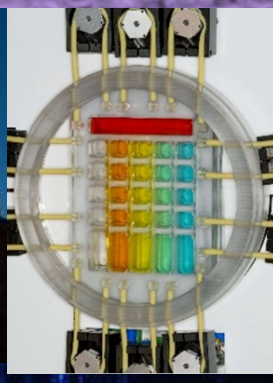

National Center for Advancing Translational Sciences

CONGRESSIONAL JUSTIFICATION
FY 2025

Department of Health and Human Services
National Institutes of Health

NIH National Center for Advancing Translational Sciences

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences (NCATS)

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General Notes

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

Cover Page

Clockwise from top left corner: a) Robot sampling the NCATS Tox21 compound collection. Samples reformatted by NCATS Compound Management staff can be used in a variety of tests, from single test tubes to 1536-well plates. Credit: NCATS. b) Individually-barcoded samples in the Tox21 compound collection. Sample retrieval and management are automated inside a -20°C system. Credit: NCATS. c) National COVID Cohort Collaborative (N3C) illustration representing its national reach and impact. Credit: NCATS. d) A high-throughput screening robot in NCATS' laboratories. Credit: NCATS. e) Five separate tissue systems (heart, liver, blood vessels, skin and cancer), each within its own custom-designed chamber, are shown on a single 'chip' (colors denote different tissue types). Credit: Columbia University. f) In recognition of Rare Disease Day at NIH, NIH lights up Building 1 on the Bethesda campus in Rare Disease Day colors. Credit: NCATS.

Director's Overview

To make real, positive impacts on human health, scientific discoveries need to reach people through the translation of research discoveries into tangible health interventions, such as drug therapies, medical devices, and clinical practice. At the National Center for Advancing Translational Sciences (NCATS), we break through barriers that slow down how research discoveries become real-world results.

Joni L. Rutter, Ph.D.
Director of the National Center for Advancing Translational Sciences (NCATS)

Translational science is vital to turning lab discoveries into health solutions. For example, treatment of rare diseases is sometimes not only hindered by a lack of basic scientific knowledge, but also impeded by how long it takes for patients to receive a correct diagnosis (an average of seven years), and the lack of a standard, streamlined pathway for development and delivery of a customized gene therapy. In addition to these rare disease challenges, therapeutic development overall needs new approaches that can better predict safety and efficacy in humans, such as human cell-based 3-D models for drug testing. Translational science is also instrumental in speeding up the many stages in launching a clinical trial: from study design to study startup and ethical review, to patient engagement, recruitment, and retention, through study completion. At NCATS, we support innovations across each of these stages of the translational research pipeline, and the dissemination and implementation of research advances. We not only serve as a bridge from the bench to the bedside, we learn and share how to build these bridges better.

NCATS' Approach to Advancing Translation

NCATS' programs are designed to study many diseases at one time, leverage team science, and apply cutting-edge technologies to translational research problems. For example, across many NCATS research areas, we are harnessing the power of data science and applying it across the translational research spectrum: from applying artificial intelligence/machine learning (AI/ML) to drug discovery and development, to using data from electronic health records to better understand disease progression. Our work on sharing viral screening and test data through the OpenData Portal and harmonizing clinical data for research through the National COVID Cohort Collaborative (N3C) has received the highest levels of HHS awards in 2023. Our commitment to data science also includes prize competitions for bias-detection tools in (AI/ML), to promote trustworthiness and transparency in health informatics. We are also taking an active leadership role across NIH on the integration of AI/ML with quantum computing to improve biomedical research and clinical care. Such platform approaches allow us to work towards creating more treatments, for all people, more quickly.

Fulfilling the Vision of "*More Treatments, for All People, More Quickly*"

NCATS' approach to turn biomedical research discoveries into health solutions is critical to fulfilling our vision of "More Treatments, for All People, More Quickly." Many of our projects are cross-cutting, collaborative, and support several of these three pillars, amplifying their impact.

Our research supports efforts to enrich the therapeutic development pipeline with promising candidates, while also increasing the number of candidates that demonstrate clinical readiness. This is especially important given only about 5 percent of over 10,000 known diseases have therapies. For example, our investment to create A Specialized Platform for Innovative Research Exploration (ASPIRE) is helping us find ways to streamline the time-intensive and labor-intensive drug discovery process. ASPIRE will apply informatics and data science to chemical compound development and testing, to deepen our understanding of the chemical and biological interfaces that are so crucial to drug development.

Testing the safety and efficacy of novel drugs has historically relied on animal models. NCATS has proactively funded and engaged partners to create new approach methodologies, sometimes referred to as novel alternative methods (NAMS), that may be more relevant to human physiology, and more predictive of clinical outcomes. Our productive partnership with the National Aeronautics and Space Administration (NASA) and our engagement with academic and private-sector research communities demonstrate the innovative way we can accelerate the transition of novel preclinical candidate therapies to first-in-human studies.

Supporting translational innovations that address the health needs for all people is a core goal at NCATS. In FY 2025, we will further leverage our Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) portfolio to support research that addresses health inequities in clinical diagnostics, so that tools for monitoring and testing indicators of health work for all.

Another example of research programs we support that benefit all people is our continued support of the Clinical and Translational Science Awards (CTSA) Trial Innovation Network (TIN). The TIN tests innovations to improve translational research, particularly multisite clinical trials. The TIN also consults on and provides resources for multicenter clinical trials and studies and facilitates recruitment and retention strategies. These efforts aim to improve clinical trial enrollment, clinical trial participant diversity, as well as lower the barriers that prevent patients from participating, so that clinical research truly benefits all people. (Read more in the Program Portrait in the pages that follow.)

Particularly for the over 30 million of patients in the United States affected by rare diseases, NCATS' work to speed translational research is critical and urgent. NCATS supports many rare disease innovations, including small grant programs to support the efficient and effective progress of rare disease candidate therapeutics or diagnostics toward clinical trial readiness. This ongoing research helps provide the data necessary for the design of rigorous and successful clinical trials, thus accelerating a key stage of the translational research process.

Stimulated by previous budget increases that expanded our work in gene therapy, NCATS launched a major gene therapy pilot program for four different rare diseases – the Platform Vector Gene Therapy (PaVe-GT) program – with the goal of shortening the time of clinical trial startup using a single gene delivery system and manufacturing methods. This pilot program has already made regulatory documents publicly available, with the intent of benefiting future gene therapy clinical trials for very rare diseases. This pioneering program is also paving the way for other partnership programs we lead and help support, such as the Accelerating Medicines Partnership® (AMP®) Bespoke Gene Therapy Consortium and the NIH Common Fund Somatic Cell Gene Editing program.

NCATS Now and in the Future: Strategic Directions and Engagement

Through strategic investments to advance translational science, there are many opportunities for NCATS to contribute to saving lives through translational science. The NCATS strategic planning process for the next five years is underway. Throughout this process, we have continued to engage individuals and organizations representing many different sectors, including other NIH institutes, centers, and offices; patient advocacy groups; trainees, principal investigators, and others supported by our robust CTSA network and the Rare Disease Clinical Research Network (RDCRN); and partners at other government agencies. By engaging across research and patient communities through workshops, roundtables, and strategic planning efforts, we embody the team-based, collaborative science approaches that will allow us to move further together, fulfilling the NCATS mission.

Audacious Goals

As NCATS enters its second decade, it has set audacious goals for the next 10 years:

- ✓ **More treatments** — Increase the number of treatments in development by fivefold.
- ✓ **For all people** — Dramatically increase diversity, equity, inclusion and access across every area NCATS supports.
- ✓ **More quickly** — Enable diagnostics and therapeutics to reach people twice as fast.

