NCATS

COLLABORATE. INNOVATE. ACCELERATE.

Where Science Goes to Become Health: NCATS Mission, Vision, & Goals

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Director

National Center for Advancing Translational Sciences (NCATS)

Research!America Alliance Discussion
October 15, 2024

The Public Health Challenge

10,000

Diseases

and only

5%

Have Treatments or Cures

Time from early development to the medicine cabinet takes 10-15 years.

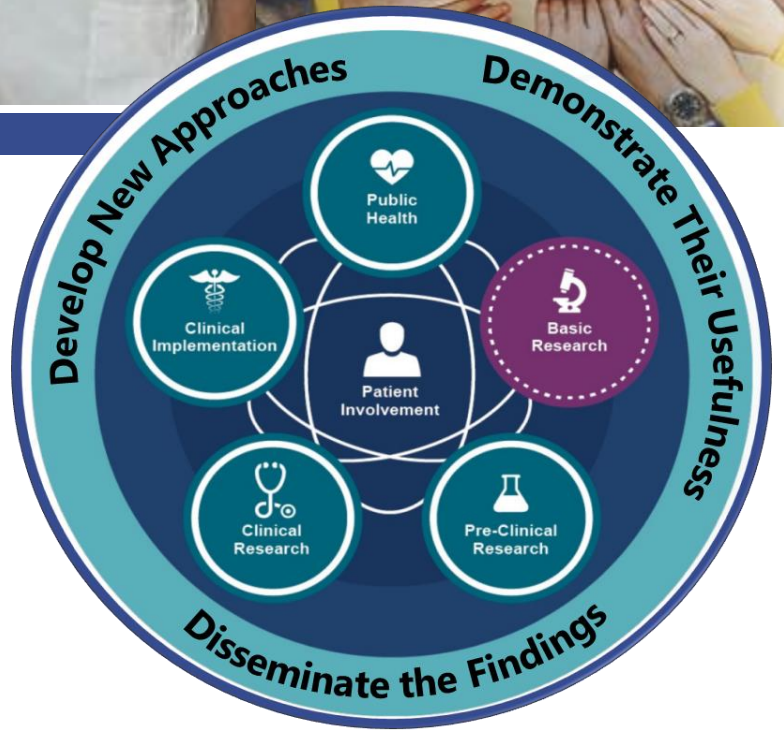
9 **out of** **10**

Promising therapeutic candidates that enter clinical trials fail.

NIH National Center for Advancing Translational Sciences

NCATS' Mission

Turn research observations into health solutions through translational science



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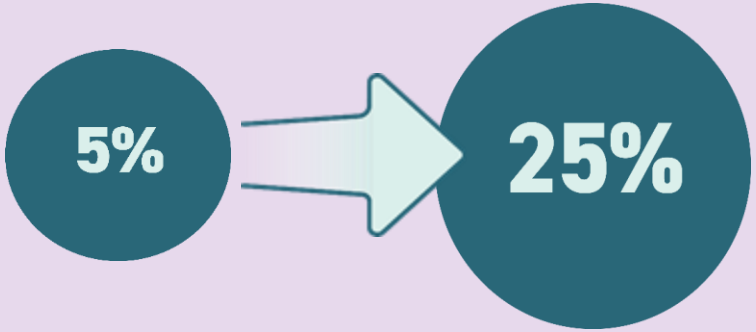
NCATS Vision: Three Audacious Goals

More Treatments



Five-Fold Increase in Number of Diseases with Treatments

All People

Dramatically Increase Inclusivity Across Every Area We Support

More Quickly

Enable Diagnostics and Therapeutics to Reach People Twice as Fast

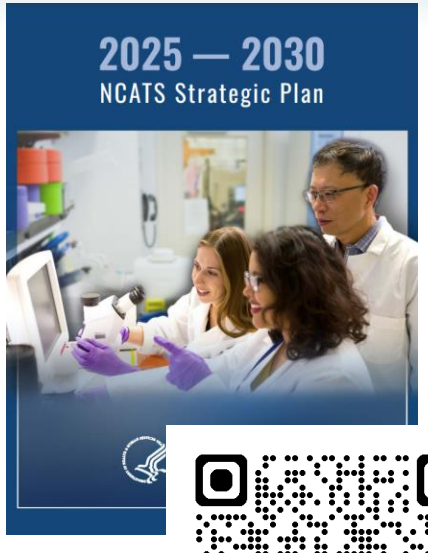
NCATS Strategic Plan for 2025-2030

1,700+ unique comments

1,150+ individuals engaged

44+ formal meetings

70+ written responses



Read the Strategic Plan here

Turning Vision into Action

Goal 1

Advance Development of and Access to More Treatments, Particularly for Diseases With Unmet Needs

Goal 2

Empower Everyone to Contribute to and Benefit From Translational Science

Goal 3

Accelerate Translational Science by Breaking Barriers and Boosting Efficiency

Goal 4

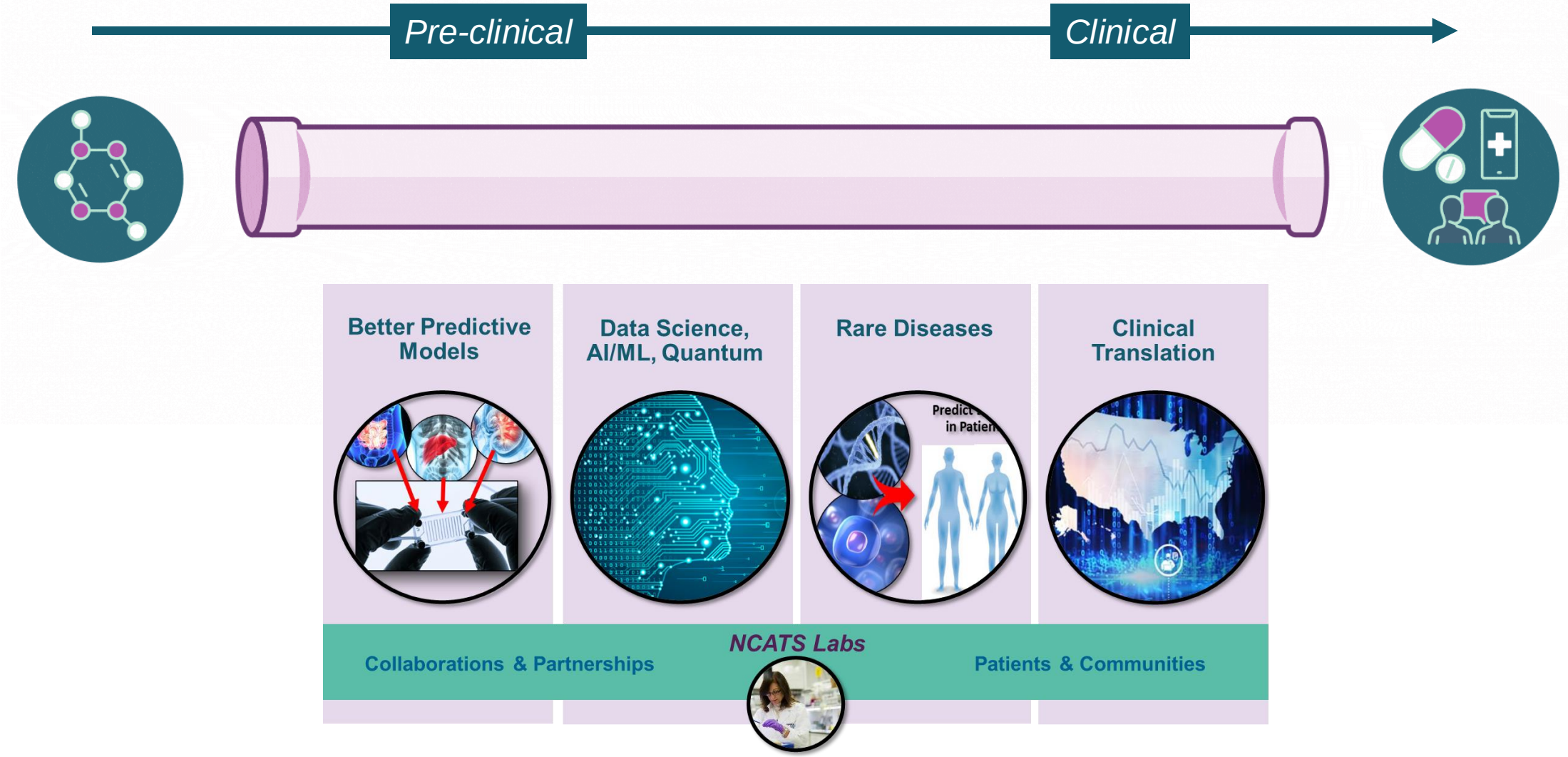
Leverage Crosscutting Strategies to Enhance Translational Science

