

# Catalyzing Translational Innovation in the Age of COVID-19

### Christopher P. Austin, M.D. Director, NCATS

Federal Demonstration Partnership January 11, 2021



### The COVID-19 Pandemic A public health crisis unrivalled in modern times





# **People at Increased Risk for Severe COVID-19 Illness**

# Older adults

### People of any age with certain underlying medical conditions



# Underlying Medical Conditions Strongly Associated with Increased Risk for Severe COVID-19 Illness

- Serious heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)
- Chronic kidney disease
- Chronic obstructive pulmonary disease (COPD)
- Diabetes, type 2
- Obesity (BMI ≥ 30)
- Cancer
- Sickle cell disease
- Immunocompromised state from solid organ transplant



# Viewpoint COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

"The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations."

### Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – September 19, 2020



**AS Fauci/NIAID** 

Source: CDC COVID-NET. Data from 14 states.



#### A Translational Approach to Addressing COVID-18

Eallaboration Speeds COVID-19 Beneversh

National Network Accelerates COVID-19 Clinical Trial Startup

▶ Platform Approaches Plyst to COVID-15 Efforta

#### 1.447 periods 27.48.2021

where translational science comes in.

trianalation)

A Translational Approach to Addressing COVID-19

#### LATEST NEWS

A team of researchers used organiseds ---timy 3-D trasse models of human brain development - to better understand brass Warthing caused by SMIS-OW-2

Lauren Moren

resourch across all diseasory, NCAPS has developed research basis. technologies, expertise and collaborative networks that can quickly pivot to addressi urgant public haatth issues. In addition, by using its natworks to draw together orderts with receisary and complementary skills, invariedge and experience, 6CATS is enabling projects to out through operational readblacks.

The process of developing new thirs appen and getting them to patients is long.

and difficult. During public health emergencies, science --- and the process of

Translational science is focused or streambring the process of reaving

health and well-being. NEATS is focused on advancing the science of

Chandiating") lab findings into medical practice and treatments to improve

NCATS is supporting research activities spanning the translational science

spectrum to address the novel spronavirus 3019-ISARS-CeV-25 and the alsonne it causes (COVID-19). With the arm of accelerating translational

traving observations into new therapers -- must move faster than ever. That is

#### **VIDEO SPOTLIGHT**

Watch this video for a behind the scenes look at how a collaborative NIH study to measure undetected coronavirus cases came together.

#### Research Activities





Learn about collaborations that are Learn about ACATS projects that are inverseing existing platform approaches speeding research related to COVID-19. to help detect coronavirus cases and first ways to the treat infaction.

Learn hime coordination by an NERTSsupported network of research institutions beigs clinical trials get startiel suichly.

NCATS took an unprecedentedly open, collaboration-based approach to COVID-19

#### https://ncats.nih.gov/covid19-translational-approach



National Center for Advancing ranalational Sciences



### **COVID-19 OpenData Portal**

This online data resource launched in May to openly and quickly share COVID-19-related drug discovery data and experiments for all approved drugs

NCATS is sharing complete data from 13 SARS-CoV-2-related experiments screened against ~10,000 approved drugs/candidates (>500,000 data points)

>27,000 visitors and 85,000 views since launch

Expanding this data-sharing resource to include more complex types of data (e.g. image-based screens)





- Recursion Pharmaceuticals (UT, USA)
- University of Michigan (MI, USA)
- Fraunhofer Institute for Molecular Biology (Aachen, Germany)
- Beijing University of Chemical Technology (Beijing, China)
- Karolinska Institutet/SciLifeLab (Sweden)

#### https://opendata.ncats.nih.gov/covid19/

https://ncats.nih.gov/expertise/covid19-open-data-portal



Niclos	samide	Next the leader a survey of the set of the set
STAT-1 in	mbitor	Now includes compound-level summarie
Sackgro	und Single Agent Screening Dat	of SARS-CoV-2 activity
Identifi	ers	
Sample !	Name Niciosamide	
NCATS I	NCGC00016735	
CAS	50-65-7	
Pubchen	NSID N/A	YY YO
NCATSI	rolght Link (3*	on Bertago
ACTO	NR IINGG	
	244 9.06 1144	Table 1948 1948 1948
	Lines B	Spike - ACE2 protein - protein interaction outpractive
	2.044	APRIL POLICE POLICE POLICE POLICE (TARK CONTRICTION)
		TMPRSS2 enzywatic activity
		17.75 av
No.	8.2240	SARS-CoV Pseudotyped particle entity
4	13844	SARS-CoV Pseudotyped particle entry (VeroE6 tox counterscreen
oter	2.00644	MDRS Pseudotyped particle antry
4	3.35gW	MERS Pseudotyped particle entry 04uh7 tox counterscreen)
	R11pm	SARS-CoV-2 cytopathic effect (EPE)
	A LINE	SARS-CoV-2 cytogathic effect thost tox counterscreent
	THE REAL PROPERTY AND A DESCRIPTION OF A	HEK293 cell line toxicity
		an read Human Revolution