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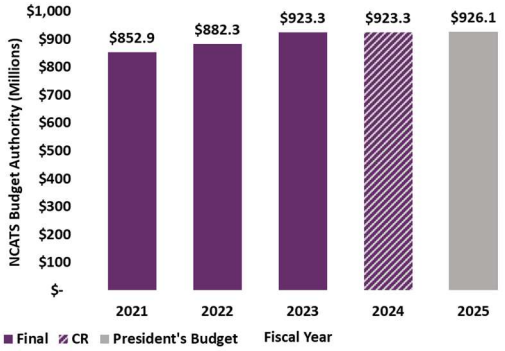
National Center for Advancing Translational Sciences

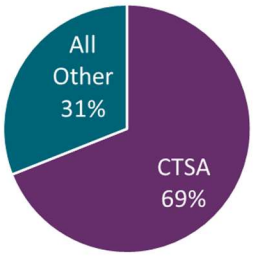
More Treatments for All People More Quickly

NCATS' Approach

NIH's National Center for Advancing Translational Sciences (NCATS) works with patient organizations, researchers, industry, clinicians, and other partners to focus on what's common across diseases. Together, we develop tools, technologies, and approaches that overcome roadblocks slowing medical progress — from high failure rates in the therapy development pipeline to inequities in clinical outcomes. We support a range of initiatives to achieve a future that offers ***more treatments, for all people, more quickly.***

Funding History





NCATS Appropriations

NCATS by the Numbers

>60 medical research institutions in NCATS' Clinical and Translational Science Awards (CTSA) program network

240 intramural collaborations active across all sectors

395 patents issued to NCATS since 2010, including **94** U.S. and **301** foreign patents

55 approved Investigational New Drug (IND) applications built on a decade of NCATS' advances

*Of the more than **10,000 known rare diseases,** only about 500 have treatments. That means that millions of people with illnesses or diseases are waiting for safe and effective treatments. The therapeutic challenge is particularly great for the **30 million people** living with a rare disease in the United States, for whom a lack of treatments and diagnostic tools leads to annual direct medical costs of **$400 billion and nearly $1 trillion total costs**. To overcome these formidable challenges, NCATS is speeding the translation of scientific discoveries into health solutions.*

More Treatments

- New Approach Methodologies (NAMs), such as 3-D tissue bioprinting and tissue chips, are designed to better predict efficacy, improve drug development success rates, and lower the number of costly therapies.
- The Platform Vector Gene Therapy (PaVe-GT) program and the Bespoke Gene Therapy Consortium (BGTC) will lead to more therapies for rare diseases.
- The Rare Diseases Clinical Research Network (RDCRN) and the Biomedical Data Translator seek solutions that can be applied across conditions and diseases.

All People

- NCATS builds and supports organizational cultures that support diversity, equity, inclusion, and accessibility.
- NCATS' CTSA institutions are increasing participation among underrepresented groups in clinical research and the translational science workforce. CTSA institutions collaborate with many partners, including minority-serving institutions and rural organizations, across the United States.

More Quickly

- The Streamlined, Multisite, Accelerated Resources for Trials (SMART) Institutional Review Board (IRB) Platform and the Trial Innovation Network (TIN) overcome roadblocks in clinical trials to cut study start-up time.
- Rapid screening of the NCATS Pharmaceutical Collection of approved drugs is enabling researchers to find leads for rare and common diseases, to move quickly into preclinical and clinical testing.

Rare Diseases Research Innovation

NCATS is the heart of rare diseases research at NIH. We support programs that find solutions for rare diseases, including:

- The RDCRN consists of 20 consortia that include physicians, scientists, and patient advocacy groups delivering insights into more than 200 rare diseases. The network plays a pivotal role in developing therapies, including a U.S. Food and Drug Administration–approved drug to treat acute intermittent porphyria.
- The Impact of Rare Diseases on Patients and Healthcare Systems (IDeaS) pilot study, which mapped the lengthy and arduous diagnostic odyssey many people with rare diseases face. The study revealed that the annual direct medical costs for people in the United States with rare diseases are $400 billion.
- The PaVe-GT program, which uses the same gene therapy delivery system and manufacturing methods in multiple gene therapy trials. The trials are targeting rare liver and neuromuscular conditions.

Audacious Goals

As NCATS advances into its second decade, we have set audacious goals for the next 10 years:

More treatments
Increase the number of treatments in development by fivefold.

For all people
Dramatically increase diversity, equity, inclusion, and access across every area NCATS supports.

More quickly
Enable diagnostics and therapeutics to reach people twice as fast.

Emerging Public Health Needs

We develop and support research initiatives to meet urgent public health demands, including:

- Clinical trials conducted through NCATS' nationwide CTSA Program network: By reaching people where they are, NCATS makes research participation easier through innovations in clinical trial recruitment, design, and management.
- Drug repurposing and human cell-based screening: NCATS' already-established capabilities have been pivoted towards emerging infectious disease concerns (e.g., Zika, SARS-CoV-2), rare diseases, as well as novel paths for addressing pain and addiction (NIH HEAL Initiative collaborations).
- Clinical data harmonization in cloud-based repositories: Moving towards a clinical data resource for studying many diseases, based on the National COVID Cohort Collaborative, or N3C, that harmonizes data from electronic health records to reveal critical insights into Long COVID, and how COVID-19 health outcomes vary across ages, races, chronic conditions, and treatment regimens.

Diversity, Equity, Inclusion, and Access to Research

We are committed to greater inclusion in our research and workforce to improve the health of all communities through the following initiatives:

- The CTSA TIN, which develops innovative approaches to boost diversity in clinical trials. The TIN's Recruitment Innovation Center (RIC) brings diverse groups of collaborators into the planning and implementation of clinical research.
- The expansion of research tools, such as tissue chips for drug screening and data sets, to include underserved populations and relevant health needs, in the drug discovery process.
- The NCATS Gaining Research Equity and Advancement in Translational Sciences (G.R.E.A.T.S) Program, which supports the career development of a diverse group of undergraduate and graduate students.

Major Changes in the Budget Request

The budget request for National Center for Advancing Translational Sciences (NCATS) of $926.1 million represents an increase of $2.8 million from the FY 2023 Final level. NCATS will support priority research programs. NCATS will pay non-competing grant awards at their committed levels and fund high priority new awards. NCATS will continue to turn research observations into health solutions through translational science, with the goal of developing more treatments, for all people, more quickly.

Research Project Grants (+$135.2 million; total $312.4 million):
Beginning in FY 2023, the primary funding mechanism for the Clinical and Translational Science Awards (CTSA) Program transitioned from Clinical Research Centers to Research Project Grants to make the application and awarding process more efficient, allow for enhanced and targeted application review, and to expand applicant's flexibility to leverage unique strengths and drive clinical and translational science innovation. Additional funding opportunities were made available to further enhance translational science scope and breadth. NCATS will ensure that recipients of CTSA institutional awards will receive not less than 95 percent of the core resources received in their prior award.

Research Centers (-$118.0 million; total $208.8 million):
Beginning in FY 2023, the primary funding mechanism for the Clinical and Translational Science Awards (CTSA) Program transitioned from Clinical Research Centers to Research Project Grants. NCATS will ensure that recipients of CTSA institutional awards will receive not less than 95% of the core resources received in their prior award.

Research and Development Contracts (-$28.8 million; total $93.4 million):
NCATS will prioritize research activities through other funding mechanisms and not support as many R&D contracts in FY 2025. Some activities funded through the R&D Contracts mechanism are ending or will continue through other funding mechanisms.

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences

Budget Mechanism *

(Dollars in Thousands)

Mechanism	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Research Projects:								
Noncompeting	64	$34,167	59	$140,432	96	$214,694	32	$180,527
Administrative Supplements	*(3)*	$1,210	*(2)*	$527	*(2)*	$305	*-(1)*	-$905
Competing:								
Renewal	0	$0	0	$0	0	$0	0	$0
New	52	$119,749	74	$93,453	74	$73,923	22	-$45,826
Supplements	0	$0	0	$0	0	$0	0	$0
Subtotal, Competing	**52**	**$119,749**	**74**	**$93,453**	**74**	**$73,923**	**22**	**-$45,826**
Subtotal, RPGs	116	$155,126	133	$234,412	170	$288,922	54	$133,796
SBIR/STTR	34	$22,077	37	$23,419	37	$23,499	3	$1,421
Research Project Grants	150	$177,203	170	$257,830	207	$312,421	57	$135,217
Research Centers								
Specialized/Comprehensive	0	$10,963	0	$548	0	$10,048	0	-$915
Clinical Research	47	$315,829	36	$258,968	24	$198,722	-23	-$117,107
Biotechnology	0	$0	0	$0	0	$0	0	$0
Comparative Medicine	0	$0	0	$0	0	$0	0	$0
Research Centers in Minority Institutions	0	$0	0	$0	0	$0	0	$0
Research Centers	**47**	**$326,792**	**36**	**$259,516**	**24**	**$208,770**	**-23**	**-$118,022**
Other Research:								
Research Careers	59	$60,383	58	$60,420	55	$63,173	-4	$2,790
Cancer Education	0	$0	0	$0	0	$0	0	$0
Cooperative Clinical Research	0	$0	0	$0	0	$0	0	$0
Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Minority Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Other	43	$36,534	40	$35,162	40	$38,435	-3	$1,901
Other Research	**102**	**$96,917**	**98**	**$95,582**	**95**	**$101,608**	**-7**	**$4,692**
Total Research Grants	299	$600,912	304	$612,928	326	$622,799	27	$21,887
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	442	$27,287	442	$27,105	442	$29,472	0	$2,186
Total Research Training	**442**	**$27,287**	**442**	**$27,105**	**442**	**$29,472**	**0**	**$2,186**
Research & Develop. Contracts	138	$122,232	118	$104,274	107	$93,441	-31	-$28,791
SBIR/STTR (non-add)	*(7)*	*($4,636)*	*(7)*	*($3,254)*	*(7)*	*($3,256)*	*(0)*	*-($1,379)*
Intramural Research	101	$98,586	111	$96,942	121	$96,992	20	-$1,594
Res. Management & Support	177	$74,306	187	$82,074	198	$83,382	21	$9,076
SBIR Admin. (non-add)		*($434)*		*($445)*		*($445)*		*($11)*
Construction		$0		$0		$0		$0
Buildings and Facilities		$0		$0		$0		$0
Total, NCATS	**278**	**$923,323**	**298**	**$923,323**	**319**	**$926,086**	**41**	**$2,763**

* All items in italics and brackets are non-add entries.