Goal 5

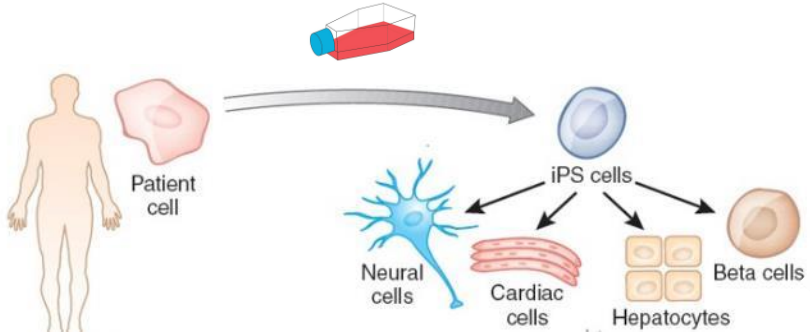
Champion Effective Stewardship of Translational Science Through Transparency, Integrity, Accountability, and Social Responsibility

NCATS is Re-engineering the Translational Pipeline

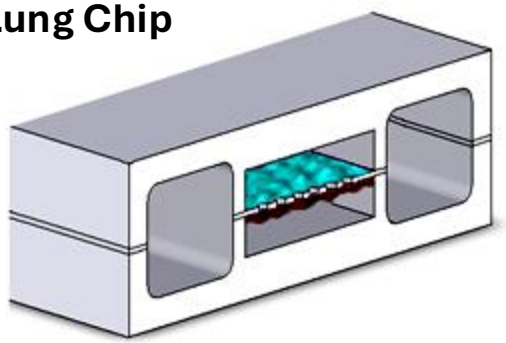
NCATS is advancing translational science by addressing long-standing scientific and operational bottlenecks in the translational pipeline so that new treatments reach people faster.

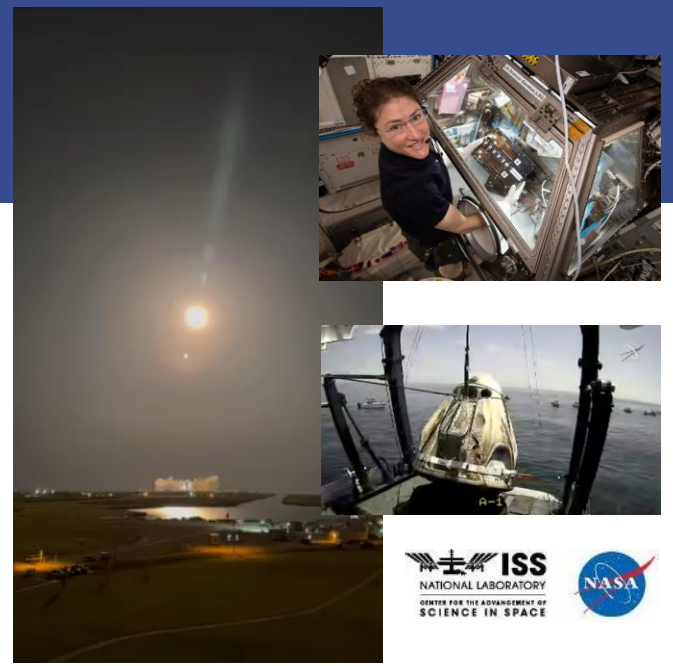


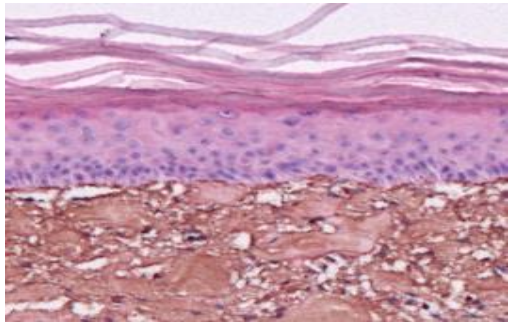
Better Predictive Models



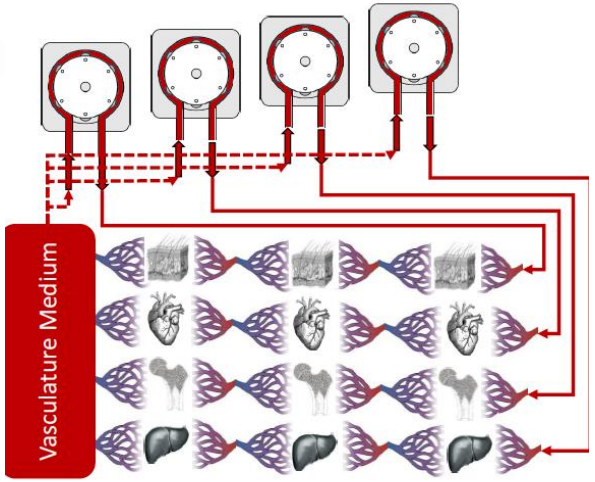
Lung Chip



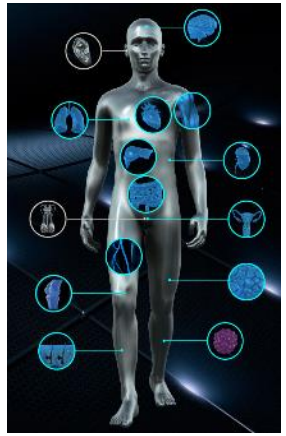




3D Bioprinted Skin Tissue



Multi-Organ Chip



Precision Medicine You-On-A-Chip

- Identify & test biomarkers
- Reduce trial risk
- Hone patient selection
- Explain variable treatment response

Courtesy of Marc Ferrer, NCATS, Dan Tagle, NCATS, and Gordana Vunjak-Novakovic, Columbia

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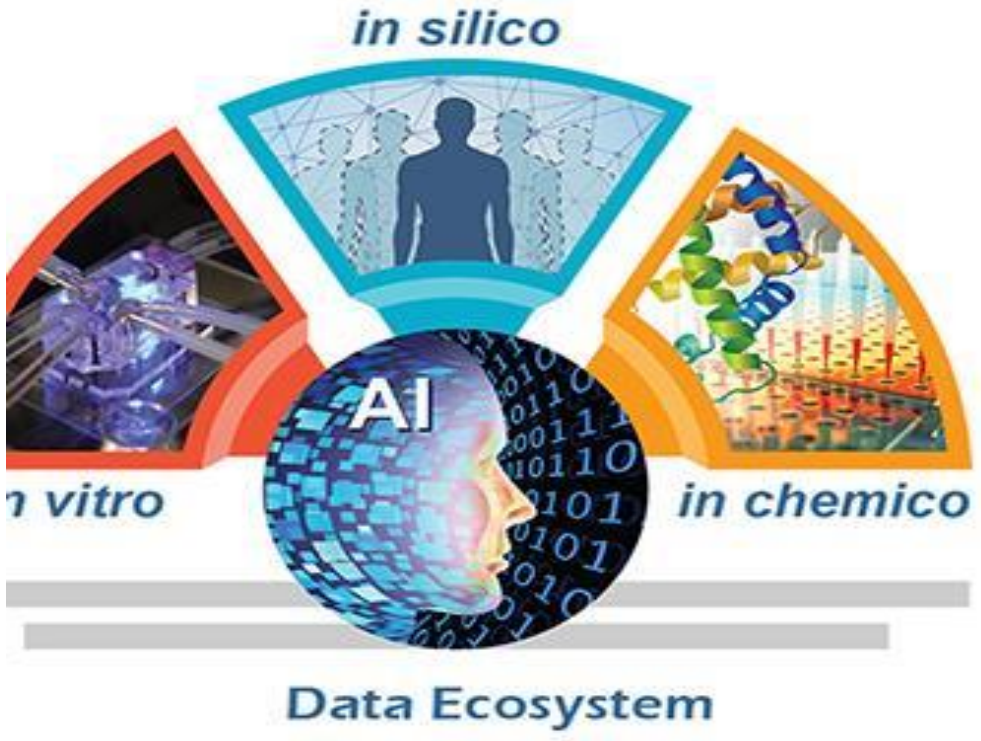
New Approach Methodologies (NAMs)

