

UNDERSTANDING THE RULES OF LIFE: PREDICTING PHENOTYPE (UROL)

UROL Funding¹ (Dollars in Millions)			
	FY 2020 Actual	FY 2021 Estimate	FY 2022 Request
Stewardship Activities (BIO)	\$29.95	\$30.00	\$30.00
Foundational Activities	\$87.47	\$53.50	\$83.50
BIO	20.77	20.00	40.00
CISE	9.04	6.00	6.00
EHR	10.38	-	-
ENG	8.40	3.00	3.00
GEO	4.00	4.00	4.00
MPS	30.11	16.00	16.00
SBE	4.77	4.50	4.50
TIP	-	-	10.00
Total	\$117.42	\$83.50	\$113.50

¹ Funding displayed may have overlap with other topics and programs

Overview

The URoL NSF Big Idea aims to create a new paradigm at the convergence of science, engineering, and technology that will elucidate theoretical frameworks, or rules, to enable prediction of the diversity of solutions that biological systems use to support life processes. Advances in understanding life at the fundamental level of the genome will enable re-engineering of cells, organisms, and ecosystems, and innovative biochemicals and biomaterials that sustain a vibrant bioeconomy and strengthen society. URoL also aims to train the next generation of researchers capable of using those rules and theories not only to predict the behavior of living systems, but to design them to benefit humankind.

Associated with URoL, NSF funds convergent research that addresses questions from the molecular to the ecosystem scale, and across biological diversity. These include foundational research on genetic variation and phenotypic emergence; ethical and social implications and societal acceptance of new biotechnologies, such as tools for genetic engineering and synthetic biology; ecological forecasting; and data science and AI to predict phenotype. In FY 2022, NSF will fund new awards in mathematical and physical sciences that utilize theory and novel experimental tools to address fundamental problems in biological systems and build capacity in a convergent research domain; new programs in synthetic biology that enable creation of novel chemicals, materials, and engineered systems; and infrastructure that further enables URoL research.

In FY 2018, NSF released several Dear Colleague Letters to announce URoL opportunities for catalytic activities. In FY 2019, NSF invested a total of \$36.0 million in 38 new awards in response to two Foundation-wide URoL solicitations: *URoL: Building a Synthetic Cell: An Ideas Lab Activity*¹ and *URoL: Epigenetics*.² In FY 2020, NSF funded 14 awards in response to the revised *URoL: Epigenetics*³ solicitation, and 26 awards in response to a new NSF-wide solicitation, *URoL: Microbiome Theory and Mechanisms (MTM)*⁴; these totaled \$40.0 million. In FY 2021, a second competition is being conducted for a revised *MTM* solicitation, and a new solicitation was issued: *URoL: Emergent Networks (URoL:EN)*.

¹ www.nsf.gov/funding/pgm_summ.jsp?pims_id=505600

² www.nsf.gov/funding/pgm_summ.jsp?pims_id=505582

³ www.nsf.gov/pubs/2020/nsf20512/nsf20512.htm

⁴ www.nsf.gov/funding/pgm_summ.jsp?pims_id=505694

Goals

1. To support a convergence of science, engineering, and technology in discovery of rules governing the emergence of robust, resilient, and adaptable phenotypes at three levels of biological organization, across the tree of life: (1) cells and cell systems; (2) multi-cellular organisms and their co-dependent microbial associations; and (3) complex networks of organisms and species involving social and ecological dynamics. Understanding the rules at these three different scales should enable the prediction of the behavior of living systems and how those systems interact with, respond to, and modify the environment, and will facilitate the engineering of biological systems and enable new forms of bio-manufacturing that are ethically sound, societally acceptable, and beneficial to humankind.
2. To support the discovery of rules governing emergent properties of networks of living systems that impinge on and are influenced by coupled natural, built, and social environments. The often unanticipated outcomes of these interactions rest on, but are not wholly or even partly predicted by, mathematical, chemical, and physical principles and unit-level (molecule/cell/organism/population) biological properties, and prediction is further hampered by accelerating perturbations in environmental circumstances and the associated occurrence of extreme events. A better understanding of the determinants of emergent network properties across various levels of organization will generate actionable information about the impact of specific environmental changes on outcomes for living communities, and vice versa, enabling improved prediction of, preparedness for, and response to natural and man-made environmental challenges, and more effective environmental management.
3. To support networks of researchers, technology developers, and educators engaged in URoL activities and thereby further the development of a robust community, with an impact that is sustained beyond the five-year investment in the URoL Big Idea. The convergent nature of research addressing emergent properties of living systems should stimulate the development of new and improved techniques in molecular, genomic, and cellular examination and manipulation; improved technologies for the capture of biological, behavioral, and social phenotypic data in free-living organisms; advances in data science, AI, and machine learning, as well as computational modeling ; more capable cyberinfrastructure to support robust, data- and computationally-enabled URoL discovery and sharing of research results; and advances in theory coming from relevant fields of science and engineering. URoL also support investments in training and workforce development to produce scientists that have a firm grounding in the life sciences as well as the mathematical, physical, computational, behavioral and/or social sciences and engineering that enable them to work collaboratively across disciplinary boundaries. Finally, URoL provides a rich context in which to expand science-literacy efforts aimed at diverse communities across the nation. Research networks provide a mechanism for sustained support of distributed groups of investigators working to achieve URoL goals.

FY 2022 Investments

URoL activities in FY 2022 will build upon the investments made in FYs 2019-2021. The FY 2021 solicitation supporting research on emergence in living systems will continue in FY 2022 (Goals 1 and 2). URoL will explore ways to build upon prior investments through synthesis activities to be developed in FY 2023, supporting networks of researchers, technology developers, and educators in different URoL domains (Goal 3). Foundational investments, aligned with URoL goals, will also provide support for convergent programs initiated in FY 2019 and planned for FY 2022. These activities laid the foundations for the URoL Big Idea; they are currently managed by NSF's directorates and offices and will continue to remain within the directorates and offices with respect to their funding and management.