#### https://opendata.ncats.nih.gov/covid19/

National Center for Advancing Translational Sciences

NCATS screen all app

are completed

#### **OpenData Portal**

Home	OpenData Browser	Assays	Animal Mo	dels Omics Effor	ts Highlig	hts Resources			
OpenD		10	NIH Nati	onal Center Advancing slational Sciences	penData	Portal			
opend			Home	OpenData Browser	Assays	Animal Models	Omics Efforts	Highlights	Resources 🕶
NCATS is gener screening a par	rating a collection of datas	ats by issays agains	tome > Animal	Models					
all approved dru	ugs		Animal Mo	dels					
These datasets generate them, the scientific co	, as well as the assay proto are being made immediate ommunity on this site as th	ocols used to ely available to ese screens	Summary Sr	nall Animal Model Field Gu	ide ACTIV Res	ources			

#### Animal Model Summary Overview

The animal model summaries and descriptions have been curated by the National Institutes of Health (NIH) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Preclinical Working Group with support from the Foundation for the National Institutes of Health (FNIH). New and updated information, including detailed individual animal model pages, will be provided as more scientific studies are shared. Please continue to check back for more information.

Feedback, comments, and guestions are highly encouraged to further develop these pages. Please contact ACTIVpreclinical@fnih.org.

#### Small Animals



ences

**SFNIH** 

### CURE ID: Capturing Clinicians' Experiences of Novel Uses of Existing Drugs During COVID-19



- **CURE ID** A mobile application and website
- Data captures clinical experience with novel uses of existing drugs Repurposing
- Data used for hypothesis generation confirming hypothesis via clinical trials integration into clinical practice
- Released Dec 2019; COVID-19 update May 2020
- Developed collaboratively by FDA and NCATS/NIH, with the support of WHO and IDSA

### CURE ID: Capturing Clinicians' Experiences of Novel Uses of Existing Drugs During COVID-19

#### CURE ID and COVID-19

- 1109 clinical case reports
- 250 repurposed drugs
- 1327 clinical trials
- 113 discussion threads

#### **Ongoing Initiative Expansion**

- Special interest collaborations to capture repurposing efforts for neonates, pregnant and lactating women
- PCOR-TF Grant Collaboration between VIRUS registry, JHU and Mayo to expand COVID-19 surveillance using EMRs
  - Bridge to randomized trial platform initiative for COVID-19 with mild to moderate disease

#### **Treatment Outcome by Drug**



■ Improved ■ Unchanged ■ Deteriorated ■ Died

#### PRESS RELEASES

June 23, 2020

PRINT PDF

### C-Path Launches CURE Drug Repurposing Collaboratory to Accelerate Identification of New Uses of Existing Drugs to Treat Infectious Diseases, Including COVID-19

#### Clinicians to report novel uses of existing drugs through FDA-NCATS CURE ID Mobile App.

**TUCSON, Ariz., June 23, 2020** — As millions of patients struggle with diseases that lack adequate treatments, there is a critical need to understand how existing drugs can be used in new ways to improve clinical outcomes. Health care professionals use drugs in novel ways as a potential life-saving intervention when no specific approved therapies are available. However, without the ability to share these experiences in a systematic manner, the clinical and research communities cannot benefit from lessons learned.

To address the challenge, the Critical Path Institute (C-Path) today announced the launch of the CURE Drug Repurposing Collaboratory (CDRC) funded by the U.S. Food and Drug Administration (FDA), in collaboration with the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH). A public-private partnership, CDRC will provide a forum for the exchange of clinical practice data to inform potential new uses of existing drugs for areas of high unmet medical need, advancing research in these areas. The Collaboratory will also create a network connecting major treatment centers, academic institutions and researchers, private practitioners, government facilities and health care professionals around the world.







National Center for Advancing ansiational Science

### **COVID-19 Serosurvey**

- NCATS with NIAID, NIBIB, and NCI quickly enrolled 10,000 participants and analyzed their samples to give NIH and other health organizations more information on the current spread of COVID-19. Results will be reported shortly.
- Two longitudinal follow-ups at 4 and 8 months are planned. Follow-up already has started.
- CTSAs: University of Alabama, University of Pittsburgh





National Center for Advancing Instational Sciences A rare disease patient serosurvey with RDCRN will be shortly underway.



https://ncats.nih.gov/covid19-translational-approach/collaboration#forming-new-collaborations Source: DPI/ETB

### National COVID Cohort Collaborative (N3C)

- A collaboration among the CTSA Program hubs and CD2H to share electronic health records in a centralized, secure location housed at NCATS.
- More than 82 projects are now approved to access the N3C Data Enclave to look at real-world clinical data to help speed COVID research and improve clinical care.
- Rapid development and execution of data agreements, assessment of Federal policy implications, and implementation of operational policies
- Ą.