The Common Fund

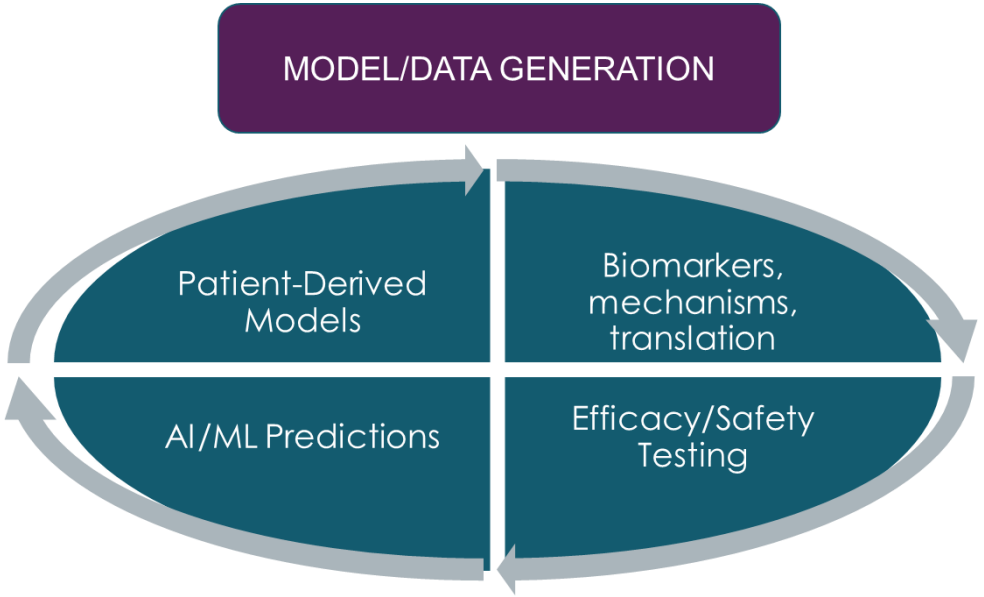
Complement Animal Research In Experimentation (Complement-ARIE)

Speeding the development, standardization, validation, and use of human-based NAMs

- Technology development projects/centers
- Data & NAM resource coordinating center
- Validation network for regulatory implementation
- Community engagement and training
- Strategic engagement

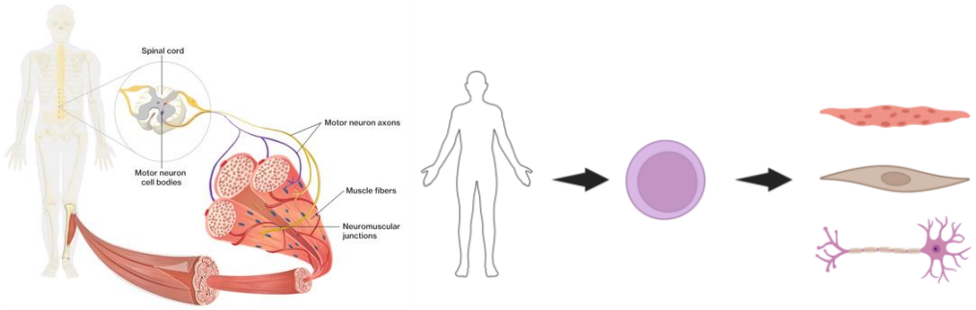


i3D-RARE: A precision medicine platform of stem cell-derived 3D cellular models to accelerate the development of therapeutics for rare diseases

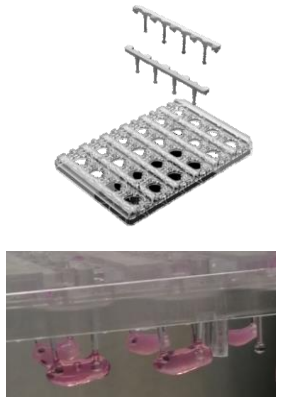


https://www.youtube.com/watch?v=T6J9ox8pCCA

Biofabricated neuromuscular junction tissue models for congenital myasthenic syndromes



CRISPR-edited iPSCs from NHLBI



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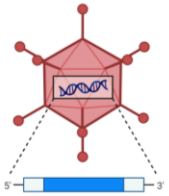
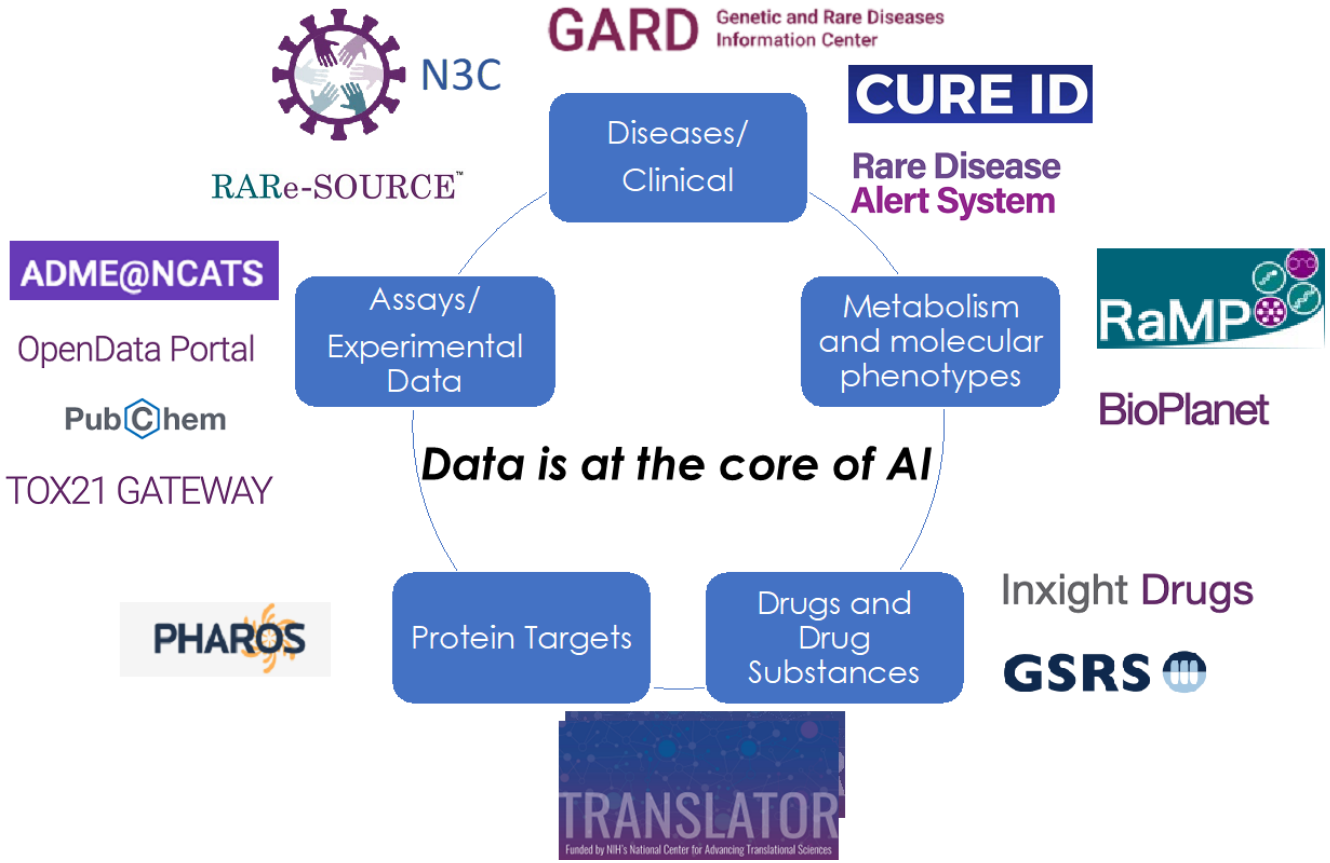


Functional Readouts

NINDS and NCATS

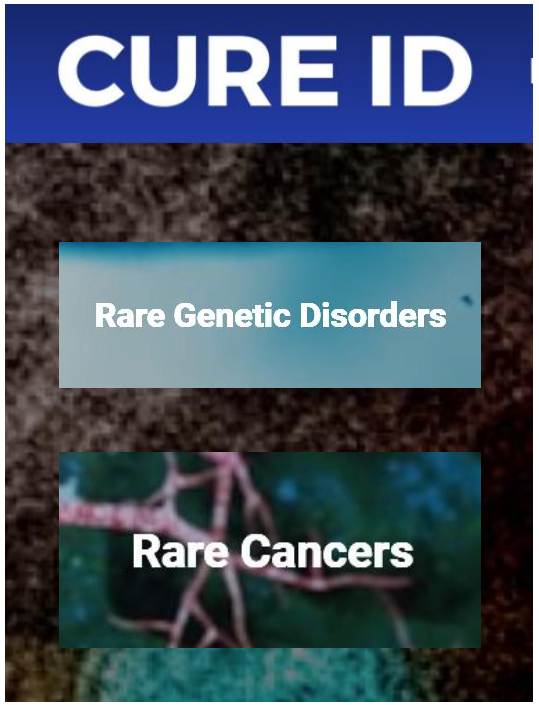
Applying Data Science to Speed Translation