NATIONAL INSTITUTES OF HEALTH

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, $926,086,000: Provided, That up to $70,000,000 shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network: Provided further, That at least $631,444,000 is provided to the Clinical and Translational Sciences Awards program.

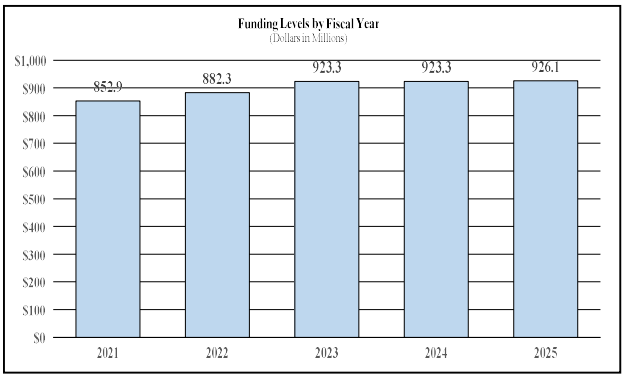
NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

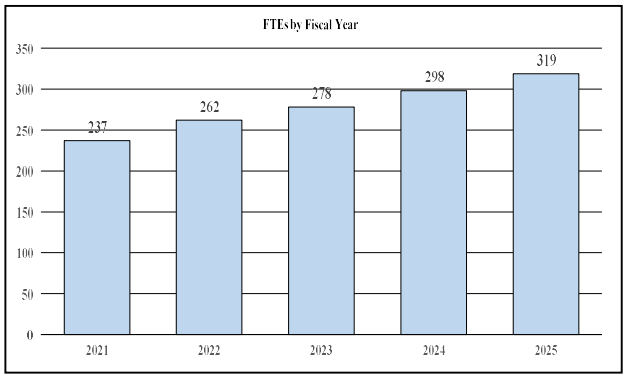
Summary of Changes
(Dollars in Thousands)

CHANGES	FY 2023 Final		FY 2025 President's Budget		Built-In Change from FY 2023 Final	
	FTEs	Budget Authority	FTEs	Budget Authority	FTEs	Budget Authority
1. Intramural Research:						
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		$20,198		$25,287		$238
b. FY 2024 effect of FY 2024 pay & benefits increase		$20,198		$25,287		$786
c. FY 2024 paid days adjustment		$20,198		$25,287		$78
d. Differences attributable to FY 2024 change in FTE		$20,198		$25,287		$4,987
e. FY 2025 effect of FY 2024 pay & benefits increase		$20,198		$25,287		$287
f. FY 2025 effect of FY 2025 pay & benefits increase		$20,198		$25,287		$391
g. FY 2025 paid days adjustment		$20,198		$25,287		$0
h. Differences attributable to FY 2025 change in FTE		$20,198		$25,287		$2,270
i. Payment for centrally furnished services		$3,009		$3,226		$217
j. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$75,379		$68,478		$4,093
Subtotal, IR built-in cost changes						$13,348
2. Research Management and Support:						
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		$33,389		$40,258		$395
b. FY 2024 effect of FY 2024 pay & benefits increase		$33,389		$40,258		$1,299
c. FY 2024 paid days adjustment		$33,389		$40,258		$129
d. Differences attributable to FY 2024 change in FTE		$33,389		$40,258		$1,999
e. FY 2025 effect of FY 2024 pay & benefits increase		$33,389		$40,258		$462
f. FY 2025 effect of FY 2025 pay & benefits increase		$33,389		$40,258		$636
g. FY 2025 paid days adjustment		$33,389		$40,258		$0
h. Differences attributable to FY 2025 change in FTE		$33,389		$40,258		$2,305
i. Payment for centrally furnished services		$0		$0		$0
j. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$40,896		$43,124		$2,329
Subtotal, RMS built-in cost changes						$9,553

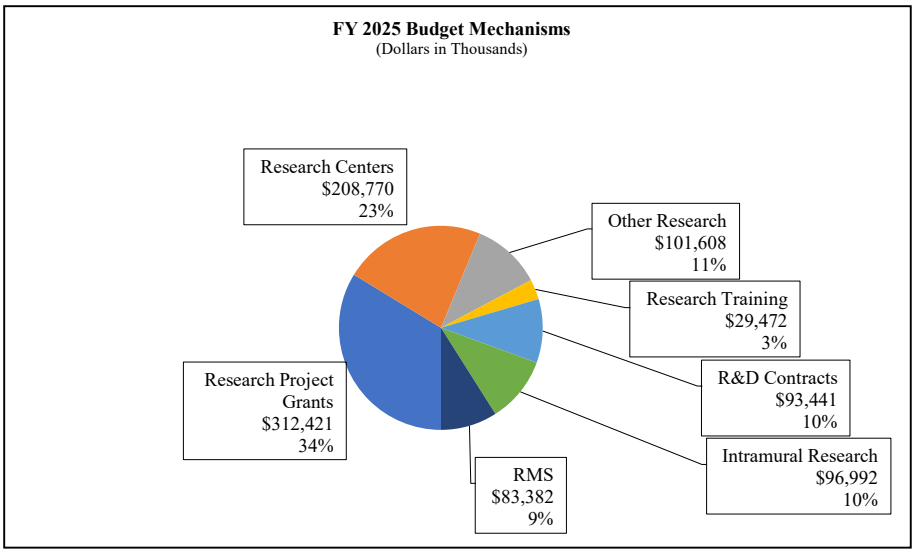
CHANGES	FY 2023 Final		FY 2025 President's Budget		Program Change from FY 2023 Final	
	No.	Amount	No.	Amount	No.	Amount
B. Program:						
1. Research Project Grants:						
a. Noncompeting	64	$35,377	96	$214,999	32	$179,622
b. Competing	52	$119,749	74	$73,923	22	-$45,826
c. SBIR/STTR	34	$22,077	37	$23,499	3	$1,421
Subtotal, RPGs	150	$177,203	207	$312,421	57	$135,217
2. Research Centers	47	$326,792	24	$208,770	-23	-$118,022
3. Other Research	102	$96,917	95	$101,608	-7	$4,692
4. Research Training	442	$27,287	442	$29,472	0	$2,186
5. Research and development contracts	138	$122,232	107	$93,441	-31	-$28,791
Subtotal, Extramural		$750,431		$745,712		-$4,719
6. Intramural Research	101	$98,586	121	$96,992	20	-$14,942
7. Research Management and Support	177	$74,306	198	$83,382	21	-$477
8. Construction		$0		$0		$0
9. Buildings and Facilities		$0		$0		$0
Subtotal, program changes						-$20,138
Total built-in and program changes	278	$923,323	319	$926,086	41	$2,763

History of Budget Authority and FTEs:

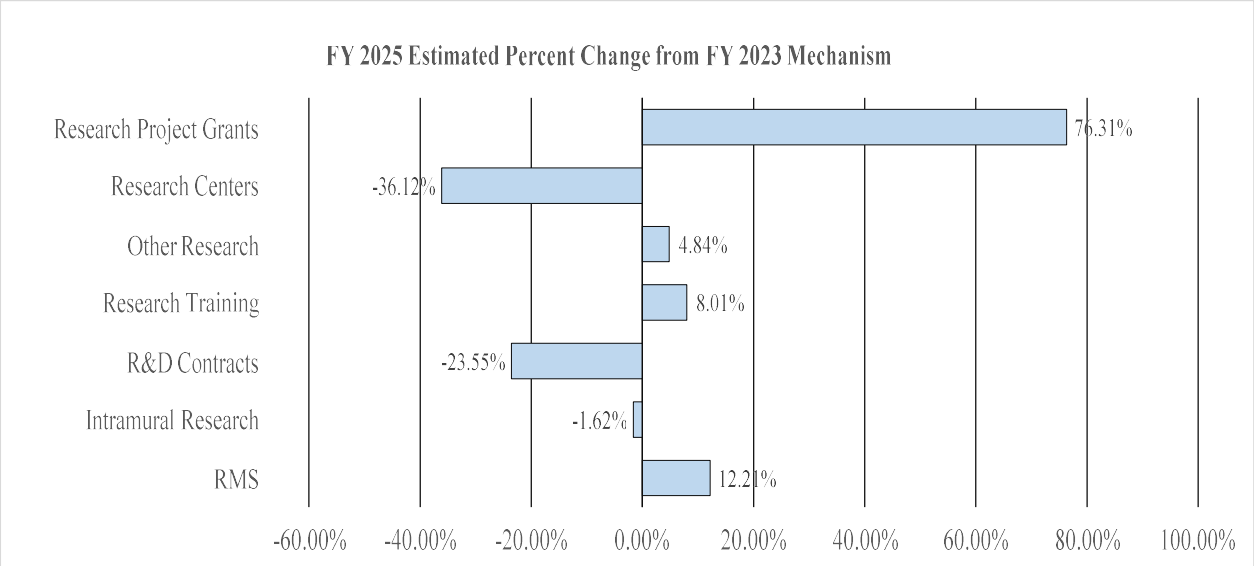




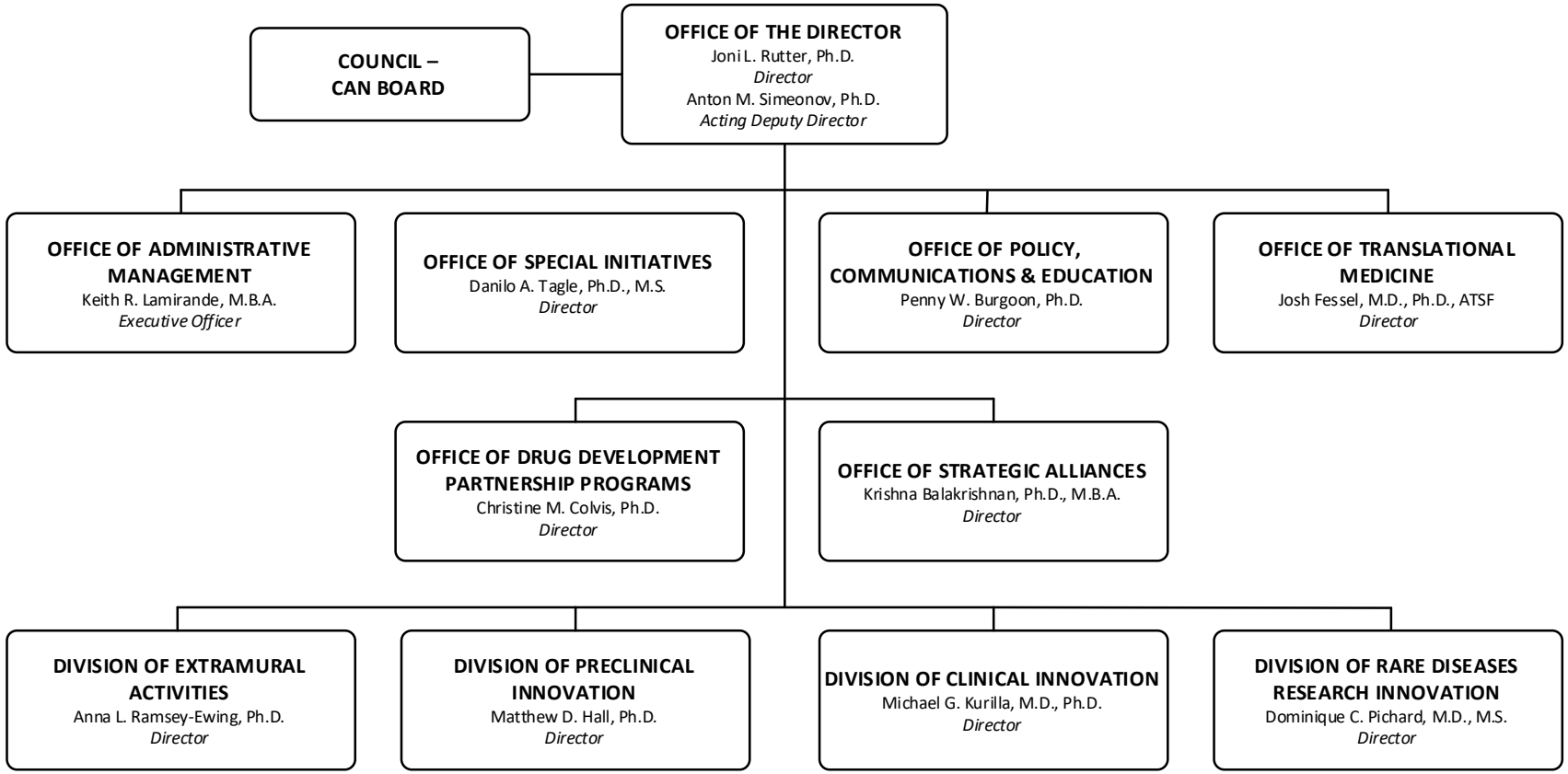
Distribution by Mechanism:



Change by Selected Mechanisms:



NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences



NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences

Budget Authority by Activity[1,2,3]
(Dollars in Thousands)

	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023 Final	
Budget Activity	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Clinical and Translational Science Activities		$629,570		$629,570		$631,454		$1,884
Reengineering Translational Sciences		$171,977		$171,977		$172,492		$515
Cures Acceleration Network		$66,000		$66,000		$66,197		$197
Rare Diseases Research and Therapeutics		$55,776		$55,776		$55,943		$167
TOTAL	**278**	**$923,323**	**298**	**$923,323**	**319**	**$926,086**	**41**	**$2,763**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund

[2] Amounts for each budget activity combine funding for extramural research, intramural research, and research management and support components of the activity

[3] NCATS funds rare diseases research in all four of its budget activities. Rare Diseases Research and Therapeutics is for those programs solely dedicated to rare diseases research.

National Center for Advancing Translational Sciences

Authorizing Legislation: Section 301 and Title IV of the Public Health Service Act, as amended, and Section 480 of the PHS Act, relating to the Cures Acceleration Network.

Budget Authority (BA):

	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
BA	$923,323,000	$923,323,000	$926,086,000	$2,763,000
FTE	278	298	319	41

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Overall Budget Policy: The FY 2025 President's Budget request for the National Center for Advancing Translational Sciences (NCATS) is $926.1 million, an increase of $2.8 million or 0.3 percent compared with the FY 2023 final level.

Program Descriptions and Accomplishments

I. Scientific and Operational Innovations to Accelerate the Translation of Clinical Research

Supporting a Broad Spectrum of Clinical and Translational Science Across the Nation
The **Clinical and Translational Science Awards (CTSA) Program** is a collaborative consortium working locally, regionally, and nationally to speed the translation of clinical research discoveries into health benefits to serve all people. A nationwide network of over 60 biomedical research institutions serves as the program's backbone, collaborating with various partners to tackle key bottlenecks in clinical research and translational science.[1]

Fostering CTSA Collaborative Activities to Reach All People
Collaborative, consortium-wide activities yield impacts across CTSA awardee institutions, with streamlined research practices, access to resources and expertise, and application of scientific problem-solving to long-standing issues that slow all phases of research and public health implementation. Collaborations extend to minority-serving institutions as well as organizations in rural areas, to address health inequities. Notable CTSA team science-based advances include:

- CTSA Collaborative and Innovation Acceleration Awards (CCIA): Through CCIA support, CTSA scientists create synergy and accelerate the translational research process through collaboration and innovation. CCIA awards are multi-site awards that support the development, demonstration, and dissemination of innovative solutions to transform

[1] ncats.nih.gov/research/research-activities/ctsa

CTSA Trial Innovation Network

The CTSA Trial Innovation Network (TIN)[1] supports accelerating the translation of novel interventions into life-saving therapies through operational innovation and collaboration on clinical trials.

The TIN's operational innovation and collaboration efforts include:
- a single institutional review board system,
- master contracting agreements,
- quality-by-design approaches, and
- a focus on evidence-based strategies to recruitment and patient engagement.

The TIN's community engagement efforts reach patients and communities through every phase of research, by providing resources from CTSA institutions and community health partners to conduct engagement, recruitment, and retention activities for clinical trials and multi-site studies.

Notable resources provided by the TIN include:
- best practices for conducting trials during public health emergencies,
- recruitment and retention toolkits, and
- a webinar for engaging racial and ethnic minority patient populations in clinical trials.

The TIN and other CTSA community engagement resources have been a critical part of NIH's efforts to address public health emergencies. For example, the **Pain Management Effectiveness Research Network**, a multisite research cooperative program through the **NIH Helping to End Addiction Long-Term (HEAL) Initiative®**, is using CTSA TIN infrastructure to support clinical trials that compare the effectiveness of existing non-addictive therapies and novel approaches for prevention and management of pain to advance new treatments for the opioid crisis.

NCATS is continuing to support this important initiative through recent renewal of several TIN awardees. Along with existing activities, the continuation of these awards will allow the TIN to expand its focus to include:
- increasing participation from minority-serving institutions and rural organizations,
- evaluating the recruitment effect of trial inclusion/exclusion criteria, and
- supporting remote and decentralized trials.