National Center for Advancing Instational Sciences Created and launched a federal Data Access Committee (DAC) with accompanying policies and procedures



The N3C Data Enclave opened to researchers in September.



# What makes the N3C unique?

- Robust Scale and Scope: Includes demographics, symptoms, laboratory test results, procedures, medications, medical conditions, physical measurements
- Harmonized Data: Makes data from different types of medical records comparable
- Collaborative Analytics: enables team-based research, machine-learning and rigorous statistical analyses
- **Centralized and Secure**: data remain in NCATS' secure FedRAMP-certified cloud, provides standardized assessment, authorization and continuous monitoring

N3C Key Project Meb Inset of positive UNIC cases disprisitio or artificial or a c	rics is televed a Segrees of I	s the number UIT? 1, the ICD-	of distinct patients 10-GM code for 15	who have at least she p DND-19, yeas identified	uative react b	nr any CDVID lab keat			
COVID-19 Positive Patients 475,729		2	Total Patie 2,623,3	337		Sites 38	Rows of Data		
Procedures 168.0m		Lab Re 1.3	seults 3b	Drug Expose 472.1	m	Visits 147.2m	Observations 204.7m		
Cohort characteristic Annory Ontercelle Alue	C9			To plot Aus	(Group				
Cohort characteristic Senery Offers to stud	C9 COVID (Hor676729)	Nue-COVID IN:21474580	Overall (N=2,623,337)	Teper (Ap	r Głoup	*			
Cohort characteristic Anney Optimized at an Gender	C6 COVID (No:475729)	Nee-COVID IN=21476880	Overali (N=2,623,337)	To pur Age	rűresza				
Colvert characteristic senses deteration of se Gender Hide	C8 00048 08x475729) 217943	Nex-COVID IN:2147600) 947579	Overall (N=2,623,337) 1195622	Topist. Aga	rGroup				
Cohort characteristic Antropy Operation of per Gender Mile Female	C9 (No-478729) 217943 227409	Nen-COVED IN-21476600 947579 1778004	Overall (N=2,623,337) 11-05622 1456273	Topter, Ap	rūreup				
Cohort characteristi Annory Orecce to Adue Dender Mule Frende Mul	C9 North Offic471729) 217943 227409	Nen-COVED IN=21476000 947579 FT98804 1116	Overali (N=2,623,337) 1455273 1455273 3116	Tratit Ap	r Group				
Cohort characteristi annory Officer IV 45 of 10 Sender Mile Freshe Mil	C0 COVED (66:475727) 217943 227409	Nen-COVID (N=2147600) 947579 119904 1116	Deerali (N=2,423,237) 1105622 1456273 3116	Topin (Ag	rGroup				
Cohort characteristic anney Overcette 46 av Male Teendae Nat Perstae Nat 9 - 17 16 - 29	C9 covid covid 217943 217943 217943 43324 44324	Nen-COVID (N=2147600) 947579 119804 1116 202986 315559	Overali (N=2,423,237) 1105622 1456273 1116 366310 419707	To plot Age	rGroup	•	ň		
Cohort characteristi Antrony Overcet in a file Sender Male Penale Male 8 - 17 10 - 22 30 - 45	C9 ments COVID (HexA75729) 217943 227409 43324 94352 12243	Nee-COVID IN-21476000 947579 1198004 1116 310986 3105599 300258	Dverali (N=2,422,137) 1165+22 1455/73 1116 39+310 415771 200731	Toper Ap	rGroup	•	1		
Cohort characteristic intervery Optimization ad un Sender Adde Presale Mail Age 0 - 17 10 - 27 30 - 47 56 - 24	C9 merin (NxA78729) 217943 227409 43324 96152 142481 142481 142481 142481	Nem-COVID 1N=21A74000 90.7679 11140 1114 1114 1114 100986 016559 506258 506258	Deerali (N=2,423,2379) 1165622 1456273 1116 366310 419791 760731 560879	- 12 - 12 - 12 - 12	rtiresp				
Cohort characteristic intervery Universitie ad un Dender Mule Frenzle Mul 8. 17 10 - 29 30 - 44 51 - 55 65 - 65	C0 COVID (No.6787279) 217943 227409 43324 94152 142541 104159 81322	Nac-COVID IN-21474600 947679 1116 210966 215539 566259 466259	Deerali (N=2,423,237) 1105622 1255273 3116 386310 410701 700731 560799 847381	Topat Ap	rGroup	*			
Cohort characteristic annory Universitie Advice Male Frenzie Male 8 - 17 10 - 29 30 - 49 51 - 40 51 -	C0 ((6475729) 217943) 227409 43334 96152 104152 104152 83322 4500	Nee-COVID 111221474600 94.7679 1119004 11155 115579 555228 456729 24702	Deerali (N=2,423,237) 1165622 1256273 3116 364310 410701 700731 560079 847381 36285	To part ( Age -19 (4-19 20-4 <sup>9</sup>	rGraap				
Cohort characteristic Jantery Overstein Alian Note Note Note Note Note Note Note Note	C0 ((%A7E729) 217943 227409 43334 96152 142481 104160 81322 4500	Nen-COVID Ne.21476000 94.76379 1136 210966 215539 25522 25522 25522 25522 25522	Degrali (N=2,423,227) 1105622 1456373 1116 366310 410701 700731 560079 847381 20285	To plat (Ap)	rtirosp				