- Predict EffectiveTreatments
- Improve Diagnosis
- Generate New Hypotheses
- Enhance Treatment Discovery
- Match Patients to Right Treatment
- Systems Viewpoint to advance at a more than one disease at a time pace

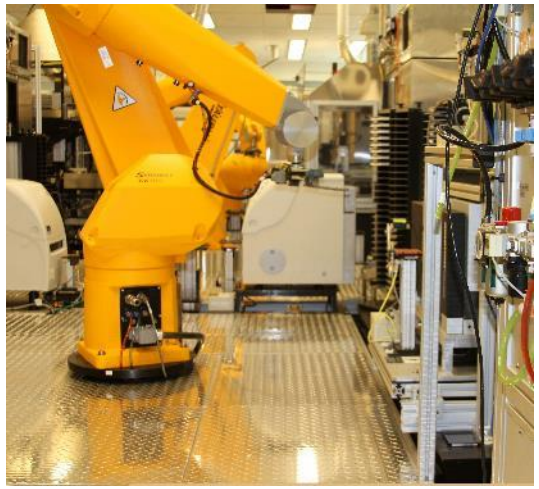


Drug Repurposing Strategies for Rare Diseases

Clinical Observation & Crowdsourcing

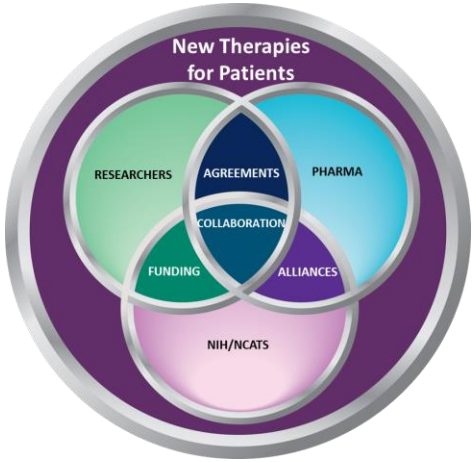


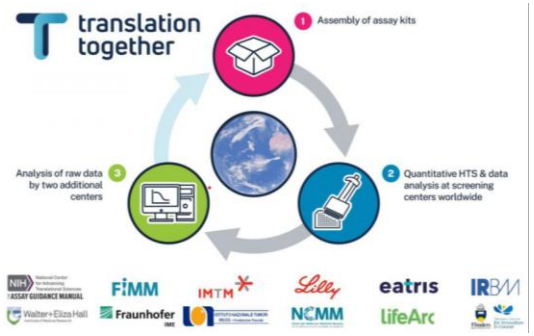
Molecular/Cellular Screening



>370,000 compounds in NCATS Libraries (3,000 FDA-approved)

Partnerships





Computationally Assisted Identification

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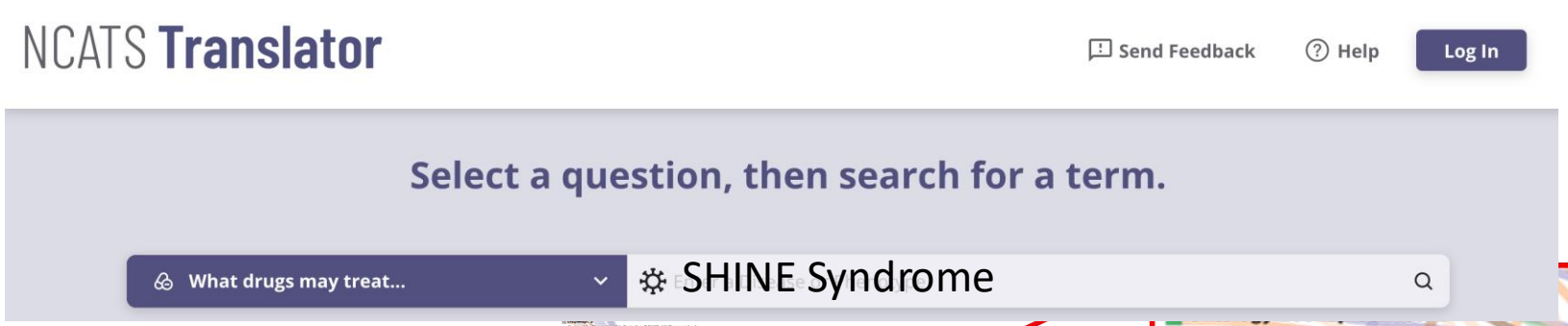
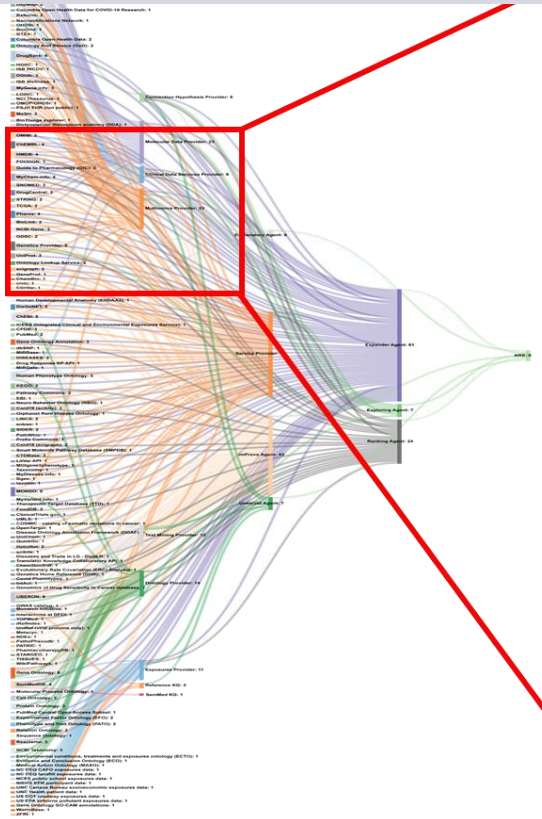
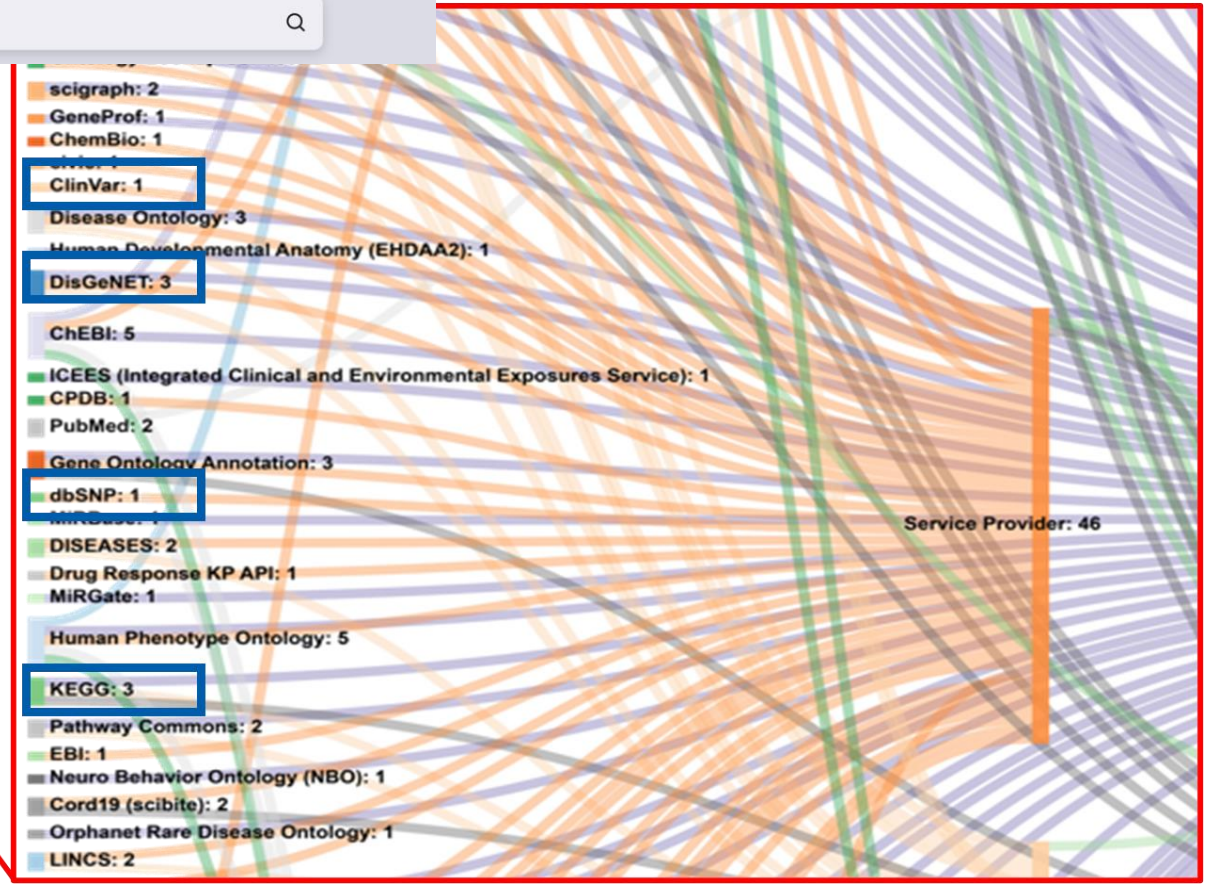
Finding Connections in Biomedical Information