[1]ncats.nih.gov/research/research-activities/ctsa/projects/tin

the field of translational science, address inefficiencies that are common across diseases, and bring more interventions to all people more quickly. CCIA projects underway include cross-CTSA collaborations to apply analytics and machine-learning approaches to maternal-health interventions; translating science to clinical practice to improve safety and efficacy of opioids in neonates, children, and nursing mothers; and applying analytics to improve risk prediction for multisystem diseases using data from electronic health records (EHR) from multiple CTSA hubs.[2]

- CTSA Rural Health Efforts: The CTSA program is committed to accelerating clinical and translational research to address health disparities and the significant burden of conditions that disproportionately affect rural, minority, and other underserved populations.[3,4] Research that supports rural health concerns include efforts to address diseases of despair,[5] the opioid epidemic,[6,7] and enhancements to primary care clinical practice.[8]

CTSA Support of Trainee and Career Development

Career development and training components of the CTSA Program enhance institutional activities by cultivating and sustaining future leaders of the clinical and translational science biomedical research workforce. The impact of the CTSA Program in fostering the development and inspiration of the next generation of translational scientists

[2] ncats.nih.gov/research/research-activities/ctsa/projects/ccia/2022
[3] ncats.nih.gov/research/research-activities/ctsa/projects/rural-health
[4] grants.nih.gov/grants/guide/notice-files/NOT-TR-19-015.html
[5] ncats.nih.gov/research/research-activities/ctsa/projects/rural-health/ctsi-psu
[6] ncats.nih.gov/research/research-activities/ctsa/projects/rural-health/consider
[7] ncats.nih.gov/research/research-activities/ctsa/projects/rural-health/proud-r2
[8] ncats.nih.gov/research/research-activities/ctsa/projects/rural-health/wprn

is substantial: in addition to supporting nearly 500 predoctoral and postdoctoral fellows a year, the CTSA awards support more than 400 senior postdoctoral fellows and junior faculty scholars a year and offer protected time for career development in clinical translational team science research.

One example of CTSA-supported training resulting in an entrepreneurial impact involves a potential neonatal opioid withdrawal syndrome (NOWS) therapy. Postdoctoral fellows at the CTSA Translational Research Institute at the University of Arkansas for Medical Sciences (UAMS) identified a deuterated form of buprenorphine thought to alter its metabolism to minimize formation of the harmful metabolite that contributes to NOWS, while still treating opioid-dependence and preventing relapse in the mother.[9] Since then, the postdoctoral fellows formed a company to bring deuterated buprenorphine through the drug development pipeline, and have been successful in several business plan prize competitions.[10]

Looking Forward

NCATS takes pride in its stewardship of the CTSA Program and its many contributions to the biomedical research enterprise across the nation. In 2022 and 2023, Dr. Joni Rutter, NCATS' director, conducted over 20 roundtables with CTSA principal investigators, directors, institutional leadership, enterprise committees, community advisors, trainees, and scholars to engage in discussions about the CTSA Program. These discussions centered on fortifying the CTSAs and collaboratively shaping its future. NCATS was excited to support the CTSA community at the first in-person CTSA meeting in over two years in November 2022, highlighting pivotal opportunities such as innovating community engagement, and leveraging electronic health records, real world data, and AI/ML technologies.

With FY 2025 funding, NCATS plans to renew its program of self-contained research projects that address a general roadblock in clinical or translational science, or operations that limit the efficiency and effectiveness of translation. This program will foster the transition of current CTSA program trainees and career award scholars to mid-career, independent academic translational science investigators.

NCATS continues to engage with the research community for continued improvement of this important national program.

Budget Policy: The FY 2025 President's Budget request for the CTSA Program is $631.5 million, an increase of $1.9 million or 0.3 percent compared to the FY 2023 level.

II. High-Risk, Transformative Efforts for High-Need Cures

Authorized by Congress,[11] the **Cures Acceleration Network (CAN)** aims to advance the development of high-need cures and reduce barriers in the path from research discovery to

[9] pubmed.ncbi.nlm.nih.gov/37229250/
[10] news.uams.edu/2023/05/24/uams-tri-training-program-helps-postdocs-develop-entrepreneurial-spirit-form-competition-winning-pharmaceutical-startup/
[11] ncats.nih.gov/sites/default/files/PHS-act-update.pdf

therapies for patients.[12] NCATS funds projects through CAN to support transformative, paradigm-shifting programs and initiatives. Examples include automated development of new chemical compounds; drug safety and efficacy testing using models of human tissues on a chip ("tissue chips") and complex 3-D functional tissues of living cells and scaffolding materials on microplates (3-D bioprinting); and development of standardized approaches to gene-directed therapies, applied to rare diseases.

The **Tissue Chips for Drug Screening Program** applies 3-D platforms called microphysiological systems (MPS) that use human cells and tissues on microfluidic chips to accurately model the structure and function of human organs, such as the lung, liver, and heart, to better predict the effectiveness and toxicity of potential drugs in humans. In FY 2025, NCATS will continue to pursue a unique opportunity to rapidly model and study age-related diseases under the microgravity of outer space and translate that understanding to improve human health on Earth. The Tissue Chips in Space program,[13] a partnership with the National Aeronautics and Space Administration (NASA), allows scientists to study certain diseases and aging processes which take years to progress on Earth, but only weeks or months to progress when brought into the microgravity of space. NCATS will build upon the successes and lessons learned from the initial Tissue Chips in Space program and significantly advance the utility of tissue chips to model accelerated aging, represent diverse population groups, and drive precision medicine approaches.

Ongoing research activities on MPS will include NCATS' partnership with the United States Food and Drug Administration (FDA) to facilitate the qualification of MPS as drug development tools via the establishment of several Translational Centers of MPS nationwide. Each center will generate specific datasets for several MPS platforms

Bespoke Gene Therapy for Rare Diseases

The NCATS-led Bespoke Gene Therapy Consortium (BGTC), part of the Foundation for the National Institutes of Health (FNIH) Accelerating Medicines Partnership® (AMP®) Program, is a public-private partnership with other NIH ICs, FDA, and FNIH, to foster development of gene therapies intended to treat rare genetic diseases, including diseases too rare to be of commercial interest. NCATS supports the BGTC work in several ways, including scientific leadership by NCATS' Division of Rare Diseases Research Innovation, financial support of the data coordination center through CAN, and research into the basic biology of the adeno-associated virus (AAV), the common gene-delivery vector being used in BGTC, in collaboration with NCATS intramural laboratories.

In May 2023, BGTC announced the selection of the eight rare diseases for its clinical trial portfolio.[1] BGTC will establish platforms and standards to streamline the regulatory approval process by establishing minimum standards for manufacturing, product analytical testing, and pre-clinical testing. These trials will demonstrate that manufacturing and testing standards can provide a streamlined approval pathway for first-in-human clinical trials.

If the trials with these eight rare diseases are successful, these approaches are expected to be applicable for other diseases caused by a single, known gene mutation. Increasing efficiency in gene therapies will help bring cutting-edge health interventions to more patients, advancing the development of needed cures by reducing significant translational barriers.

[1]fnih.org/news/the-foundation-for-the-national-institutes-of-health-announces-selection-of-eight-rare-diseases-for-the-bespoke-gene-therapy-consortium-clinical-trial-portfolio/

[12] ncats.nih.gov/about/advisory-committees/can
[13] ncats.nih.gov/research/research-activities/tissue-chip/projects/space

for qualification of MPS as drug development tools and regulatory acceptance by the FDA. The goal for this activity is the rapid commercialization and widespread use of MPS by the biomedical research community as complementary or replacement approaches to animal studies that could be part of the regulatory process.

The process of creating new chemical compounds that may one day become a treatment for diseases has historically been a slow, non-automated process. To increase the likelihood of developing treatments which may treat diseases, and to create additional variations of effective chemical compounds more quickly, NCATS aims to change the paradigm of drug discovery and development and make it more data driven through **A Specialized Platform for Innovative Research Exploration (ASPIRE)**. The greater scientific community helped identify specific areas that, if addressed, would transform the drug development process, including advancing synthetic chemistry to be more of an information-based science; remedying lack of data standardization in chemical databases; and addressing limitations of current biological assays used to identify and validate promising drug candidates. Historically, optimizing drug synthesis and testing has been a laborious, largely artisanal, and isolated process, focused on the individual experiment with limited ways to use big data or automated approaches to learn from previous experiments. In the multi-year NCATS 2020 ASPIRE Reduction-to-Practice Challenge, funded through the NIH Helping to End Addiction Long-Term (HEAL) Initiative®, collaborative teams integrated a chemistry database, electronic synthetic chemistry portal, predictive algorithms, and biological assays into a working platform that will provide greater access to tools that can catalyze the discovery and development of novel, safe, and effective treatments for pain, opioid use disorder, and overdose. The grand prize was awarded in October 2022 to a scientific team that used an AI/ML automation platform for drug discovery.[14] In parallel to the challenge, NCATS is supporting multiple scientific teams who are working with the NCATS ASPIRE Laboratory to develop an intramural ASPIRE platform that will incorporate physical and computational modules, incorporating AI and quantum-enabled approaches to automate chemical synthesis and biological testing systems. The NCATS ASPIRE Program is also using additional funding mechanisms such as Small Business Innovation Research (SBIR) contracts to spur innovation in the area of automated synthetic chemistry and drug discovery. The ultimate goal of the NCATS ASPIRE program is to allow rapid and cost-effective drug discovery and fulfill the development and the promise of safe and effective treatments and cures across a wide spectrum of diseases.