Cohort characteristi Antrony Overcet In Alian Male Feedale Male 8 - 17 10 - 29 30 - 49 55 - 56 55 - 56 55 - 56 Ontenew	C5 merits (HexA78729) 217943 227409 43324 43324 162481 104158 83322 2007 201753	Nee-COVID IN-2147660 947679 119604 1196 200966 215599 200966 215599 200966 215599 200966 215599 20096 20000000000	Dverali (N=2,423,337) 1165622 1456273 1116 366310 410791 366310 410791 560079 847381 36025 36025	To plant. Age -10 (0-10 20-47 30-48	r Greage				
Cohort characteristic intervery Ordentic The Aduet Male Prenate Mail 19 - 29 20 - 40 20 - 40 2	C6 merits (No.678729) 217043 227039 43334 96152 104160 81352 201793 2567	Nee-COVID IN=21474680 947679 1198804 1198 202886 215539 202289 444259 25702 25702	Deerali (N=2,423,2379) 1105622 1456273 13116 364310 419701 760731 560079 847381 347381 347381 347381 347381 347381 347381 347381 347381 347381 347381 347381 347381	Trapart App -12 (0-32 -23 -24 -24 -24 -24 -24 -24 -24 -24 -24 -24	r Greep				
Cohort characteristic intervery Universities at an Dender Male Frenate Male 19 - 29 30 - 49 50 - 59 50 - 54 51 - 54 55 - 55 56	C5 (HexA78729) 217943 227409 43334 94152 122481 104152 122481 104152 10249 281752 281752 2597 26371	Nes-COVID (N=21474680) 947679 11196 115579 558228) 456729 25701 14973725 31354 20330	Destall (N=2,423,237) 1105622 1255713 3116 364210 410701 700731 560799 847381 36285 117754273 38911 406701	Topat (Ap -1) (4-3) (5-3) (5-4) (5-5	r Greeup				
Cohort characteristic Interve Orientation Adue Sender Male Preside Male Preside Male Preside Male Discourse Sender Sender Male Othersen Male Othersen Male Male Sender Sen	C9 (Hu-A782749) 217943 227099 43334 96152 102461 31322 4500 281793 2961793 2961793 2961793 19609	Nes-COVID (N=2147660) 947639 1118 202866 (16599 250229 266729 266729 266729 266729 257001 1490725 31346 200300 26000	Deerali (N=2,423,237) 1165622 1356273 3116 364210 410701 200735 560079 847597 36295 17754277 362911 400701 400701 400701 400701 400701 400701	Topat Ap	rtiresp				
Cohort characteristi antery Orientation and an indef Male Fenale Male Fenale Male Fenale Bale State State State White Construction Race Vinite One Race of Atmain American Asian Pacific Datastery	C9 (HoxA783729) 2(17943) 2(179	Nee-COVID IN-2147660 947579 1196054 1196 200966 215539 200966 215539 200966 215539 200966 215539 20096 20000000000	Dverall (N=2,423,337) 1165622 1456273 1116 366210 410701 366210 410701 560079 847581 36025 36029 847581 36285 362911 406701 40701 40070000000000	Topart App -10 (0-)* 10-4* 10-4* 10-4*	rtirege				
Cohort characteristi intervery Orientation adue Male Teenale Add 1017 10-29 20-47 20-57 20-57 20-57 20-57 55- Uniterativ Back or African American Asses Pacific Infantity Net	C9 (96:478729) 217943 227039 43334 96:12 14234 96:12 14234 96:12 14234 96:12 14234 96:12 14234 96:12 14507 26:1713 1567 26:1713 16:72 16:72 16:72 16:72	Nee-COVID IN-21474680 947679 1198804 1198 200289 200289 444259 20028 20028 10000 20028	Deerali (N=2,423,2379) 1456273 1316 364310 419791 760731 560079 947381 34285 17754527 36911 480701 480701 480701 5623 281400	Triport App -12 (0-32 -23 -24 -24 -24 -24 -24 -24 -24 -24 -24 -24	r Greage				
Cohort characteristic intervery Orientet In Adue View Constraints Number 19 - 22 30 - 49 50 - 54 51 -	C9 (96:478729) 217943 227039 43334 96152 16248 83322 4500 281753 3597 26331 11652 1672 98226	Nes-COVID (N=21474580) 947639 11366 115539 555228 456229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 29705 144229 144220 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 144229 14429 144229 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14429 14444444444	Destall (N=2,423,237) 1105622 1255273 3116 265273 3116 415751 260751 260799 947381 36285 1779423 362911 400701 400701 400701 400701 5522 251600	Topot (Ap -1) (4. 3) (5. 3) (5. 4) (5. 4) (5	rGreege				
Colvort characteristic Jammery Officers to Adue State Frenale Mad B - 17 10 - 27 30 - 47 58 - 94 65 54 Unineave Race Winas Other Pacific relative Mat Black of Africat American Asse Pacific relative Mat Ethnicity Mar Itanion	C9 (Hu-A78229) 217943 227409 43334 96152 83322 85322 85322 85322 85322 85322 85322 85322 85322 85322 85322 85322 85322 85322 85322 96125 1672 96225 1672 97268	Nee-COVID (N=2147660) 947537 1118 202966 (15592 255228 255228 255228 255229 245229 2552529 255229 255229 255229 25	Overall N=2,423,337) 1165622 1455713 3116 364310 410701 560809 847881 30285 1775623 369110 410701 410701 410701 40285 5623 251600 2001885 64199	Toper: App -11 (4-1)* 30-4* -0.4	e Grenza				



