

Office of Strategic Coordination Revised Concept Clearance

TITLE: The RNomics Program

INTRODUCTION: This is a revised concept originally presented at the September 2025 council of council meeting. We were pleased that the Council members were largely enthusiastic about this broad area of research, the need for better technologies to unravel the complexity of RNA, and the high impact the proposed program will have on the field, if successful. At the same time, we heard concerns about the feasibility of the program as presented, specifically related to the timing and potential interdependency of the proposed initiatives, the broad scope of the program, and concerns about the high-risk nature of some of the proposed initiatives.

This revised concept does not propose fundamental changes to the program structure. Instead, we provide more detailed information about each of the initiatives proposed in the associated powerpoint document and presentation. **We have integrated these changes throughout the new proposal presentation and believe this presents a comprehensive package for the council to consider.**

Specifically, we address the following elements in the revised concept presentation:

- To address the concern that *the concept is too narrow scientifically and does not meet the “synergistic” requirement for Common Fund programs*, we added background on the broad relevance of RNA science, and how achieving the goals of this program will impact research across all NIH mission areas
- To address *the need for this research in the community*, we added details throughout highlighting the elements of the program designed in direct response and alignment to the NASEM report recommendations as discussed in September
- To address *the concern about whether the program is too high-risk and not feasible at this time*, we added descriptions of how initiative 1 (RNA sequencing technology) balances risk and reward by capitalizing on existing innovation
- To address the *possible interdependence of the discrete program goals*, we describe why initiative 2 does not depend on the success and output from initiative 1. We also describe why initiative 3 (molecular standards) does not need to be completed in order for initiative 1 to begin and succeed, and how the two initiatives will progress concurrently.
- Finally, we clarify milestones, goals, and deliverables.

BACKGROUND: RNA plays a central role in cellular function and is a key element of many emerging biotechnologies, diagnostics, and therapeutics. A [2024 NASEM report](#) declared that “RNA science stands at a critical crossroads,” emphasizing the urgent need for technological advancement. RNA is chemically modified in over 170 distinct ways that impact stability, structure, localization, and function. Current tools cannot adequately sequence RNA or detect these modifications, limiting our ability to decode the full scope of RNA biology. There is a pressing need for the refinement of existing and generation of new technologies to map and interpret RNA modifications with precision.

PROGRAM GOAL: The RNomics Program will develop the essential tools needed to comprehensively characterize the human RNome, defined as the entire set of RNA molecules in a cell or organism, including coding and noncoding elements and RNA base modifications. The program will propel development of transformative technologies and molecular standards that enable sequencing full-length RNAs and detection of all base modifications. It will develop the tools needed to understand the role of modifications in RNA structure, dynamics/stability, and function *in vivo* and will further establish requisite computational tools, chemical, biological and data standards, and database resources for modification-inclusive RNA sequencing data, permitting generation of first-of-their-kind reference

datasets and RNA-based clinical biomarkers. These advances will set the stage for future studies aimed at understanding the role of endogenous RNA and its modifications in human health and disease.

PROPOSED INITIATIVES:

- **Initiative 1: RNA Sequencing Technology** – Development of improved and emerging technologies and associated computational tools to enable end-to-end sequencing of RNA and its modifications, encompassing the full breadth of RNA types found in a cell, agnostic with respect to source.
- **Initiative 2: RNA Molecular and Computational Tools** – Development of novel technologies that enable functional analysis of RNA. This includes technologies needed to analyze its structure, localization, and function as well as molecular tools for manipulating and processing RNA.
- **Initiative 3: RNomics Molecular Standards** – Production and distribution of standard RNA molecules. These standards are necessary to ensure reproducibility across RNA technologies and serve as a platform for cross-comparison of tools and methods and spike in control so different laboratories can calibrate accurately, increasing interoperability of datasets.
- **Initiative 4: RNomics Coordinating Center for Technology Benchmarking and Data Standardization** – Development and adoption of data standards that facilitate harmonization of disparate RNA datasets, coordination of benchmarking, reference data generation, and outreach.

DELIVERABLES: The major deliverable will be an RNomics Toolkit—a comprehensive platform of technologies and data infrastructure enabling complete, direct RNA sequencing (including modifications) from any sample. This toolkit will contain advanced RNA sequencers, synthetic RNA standards, and molecular tools for analyzing RNA function and mechanism. A robust suite of computational models will support predictive insights into RNA function and therapeutic outcomes. The program will also provide standardized data and database resources, initial RNA sequencing reference data, and clinically relevant RNA biomarkers to advance precision medicine.

BUDGET: \$151M over 5 years

TABLE 1 - BUDGET SUMMARY

	Lead IC	FY27	FY28	FY29	FY30	FY31	Total
Initiative 1 – RNA Sequencing Technology	NHGRI, NIGMS	\$14M	\$14M	\$14M	\$14M	\$14M	\$70M
Initiative 2 – RNA Molecular and Computational Tools	NIAID, NIDA, NCI	\$6M	\$6M	\$6M	\$6M	\$6M	\$30M
Initiative 3 – RNomics Molecular Standards	NIEHS, NIA	\$8M	\$7M	\$5M	\$4M	\$3M	\$27M
Initiative 4 – RNomics Coordinating Center for Technology Benchmarking and Data Standardization.	NIEHS, NHGRI	\$2M	\$3M	\$5M	\$6M	\$7M	\$23M
RMS – for NIH staff salary and travel; NIH-organized workshops	NHGRI, NIEHS	\$250K	\$250K	\$250K	\$250K	\$250K	\$1.25M
TOTAL		\$30.25M	\$30.25M	\$30.25M	\$30.25M	\$30.25M	\$151.25M