

Office of Strategic Coordination Concept Clearance

TITLE: The RNomics Program

BACKGROUND: RNA plays a central role in cellular function and is a key element of many emerging biotechnologies, diagnostics, and therapeutics that will impact human health. 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 a new generation of 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 generate 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, 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 RNA and its modifications in human health and disease.

PROPOSED INITIATIVES:

- **RNA Sequencing Technology** - Development and implementation of novel and improved 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
- **RNA Molecular and Computational Tools** – Development and application of novel technologies that enable complete 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
- **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 newly developed tools and methods
- **RNomics Coordinating Center for Technology Benchmarking and Data Standardization.** Generation of standards in nomenclature, database requirements, and methodology to facilitate harmonization of disparate RNA datasets, benchmarking of new technologies, facilitation of data production, and outreach and promotion of methods to guide technology adoption

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 include RNA sequencing technologies, synthetic RNA standards, and molecular tools for analyzing RNA structure, localization, and interactions. A robust suite of computational models will support predictive insights into RNA function and therapeutic outcomes. The project 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