https://ncats.nih.gov/n3c



# **N3C Data Pipeline**



# **COVID-19 Tissue Chips**

- Don Ingber and team (Wyss Institute) previously funded by NCATS to model human lung-on-chip and response to influenza
- Chip used to model viral entry of SARS-CoV2 and test repurposed drugs
- Amodiaquine, toremifene, and clomiphene inhibit viral infection under physiological conditions
- Hydroxychloroquine, chloroquine and arbidol did not inhibit viral entry, consistent with clinical data
- Proof-of-concept that tissue chips can help identify existing drugs that may be repurposed for pandemic viral applications.



https://doi.org/10.1101/2020.04.13.039917 (bioRxiv)





# MPSCoRe: Microphysiological Systems for COVID-19 Research Working Group

- Joint working group to support and help coordinate global MPS efforts to study COVID-19 and future infectious disease applications.
- Partnership between NC3Rs, NICEATM, NCATS, NIAID/DMID, US Army DEVCOM CBC
- ~60 members have accepted targeted invitations so far, including stakeholders from pharma, MPS developers, academia, regulatory agencies, etc.
- Informational webinar planned for 29 January 9:00-11:00 am EST
- Workshop planned as satellite to NCATS Tissue Chip Consortium spring meeting

#### **MPSCoRe WG Objectives include:**

- Raise awareness of COVID-19 MPS research
- Facilitate connections between MPS developers and end-users
- Engage global regulatory authorities
- Characterize model performance and readiness criteria
- Support the assessment of MPS against in vivo/clinical data
- Ensure the 3Rs opportunities are recognized.





National Center for Advancing anslational Sciences

### **COVID-19 Clinical Trials**

NCATS and its CTSA Program are playing lead roles in rigorous clinical trials to test potential treatments in hospitalized adults with COVID-19:

- The ACTIV-1 Immune Modulators trial is evaluating three drugs that could reduce the harmful COVID-19 cytokine storm
- Two trials led by Einstein/NYU and Vanderbilt are evaluating blood plasma donated by people who have recovered from COVID-19



National Center for Advancing Instational Sciences

https://ncats.nih.gov/news/releases Source: DCI





The trials are currently enrolling participants.

### Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

ACTIV-1 IM: Randomized Master Protocol for Immune Modulators for Treating COVID-19

#### Infrastructure and Support:

Evaluating treatment of three therapeutic agents in moderately or severely ill hospitalized patients (adults) infected with SARS-Cov-2.

- Therapeutic agents:
  - ✓ Infliximab (Remicade) TNF-alpha blocker
  - ✓ Abatacept (Orencia) CTLA-4
  - Cenicriviroc (CVC) CCR2/CCR5 antagonist
- Target enrollment: 2,160 participants

 Leveraging existing NCATS CTSA Program Trial Innovation Network

- Supported by Operation Warp Speed (OWS) via a Biomedical Advanced Research and Development Authority (BARDA) Task Order awarded to Technical Resources International (TRI, Inc.)
- Coordination and oversight by NCATS

#### Major Milestones and Progress

- Launched on October 16, 2020
- 25 active sites in the U.S.

#### Study Snapshot





National Center for Advancing franslational Sciences



# NCATS Convalescent Plasma RCTs Multisite trials run through CTSA hubs

### CONTAIN COVID-19

RANDOMIZED CONTROLLED TRIAL STUDYING THE EFFICACY AND SAFETY OF CONVALESCENT PLASMA IN LIMITING COVID-19 COMPLICATIONS Enrollment: 725 Active Sites: 17

**Anticipated Completion: February** 



Enrollment: 532 Active Sites: 20 Anticipated Completion: March



NIH

National Center for Advancing Instational Sciences **NCATS Accelerating Translation by:** *Establishing format for direct data submission to FDA Promoting harmonization of plasma assays* 



### **Community Engagement to Address COVID-19**

NCATS' CTSA Program hubs are trusted community partners, which allowed them to rapidly pivot to address COVID-19 health disparities.