Budget Policy: The FY 2025 President's Budget request for the Cures Acceleration Network is $66.2 million, an increase of $0.2 million or 0.3 percent compared to the FY 2023 level.

III. Reengineering Translational Science for More Therapies to Reach All Patients

Accelerating Therapeutics Development by Solving Translational Challenges

Several NCATS projects and initiatives address challenges in the therapeutics development pipeline to accelerate therapeutic development and delivery. NCATS' innovations range from harnessing human cell-based solutions for testing drug toxicity and efficacy, repurposing approved drugs for use as therapies for other diseases, capitalizing on the growing field of data

[14] ncats.nih.gov/funding/challenges/winners/aspire-2020#c1

science approaches for clinical discovery, and fostering the development of the next generation of translational scientists.

One strategy for bringing more treatments to all people is to use already-approved drugs in new ways. **Drug repurposing** can shorten the time it takes for drug evaluation and approval, as safety and efficacy profiles already exist for these drugs. One example of this comes from the efforts of a collaborative research team of scientists from Duke University, the University of Florida, and NCATS. The team showed that an existing antiviral drug approved for use against HIV infection called ritonavir may prove helpful in treating DYT1, the most common inherited form of dystonia, a group of rare, potentially disabling muscle disorders characterized by abnormal, involuntary movements with few treatments and no cure.[15] To find a potential treatment, NCATS translational scientists first assessed the effectiveness of the nearly 3,000 FDA–approved drugs in the NCATS Pharmaceutical Collection.[16] They did this by developing an assay to test the ability of drugs to correct the protein defect, and, using high-throughput screening, rapidly identified 18 promising drugs. Further experiments demonstrated that ritonavir could correct the brain abnormalities seen in DYT1. The promising results, seen both in cell-based tests and in an animal model of the disease, show this drug is well-positioned for planned further development as a potential therapy for dystonia.[17]

Forging Strategic Alliances and Supporting Small Businesses

Establishing research agreements is critical to collaborative research, as demonstrated through the clinical trials conducted through CTSA hubs (such as the Accelerating COVID-19 Therapeutic Interventions and Vaccines, or ACTIV, trials), the National COVID Cohort Collaborative (N3C), and intramural partnerships with academia and industry. In FY 2023 alone, NCATS facilitated over 300 agreements to support these and many other projects.

The NCATS Office of Strategic Alliances supports execution of these agreements, as well as further advancement of high priority NCATS goals through small business program funding. One scientific team supported by a Small Business Innovation Research (SBIR) grant from NCATS created a tiny, bioengineered 3-D model that mimics the biology of two rare, devastating neuromuscular diseases — chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy.[18] The researchers used an organ-on-a-chip, or "tissue chip," model of these diseases to generate key preclinical data used in an FDA Investigational New Drug application. The resulting authorization enabled testing of a candidate drug in a Phase 2 clinical trial. This study may open the door to studying and developing new candidate therapies for other rare diseases by establishing a new avenue for testing new and existing drugs for rare diseases.

Recently, a partnership between an NCATS SBIR grantee and one of NCATS' CTSA Program institutions led to the creation of Natural Language Processing (NLP) software called the

[15] pubmed.ncbi.nlm.nih.gov/34408078/
[16] ncats.nih.gov/research/research-resources/preclinical-research-toolbox/npc
[17] ncats.nih.gov/news-events/news/drug-repurposing-approaches-reveal-HIV-drug-holds-promise-against-a-rare-disabling-muscle-disorder
[18] ncats.nih.gov/news-events/news/2022/researchers-create-3-D-model-for-rare-neuromuscular-disorders-setting-stage-for-clinical-trial

Clinical Language Annotation, Modeling, and Processing, or CLAMP, toolkit.[19] The CLAMP modular system has a workbench-style interface that can be used both by data scientists and researchers who do not explicitly focus on data science, and can take the non-standardized, hard-to-analyze descriptions found in patient health records, reports, and scientific literature, to search, identify, and organize these descriptions into standardized information. CLAMP then led to the development of Meric NLP, a cloud-based version of CLAMP, with the purpose of helping to improve healthcare research through text extraction and standardization.

NCATS is also supporting technologies for improving minority health and eliminating health disparities, as demonstrated by participation in a small business funding opportunity with several other NIH ICs.[20] In addition, NCATS is planning a program to address health inequities in clinical diagnostics for FY 2025.

NCATS is also committed to outreach to a diverse small business workforce. For example, the NCATS small business program is engaged in entrepreneurship training and outreach focused on diversity, including hosting an outreach webinar event where speakers from NCATS and NHLBI talked about the SBIR and Small Business Technology Transfer (STTR) funding programs. [21] They were joined by leaders of multiple programs to help prepare and support researchers looking to commercialize their innovations, including programs specially designed for researchers from Historically Black Colleges and Universities, Hispanic-Serving Institutions, and women-owned businesses. The event had 160 registrants from 34 states and territories (including 8 Institutional Development Award [IDeA] states) and 42 percent of the registrants were from women-owned businesses. Reaching a broad representation of scientist-entrepreneurs is critical for bridging disparity gaps in technology.

Inspiring the Next Generation of Translational Scientists

In addition to supporting training and career awards through the CTSA Program, NCATS develops and disseminates evidence-informed resources and approaches to educate and train the translational science workforce. Examples include:

- Translational Science Interagency Fellowships (TSIF):[22] The TSIF program is a joint three-year postdoctoral fellowship opportunity where fellows receive training from a mentoring team consisting of NCATS and FDA scientists in preclinical translational science, therapeutic technology development, and regulatory research and review. Fellows exit with skills that enable them to navigate translational science whether in academia, the pharmaceutical industry, or government.
- Gaining Research Equity and Advancement in Translational Sciences (G.R.E.A.T.S):[23] This program provides an avenue for a diverse, underrepresented pool of applicants to enter the translational science workforce through summer internships at NCATS' Division of Preclinical Innovation research laboratories. G.R.E.A.T.S. interns have been

[19] ncats.nih.gov/news-events/news/artificial-intelligence-is-advancing-clinical-research-and-data-quality
[20] grants.nih.gov/grants/guide/rfa-files/RFA-MD-23-002.html
[21] ncats.nih.gov/funding/small-business-program/about-funding
[22] ncats.nih.gov/research/training-education/training-at-ncats/TSIF
[23] ncats.nih.gov/research/training-education/training-at-ncats/training-opportunities#GREATS

co-authors on research publications[24] and been featured in a blog of the NIH Intramural Research Program weekly newsletter.[25]

- Bringing Access to NCATS' Translational Science Knowledge to the Scientific Workforce: Since 2020, NCATS has taught a highly innovative fully online short course in preclinical translational science, moving it to an open access platform in 2023 to ensure the broadest possible reach. The course uses case study teaching approaches and focuses on transmitting principles and practices for effective preclinical translational science typically only learned through postdoctoral training and professional activities. Over 250 students have participated in this course, from early career through senior career, and with a range of backgrounds, including in preclinical research, clinical research, science administration, and patient engagement in research.

Budget Policy: The FY 2025 President's Budget request for Reengineering Translational Sciences is $172.5 million, an increase of $0.5 million or 0.3 percent compared to the FY 2023 level.

IV. Harnessing Translational Science Strategies for Rare Diseases Research and Therapies

Rare diseases, defined as conditions affecting fewer than 200,000 people in the United States, are a significant health problem that is underserved and underestimated. Over 10,000 different rare diseases collectively[26] affect an estimated 30 million people in the United States (or one in 10 people — about the same number as those living with diabetes), and 95 percent of rare diseases have no approved treatment. Additionally, the economic burden of rare diseases is serious, resulting in over $1 trillion in total health care costs, disability, and early death.[27]

The impact of rare diseases on patients is significant, underscoring the need for continued innovations in rare diseases research. Greater access to early genetic/genomic testing and investments in rare diseases research networks, diagnostic strategies, precision gene-directed therapies, as well as strategies that can quickly redirect to address another disease, could meaningfully advance research and therapeutics development to help those affected by these disorders. NCATS invests in efforts designed to either create platforms that can address multiple diseases at once or develop an intervention for one disease that can be readily adapted to apply to other diseases. NCATS utilizes both its intramural and extramural programs, and its Division of Rare Diseases Research Innovation (DRDRI) works collaboratively with NIH Institutes, Centers, and Offices, to address and support research on rare diseases, as well as providing leadership, direction, and coordination for rare diseases research at NIH.

