managed database** that maintains up-to-date, curated information about RNAs and their modifications.

Recommendation 6 (abbr.): To develop a **strong workforce**, institutions and funding agencies, such as HHMI, NIGMS, and NSF, in partnership with education experts, scientific societies, and industry groups, should build upon existing educational materials and training opportunities for students and the public.

Visit the **Summary** or **Chapter 6** for more details on Recommendations

Potential outcomes and broader impacts

- Novel sequencing tools, technologies, and computational methods
- Improved data infrastructure
- A well-trained, impassioned, diverse U.S. workforce

- Discovery of new linkages between RNA modifications and genetic disorders
- Improved disease control, prevention, and preparation for future pandemics
- Development of better vaccines to fight viruses
- New immunotherapies to treat cancer
- New antibiotics and antivirals
- Enhanced efficacy of RNAs used in gene therapy
- New diagnostic protocols for viral detection, tumor testing, and detection of inherited diseases
- New methods for improving crop yields and drought resilience, thus enhancing agricultural production and greater global food security
- Bolstered synthetic biology capabilities
- Advances in computer science

NATIONAL ACADEMIES *Sciences Engineering Medicine*

Thanks for listening!

We invite your questions

Q&A Panel

Brenda Bass

TJ Ha

Juan Alfonzo

Lydia Contreras

Patrick Limbach

Kate Meyer

Download the report

Critical challenges and roadblocks

Despite notable progress and economic value in this growing field, much about how RNA modifications affect the fate and function of RNA molecules in living systems is still unknown.

Existing technologies cannot currently discover all RNA modifications, let alone comprehensively sequence them on every RNA molecule.

Several types of standards are needed, specifically modified RNA reference materials, data standards around nomenclature and clear guidelines for data deposition and exchange, and robust and sustainable platforms for the curation and indexing of vast amounts of RNA data.

A sustainably funded and centrally managed database (or ensemble of databases) that maintains up-to-date, curated information about RNAs and their modifications is urgently needed.

To meet the future demands, the field needs a well-trained, impassioned, diverse U.S. workforce with interdisciplinary expertise and strong quantitative and computational skills

Highlights: Expanding Research

Conclusion 5: Discovery efforts and fundamental research in the field of epitranscriptomics will reinforce the importance and impact of RNA modifications and fuel technological advances that will improve scientists' ability to sequence them.

(cont.) New funding mechanisms, public and private, that encourage collaboration, spur innovation, and increase interest in RNA modifications will be critical.

Highlights: Advancing Technology

Conclusion 6: The current tools, technologies, and methodologies for end-to-end sequencing of RNA and all of its modifications are insufficient.

(cont.) The field of RNA biology will be driven forward by improving upon existing approaches and advancing new technologies that are robust and quantitative, and that preserve the information of full-length RNAs.

Conclusion 7: Improving the sensitivity of methodologies for cataloging and quantifying all RNA modifications in a sample, even without positional information, is an important enabling step that will inform the development of future RNA sequencing technologies and facilitate discovery of additional RNA modifications.

(cont.) Achieving this crucial intermediate goal will be spurred by an expanded repertoire of modified nucleosides for use as reference standards and more sensitive instrumentation.

Highlights: Advancing Technology (cont.)

Conclusion 8: Efforts directed toward enabling end-to-end sequencing of RNA and its modifications will accelerate innovation in the life sciences research enterprise but will also pave the way for developing new biotechnologies (e.g., biotherapeutics, vaccines, diagnostics, nanomaterials) and novel approaches that open new doors in life sciences research and other areas that are not yet apparent.

Recommendation 2 (abbr.): Federal funders of research such as NIH, NSF, DOD, and DOE should invest in and prioritize closing gaps in the existing tools, exploring new technologies, and centralizing resources for available tools and methods.

Highlights: Developing Standards

Conclusion 9: Several types of standards are needed:

- Technology-agnostic modified RNA reference materials
- Data standards around nomenclature and clear guidelines for data deposition and exchange
- Robust and sustainable platforms for the curation and indexing of vast amounts of RNA data

Recommendation 3 (abbr.): NIST should develop, curate, and promote standards to support the field of epitranscriptomics. Specifically, modified RNA reference materials should be developed with a focus on making them widely available and affordable.

Recommendation 4 (abbr.): NCBI should establish and promote standards for databases, data deposition and exchange, and nomenclature for RNA modifications.

Highlights: Centralizing Data Resources

Conclusion 10: The prevalence of "home-grown," small-group-supported RNA databases has been vital to advancing the field of RNA biology.