They are working closely with community partners on initiatives to speed the discovery and delivery of COVID-19 treatments and vaccines to those in greatest need.



COLLABORATE. INNOVATE. ACCELERATE.





National Center for Advancing Inslational Sciences

https://ncats.nih.gov/ctsa/projects/community-engagement-at-CTSA-hubs-during-the-COVID-19-pandemic Source: DCI

### **Community Engagement to Reduce COVID-19 Health Disparities**



### Community Engagement Alliance (<u>CEAL</u>) Against COVID-19 Disparities

 To provide trustworthy information through active community engagement with, investment in, and outreach to underserved communities, building long-lasting partnerships to improve diversity and inclusion in our scientific response to the COVID-19 pandemic

### Rapid Acceleration of Diagnostics (<u>RADX</u>) Initiative

- To speed innovation in the development, commercialization, and implementation of technologies for COVID-19 testing
- <u>RADx-UP</u>: Rapid Acceleration of Diagnostics for Underserved Populations





### **NIH-Funded Community Engagement Alliance (CEAL) Against COVID-19 Disparities Research Teams**



#### **CEAL Awardee States / Pls**

- 1. Alabama\* Mona Fouad, M.D., M.P.H.
- 2. California\* Arleen F. Brown, M.D., Ph.D.
- 3. Florida\* Olveen Carrasquillo, M.D., M.P.H.
- 4. Georgia\* Tabia Henry Akintobi, Ph.D., M.P.H.
- 5. Michigan\* Erica Marsh, M.D.
- 6. North Carolina\* Anissa I. Vines, Ph.D.
- 7. Tennessee\* Paul Juarez, Ph.D.
- 8. Texas\* Jamboor Vishwanatha, Ph.D.
- 9. Mississippi Caroline Compretta, Ph.D.
- 10. Arizona Sairam Parthasarathy, M.D.
- 11. Louisiana Marie A. Krousel-Wood, M.D.

National Institutes of Health

\*CTSA affiliation





#### RADx<sup>™</sup> Tech

The RADx Tech initiative aims to speed the development, validation, and commercialization of innovative point-of-care and home-based tests, as well as improve clinical laboratory tests, that can directly detect the virus. Budget: \$500 Million



id Acceleration Diagnostics (RADX)

#### **RADx Underserved Populations (RADx-UP)**

The overarching goal of the RADx-UP initiative is to understand the factors associated with disparities in COVID-19 morbidity and mortality and to lay the foundation to reduce disparities for those underserved and vulnerable populations who are disproportionately affected by, have the highest infection rates of, and/or are most at risk for complications or poor outcomes from the COVID-19 pandemic.

Budget: \$500 Million



#### RADx Advanced Technology Platforms (RADx-ATP)

The RADx-ATP program seeks to increase testing capacity and throughput by identifying existing and late stage testing platforms for COVID-19 that are far enough advanced to achieve rapid scaleup or expanded geographical placement in a short amount of time. These efforts will focus on scaling up technologies, including improving existing high-throughput platforms, to increase performance. Budget: \$230 Million



#### RADx Radical (RADx-rad)

RADx-rad will support new, non-traditional approaches, including rapid detection devices and home-based testing technologies, that address current gaps in COVID-19 testing. The program will also support new or non-traditional applications of existing approaches to make them more usable, accessible, or accurate. These may lead to new ways to identify the current SARS-CoV-2 virus as well as potential future viruses.

Budget: \$200 Million



National Institutes of Health



# RADx-UP

- > A collaborative clinical research network of existing large-scale programs that have adequate capacity, infrastructure and relationships with underserved communities.
- Research on the social, ethical and behavioral implications of these health disparities to inform the development and evaluation of testing programs.
- A coordination and data collection center, providing overarching support and guidance on administrative operations and logistics, facilitating effective use of COVID-19 testing technologies, supporting community and health system engagement and providing overall infrastructure for data collection, integration and sharing.







# **RADx-UP CTSA Supplement Sites**



- Medical College of Wisconsin
- The Ohio State University
- The University of Utah
- Rutgers
   Biomedical and
   Health Sciences
- The University of Texas Health Science Center at Houston
- University of Kansas Medical Center

https://www.nih.gov/research-training/medical-research-initiatives/radx/funding#radx-up-funded





\*Out of 32 institutions received supplements

### Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

### LAUNCH

On April 17, NIH announced the launch of a public-private partnership, **Accelerating COVID-19 Therapeutic Interventions and Vaccines(ACTIV)** 

#### MISSION

Develop a coordinated research response to speed COVID-19 treatment and vaccine options





### **ACTIV Stakeholders**

ACTIV is being coordinated by the Foundation for the National Institutes of Health (FNIH), and has brought together multiple partners from government, industry and non-profits.



