NCATS

COLLABORATE. INNOVATE. ACCELERATE.

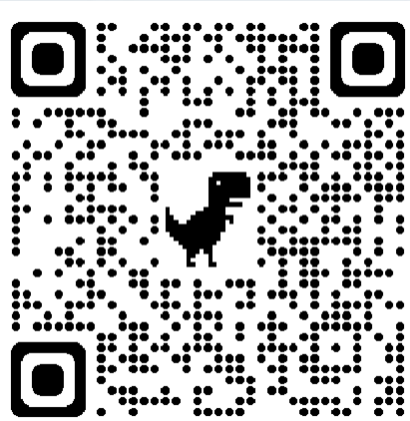
Research at the Intersection of Translational Science and Children's Health

Joni L. Rutter, PhD

Director

National Center for Advancing Translational Sciences

National Advisory Child Health and Human Development
September 6, 2023



NIH National Center for Advancing Translational Sciences

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.

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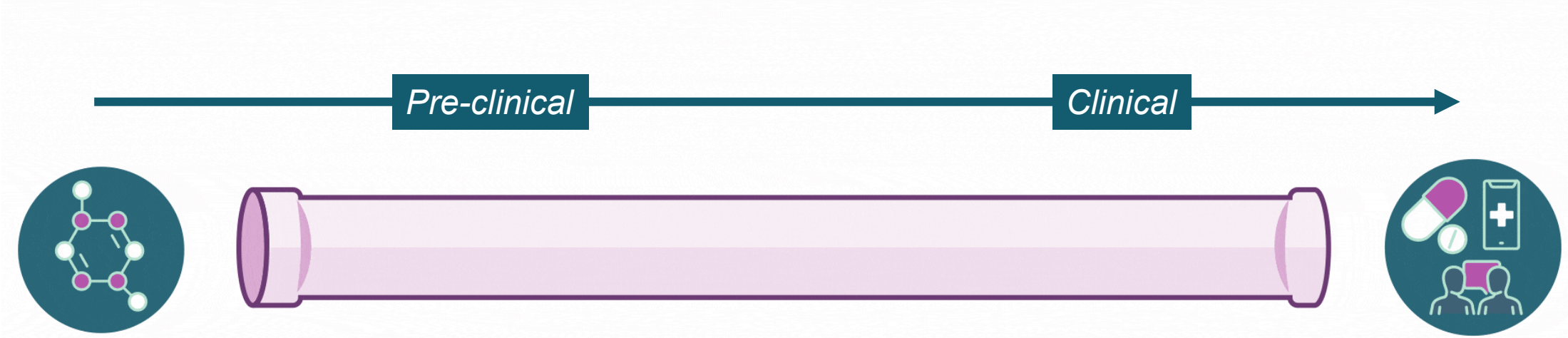
NCATS' MISSION

Turn research observations into health solutions through translational science

National Center for Advancing Translational Sciences

NCATS is Re-engineering the Translational Pipeline

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



Examples of bottlenecks

- And solutions

Operational

"One size fits all" approach

- **Adaptive clinical trial design, master protocols**
- **N of small CTs, RDCRN basket/umbrella trials**

Low enrollment and diversity in clinical trials

- **Patient Advisory Groups, Enhanced community engagement efforts (TIN)**

Administrative/Workforce Dev

Administrative burden for study start-up

- **Streamlined business and regulatory processes (SMART IRB)**

Shortage of qualified translational investigators

- **Training and career development best practices (CTSA K, T, R25, R03, DPI)**

Scientific

Insufficient tools and technologies to predict toxicity and efficacy of new drugs

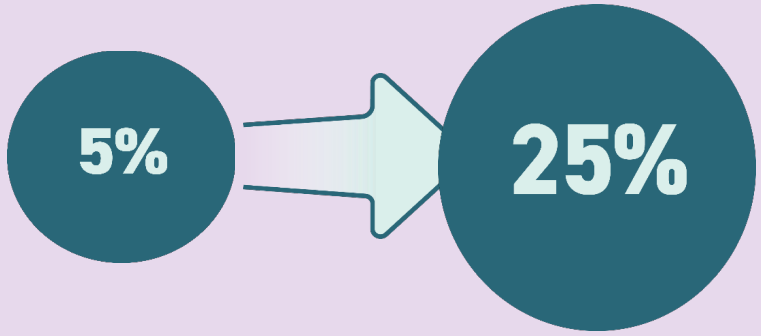
- **Platform-based Tissue/Organ on chips; 3D biofabrication**
- **Gene targeted therapies**
- **AI/ML drug development (ASPIRE)**

Incompatible databases to advance data science

- **Data, interoperability and integration (Translator, N3C, GARD, RARESource)**

NCATS Vision: Three Audacious Goals

More Treatments



Five-Fold Increase in Number of Diseases with Treatments

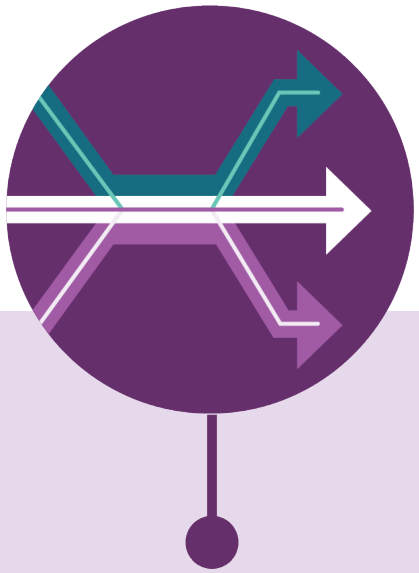
All People

Dramatically Increase Inclusivity Across Every Area We Support

More Quickly

Enable Diagnostics and Therapeutics to Reach People Twice as Fast

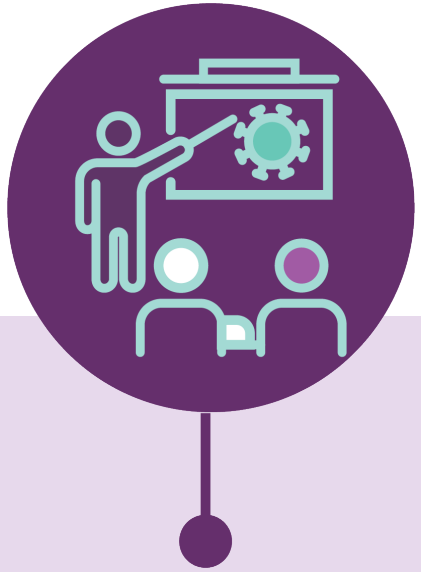
Key NCATS Approaches



Understanding what's similar across diseases to spur multiple treatments at a time

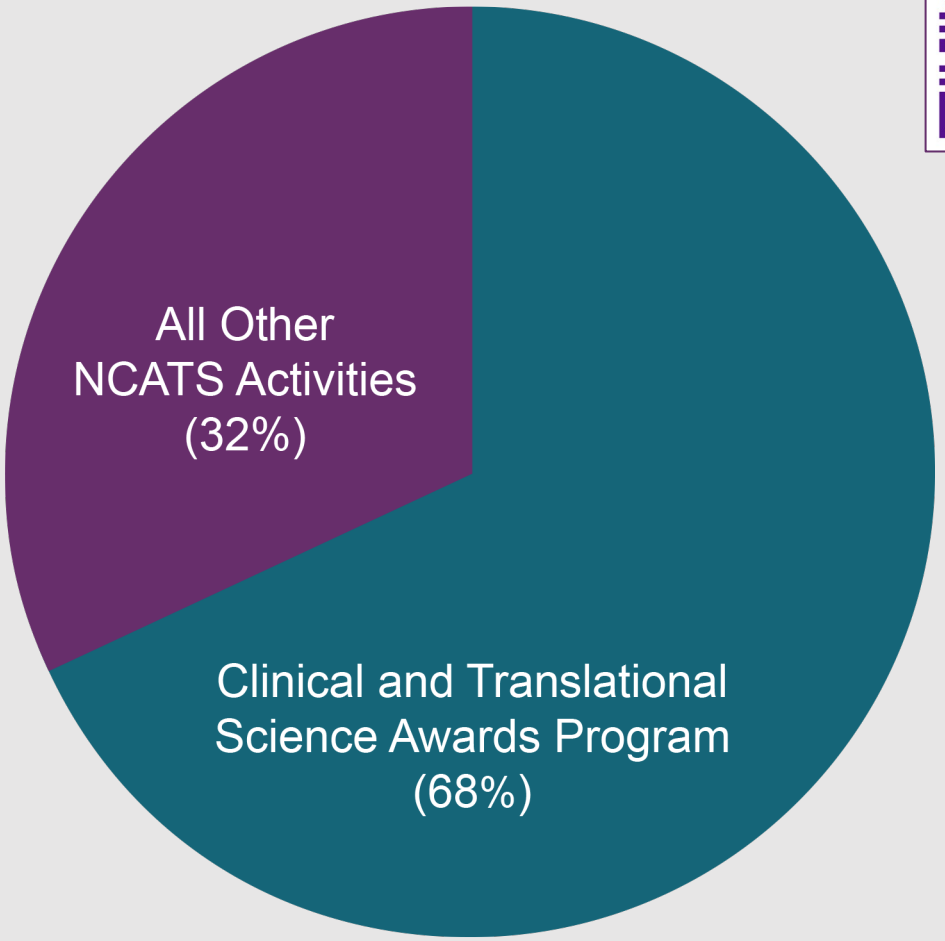
Developing models that better predict a person's reaction to a treatment

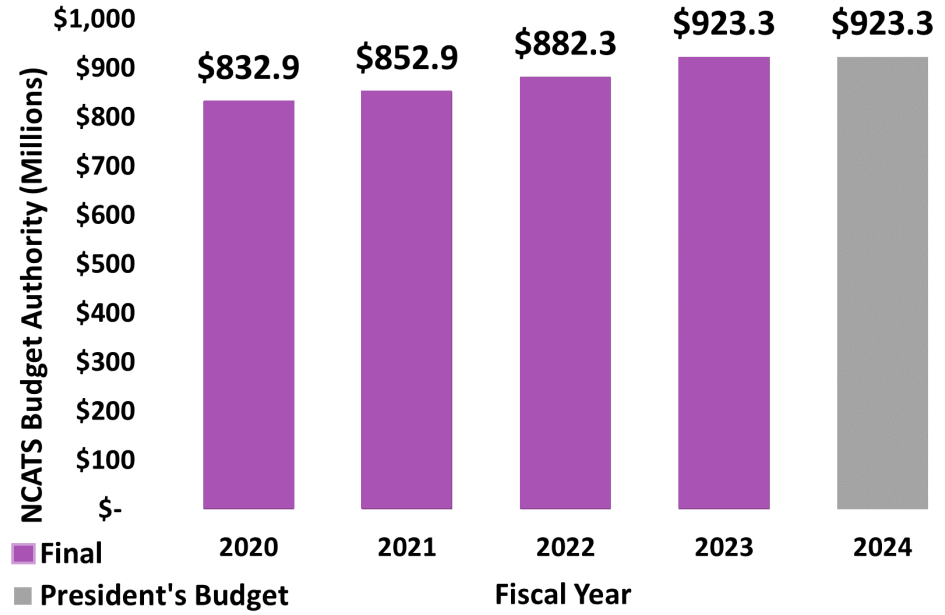
Enhancing clinical trials so the results more accurately reflect the patient population