TRANSLATOR
Funded by NIH's National Center for Advancing Translational Sciences

Turning data into knowledge graphs to get insights into how drugs might relate to diseases





https://ui.transltr.io/demo

Use Case – SHINE Syndrome

- “What drugs/chemicals may up/downregulate my gene of interest?”
- SHINE syndrome:
  - **S**leep Disturbances
  - **H**ypotonia
  - **I**ntellectual Disabilities
  - **N**eurological Disorders (including motor issues)
  - **E**pilepsy

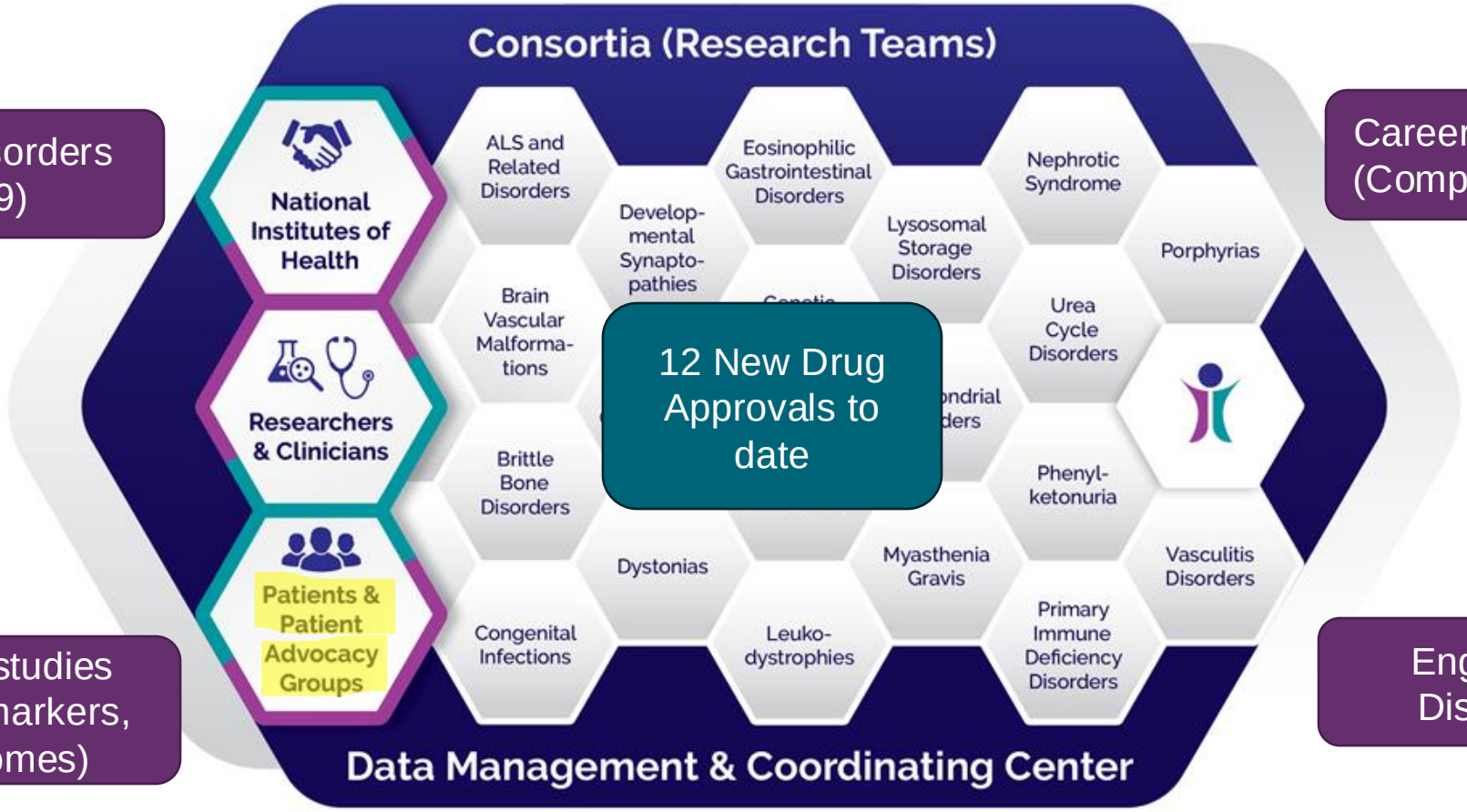
- Gene: *DLG4* (discs large MAGUK scaffold protein 4); predicted impact of variants: LOF, haploinsufficiency
- Translator result: Guanfacine may increase *DLG4*
- Five months post-treatment
- Translator can show value for research of all stages – early preclinical to clinical

TRANSLATOR
Funded by NIH's National Center for Advancing Translational Sciences

RARE DISEASES CLINICAL RESEARCH NETWORK

A network of 20 research teams collaborating to achieve faster diagnosis and better treatments for patients with rare diseases

3 or more disorders (mean=9)



12 New Drug Approvals to date

Career enhancements (Competitive scholars)

3-5 clinical studies (Nat hx, biomarkers, CTs, outcomes)

Engagement & Dissemination

National Center for Advancing Translational Sciences

NIH National Center for Advancing Translational Sciences

NIH National Institute of Dental and Craniofacial Research

NIH National Institute of Diabetes and Digestive and Kidney Diseases

NIH National Institute of Allergy and Infectious Diseases

NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIH National Institute of Neurological Disorders and Stroke

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

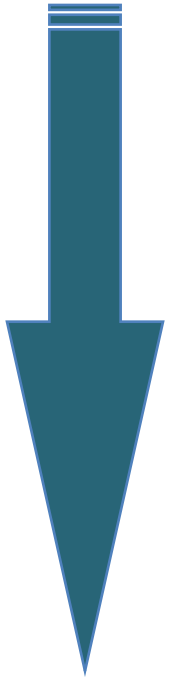
NIH National Institute of Mental Health

NIH National Heart, Lung, and Blood Institute

NIH National Institutes of Health *Office of Dietary Supplements*

Gene-Based Therapies for Rare Diseases

Development



Clinical Trials

1) Somatic Cell Gene Editing (SCGE)

- NIH Common Fund Program
- Moving to clinical studies for second phase
- Toolkit – data on performance of delivery technologies

2) Accelerated Medicines Program® – Bespoke Gene Therapy Consortium (BGTC)

- Enhancing vector manufacturing
- Enhancing gene expression
- Regulatory playbook

3) Platform Vector Gene Therapy

- Single AAV vector as a platform for multiple therapeutic genes
- Testing ability to increase efficiency to clinical trial start-up

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Accelerating Medicines Partnership®
Bespoke Gene Therapy Consortium (BGTC)

https://fnih.org/BGTC

Mission: Streamlining regulatory frameworks to accelerate gene therapies for rare

Gene Therapy and Manufacturing Pairs Selected for Clinical Trials	Rare Pediatric Disease Designation	Orphan Drug Designation
Adeno-Associated Virus 9 (AAV9-hPCCB) for **propionic acidemia**	✓	✓
Adeno-Associated Virus 9 (AAV9-SUMF1) for **multiple sulfatase deficiency**	✓	✓
Adeno-Associated Virus Nephrocystin 5 (AAV-NPHP5) for **NPHPR mutation-associated retinal dystrophy**	✓	✓
Adeno-Associated Virus 5 (AAV5-CNGB1) for **autosomal recessive retinitis pigmentosa due to CNGB1 mutation**	✓	✓
Adeno-Associated Virus 8 (AAV8-hGALNS) for **mucopolysaccharidosis IVA (Morquio A syndrome)**	✓	✓
Adeno-Associated Virus 8 (AAV8-hSLC4A11) for **congenital hereditary endothelial dystrophy**	✓	✓

