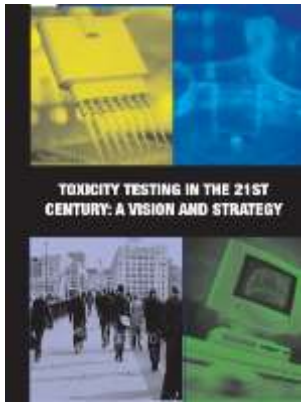
NCATS-NTP collaboration

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

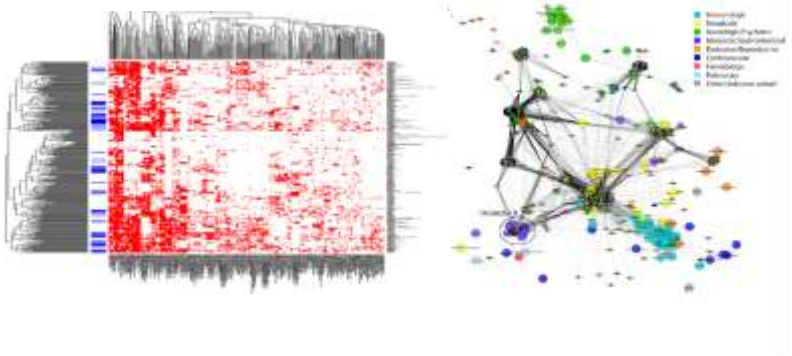
National Toxicology Program Board of Scientific Counselors

June 17, 2019

The Toxicology in the 21st Century (Tox21) Program



- Initiated 2005 with NTP; made official 2008 w NTP, EPA; FDA added 2010
- Identify patterns of compound-induced biological response in order to:
  - characterize toxicity/disease pathways
  - facilitate cross-species extrapolation
  - model low-dose extrapolation
- Prioritize compounds for more extensive toxicological evaluation
- Develop predictive models for biological response in humans



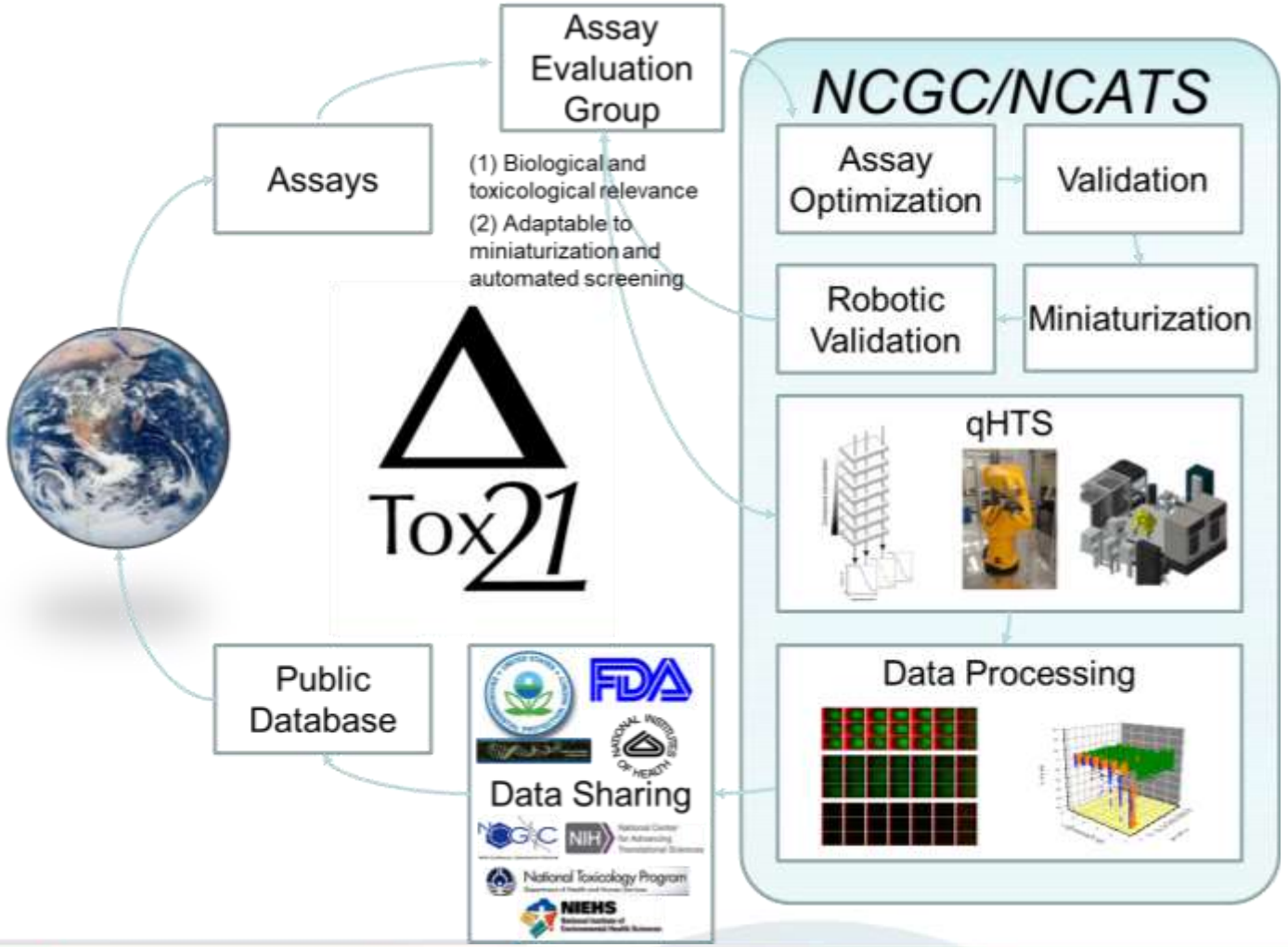
NIH National Center for Advancing Translational Sciences