Leveraging real-world data and data science approaches to address public health needs

NCATS' Budget At-a-Glance





$ (in millions)	FY 2023	FY 2024	
NCATS	Enacted	President's Budget	FY24 PB +/- FY23 Enacted
Total	**923.3**	**923.3**	**0 (0%)**
CTSA	629.6	629.6	0 (0%)
Non-CTSA	293.8	293.8	0 (0%)

Reflects Fiscal Year 2023 Enacted Appropriations
NCATS Budget: $923,323,000

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NCATS

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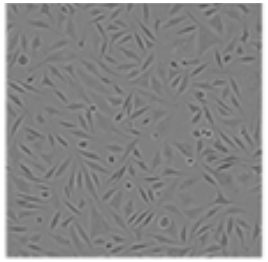
Specific Efforts in Translational Science for Children's Health

Pre-clinical --- Clinical --- Data Science

Revolutionizing Drug Development Approaches

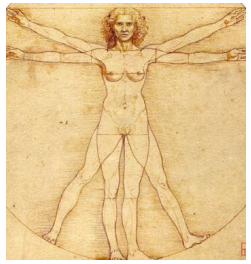
*(**PhRMA**, Biopharmaceutical Research Industry Profile, 2016)*

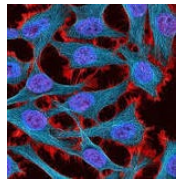
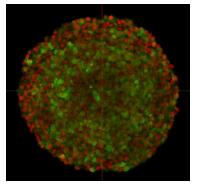
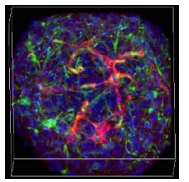
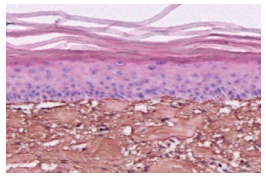
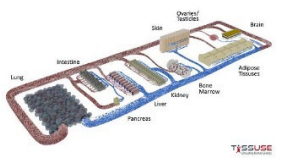
2D Cell Lines

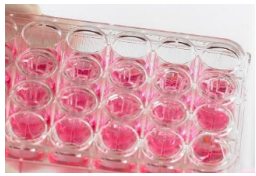


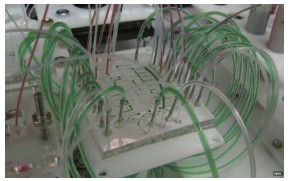
Human

Mouse



2D	Spheroids	Organoids	Printed Tissues	Organ-on-a-chip
				





Need for new technologies and better predictive tools across the translational pipeline

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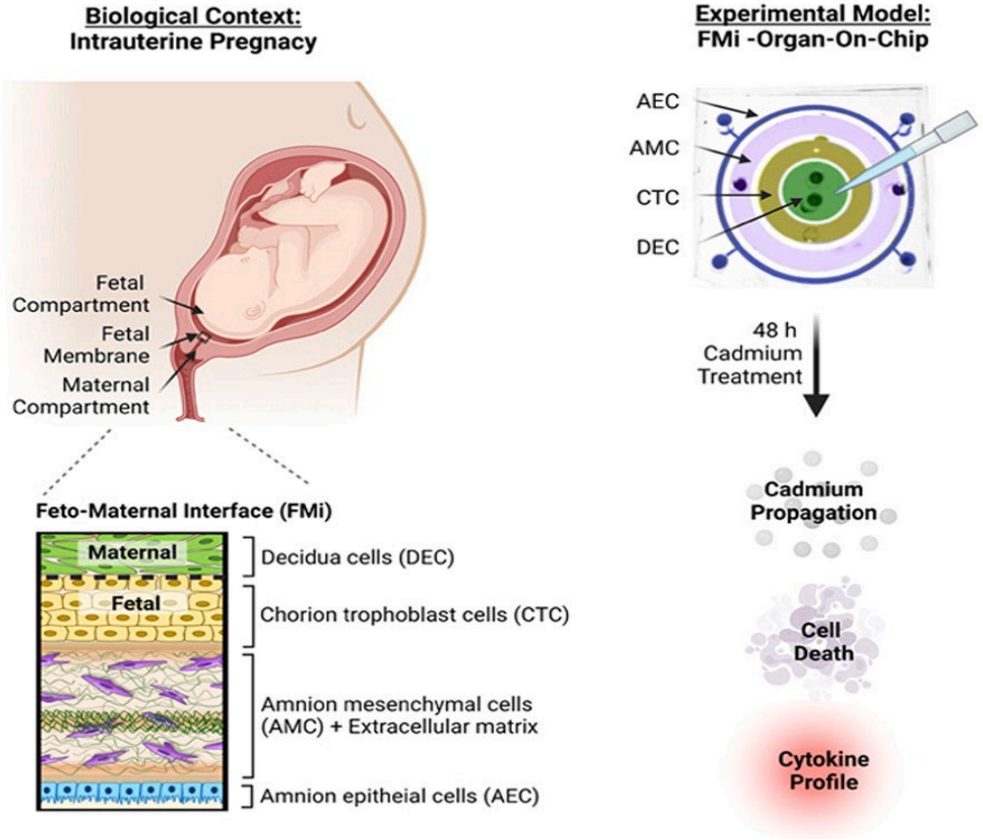
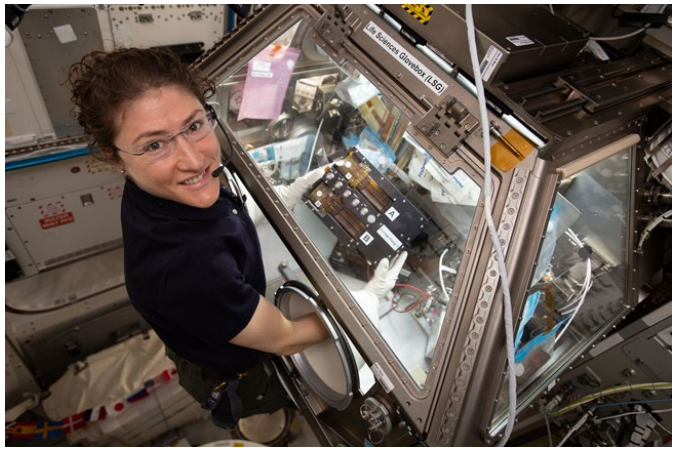
Using 3-D Tissue Bioprinting and Tissue Chip to Improve Health in Pregnancy

- The Fetal-Maternal Interface (FMI) on a Chip aims to reproduce the structure, function, and responses of the FMI, mimicking health and inflammation
- The goal is to offer a personalized FMI model to test potential treatments and streamline clinical trials.
- One study tested the effect of maternal exposure to cadmium (Cd), an environmental toxin, and found significant cell death in maternal cells, but minimal effect on fetal cells. (PMID: 34391970)



Kim S, Richardson L, Radnaa E, Chen Z, Rusyn I, Menon R, Han A. Molecular mechanisms of environmental toxin cadmium at the feto-maternal interface investigated using an organ-on-chip (FMi-OOC) model. J Hazard Mater. 2022 Jan 15;422:126759. doi: 10.1016/j.jhazmat.2021.126759. Epub 2021 Aug 2. PMID: 34391970; PMCID: PMC8595660.

Physiological Changes under Prolonged Microgravity: Chips in Space



Resupply Mission
March 14, 2023

TISSUE CHIPS IN SPACE

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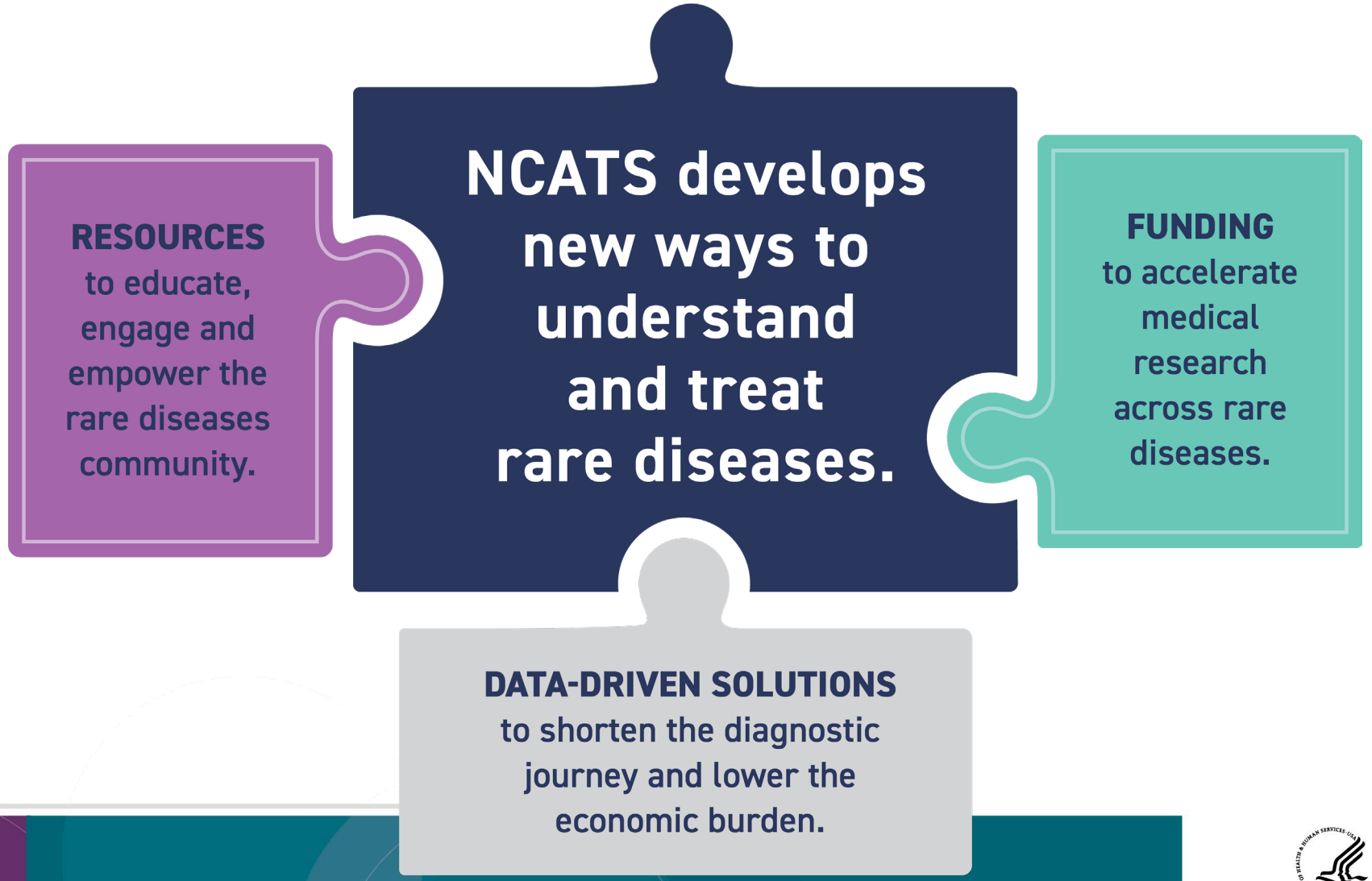
NCATS Has a Home for Rare Diseases