NCATS Labs: A Record of Clinical Success

>50
IND applications

3
New drug approvals

Chronic yeast infections
(approved by FDA)

Upstaza™
(eladocagene exuparvovec)

AADC deficiency
(approved by EMA)

aGamree®
(vamorolone) oral suspension 40mg/mL

Duchenne muscular dystrophy
(approved by FDA and EMA)

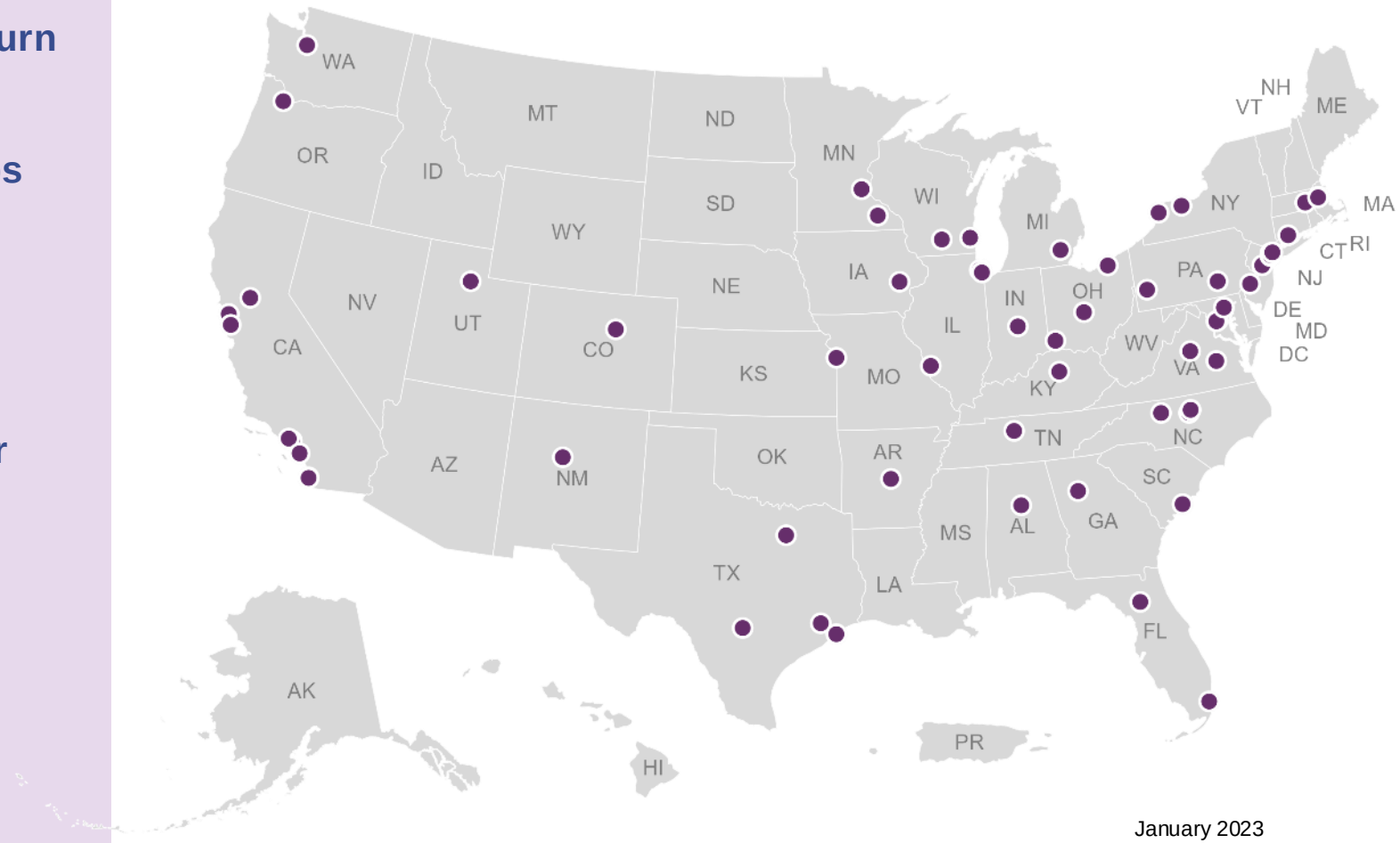
NIH National Center for Advancing Translational Sciences

CTSA Program: Premier National Network Speeds Health Solutions

#CTSAProgram

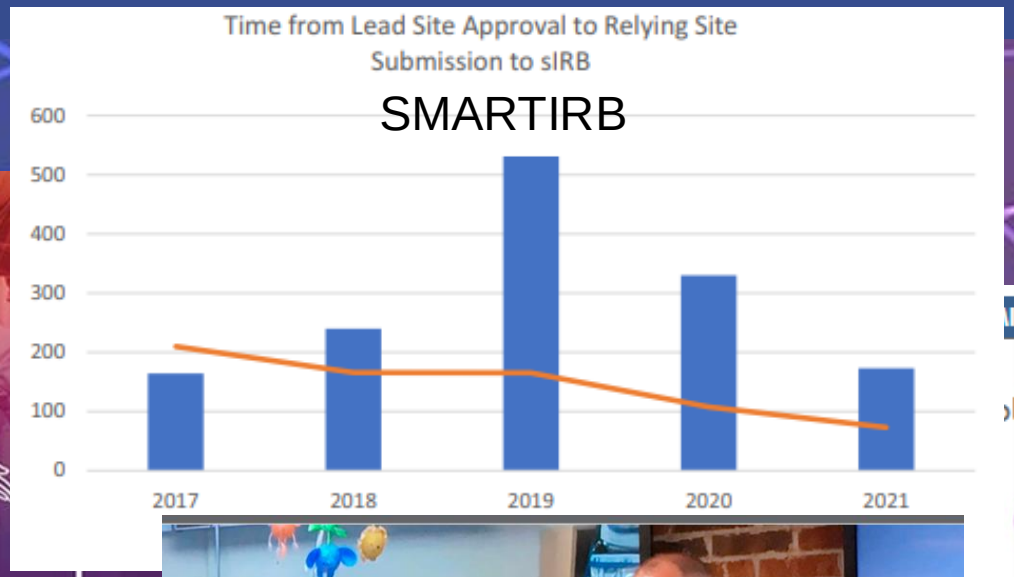
- **Develop, demonstrate, and disseminate innovations that turn science into health faster**
- **Promote impactful partnerships and collaborations**
- **Address health disparities**
- **Provide a national resource for the rapid response to urgent public health needs**
- **Promote training and career support**
- **Nurture the field of translational science**

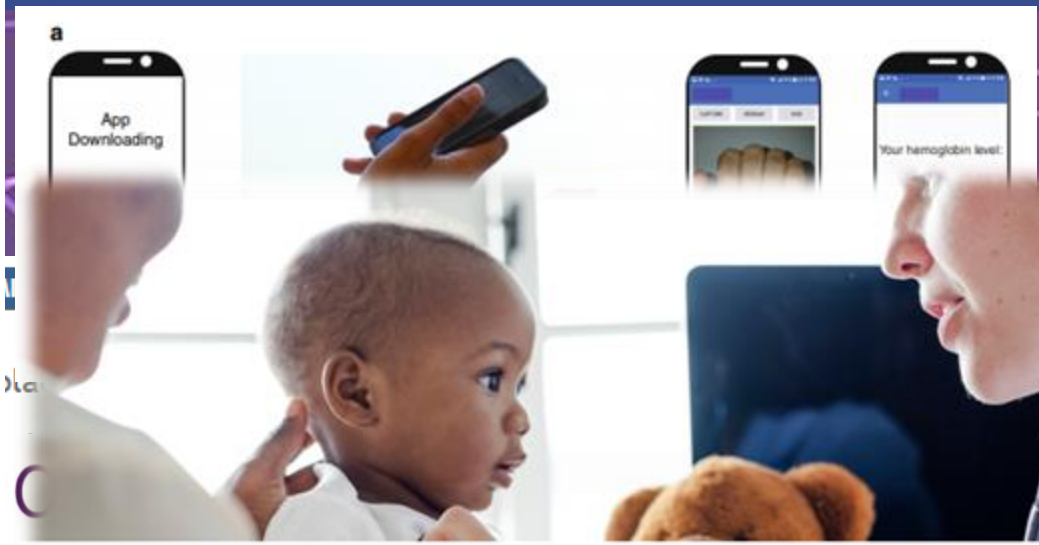
Clinical and Translational Science Awards Primary Institutions