[24] pubmed.ncbi.nlm.nih.gov/36049119/
[25] irp.nih.gov/blog/post/2023/08/scouting-out-summer-poster-day
[26] pubmed.ncbi.nlm.nih.gov/32020066
[27] healthaffairs.org/content/forefront/economic-burden-rare-diseases-quantifying-sizeable-collective-burden-and-offering

Raising Awareness and Knowledge about Rare Diseases

As part of the global observance of Rare Disease Day® in February every year, NCATS organizes Rare Disease Day at NIH, cosponsored with the NIH Clinical Center, to raise awareness about rare diseases, the people they affect, and the NIH collaborations that address the scientific challenges. On February 28, 2023, Rare Disease Day at NIH was held in person for the first time since 2020, with sessions highlighting rare diseases programs and resources; the needs of adolescent and young adult rare diseases patients; diversity, equity, inclusion, and accessibility (DEIA) as related to genetics and gene-targeted therapies; and the role of advocacy and industry partnerships in developing treatments for rare diseases. The event spotlighted the points of view of the rare disease community and emphasized the need to foster DEIA in rare diseases research. The day culminated with an unexpected and emotional announcement by Ronald J. Bartek, co-founder and president of Friedreich's Ataxia Research Alliance and a past co-chair of NCATS' Cures Acceleration Network Review Board, that the FDA had approved the first drug for Friedreich's ataxia, a rare disorder that affects the nervous system (Figure 1). The news marked a great moment for the rare diseases community and underscored the importance of continuing to work together to turn hope into action for more rare diseases.

Figure 1. NCATS Program Officer Eric Sid congratulates Ron Bartek on the announcement that U.S. FDA approved the first drug for Friedreich's ataxia.
Photo credit: NCATS

Another way NCATS provides the public with health information and knowledge of rare diseases is the **Genetics and Rare Diseases (GARD) Information Center,**[28] which provides clear, accessible information for patients, families, caregivers, and the public on rare diseases. NCATS will continue the modernization of the GARD website to provide updated information about rare diseases, their symptoms and causes, and patient organizations in a more user-friendly way, as well as explaining the knowledge from large data sources developed for clinicians and scientists so that it is easy for visitors to use and understand. One of NIH's most frequently visited public websites with over a million unique visitors each month, GARD also provides contact information for support and advocacy groups, as well as a free inquiry service for people seeking additional information.

Driving Innovations in Rare Diseases Research

The Rare Diseases Clinical Research Network (RDCRN) is a cross-NIH program of 20 clinical research consortia that promotes highly collaborative, multi-site, patient-centric, translational and clinical research to advance the diagnosis, management, and treatment of rare diseases.[29, 30] Working as a network, multidisciplinary teams of researchers located at 273 sites across the United States and internationally share research tools and resources to study over 200 rare diseases in partnership with patients, patient advocates, and the NIH. RDCRN research aims to reduce the risk of failure of treatments in clinical trials by emphasizing clinical trial readiness; identifying biomarkers for predicting disease diagnosis, prognosis, and outcome; and developing sensitive and specific outcome measures. In FY 2025, the RDCRN Program will be renewed,

[28] rarediseases.info.nih.gov/
[29] ncats.nih.gov/research/research-activities/RDCRN
[30] rdcrn.org/

beginning the program's fifth funding cycle. NCATS will continue directly supporting RDCRN data coordination, including the establishment of an RDCRN data warehouse to provide data from network activities to the rare diseases research community. NCATS will also provide support in collaboration with other NIH Institutes and Centers to specific RDCRN research consortia. NCATS hopes to build bridges between major research networks, such as the RDCRN, and academic medical centers that provide clinical care, such as CTSA institutions, to further the collaboration and sharing of rare diseases expertise, tools, and resources.

NCATS leads highly collaborative efforts for developing, testing, and delivering gene-directed therapy platforms for rare disease treatment needs. NCATS seeks to demystify the gene therapy development process through several efforts. The **Platform Vector Gene Therapy (PaVe-GT)** program was launched by NCATS in FY 2019 to improve the efficiency of clinical trial startup by using the same gene delivery system and manufacturing methods for multiple rare disease gene therapies.[31] PaVe-GT is starting with a pilot project focused on two inherited muscle weakness/neuromuscular junction disorders and two inherited metabolic diseases. PaVe-GT is a public model of how to plan and conduct a clinical trial for gene therapies for these rare diseases, and researchers are making their project results and documents publicly available so they can be used to benefit subsequent gene therapy efforts that use the same vector. PaVe-GT's key accomplishments thus far include receiving two regulatory approvals which will incentivize bringing rare disease treatments to market: an orphan drug designation for investigational gene therapy, and the regulatory designation of one of the pilot program diseases as a rare pediatric disease.[32] This work informs roadmaps for how to get preclinical data necessary to move a gene therapy program forward.

PaVE-GT efforts have also inspired further engagement across NIH, FDA, and beyond, resulting in the Bespoke Gene Therapy Consortium, an Accelerating Medicines Partnership initiative co-led by NCATS (see Program Portrait above).

Gene-targeted therapies such as gene therapy and gene editing are therapeutic platforms that, in principle, are applicable to thousands of rare diseases (specifically monogenic diseases, which are caused by the inheritance of single gene mutations). For these cutting-edge treatments to achieve their potential, NCATS realizes the importance of involving multiple public perspectives. In March 2023, a special issue of the American Journal of Medical Genetics, Gene-Targeted Therapies: Early Diagnosis and Equitable Delivery,[33] published nine commentaries from the June 2021 workshop, "Gene-Targeted Therapies: Early Diagnosis and Equitable Delivery." The meeting and the resulting papers called attention to the challenges being faced as these therapeutic platforms move from the research environment to a public health environment, and identified ways to ensure early diagnosis of diseases and the equitable delivery of gene-targeted therapies.

Improving Therapeutic Development for Rare Diseases

NCATS is continuing to support research that will improve therapeutic development for

[31] pave-gt.ncats.nih.gov

[32] ncats.nih.gov/news-events/news/2023/NIH-Gene-Therapy-Team-Reveals-Its-Path-to-FDA-Orphan-Drug-and-Rare-Pediatric-Disease-Designations

[33] onlinelibrary.wiley.com/toc/15524876/2023/193/1

rare diseases through both its intramural activities and through extramural funding opportunities available to organizations across the United States. In a recently released initiative, NCATS is jumpstarting basic biochemical and biological research to better understand and characterize the role of understudied proteins in rare diseases, with the goals of generating preliminary data to promote broader investigation of understudied proteins in the context of rare disease and encouraging the development of novel candidate rare disease therapies.[34] To bridge the gap between early preclinical development activities and initiation of Investigational New Drug (IND) enabling studies, and to spur therapeutic development for rare diseases, another NCATS funding opportunity aims to support efficacy studies in established and validated rare disease preclinical models of meritorious agents of interest to demonstrate that a proposed therapeutic agent warrants further development.[35]

Budget Policy: The FY 2025 President's Budget request for Harnessing Translational Science Strategies for Rare Diseases Research and Therapies is $55.9 million, an increase of $0.2 million or 0.3 percent compared to the FY 2023 level.

Summary

NCATS is making progress in delivering more treatments, for all people, more quickly, and in pivoting to meet critical and unmet public health needs. There is, however, much more to do to speed the translation of scientific discovery into advancements that improve human health. Particularly for the 30 million Americans affected by rare diseases, continued investments in translational science research activities and a diverse translational science research workforce provide hope for the future.

[34] grants.nih.gov/grants/guide/rfa-files/RFA-TR-22-030.html
[35] grants.nih.gov/grants/guide/rfa-files/RFA-TR-23-016.html

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2016	$660,131,000	$643,111,000	$699,319,000	$685,417,000
Rescission				$0
2017 [1]	$685,417,000	$707,335,000	$713,849,000	$705,903,000
Rescission				$0
2018	$557,373,000	$718,867,000	$729,094,000	$742,354,000
Rescission				$0
2019	$685,087,000	$751,219,000	$806,787,000	$806,373,000
Rescission				$0
2020	$694,112,000	$845,783,000	$849,159,000	$832,888,000
Rescission				$0
Supplemental				$36,000,000
2021	$787,703,000	$840,051,000	$890,009,000	$855,421,000
Rescission				$0
2022	$878,957,000	$897,812,000	$878,072,000	$882,265,000
Rescission				$0
2023	$873,654,000	$901,678,000	$907,756,000	$923,323,000
Rescission				$0
2024	$923,323,000	$923,323,000	$923,323,000	$923,323,000
Rescission				$0
2025	$926,086,000			

[1] Budget Estimate to Congress includes mandatory financing.