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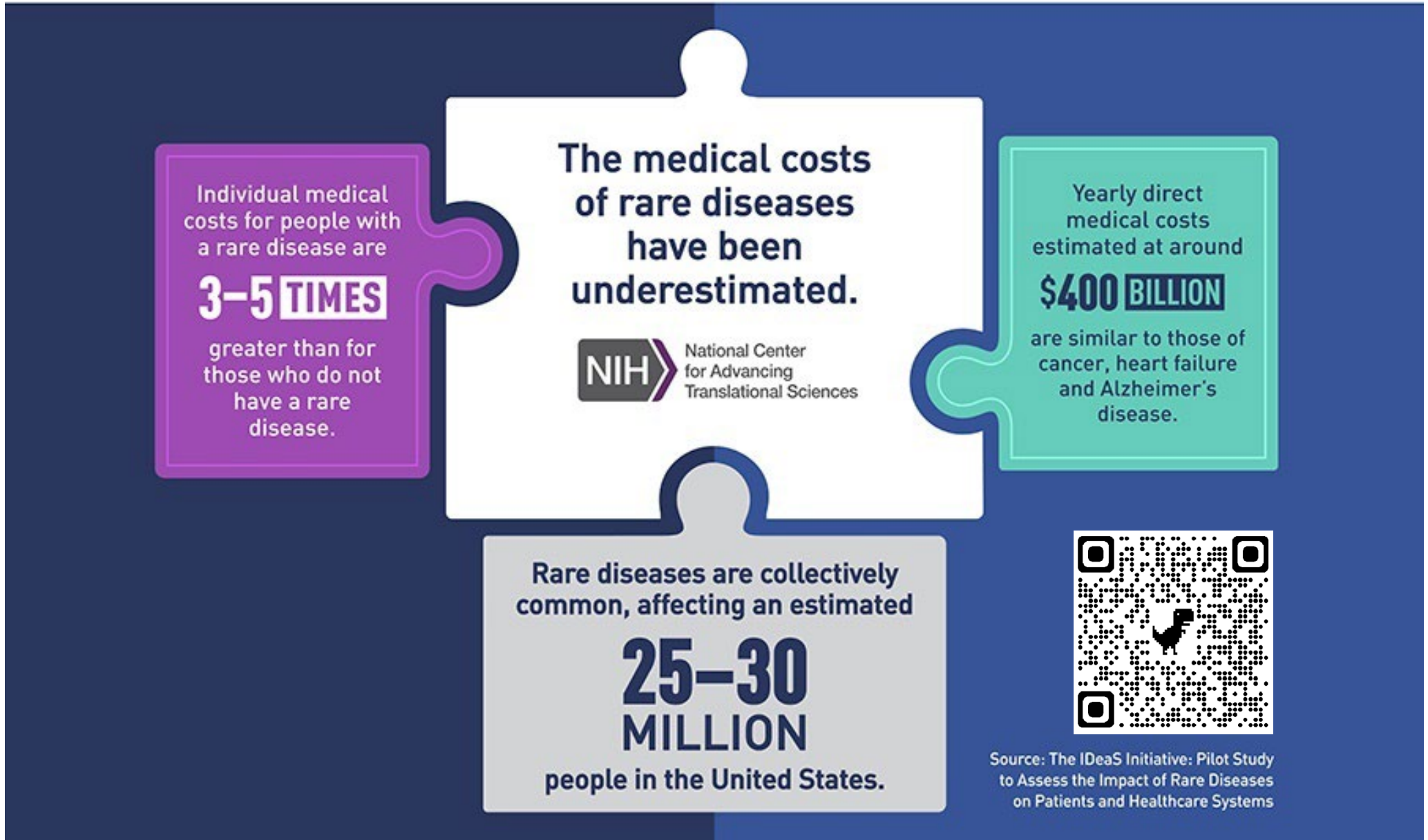
NCATS Study Suggests People with Rare Diseases Face Significantly Higher Health Care Costs



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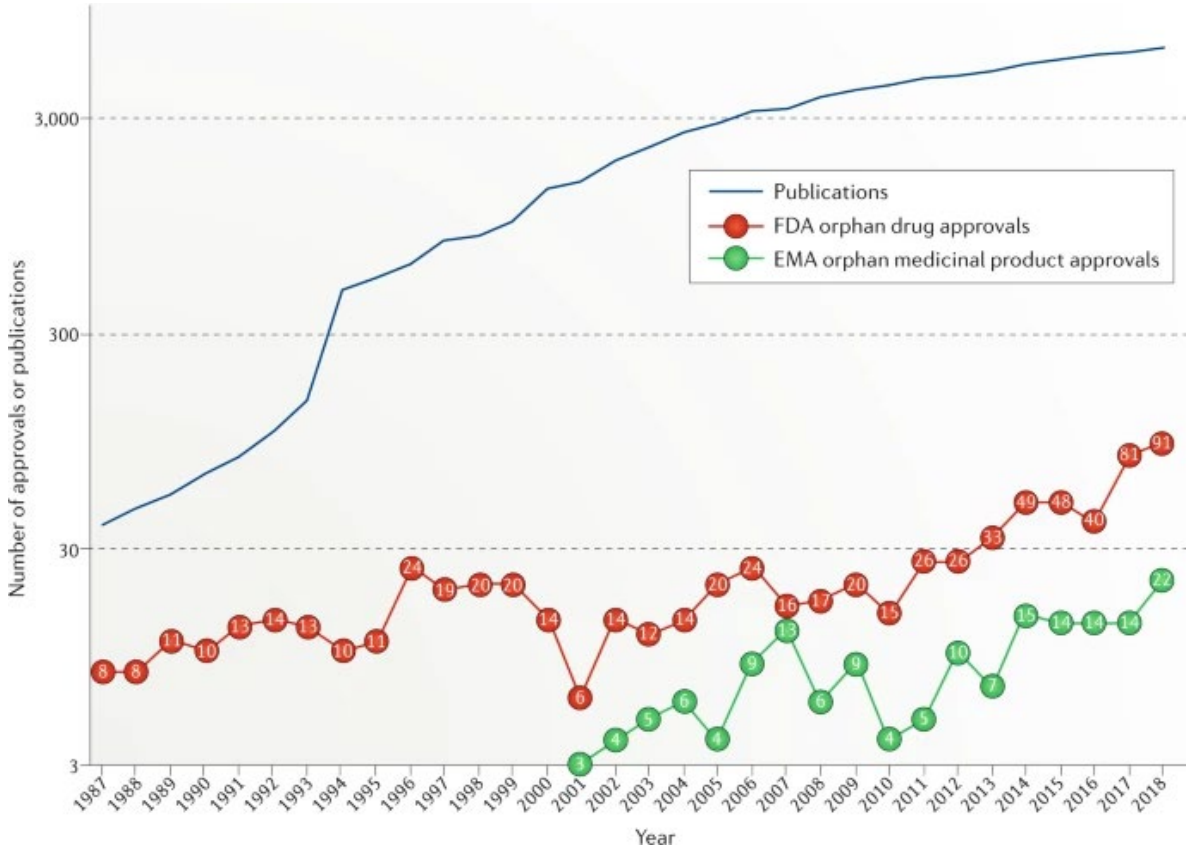
Gap Between Scientific Research and Translation to Therapies for Rare Diseases



Tambuyzer, E. et al. Nat Rev Drug Discov. 2020 Feb;19(2):93-111.

Challenges:

- Small number of patients
  - clinical phenotypes often overlap
  - different mutations a single gene can lead to different phenotypes
- Categorizing the genetic variants that cause disease, associating phenotypes, & grouping diseases based on common mechanisms
- ***Data exists but it is not collectively organized and shared to extract knowledge***

Opportunities:

- Apply advances in data and information technologies
- Build bioinformatics platform to make rare disease data more accessible

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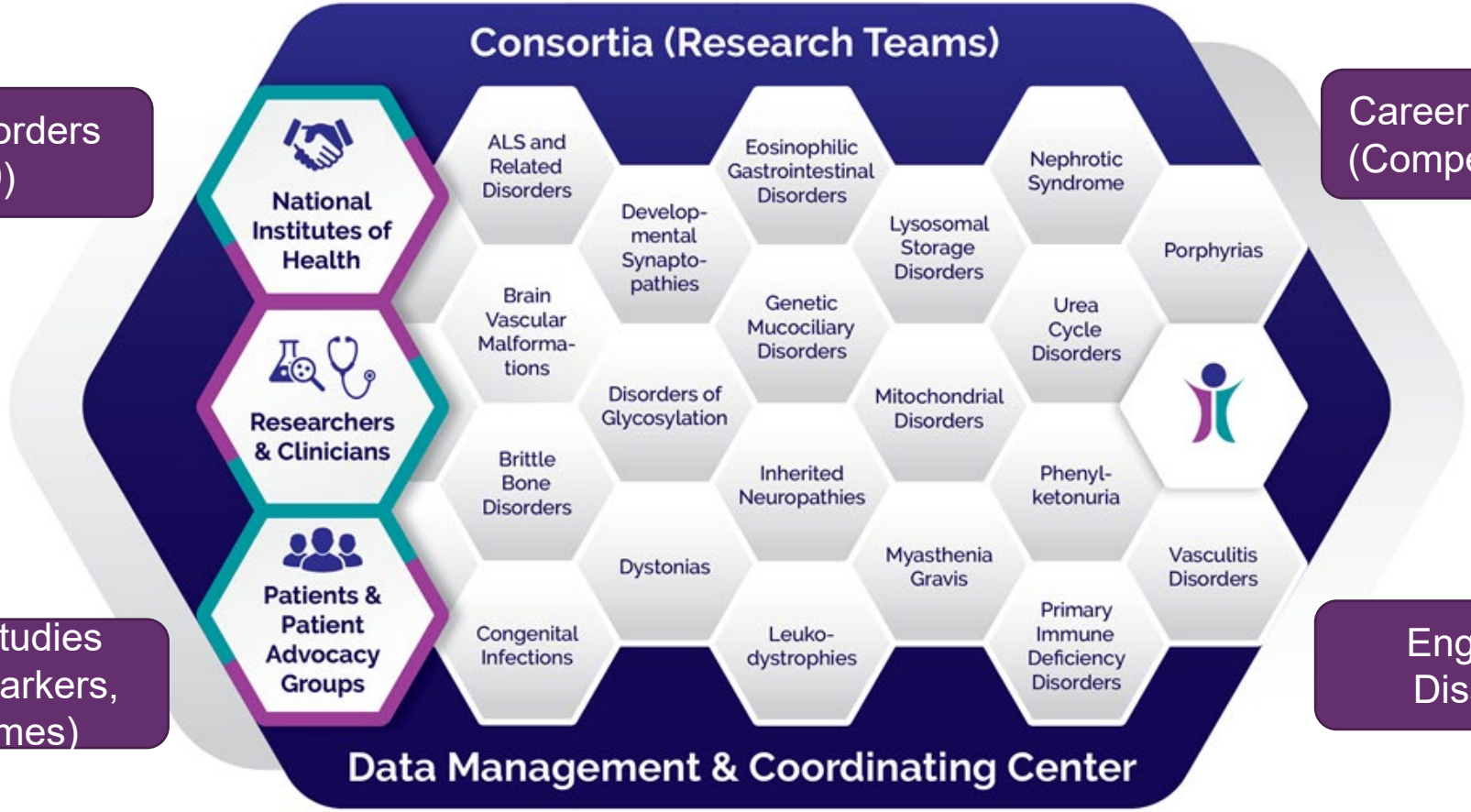
RARE DISEASES CLINICAL RESEARCH NETWORK