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

FDA

National Toxicology Program
Department of Health and Human Services

Tox21 Screening Process



Attene Ramos et al., 2013, Drug Discovery Today 18:716 723

National Center for Advancing Translational Sciences

Tox21 Robot System: “Linda”

Pintool Station

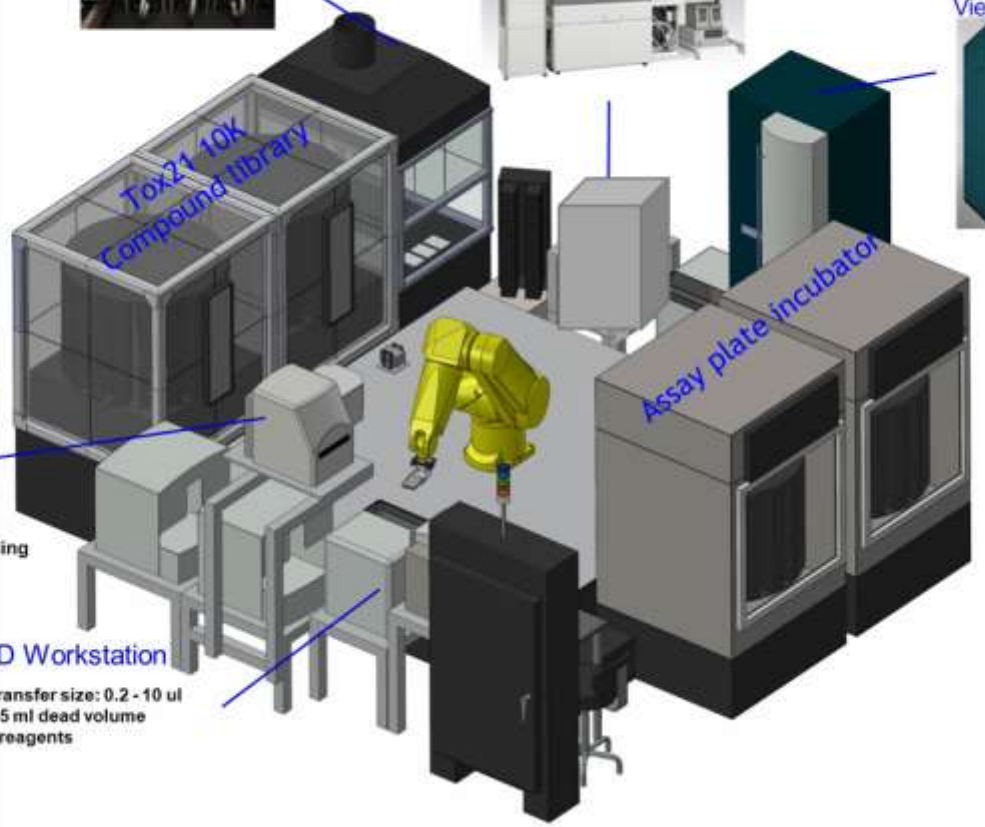
- Transfer size: 20 nl
- Pins washed in 3 solvents