### **ACTIV Governance**

ACTIV Governance includes representation from key stakeholders in both the private and public sector.





### **ACTIV Governance & Coordination with Operation Warp Speed**

OWS and ACTIV working groups have been closely collaborating to ensure alignment across both efforts.





### **Focus Area Objectives & Composition**

Each focus area is a Working Group that contains several sub groups to oversee tactical operations :





### **Preclinical Working Group**

#### OBJECTIVE

Standardize and share preclinical evaluation methods and sharing testing resources in an open forum that allows for effective validation and comparison of therapeutic candidates.

#### ACCOMPLISHMENTS TO DATE

- ✓ Developed a **master inventory of preclinical testing** resources
- ✓ Established SOPs for accelerated preclinical agent development in response to a pandemic
- Developed a National Strategy for NHP Research and a process to coordinate NHP studies centrally through NIH, and "field guides" for the use of small animal testing models
- ✓ Created and published online 9 "field guide" videos for use of small animal models in COVID-19 preclinical development
- ✓ Established a process for **prioritizing in vitro assays** and **evaluating preclinical compounds**
- ✓ Created a **public database** for sharing preclinical data (NCATS Open Science Portal)
- Conducting a "matchmaking" process to pair promising compounds with available preclinical resources and funding, on an ongoing basis
- □ Assess the impact of emerging viral mutations on efficacy of vaccines and therapeutics



-7



### OpenData Portal

Translational Sciences

]	Home OpenData Brow		wser	Assays Animal Models				Omics	s Effo	orts	Highlights	Resources 🔻	
Small	Animals								5	F١	<b>NIF</b>	-	
Species	Modification	Model Name/Nomenclatu	Non-Hu	iman Prima	and anison setmonement								FNIH
Ferret	Outbred Stock	Ferret	T ton r to							.5			
Guinea Pig	Wild Type	Guinea Pig							mitt	die.es		ncement	
Hamster	Inbred Strain	Syrian Golden					ines	inals .	altring th	stappingt	anissio	ase tribe	
Hamster	Transgenic	Tg(K18-hACE2)	Species	Geographic Origin	Route of Exposure	A	1900, 1	stin, Henn	other	Intect 4	rano ol	Disease Manifestation & Pathology	Extent of disease
Mouse	ACE2 Transduced	Adenovirus transduced hACE2	African Green	St. Kitts (wild- caught)	Intratracheal/intranasal, aerosol	V		¥	۷	TBD	TBD	Lung lesions;interstitial pneumonia; recovery	Mild to moderate
Mouse	Inbred Strain	BALB/c (adapted virus)	Aged African	St. Kitts (wild-	Intratracheal/intranasal,	 V		~	Y	TBD	TBD	Lung lesions, interstitial pneumonia,	Severe
Mause	Knock-In	C57BL/6-	Green	caught)	intratracheal, aerosol							cytokine storm; ARDS; varied death and necovery	
		Ace2 <sup>ern1(ACE2)Vowa</sup>	Cynomolous	Cambodia	Intratracheal/intranasal.		4	4	Y	TBD	TBD	Lung lesions: interstitial pneumonia:	Mild
Mouse	Transgenic	B6.Cg-Tg(K1B-	macaque		intratracheal							recovery	
		NoLejzenniva.	Rhesus macaque	China or India	Intratracheal/intranasal, intratracheal, ocular, oral, aerosol	×	4	4	۷	TBD	TBD	Lung lesions; interstitial pneumonia; recovery	Mild

https://opendata.ncats.nih.gov/covid19

### **Therapeutics – Clinical Working Group**

#### OBJECTIVE

Prioritize promising therapeutic candidates and accelerate their clinical evaluation by establishing large-scale master protocol trials.

#### ACCOMPLISHMENTS TO DATE

- Developed and continuously enhanced a world-class process for prioritizing clinical agents for rapid testing
- Evaluated ~500 available agents with potential relevance for COVID-19 therapies and prioritized the most promising agents for further study (agent prioritization continues on a rolling basis)
- ✓ Assessed, designed, and harmonized seven master protocols for ACTIV clinical trials, focusing on candidates selected through the agent prioritization process
- Selected clinical trial networks best suited to execute these master protocols and supported NIH efforts to launch them; six protocols have been launched to date
- Actively working with NIH and OWS across all protocols to ensure they are effectively coordinated, efficiently managed, and meet recruitment targets



### Prioritizing the most promising therapeutic agents for COVID-19

The Working Group continues to Identify agents that stop the virus or that treat its symptoms so they can be placed in a master protocol for a Phase II/II Progressive trial – so far ACTIV has reviewed more than 500 agents.



36

### **Clinical Trial Capacity Working Group**

The Working Group developed an inventory of clinical trial capacity, including networks of NIH ICs, industry, and other organizations, that will serve as a guide for how and where to implement effective COVID-19 clinical trials.