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)



Career enhancements (Competitive scholars)

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

Engagement & Dissemination

National Center for Advancing Translational Sciences

National Center for Advancing Translational Sciences

National Institute of Dental and Craniofacial Research

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Allergy and Infectious Diseases

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institute of Neurological Disorders and Stroke

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institute of Mental Health

National Heart, Lung, and Blood Institute

National Institutes of Health
Office of Dietary Supplements

RDCRN Clinical Sites

Active Sites	Unique Locations	Site co-located with CTSA
358	197	144

Average of 19 sites per consortia (range 5 – 42)

Site	# of consortia
Children's Hospital of Philadelphia	9
Baylor College of Medicine	8
Mayo Clinic	8
University of Minnesota	8
University of Utah	8
Children's Hospital Colorado	7
Seattle Children's Hospital	7
Stanford University	7
Boston Children's Hospital	6
Children's National Medical Center	6
Duke University	6
Massachusetts General Hospital	6
Washington University in St. Louis	6
Cleveland Clinic	5
Johns Hopkins University	5
University of Alabama at Birmingham	5
University of California, Los Angeles	5
University of California, San Francisco	5
University of Miami	5
University of Pennsylvania	5

Country	# of sites
Australia	2
Belgium	1
Canada	18
England	13
Germany	3
India	1
Ireland	1
Italy	2
Netherlands	1
South Africa	1
Switzerland	1

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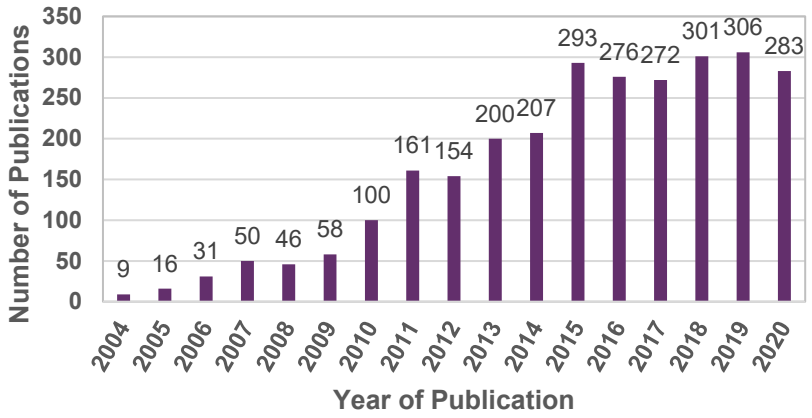
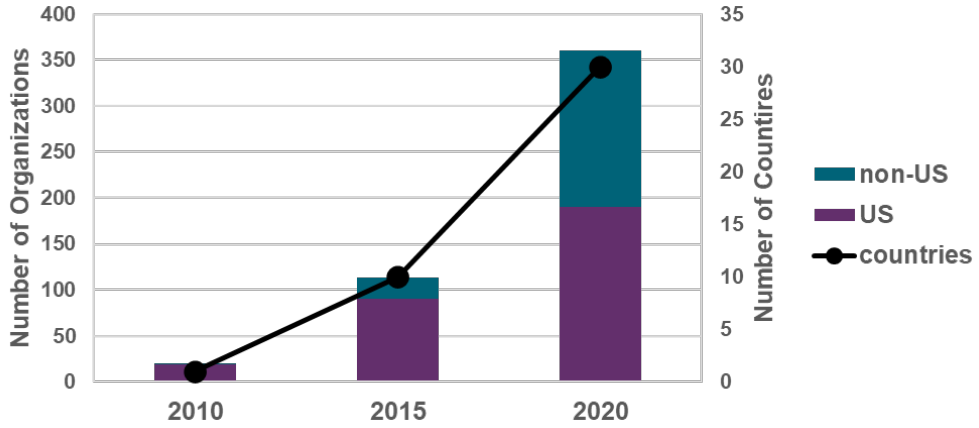
RARE DISEASES CLINICAL RESEARCH NETWORK

RDCRN Publications, International Collaborations, and Co-author Networks

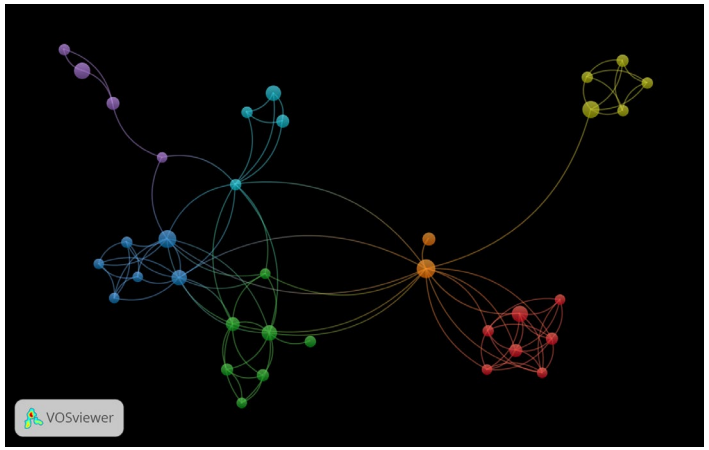
Number of RDCRN publications per year



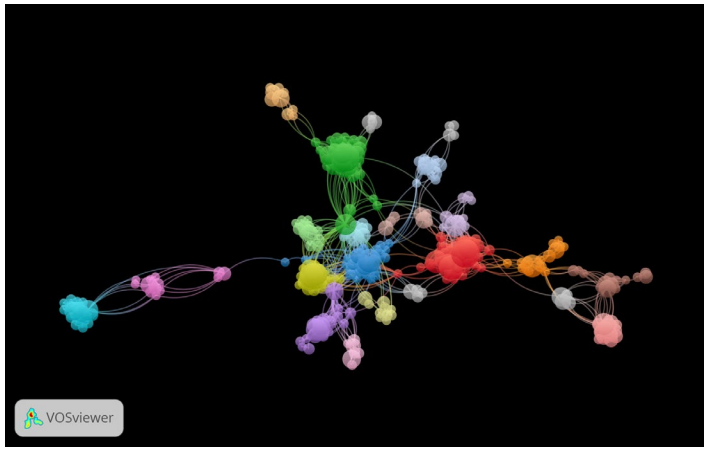
Number of organizations* and countries over time



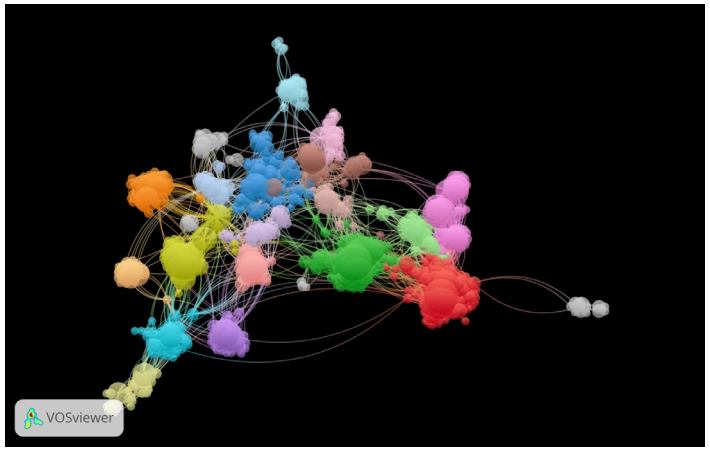
2004-2010 52 authors*



2004-2015 340 authors



2004-2020 946 authors



*Authors or organizations that contributed to at least 5 publications
28 consortia funded during first three U54-grant cycles
Analysis performed using iCite (NIH) and VOSViewer (Leiden University)

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RARE DISEASES CLINICAL RESEARCH NETWORK

RDCRN Translational Impact

RARE DISEASES CLINICAL RESEARCH NETWORK

Clinical Trials directly funded by U54 grant

- Predominantly small **Phase 1/Phase 2**
- **81 clinical trials** total since 2003
- Currently **18 trials** funded in **RDCRN4**
- **22 of 33 consortia** have conducted at least one CT

RDCRN-associated Clinical Trials

- Predominantly **Phase 2/Phase 3**
- **At least 13 ongoing clinical trials**
- Funded by industry, IC-specific grants, FDA, patient advocacy groups...
- **Leveraging** patient populations, clinical endpoints, biomarkers, safety/efficacy data…
- *No NCATS $$ involved*

8 FDA-approved treatments for 9 rare diseases

Consortium	Drug	Other Name	Indication	Company	Approval Date
RLDC	RAPAMUNE®	sirolimus	lymphangioleiomyomatosis (**LAM**)	Pfizer	May 2015
UCDC	CARBAGLU®	carglumic acid	N-acetylglutamate synthetase (**NAGS**) deficiency	Orphan Europe	March 2010
VCRC	RITUXAN®	rituximab in combination with corticosteroids	Wegener's granulomatosis (**WG**) and microscopic polyangiitis (**MPA**)	Genentech and Biogen	April 2011
UCDC	RAVICTI®	glycerol phenylbutyrate	urea cycle disorders (**UCD**)	Hyperion Therapeutics	February 2013
PC	SCENESSE®	afamelanotide	erythropoietic protoporphyria (**EPP**)	Clinuvel	October 2019
PC	GIVLAARI®	givosiran	acute hepatic porphyria (**AHP**)	Alnylam Pharmaceuticals	November 2019
CEGIR	DUPIXENT®	dupilumab	eosinophilic esophagitis (**EoE**)	Regeneron	May 2022
RTT	DAYBUE™	trofinetide	**Rett** syndrome	Acadia Pharmaceuticals	March 2023