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2024 Amount Authorized	FY 2024 CR	2025 Amount Authorized	FY 2025 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$923,323,000	Indefinite	$926,086,000
National Center for Advancing Translational Sciences	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$923,323,000		$926,086,000

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences

Amounts Available for Obligation [1]

(Dollars in Thousands)

Source of Funding	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Appropriation	$923,323	$923,323	$926,086
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*($0)*	*($0)*	*($0)*
Other Mandatory financing	*($0)*	*($0)*	*($0)*
Subtotal, adjusted appropriation	$923,323	$923,323	$926,086
OAR HIV/AIDS Transfers	$0	$0	$0
Subtotal, adjusted budget authority	$923,323	$923,323	$926,086
Unobligated balance, start of year	$0	$0	$0
Unobligated balance, end of year (carryover)	$0	$0	$0
Subtotal, adjusted budget authority	**$923,323**	**$923,323**	**$926,086**
Unobligated balance lapsing	-$22	$0	$0
Total obligations	$923,301	$923,323	$926,086

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account: FY 2023 - $62,863
FY 2024 - $37,655 FY 2025 - $37,655

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Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2024 CR	FY 2025 President's Budget
Total compensable workyears:			
	Full-time equivalent	298	319
	Full-time equivalent of overtime and holiday hours	0	0
	Average ES salary	$216	$221
	Average GM/GS grade	13.5	13.7
	Average GM/GS salary	$141	$144
	Average salary, Commissioned Corps (42 U.S.C. 207)	$143	$146
	Average salary of ungraded positions	$209	$213
	OBJECT CLASSES	**FY 2024 CR**	**FY 2025 President's Budget**
	Personnel Compensation		
11.1	Full-Time Permanent	$23,625	$25,715
11.3	Other Than Full-Time Permanent	$14,211	$15,851
11.5	Other Personnel Compensation	$1,900	$2,001
11.7	Military Personnel	$549	$574
11.8	Special Personnel Services Payments	$4,485	$4,610
11.9	**Subtotal Personnel Compensation**	**$44,768**	**$48,752**
12.1	Civilian Personnel Benefits	$15,093	$16,634
12.2	Military Personnel Benefits	$153	$160
13.0	Benefits to Former Personnel	$0	$0
	Subtotal Pay Costs	**$60,015**	**$65,546**
21.0	Travel & Transportation of Persons	$594	$607
22.0	Transportation of Things	$77	$78
23.1	Rental Payments to GSA	$0	$0
23.2	Rental Payments to Others	$0	$0
23.3	Communications, Utilities & Misc. Charges	$45	$46
24.0	Printing & Reproduction	$0	$0
25.1	Consulting Services	$14,992	$15,361
25.2	Other Services	$107,882	$94,331
25.3	Purchase of Goods and Services from Government Accounts	$61,139	$62,334
25.4	Operation & Maintenance of Facilities	$505	$505
25.5	R&D Contracts	$3,053	$3,120
25.6	Medical Care	$1,379	$1,433
25.7	Operation & Maintenance of Equipment	$17,074	$17,444
25.8	Subsistence & Support of Persons	$0	$0
25.0	**Subtotal Other Contractual Services**	**$206,024**	**$194,528**
26.0	Supplies & Materials	$8,534	$8,722
31.0	Equipment	$4,184	$4,276
32.0	Land and Structures	$3,806	$0
33.0	Investments & Loans	$0	$0
41.0	Grants, Subsidies & Contributions	$640,033	$652,271
42.0	Insurance Claims & Indemnities	$0	$0
43.0	Interest & Dividends	$12	$12
44.0	Refunds	$0	$0
	Subtotal Non-Pay Costs	**$863,308**	**$860,540**
	Total Budget Authority by Object Class	**$923,323**	**$926,086**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

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Salaries and Expenses
(Dollars in Thousands)

Object Classes	FY 2024 CR	FY 2025 President's Budget
Personnel Compensation		
Full-Time Permanent (11.1)	$23,625	$25,715
Other Than Full-Time Permanent (11.3)	$14,211	$15,851
Other Personnel Compensation (11.5)	$1,900	$2,001
Military Personnel (11.7)	$549	$574
Special Personnel Services Payments (11.8)	$4,485	$4,610
Subtotal, Personnel Compensation (11.9)	**$44,768**	**$48,752**
Civilian Personnel Benefits (12.1)	$15,093	$16,634
Military Personnel Benefits (12.2)	$153	$160
Benefits to Former Personnel (13.0)	$0	$0
Subtotal Pay Costs	**$60,015**	**$65,546**
Travel & Transportation of Persons (21.0)	$594	$607
Transportation of Things (22.0)	$77	$78
Rental Payments to Others (23.2)	$0	$0
Communications, Utilities & Misc. Charges (23.3)	$45	$46
Printing & Reproduction (24.0)	$0	$0
Other Contractual Services		
Consultant Services (25.1)	$5,709	$5,874
Other Services (25.2)	$107,882	$94,331
Purchase of Goods and Services from Government Accounts (25.3)	$36,275	$37,361
Operation & Maintenance of Facilities (25.4)	$505	$505
Operation & Maintenance of Equipment (25.7)	$17,074	$17,444
Subsistence & Support of Persons (25.8)	$0	$0
Subtotal Other Contractual Services	**$167,445**	**$155,516**
Supplies & Materials (26.0)	$8,534	$8,722
Subtotal Non-Pay Costs	**$176,694**	**$164,969**
Total Administrative Costs	**$236,709**	**$230,514**

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Detail of Full-Time Equivalent Employment (FTE)

Office	FY 2023 Final			FY 2024 CR			FY 2025 President's		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director									
Direct:	8	-	8	10	-	10	11	-	11
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	8	-	8	10	-	10	11	-	11
Office of Administrative									
Direct:	51	-	51	52	-	52	54	-	54
Total:	51	-	51	52	-	52	54	-	54
Division of Extramural Activties									
Direct:	30	-	30	34	-	34	36	-	36
Total:	30	-	30	34	-	34	36	-	36
Division of Rare Diseases Research									
Direct:	8	-	8	10	-	10	10	-	10
Total:	8	-	8	10	-	10	10	-	10
Office of Policy, Communications,									
Direct:	15	-	15	17	-	17	18	-	18
Total:	15	-	15	17	-	17	18	-	18
Office of Strategic Alliances									
Direct:	8	-	8	9	-	9	10	-	10
Total:	8	-	8	9	-	9	10	-	10
Office of Special Initiatives									
Direct:	5	-	5	5	-	5	5	-	5
Reimbursable:	2	-	2	2	-	2	2	-	2
Total:	7	-	7	7	-	7	7	-	7
Office of Drug Development									
Direct:	3	-	3	3	-	3	3	-	3
Reimbursable:	2	-	2	2	-	2	2	-	2
Total:	5	-	5	5	-	5	5	-	5
Office of Translational Medicine									
Direct:	3	-	3	3	-	3	4	-	4
Total:	3	-	3	3	-	3	4	-	4
Division of Pre-Clinical Innovation									
Direct:	80	2	82	98	2	100	109	2	111
Reimbursable:	20	-	20	10	-	10	10	-	10
Total:	100	2	102	108	2	110	119	2	121
Division of Clinical Innovation									
Direct:	34	1	35	34	1	35	36	1	37
Total:	34	1	35	34	1	35	36	1	37
Office of Grants Management and Scientific Review									
Reimbursable:	6	-	6	6	-	6	6	-	6
Total:	6	-	6	6	-	6	6	-	6
Total	275	3	278	295	3	298	316	3	319
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2021	13.2
2022	13.2
2023	13.2
2024	13.5
2025	13.7

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Detail of Positions[1]

GRADE	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	$212,100	$216,342	$220,668
General Schedule			
GM/GS-15	32	34	36
GM/GS-14	57	59	61
GM/GS-13	77	79	81
GS-12	17	19	21
GS-11	9	11	13
GS-10	0	0	0
GS-9	1	2	4
GS-8	0	0	0
GS-7	4	6	8
GS-6	0	0	0
GS-5	1	2	4
GS-4	1	2	4
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	199	214	232
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	1	1	1
Senior Grade	2	2	2
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Junior Assistant	0	0	0
Subtotal	3	3	3
Ungraded	87	89	91
Total permanent positions	203	205	207
Total positions, end of year	290	307	327
Total full-time equivalent (FTE) employment, end of year	278	298	319
Average ES salary	$212,100	$216,342	$220,668
Average GM/GS grade	13.2	13.5	13.7
Average GM/GS salary	$138,050	$140,811	$143,627

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.