### **Current Portfolio of ACTIV Master Protocols**

ACTIV Therapeutics has been taking a portfolio approach to address the dramatic health and economic challenges posed by the pandemic, with harmonized "master protocol" trials.

	DESIRED OUTCOMES	STATUS
ACTIV-1	<ul> <li>Phase III trial of 3 host-targeted immune modulators</li> <li>Inpatient (hospitalized) patient population</li> <li>NCATS Trial Innovation Network + CRO</li> </ul>	<ul> <li><u>Trial launched October 16</u></li> <li>First 3 agents selected – Abatacept, Infliximab, and Cenicriviroc</li> </ul>
ACTIV-2	<ul> <li>Phase II/III trial of up to 5-7 Neutralizing Antibodies and Oral Antivirals</li> <li>Outpatient population</li> <li>NIAID ACTG network + CRO</li> </ul>	<ul> <li><u>Trial launched August 3</u></li> <li>Initial agent: nAb from Lilly; onboarding other agents</li> </ul>
ACTIV-3	<ul> <li>Phase III trial of 5-7 Neutralizing Antibodies and Oral Antivirals</li> <li>Inpatient population</li> <li>NIAID INSIGHT + NHLBI PETAL + NHLBI CSTN + VA networks +CRO</li> </ul>	<ul> <li><u>Trial launched August 4</u></li> <li>Initial agent: nAb from Lilly (halted for futility Oct. 26); onboarding other agents</li> </ul>
ACTIV-4	<ul> <li>Phase III trial of anticoagulants (heparin, aspirin) and antiplatelet drug</li> <li>Three different populations: pre-hospitalized, hospitalized, &amp; post-hospitalized</li> <li>NHLBI-NINDS CONNECTS network</li> </ul>	<ul> <li><u>Hospitalized and Pre-Hospitalized cohorts launched Sept</u> <u>17, Post-hospitalized cohort launched early December</u></li> <li>First agents – LMWH and UFH (hospitalized) and low dose aspirin, high dose aspirin, and apixaban (pre-hospitalized)</li> </ul>
ACTIV-5 (Big Effect Trial)	<ul> <li>Phase II "proof of concept" study to identify multiple promising treatments</li> <li>Inpatient population</li> <li>NIAID networks + CRO</li> </ul>	<ul> <li><u>Trial launched October 12</u></li> <li>Two initial agents selected – Risankizumab + Lenzilumab</li> <li>Prioritizing additional agents</li> </ul>

### Where do I go for more information on ACTIV?

For:	Page / Link
Concerction	✓ NIH ACTIV Website: [https://www.nih.gov/research-training/medical-research- initiatives/activ]
General Information:	<ul> <li>✓ FNIH Website: [<u>https://fnih.org/news/press-releases/nih-launches-partnership-to-speed-covid19-vaccines-treatments</u>]</li> </ul>
To submit information for a diagnostic, vaccine, technology, or other information for the awareness of NIH:	<ul> <li>NIH COVID-19 Candidate and Technologies Portal: [<u>https://grants.nih.gov/grants/rfi/rfi.cfm?ID=107</u>]</li> </ul>
Formal submission of agents for testing in ACTIV:	<ul> <li>✓ ACTIV Preclinical and Clinical Asset Data Survey: [https://redcap.ncats.nih.gov/redcap/surveys/index.php?s=DAE87WPTE7]</li> </ul>
	<ul> <li>Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): An Unprecedented Partnership for Unprecedented Times [https://jamanetwork.com/journals/jama/fullarticle/2766371]</li> </ul>
Publications to date:	<ul> <li>Accelerating Development of SARS-CoV-2 Vaccines — The Role for Controlled Human Infection Models [<u>https://www.nejm.org/doi/full/10.1056/NEJMp2020076</u>]</li> </ul>
	<ul> <li>Bridging the Gap at Warp Speed — Delivering Options for Preventing and Treating Covid-19 [https://www.nejm.org/doi/full/10.1056/NEJMp2028535?query=TOC]</li> </ul>
	✓ A strategic approach to COVID-19 vaccine R&D [https://science.sciencemag.org/content/368/6494/948]
SFNIH	39

### What have we learned?

- It is possible to go from fundamental discovery to therapeutics and vaccines much more quickly than has historically occurred
- Ingredients for this are
  - Feeling of urgency in all participants in the research ecosystem
  - Recalculation of benefit:risk based on urgency
  - Willingness to share based on recalculation of benefit:risk
  - Proactive collaboration among public sector, private sector, and public-private orgs that derives from *desire* to share
- This is a potentially positively self-reinforcing cycle since increased efficiencies lead to increased productivity which has potential to increase return on investment despite sharing of credit/profits
- But many of the conditions, regulatory/policy exemptions, and additional funding will likely not continue without proactive steps by all participants in the university, industry, and government sectors





# NCATS

## COLLABORATE. INNOVATE. ACCELERATE.