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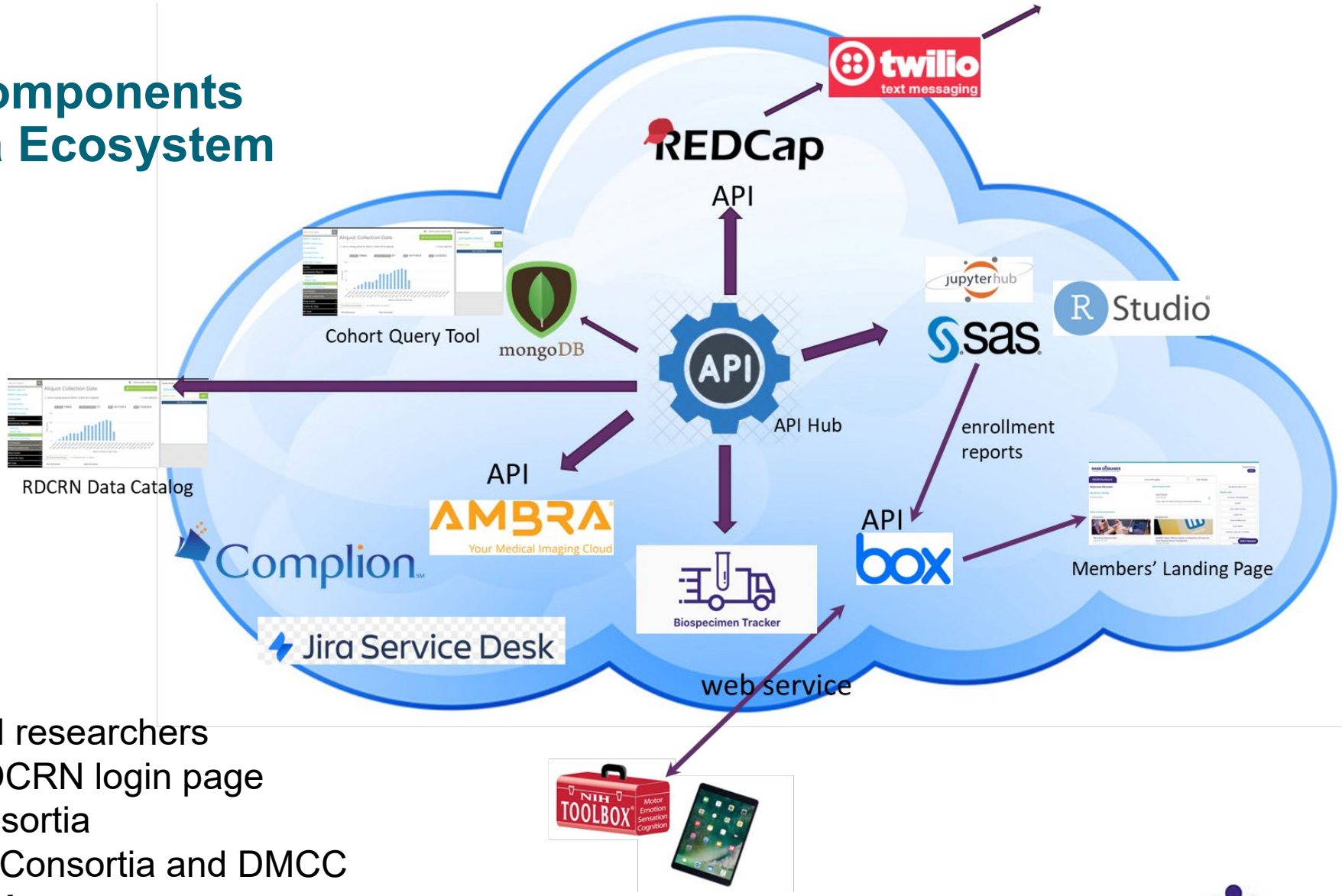
Operational Environment

Turning Components into a Data Ecosystem



Audience: RDCRN researchers
Authentication: RDCRN login page
Authorization: Consortia
Data governance: Consortia and DMCC
***Internal* data sharing**

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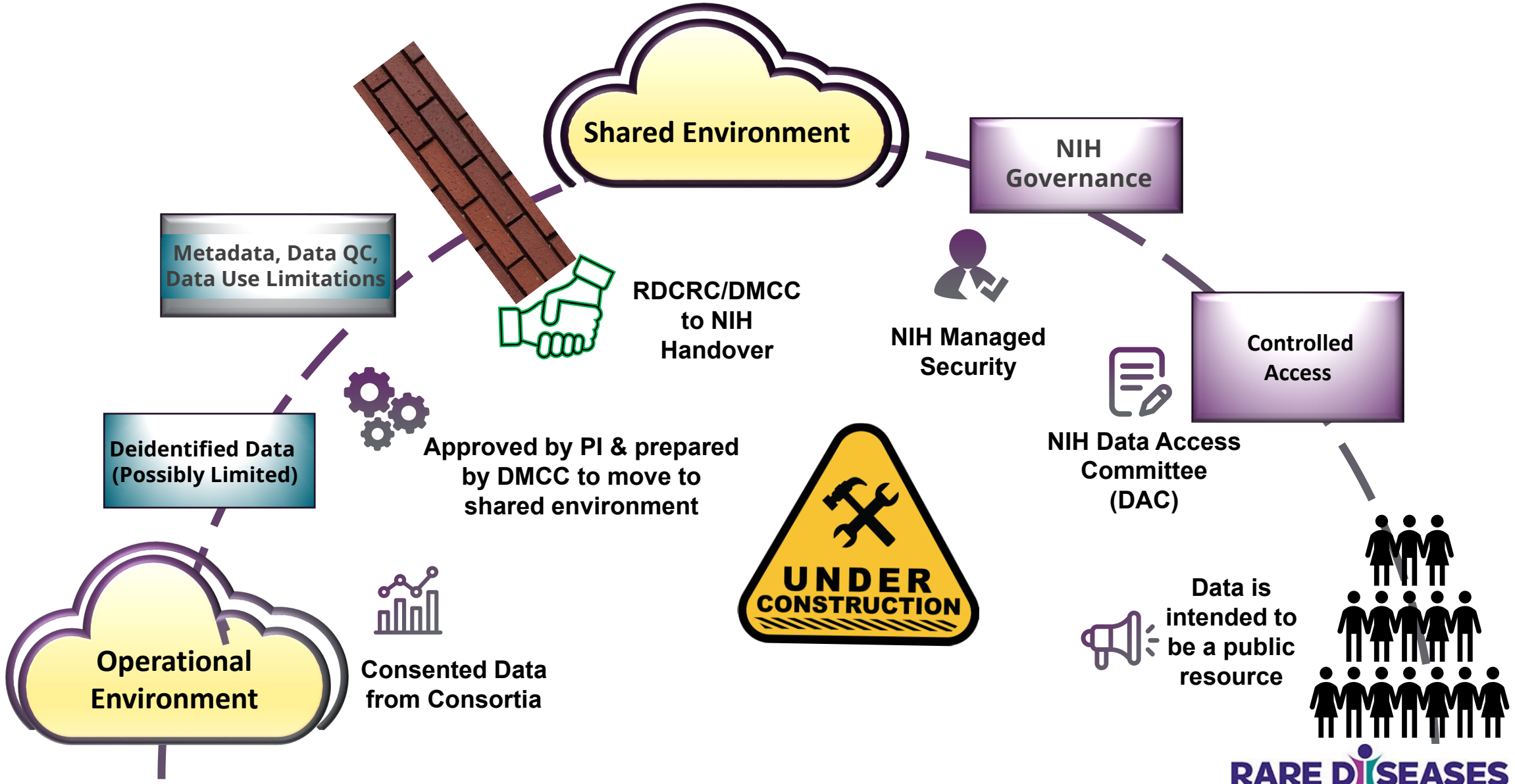
RARE DISEASES CLINICAL RESEARCH NETWORK

RDCRN Shared Data Environment



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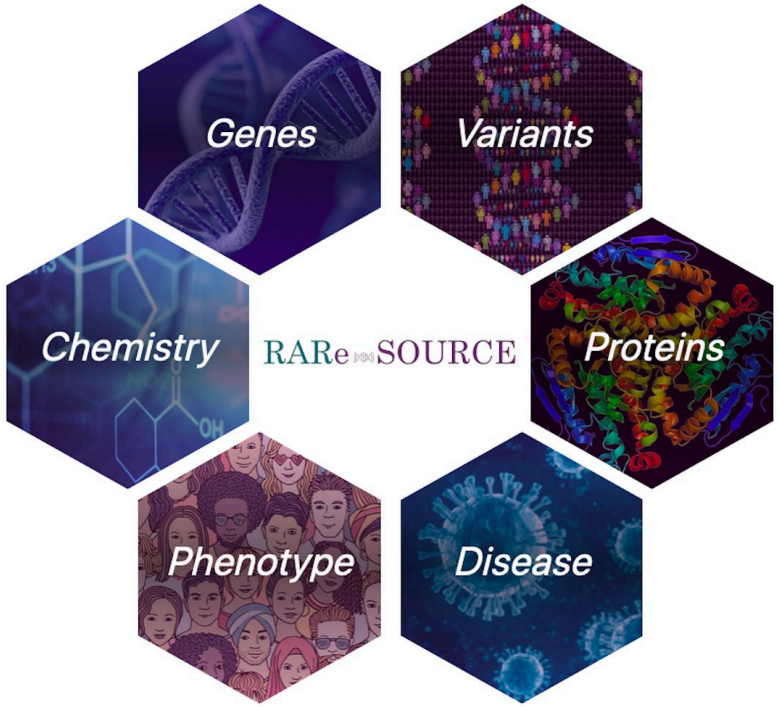
RARE DISEASES CLINICAL RESEARCH NETWORK

RARe-SOURCE

Unlocking novel insights into rare disease commonalities through multimodal data integration



Using a big data approach to understand how rare diseases can be grouped to be treated by the same drug

Collaborative Effort

NIH National Center for Advancing Translational Sciences

NIH NATIONAL CANCER INSTITUTE NCIatFrederick

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

NIH National Institute of Neurological Disorders and Stroke

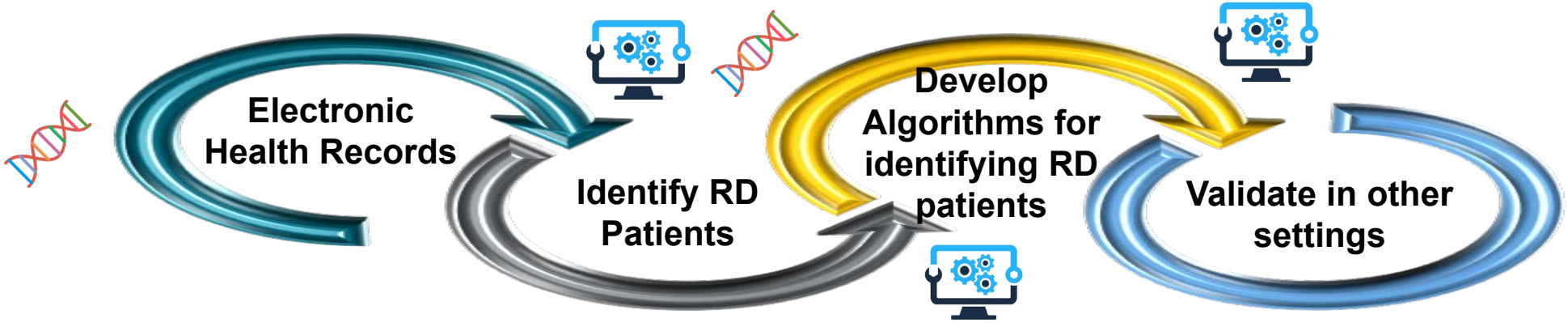
Shortening the Diagnostic Odyssey

For more information, contact Alice Chen Grady, M.D.