(cont.) Nonetheless, a major concern is the loss of resources (e.g., funding, staff) leading to a lack of maintenance of these laboratory-housed databases. Abandoning carefully curated databases may limit scientific growth and understanding, and waste time, effort, and resources.

Recommendation 5 (abbr.): NIH should establish and maintain a sustainably funded and centrally managed database that maintains up-to-date, curated information about RNAs and their modifications.

Highlights: Cultivating Innovation

Conclusion 11: Greater emphasis on RNA science in undergraduate courses is needed to build a better infrastructure for embracing future generations in the workforce.

(cont.) In addition to further education, the existing and future workforce needs interdisciplinary training with strong quantitative and computational skills.

Conclusion 12: Educational efforts in the RNA modifications field need to:

- Use methods that promote engagement
- Reflect the interdisciplinary nature of the science in education and related workforce development efforts,
- Invest in reaching and engaging students and trainees from diverse backgrounds, and
- Scale up proven strategies for retaining trainees in piloted programs.

Highlights: Cultivating Innovation (cont.)

Recommendation 6 (abbr.): To develop a strong workforce, institutions and funding agencies, such as HHMI, NIGMS, and NSF, in partnership with education experts, scientific societies, and industry groups, should build upon existing educational materials and training opportunities for students and the public.

(cont.) The materials and opportunities should be age appropriate and engaging for the interests of different groups, while covering the basic biological and chemical principles of RNA modifications, the tools available for their study, and their potential application in future medicines and useful biotechnologies.

A Roadmap for Advancing Technology

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Advancing Technology	• Standardize sample isolation, preparation, and handling for global analyses • Refine and optimize existing experimental and computational approaches • Centralize information about available technology, tools, methods, and computational toolkits • Explore novel experimental and computational approaches ✓ **RNA core centers that offer a range of sequencing and computational services and associated expertise in house** ✓ **Maps for abundant RNA types (e.g., tRNAs) for multicellular eukaryotic organisms in single, well-defined states** ✓ **Viral epitranscriptomes (e.g., SARS-CoV-2, HIV, influenza)**	• Establish high-throughput, low-cost, highly sensitive clinical assays for multiple RNA modifications • Facilitate broad access to epitranscriptome sequencing by driving down cost and improving usability • Accurately measure changes in modification stoichiometry across multiple defined cellular conditions for tRNAs • Understand modification cross-talk via modification measurements at the single molecular level for tRNAs ✓ **Epitranscriptomes for cultured cell lines and tissues in single, well-defined states** ✓ **Complete epitranscriptome for simple multicellular eukaryotic organisms (e.g., flies, worms, zebra fish) in single, well-defined state**	• Enable end-to-end sequencing and mapping of all RNA molecules and their modifications • Apply tools and technologies to answer important questions and provide insights into human health and disease • Leverage knowledge of RNA modifications for applications beyond health and medicine • Continue to move epitranscriptomics toward single-cell and single-molecule applications ✓ **Complete epitranscriptome of complex multicellular organisms under multiple defined cellular conditions** ✓ **Epitranscriptomes for human disease profiling**

A Roadmap for Developing Standards and Databases

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Physical Standards	• Establish modified nucleoside standards for 25–30 known modifications • Create 50–100 modified oligonucleotides for use as reference standards ✓ **Commercially available standard kit**	• Synthesize longer modified oligonucleotides and expand repertoire of available modifications • Develop isotopically enriched modified nucleosides for quantification of modification stoichiometry ✓ **Commercial kits with expanded repertoire of available modifications and isotopically labeled oligonucleotide standards**	✓ **Readily available, affordable oligonucleotides of any custom-ordered sequence, length, modification stoichiometry, and structure**