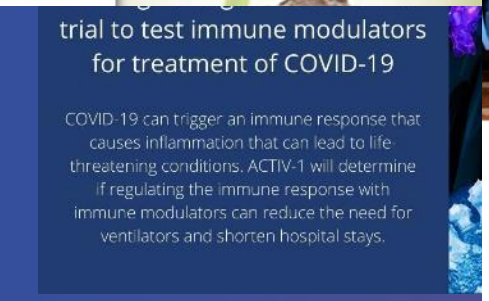


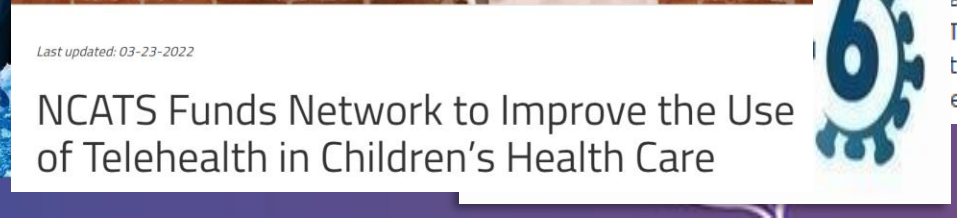
January 2023

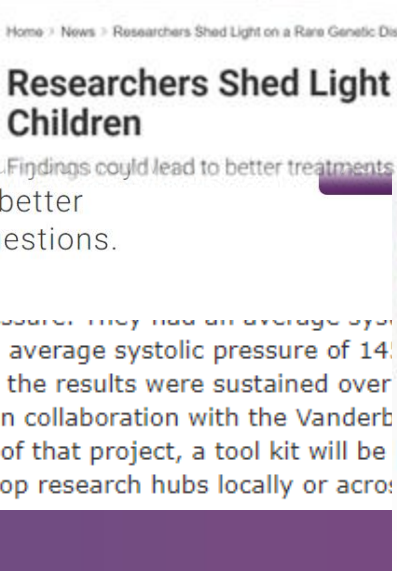
…Local strengths enable nimble, rapid, and robust responses to national public health challenges



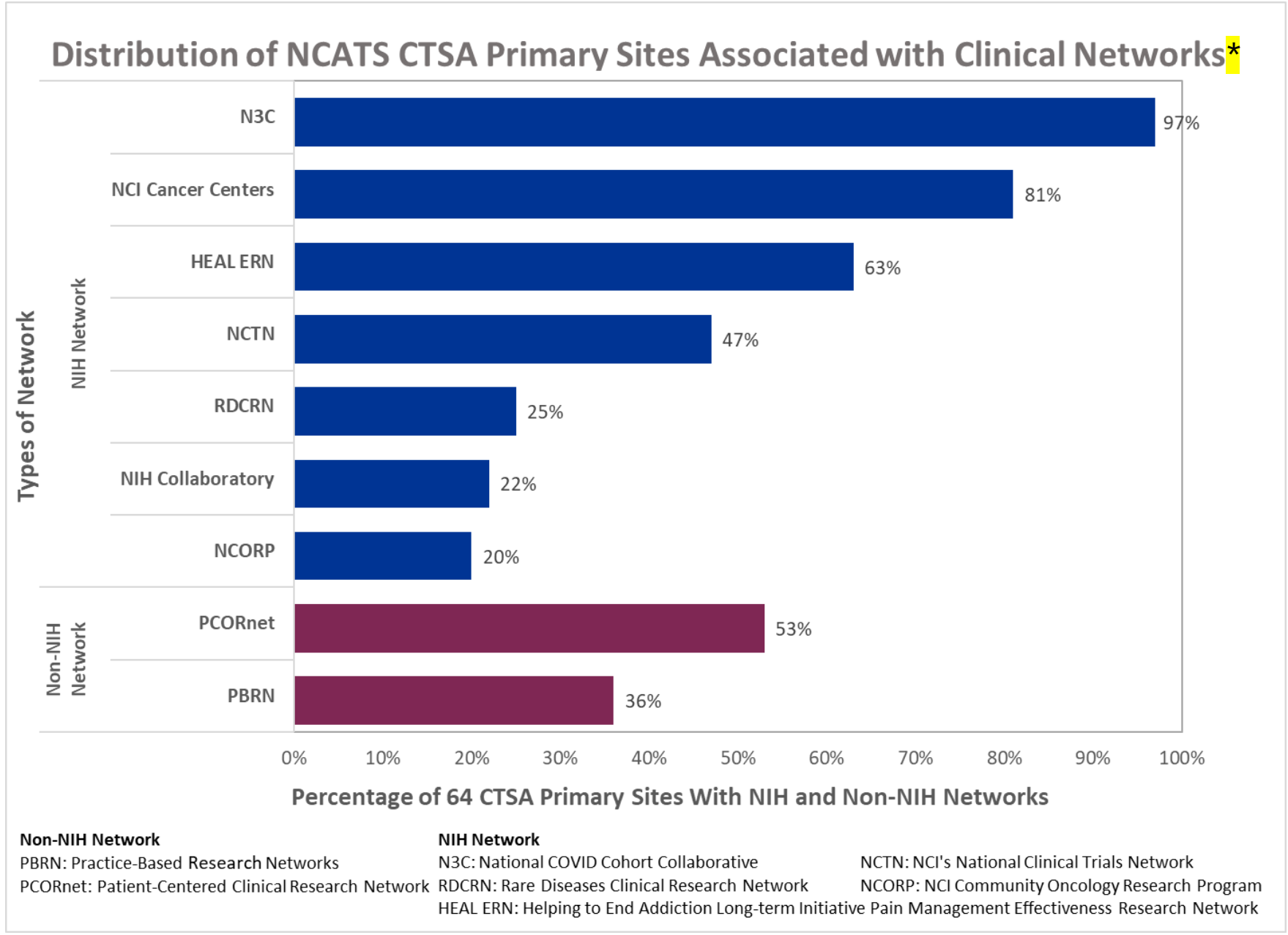








Mobile health vehicles offer health resources, vaccine education and outreach opportunities through the Our Community, Our Health programs.



Non-NIH Network

PBRN: Practice-Based Research Networks

PCORnet: Patient-Centered Clinical Research Network

NIH Network

N3C: National COVID Cohort Collaborative

RDCRN: Rare Diseases Clinical Research Network

HEAL ERN: Helping to End Addiction Long-term Initiative Pain Management Effectiveness Research Network

NCTN: NCI's National Clinical Trials Network

NCORP: NCI Community Oncology Research Program

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*FQHCs are partners with variable participation across the institutions

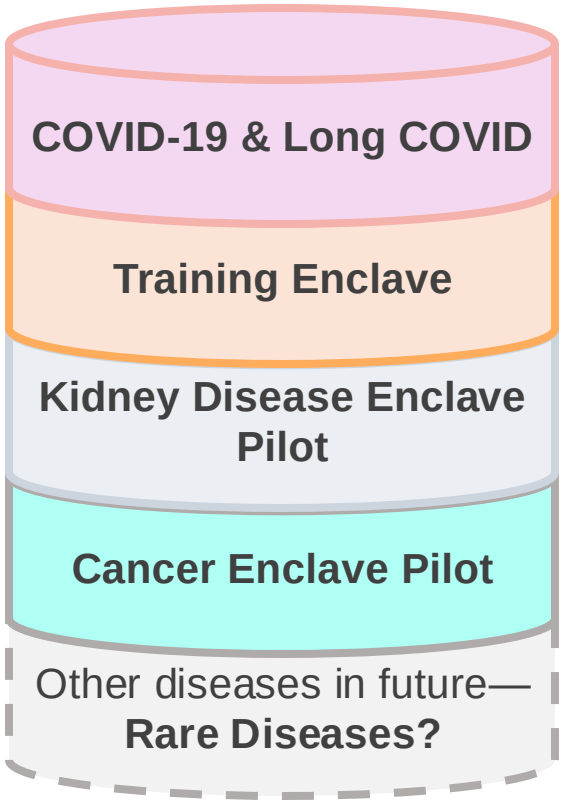
N3C-Clinical Pilot: Tenant Infrastructure and Clinical Research Enclaves