Multidisciplinary Machine-Assisted, Genomic Analysis and Clinical Approaches to Shortening the Rare Diseases Diagnostic Odyssey (UG3/UH3 Clinical Trial Optional)

Principal Investigator(s)	Year Awarded	Institution	Title
Gelb, Bruce D.; Chen, Rong; Balwani, Manisha	2022	Icahn School of Medicine at Mount Sinai	Using Electronic Medical Record Data to Shorten Diagnostic Odysseys for Rare Genetic Disorders in Children and Adults in Two New York City Health Care Settings
Gropman, Andrea Lynne; Berger, Seth I.; Vilain, Eric J.	2022	Children's Research Institute	Machine-Assisted Interdisciplinary Approach for Early Clinical Evaluation of Neurodevelopmental Disorders
Lalani, Seema R.; Lee, Brendan	2022	Baylor College of Medicine	Virtual Platforms for Genetics Evaluation in the Medically Underserved

https://ncats.nih.gov/programs/diagnostic-odyssey



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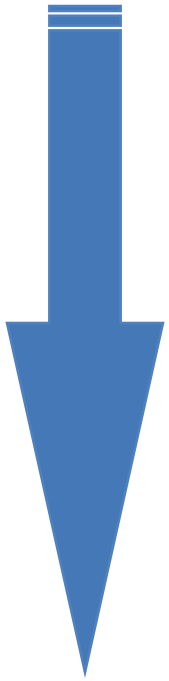
Developing and Streamlining Delivery Approaches

Development



Clinical Trials

1) Somatic Cell Gene Editing – (SCGE)
    1) NIH Common Fund Program
    2) Moving to clinical studies for second phase
    3) Toolkit – data on performance of delivery technologies

2) Accelerated Medicines Program® – Bespoke Gene Therapy Consortium (BGTC)
    1) Enhancing vector manufacturing
    2) Enhancing gene expression
    3) Regulatory playbook

3) Platform Vector Gene Therapy – (PaVe-GT)
    1) Single AAV vector as a platform for multiple therapeutic genes
    2) Testing ability to increase efficiency to clinical trial start-up

NIH
The Common Fund

NIH will award up to $6M USD in prize money and provide independent testing for the most promising delivery vehicles in two Target Areas:

- **Programmable Target Area**: highly efficient programmable delivery system delivering genome editing machinery which targets at least 3 distinct cells, tissues or organs and be at least as efficient as the current state of the art
- **Crossing BBB Target Area**: highly efficient nonviral delivery system capable of crossing the BBB to deliver genome editing machinery to a majority of target cell types in the central nervous system

Award: Top competitors could win up to $1M in prize money and have solution independently tested and validated

3 **Phase 1 Deadline**
5 October 2023

https://qrco.de/bdveZP

Accelerating Medicines Partnership®
Bespoke Gene Therapy Consortium (BGTC)

Program Website

https://fnih.org/BGTC

Highlights and progress:

- Basic AAV Biology awardees selected
- List of disease candidates for clinical trial component down to 14; Final selection by Ma 2023
- Manufacturing subteam met with FDA CBER t discuss minimal set of critical quality attribute for clinical AAV vectors
- BGTC session at American Society of Gene an Cell Therapy meeting (May 2023)

Government

NIH National Center for Advancing Translational Sciences
NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development
NIH National Eye Institute
NIH National Heart, Lung, and Blood Institute
NIH National Human Genome Research Institute
BRAIN INITIATIVE
NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH National Institute of Dental and Craniofacial Research
NIH National Institute of Mental Health
NIH National Institute of Neurological Disorders and Stroke
NIH National Institute on Deafness and Other Communication Disorders
FDA

Industry

ASC Therapeutics
Biogen
DANAHER
janssen
NOVARTIS
Ovid Therapeutics
Pfizer
REGENXBIO
Spark THERAPEUTICS
Takeda
TAYSHA GENE THERAPIES
ThermoFisher SCIENTIFIC
ultragenyx pharmaceutical

Non-Profit

Alliance for Regenerative Medicine
American Society of Gene • Cell Therapy
CIRM CALIFORNIA'S STEM CELL AGENCY
Cure Duchenne
FOUNDATION FIGHTING BLINDNESS
GENETHON CURE THROUGH INNOVATION
NIMBL
NORD National Organization for Rare Disorders
rett syndrome research trust
RTW Charitable Foundation

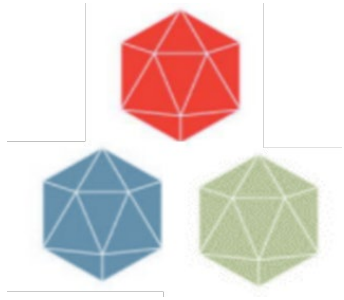
FNIH

Program Management:
Juan Esparza-Trujillo (FNIH)
Brad Garrison (FNIH)
Courtney Silverthorn, PhD (FNIH)

Steering Committee Co-Chairs:
PJ Brooks, PhD (NCATS/NIH)
Tim Miller, MD (Thermo Fisher)
Peter Marks, MD, PhD (CBER/FDA)

AMP® Bespoke Gene Therapy Consortium Components

1 AAV Basic Biology Translational Implications



- Enhancing Vector Generation
- Enhancing therapeutic gene expression

Eight research proposals selected for funding

Goal: Increase efficiency by orders of magnitude.

Therapies for patients

2 Advancing Access to AAV Technologies and Vectors for Bespoke Clinical Applications

Gene therapy target for rare disease (62 initial submissions)

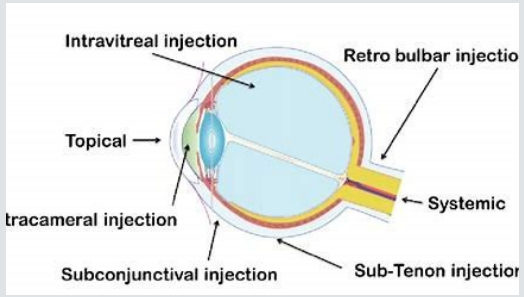
- Create & Build Capacity: Manufacture of therapeutic
- Harmonize best practices: Pre-clinical testing
- Streamline Regulatory Paths: Clinical ability to treat patients

Goal: Standardized, faster, reduced $

- CQAs (FDA Meeting held 9/29/22)
- GLP/Tox (FDA meeting June 2023)

FNIH

Clinical portfolio announced May 16, 2023



Ocular

- **Congenital Hereditary Endothelial Dystrophy (CHED)**
- **Retinal Degeneration (NPHP5)**
- **Retinitis pigmentosa 45 (CNGB1)**

Neurological

- **Multiple Sulfatase Deficiency**
- **Charcot Marie Tooth disease type 4J**
- **Spastic Paraplegia type 50**

Systemic

- **Propionic Acidemia**
- **Morquio A syndrome (Mucopolysaccharidosis IVA)**

Platform Vector-Gene Therapy (PaVe-GT) Milestones

Orphan Drug and Rare Pediatric Disease Designation Templates

RARE DISEASE DAY at NIH

https://pave-gt.ncats.nih.gov/publications/

This page lists project-relevant scientific publications authored by the PaVe-GT project team.

2023

Human Gene Therapy > Vol. 34, No. 5-6 > Clinical Developments | Open Access

Successfully Navigating Food and Drug Administration Orphan Drug and Rare Pediatric Disease Designations for AAV9-hPCCA Gene Therapy: The National Institutes of Health Platform Vector Gene Therapy Experience

Richa Madan Lomash, Oleg Shchelochkov, Randy J. Chandler, NIH PaVe-GT Team†, Charles P. Venditti, Anne R. Pariser, Elizabeth A. Ottinger, Averion Gilberto V., Balakrishnan Krishna, Bönnemann Carsten G., Brooks Philip J., Burden Steven J., Campbell Eggerton, Chen Catherine, Choi Eun-Young, Driscoll Claire, Dukhanina Oksana, Ferry Susan, Foley A. Reghan, Hauserman Janelle Geist, Li Lina, Lo Donald C., Mangalampalli Venkata, Manoli Irini, Mendoza Christopher, Oury Julien, Porter Forbes D., Portero Deanna, Portilla Lili, Rooney Jachinta, Saade Dimah, Sloan Jennifer L., Tambe Mitali, Terse Pramod, Todd Joshua, Toney London, Van Ryzin Carol, Stan Rodica, Vepa Sury, Wagner Erik, Wang Amy, Xu Xin, Zou Yaqun See fewer authors

Published Online: 20 Mar 2023 | https://doi.org/10.1089/hum.2022.232

https://www.liebertpub.com/doi/10.1089/hum.2022.232

SUBSCRIBE

Sign-up for PaVe-GT updates.

Subscribe

PAVE-GT RESOURCES

Rare Pediatric Disease (RPD) Designation Request for AAV9-hPCCA

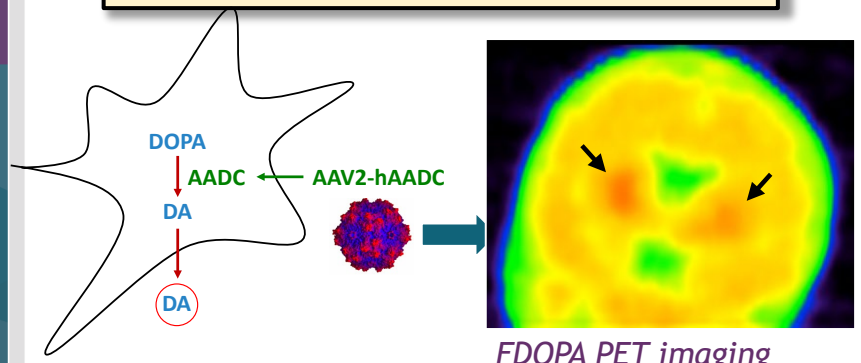
This pdf file contains the RPD designation request for AAV9-hPCCA (NCATSBL-0746) and associated communications between NCATS and FDA OOPD.

https://pave-gt.ncats.nih.gov/outputs

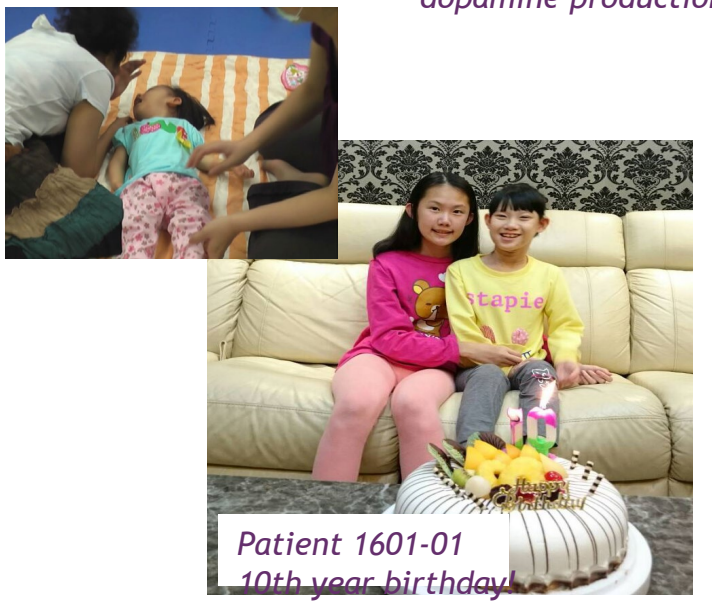
ODD: *Orphan Drug Designation;* ***RPDD:*** *Rare Pediatric Disease Designation*

Gene therapy approval from TRND/Therapeutic Development Branch collaboration

Upstaza™
eladocagene exuparvovec



FDOPA PET imaging shows de novo *dopamine production*



Patient 1601-01 10th year birthday!