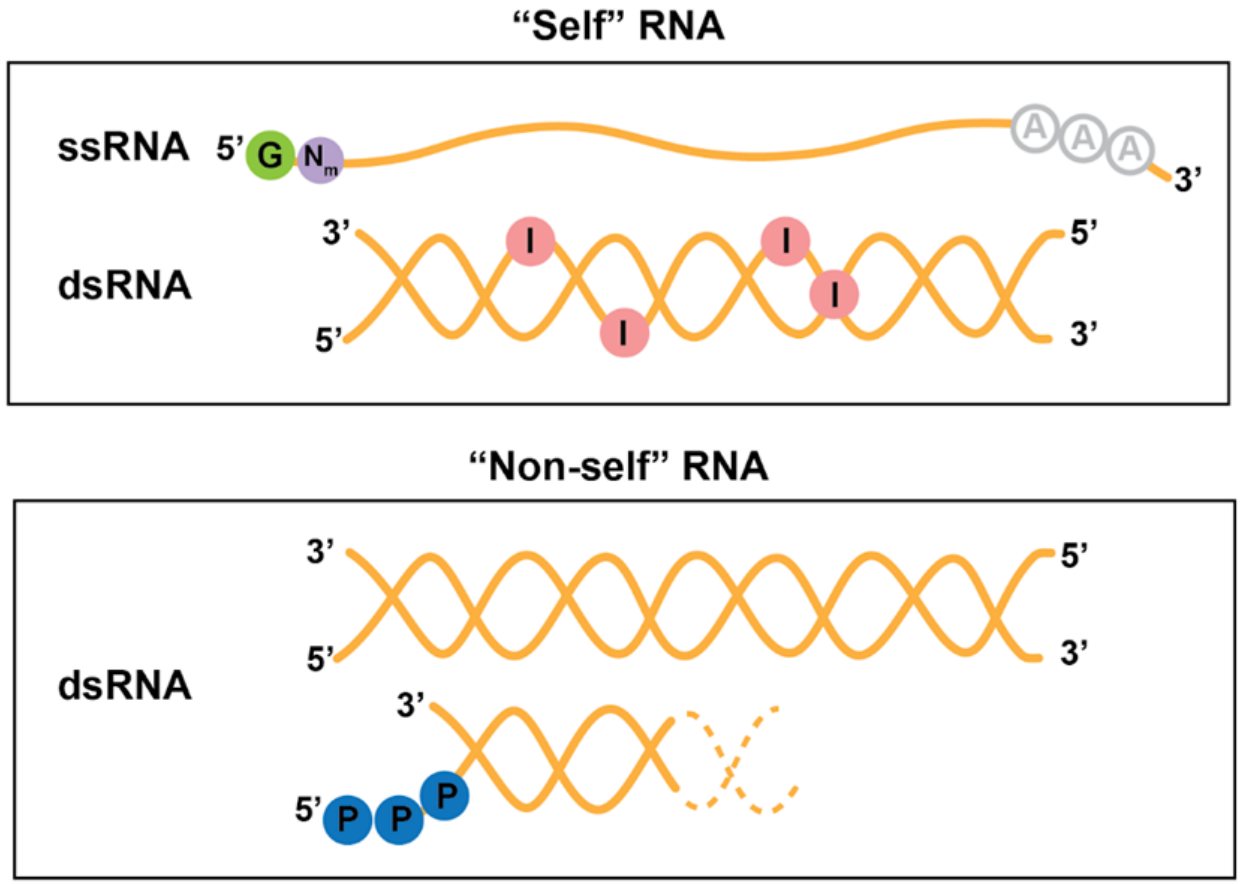
A Roadmap for Developing Standards and Databases (cont.)

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Data and Database Standards	• Establish universal standards for RNA modification nomenclature and common ontologies for use in publications and databases • Establish guidelines and standards for raw data submissions • Require that raw and processed datasets be made publicly available ✓ **A model for RNA modification data resource with guidelines for data inclusion, sharing, and accessibility**	• Put in place a financial mechanism for ensuring the long-term sustainability of critical RNA data resources ✓ **A sustainably funded, stable, integrated, and centrally managed data resource that is a long-lasting and always current source of curated information about modified RNAs**	✓ **Seamless access to universally available and shareable information on modified RNAs from any defined set of cellular conditions**

A Roadmap for Cultivating the Future Workforce

	Phase I (5 years)	Phase 2 (10 years)	Phase 3 (15 years)
Cultivating the Future Workforce	• Design multidisciplinary modules and training curricula for different educational levels • Develop experiential learning modules for high school and college students • Create learning materials for professional development and retraining programs • Organize courses and workshops that provide hands-on training in wet-lab techniques • Create dedicated conferences and funding mechanisms to convene professionals from different disciplines ✓ **A suite of cross-disciplinary educational resources and training materials well-suited for a variety of levels**	• Include information about the importance and impacts of RNA modifications in high school and college courses • Equip members of the existing workforce to contribute to advancing and applying RNA science through professional development and training programs	✓ **A well-trained, impassioned, diverse U.S. workforce with interdisciplinary expertise that is engaged in advancing and applying RNA biology and epitranscriptomics across the public and private sectors, academia, and industry**

Chapter 2, Figure 2-1



Chapter 2, Figure 2-2