Common Infrastructure

- Governance
- Common data format (OMOP)
- Data Cleaning & Harmonization
- Data Quality
- Data Lineage
- Granular/Purpose-Based Access Controls
- De-identification
- AI/ML Environment
- Code Workbooks
- Analytical Tools

Clinical Research Enclave Pilots and Future Potential

Collaborative analytics within the N3C common infrastructure



Adding top 8-10 highest burden disease areas

Research Datasets

- CMS Data
- N3C Clinical Data
- SDOH Data
- Viral Variant
- Mortality Data
- *Vaccine data*
- **Imaging MIDRC*
- SEER, SRTR

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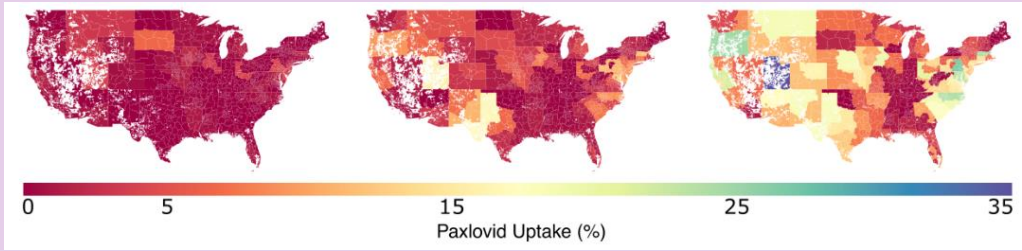
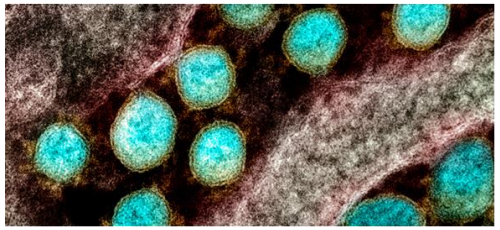
N3C Answers Public Health Questions

N3C helped the White House COVID-19 Response Team assess national use of Paxlovid.



Broader uptake of key COVID-19 drug could have saved more lives.

N3C data predicted that if 50% of people eligible for Paxlovid had taken the drug, **it would have saved 51,000 lives and spared 168,000 patients from hospital admissions.**



Reinfection

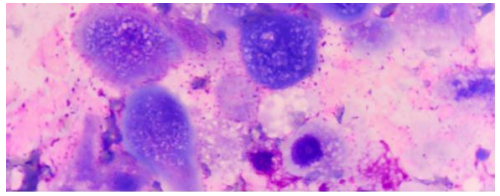
Long COVID diagnoses appear to occur more often and closer to the time of reinfection.

Vaccination

People who were vaccinated before COVID infection had a reduced risk of long COVID.

Health Disparities

Long COVID affects Black and Hispanic Americans more than white people, but these groups are less likely to be diagnosed.



Cancer Patients

While cancer patients with COVID had a higher risk of death, their race and recent cancer treatments did not significantly increase that risk.

Transplant Recipients

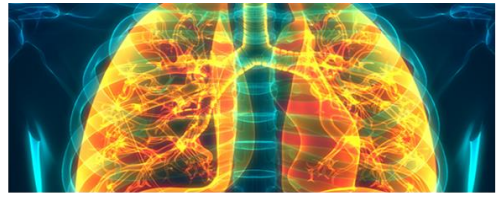
Impact of COVID infection varied by organ transplant type, putting lung recipients at high risker and liver recipients at lower risk.

Living with HIV

People with HIV had higher odds of dying from COVID but lower odds of mild or moderate COVID infection than those without HIV.

Diabetes

For those with diabetes, blood sugar levels above the ideal amount increased their odds of hospitalization, ventilation and death from COVID infection.



COPD

COVID infection was twice as likely to be fatal for people with a common chronic inflammatory lung disease called COPD.

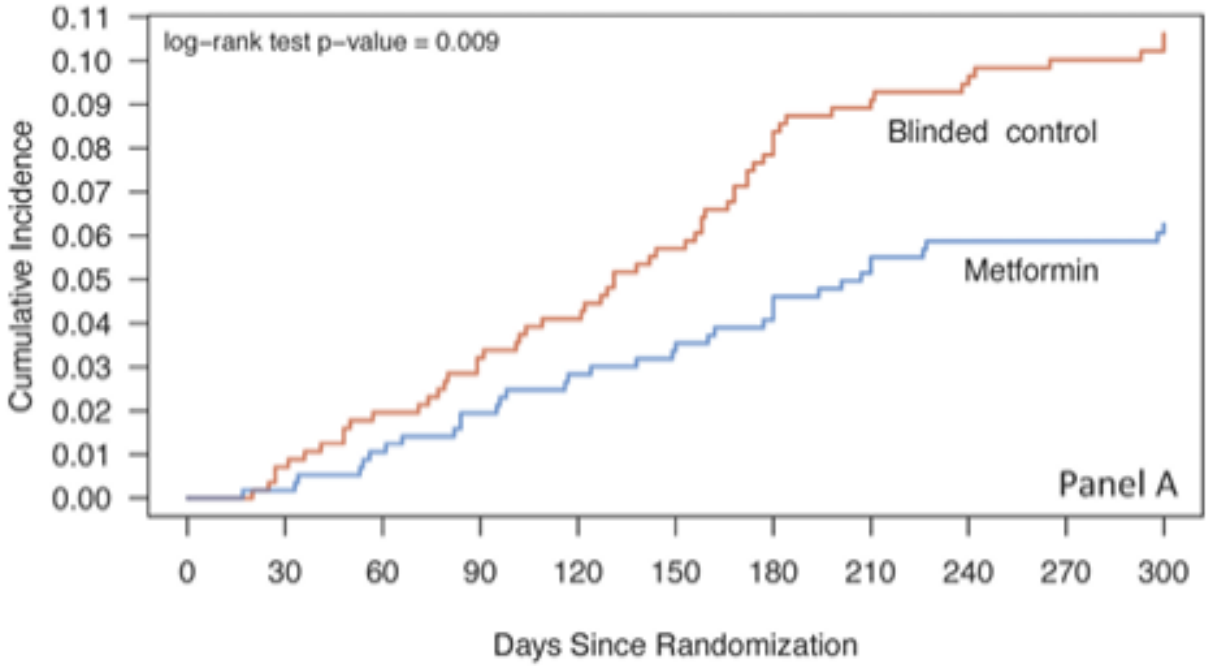
MIS-C

Kids who were male, Black/African American, or obese were more likely to develop dangerous organ inflammation called MIS-C after COVID infection.

Metformin, COVID-19, and Long COVID

COVID-OUT Clinical Trial Results

Suggesting that Acute Metformin Treatment Prevents Long COVID



https://www.medrxiv.org/content/10.1101/2022.12.21.22283753v1

ACTIV-6

COVID-19 and Long COVID to be Studied through Participant Follow-up Questions and N3C Analyses

- Primary endpoint will continue to be Time To Recovery from Acute Symptoms
- ACTIV-6 Metformin participants will be followed for up to six months
- Follow-up questions for ACTIV-6 metformin participants include:
  - Have you been told by a medical provider that you have long COVID?
  - Long COVID-specific symptom questions, i.e. What level of fatigue (being tired) have you experienced?

ACTIV-6 and Long COVID

Enhancing Public Health Impact Through Associated Analyses of Real World Data

METFORMIN

Randomized Controlled Clinical Trial Data
+
Real World Usage under Similar Conditions

Use Case for Trial Emulation Methodology

ACTIV-6

Participant-Reported Outcomes
from 3000 participants for
6 months after metformin treatment
(opened September 5;
enrolled 1485 participants)

N3C PHASTR

Electronic Health Record Data
from 110,000 outpatients who
started taking metformin
after a positive COVID-19 test

Learn more:
[Can Metformin Treat COVID-19 and Prevent Long COVID? NCATS and Partners Pursue Answers]

NIH National Center for Advancing Translational Sciences

Strategic Planning → Strategic DOING

NCATS communities have a critical role in helping us achieve our audacious goals and address emerging national research priorities.

Expanding clinical research capacity	Using RWD and clinical Informatics to improve public health	Training the next generation of the research workforce	Other things we're watching
• Jumpstart NIH director's visions • Leverage existing networks • Engage in new clinical trial modalities	• AI/ML • Platform technology • Predictive models	• Inclusivity • AIM-AHEAD • Career development	• Women's health • Quantum science

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Co-Chairs

Connecting Research to Clinical Care

- **Research in primary care settings in collaboration with clinical sites**
- **Innovations in clinical study design**
- **Participant and community engagement**
- **Participation in coordinated infrastructure supporting research in primary care settings**

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Thank You!

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