- *First disease-modifying treatment for aromatic L-amino acid decarboxylase (AADC) deficiency*
- *Global prevalence of 4,000 to 6,000 patients; life expectancy of 4-8 years*
- *First marketed gene therapy directly infused into the brain*

- Therapeutics for Rare and Neglected Diseases (TRND) program collaboration with Agilis Therapeutics and National Taiwan University begins in 2016
- NCATS develops GMP-grade manufacturing process and completes GLP safety evaluations
- Clear patient benefit in clinical studies (>5 years)
- FDA allows direct BLA filing after Phase II
- Agilis acquired by PTC Therapeutics in 2018
- ➢ **PTC granted European Commission approval in July 2022 for patients 18 months and older**

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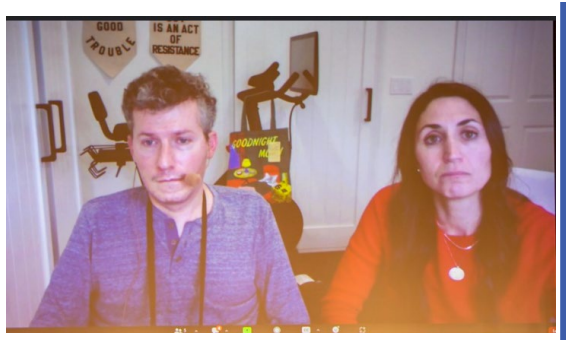


RARE DISEASE DAY at NIH

Feb. 28, 2023 | #RDDNIH

Natcher Conference Center • Bethesda, MD

National Institutes of Health
Turning Discovery Into Health

- Comments from Congressional Rare Disease Caucus chairs and NIH Acting Director
- NCATS resources and programs
- NIH Children's Inn
- Needs of adolescent/young-adult [illegible]ease patients; transitioning pediatric–adult h[illegible]are
- Genetics, gene-targets[illegible]ples, and diversity, equity, and inclusion
- Role of pati[illegible]d patient advocates in research and rare disea[illegible]herapeutics development and collaborations with industry
- Storybook ending

Stay Tuned for RDD@NIH Feb. 2024

NIH lit up Building 38A in Rare Disease Day colors.
PHOTO: NCATS

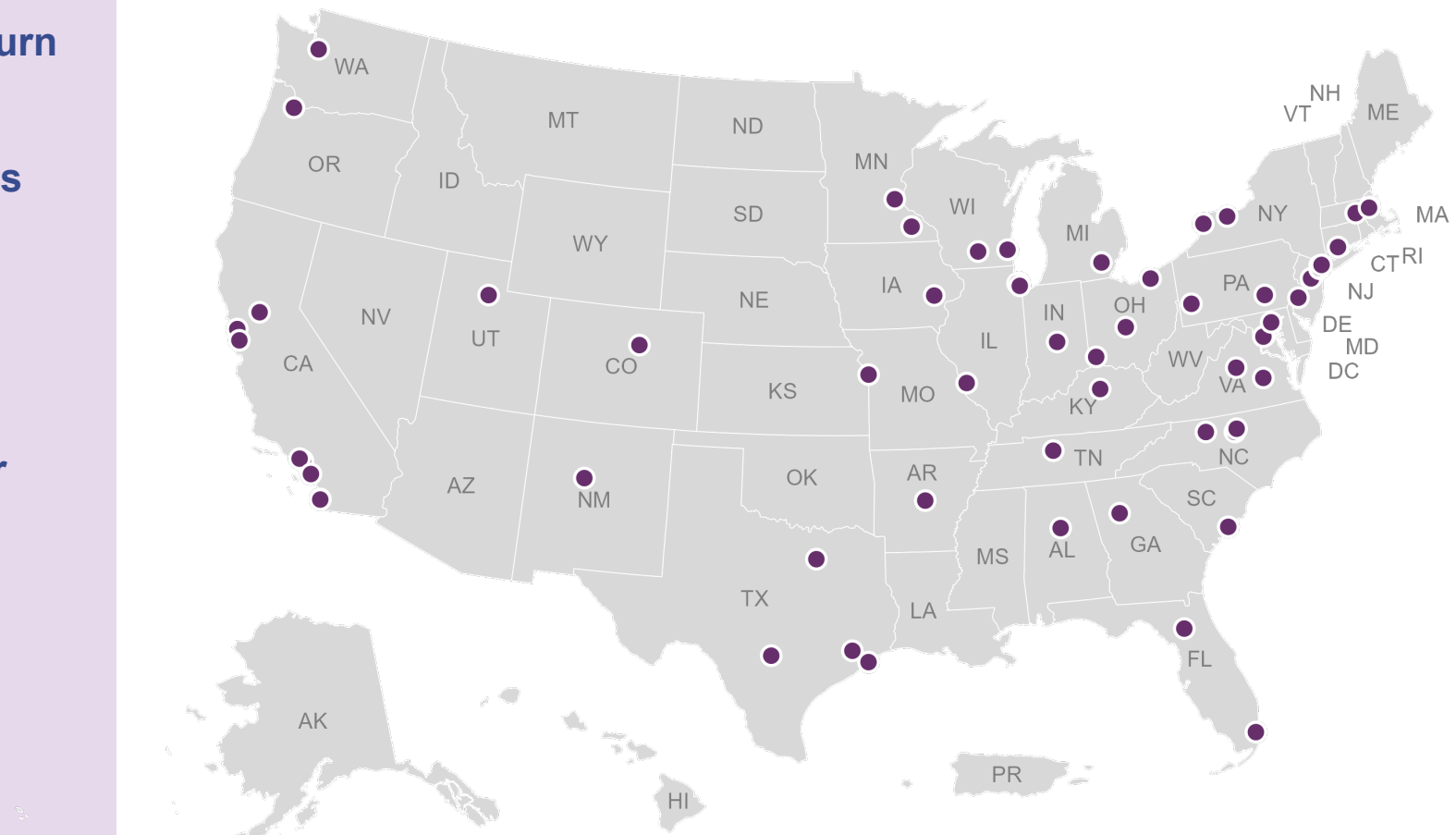
National Center for Advancing Translational Sciences

CTSA Program: Premier National Network Speeds Health Solutions

#CTSAProgram

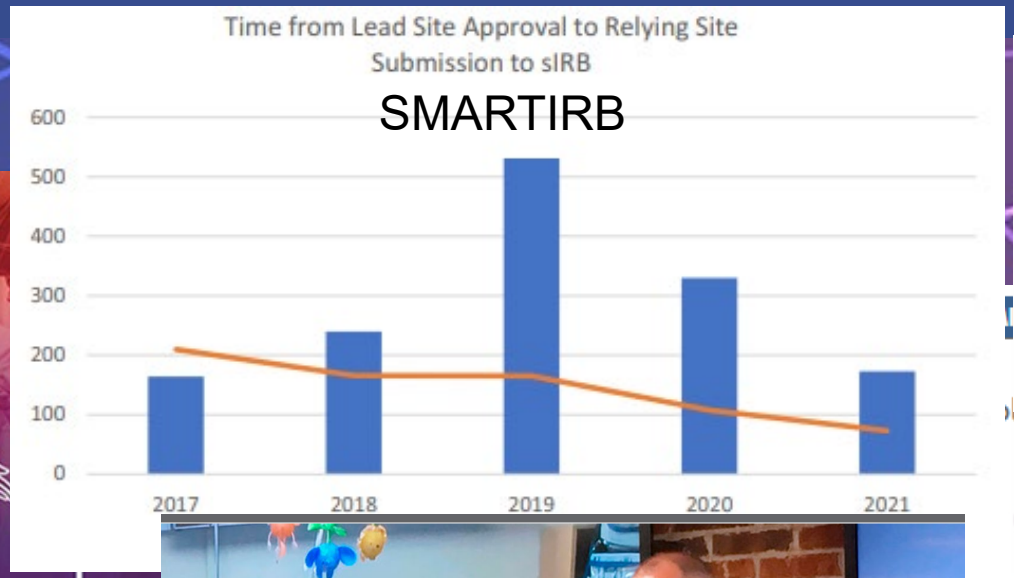
- **Develop, demonstrate, and disseminate innovations that turn science into health faster**
- **Promote impactful partnerships and collaborations**
- **Address health disparities**
- **Provide a national resource for the rapid response to urgent public health needs**
- **Promote training and career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

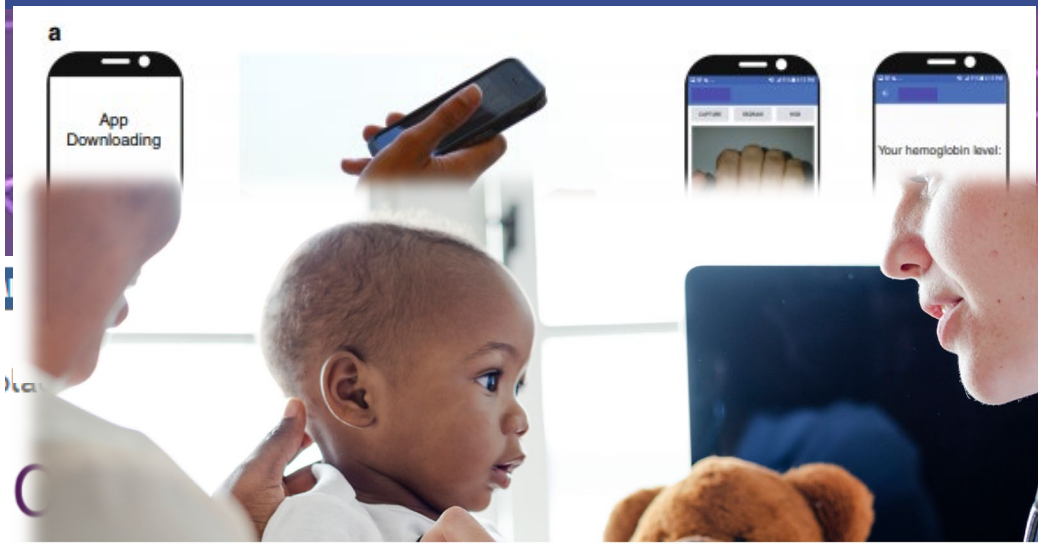
Clinical and Translational Science Awards Primary Institutions



January 2023

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





trial to test immune modulators for treatment of COVID-19

COVID-19 can trigger an immune response that causes inflammation that can lead to life-threatening conditions. ACTIV-1 will determine if regulating the immune response with immune modulators can reduce the need for ventilators and shorten hospital stays.

Last updated: 03-23-2022

NCATS Funds Network to Improve the Use of Telehealth in Children's Health Care

Home › News › Researchers Shed Light on a Rare Genetic Disease in Children

Researchers Shed Light on a Rare Genetic Disease in Children

Findings could lead to better treatments for primary ciliary dyskinesia

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

Pediatric Reach of the CTSA Program at Active Hubs in FY22

53

With an associated children's hospital

13

Have a PI or MPI that are pediatricians

10

Have children's hospitals as a partner

Pediatrics at CTSA Hubs – KL2 Scholars and TL1 Trainees in FY22

6%

Board certified in pediatrics

3%

Pediatric training but not pediatric board certified*

National Center for Advancing Translational Sciences

Pediatrica Therapeutics – UAMS TRI Trainee Startup

Addressing problem of infants born physically dependent on opioids due to maternal opioid use disorder, through development of a novel drug based on a proprietary technology which has shown promise to protect fetal development against neonatal opioid withdrawal syndrome.

Publication

- Every 15 min a newborn suffers from opioid withdrawal.
- Improving an already FDA-approved drug by “tweaking” its pharmacology to produce less fetal/neonatal opioid exposure.
- Neonatal opioid withdrawal syndrome costs $2.5B yearly.

Pediatrica THERAPEUTICS

Julia Tobacyk, PhD, CSO | Hayot Tuychiev, CMO | Veronica Garcia, COO | Megan Reed, PhD, CEO

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Towards a National Health Data Ecosystem: *National COVID Cohort Collaborative (N3C)*

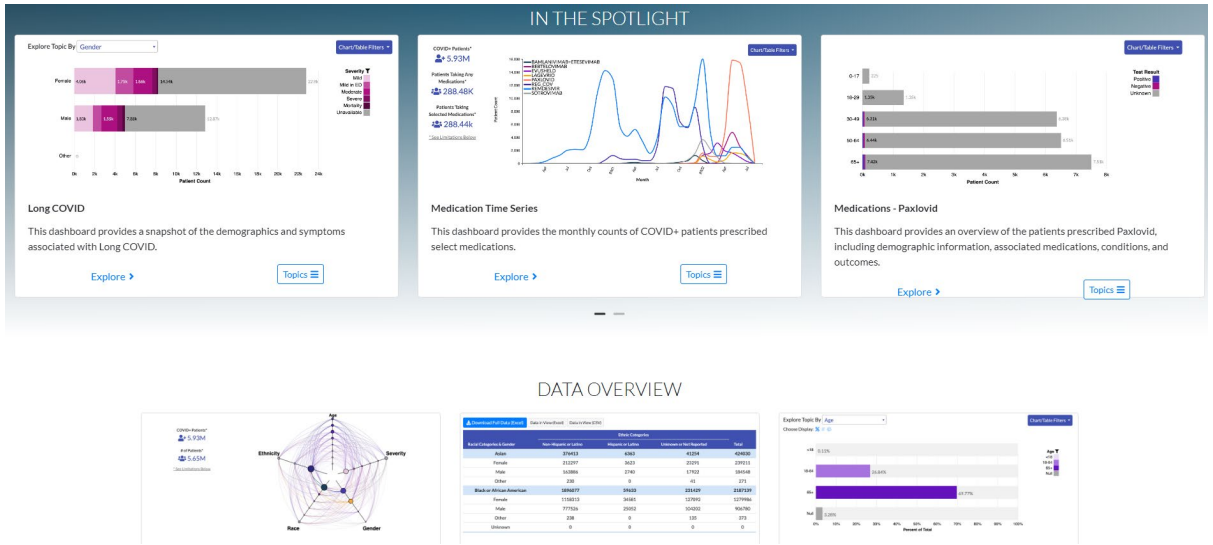
The N3C data enclave is the largest collection of real-world COVID-19 data in the United States

- **Sites**: 80
- **Persons**: Over 20 million
- **COVID+:** Over 7.9 million
- **Rows of data**: 27.1 billon
- **Clinical observations**: 2.5 billion
- **Publications and preprints**: Over 117
- **Google citations**: Over 1,000
- **Informs public health questions**
  - Long-COVID risk
  - mAB effectiveness across variants
  - Paxlovid use

EHRs * CMS * Vaccine Data * Viral Variant Seq
Updated every 2 weeks

https://covid.cd2h.org/dashboard/

NCATS N3C Dashboard



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The National COVID Cohort Collaborative (N3C): EHRs and RWD

N3C is being used to study COVID-19, identify potential treatments, and validate existing therapies

The Pregnancy Clinical Domain Team aims to leverage N3C data to gain insights into pressing COVID-19 questions around pregnancy.

These include understanding the incidence, timing, and severity of COVID-19 in pregnant women and the associated maternal and infant outcomes.

Risk for stillbirth among pregnant individuals with SARS-CoV-2 infection varied by gestational age

Tianchu Lyu [1], Chen Liang [2], Jihong Liu [3], Peiyin Hung [1], Jiajia Zhang [3], Berry Campbell [4], Nadia Ghumman [1], Bankole Olatosi [1], Neset Hikmet [5], Manting Zhang [6], Honggang Yi [6], Xiaoming Li [7]; of the National COVID Cohort Collaborative Consortium

Collaborators, Affiliations + expand

PMID: 36858096 PMCID: PMC9970919 DOI: 10.1016/j.ajog.2023.02.022

Free PMC article

Temporal Events Detector for Pregnancy Care (TED-PC): A rule-based algorithm to infer gestational age and delivery date from electronic health records of pregnant women with and without COVID-19

Tianchu Lyu [1], Chen Liang [1], Jihong Liu [2], Berry Campbell [3], Peiyin Hung [1], Yi-Wen Shih [1], Nadia Ghumman [1], Xiaoming Li [4]; National COVID Cohort Collaborative Consortium

Affiliations + expand

PMID: 36315520 PMCID: PMC9621451 DOI: 10.1371/journal.pone.0276923

Characteristics, Outcomes, and Severity Risk Factors Associated With SARS-CoV-2 Infection Among Children in the US National COVID Cohort Collaborative

Blake Martin [1], Peter E DeWitt [2], Seth Russell [2], Adit Anand [3], Katie R Bradwell [4], Carolyn Bremer [3], Davera Gabriel [5], Andrew T Girvin [4], Janos G Hajagos [3], Julie A McMurry [6 7], Andrew J Neumann [6 7], Emily R Pfaff [8], Anita Walden [7], Jacob T Wooldridge [3], Yun Jae Yoo [3], Joel Saltz [3], Ken R Gersing [9], Christopher G Chute [5 10], Melissa A Haendel [7], Richard Moffitt [3], Tellen D Bennett [1 2]

Affiliations + expand

PMID: 35133437 PMCID: PMC8826172 DOI: 10.1001/jamanetworkopen.2021.43151

Free PMC article

Multilevel determinants of racial/ethnic disparities in severe maternal morbidity and mortality in the context of the COVID-19 pandemic in the USA: protocol for a concurrent triangulation, mixed-methods study

Jihong Liu [1], Peiyin Hung [2], Chen Liang [2], Jiajia Zhang [3], Shan Qiao [4], Berry A Campbell [2 5], Bankole Olatosi [2], Myriam E Torres [3], Neset Hikmet [6], Xiaoming Li [4]

Affiliations + expand

PMID: 35688597 PMCID: PMC9189547 DOI: 10.1136/bmjopen-2022-062294

Free PMC article

Implementation of Whole Genome Sequencing (WGS) as Screening in a Diverse Cohort of Healthy Infants

- First RCT to explore the impact of WGS in ethnically and racially diverse population of healthy infants
- Develop, implement, and evaluate a sustainable approach to Genome Sequencing (GS) as screening that leverages underserved community
- To generate much-needed evidence of the value of GS in infants
- Addresses central questions that need to be answered before GS becomes routine in pediatric care

U01TR003201 (PI: Green) *with co-funding from NICHD; Collaboration with Brigham and Women's Hospital (Harvard Medical School hub), Boston Children's Hospital, Icahn School of Medicine at Mount Sinai, University of Alabama at Birmingham, Baylor College of Medicine, and The Broad Institute, Inc.

13 Years to 13 Hours

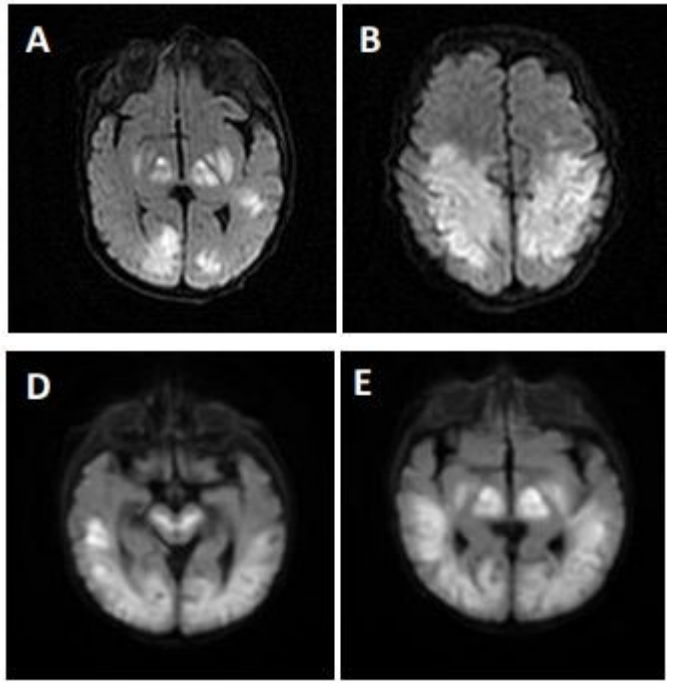
"A 5-week-old, previously healthy male infant was admitted after 2 hours of inconsolable, atypical crying and irritability. Examination revealed downward eye deviation when he cried. Computed tomography of the head showed multiple large, bilateral hypodensities."

"Infantile encephalopathy is associated with approximately 1500 genetic diseases, many of which are clinically indistinguishable but have unique, effective treatments."

"… 13 hours after we initiated sequencing,

"The results led to a clinical diagnosis of *thiamine metabolism dysfunction syndrome 2 (THMD2)"*

"Thiamine and biotin administration was started 37.5 hours after admission... Six hours later, the patient was alert, calm, and bottle feeding."



Rapid Sequencing-Based Diagnosis of Thiamine Metabolism Dysfunction Syndrome

CTSA Program Grant UL1TR002550, Scripps Translational Science Institute

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NCATS Strategic Planning Process 2024-2029: Stakeholder Engagement

Start: November 2022

Target for rollout: Late 2023/Early 2024

Getting organized → Initial stakeholder engagement → Build an outline and draft → Gather feedback on draft plan → Finalize plan and initiate rollout plans → Strategic Plan rollout and implementation

Initial stakeholder engagement

Director's Presentation

- Overview of NCATS, Translational Science principles, audacious goals
- Icebreaker questions

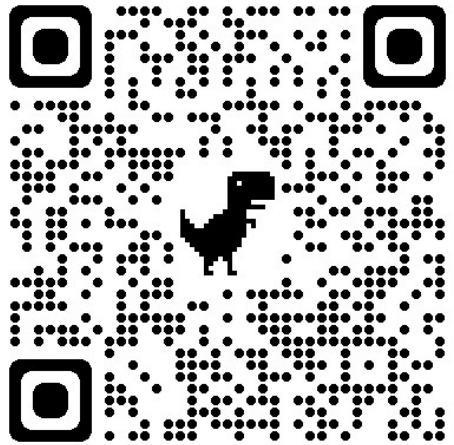
Staff Meetings and Public Roundtables

- Discussion guided by questions to get different groups' perspectives

We Are Here

RFI/ Written input (NIH/HHS Engagement)

- Focused questions to gain additional insight from individuals and/or groups



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