Kinetic Reader

- Fluorescence
- Kinetic measurement
- Bottom reading

ViewLux Multilabel Reader

- Absorbance
- Fluorescence
- F.P.
- Luminescence
- TR-FRET
- Top reading



EnVision Multilabel Reader

- Absorbance
- Fluorescence
- F.P.
- Luminescence
- TR-FRET
- AlphaScreen
- Top/Bottom reading

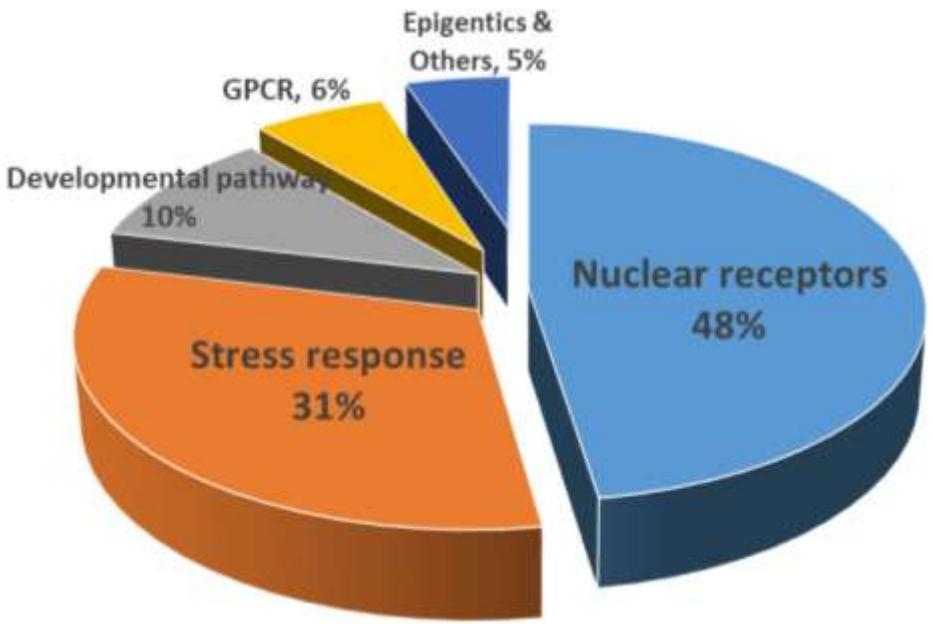
BioRAPTR FRD Workstation

- Transfer size: 0.2 - 10 ul
- 0.5 ml dead volume
- 4 reagents

Operetta Imaging System

Assays Screened in first epoch of the Tox21 Program

- **Endocrine disruption** (e.g., AR, AhR, aromatase, ER, ERR, CAR, FXR, RORr, PPARr, PPARd, PR, RXR, VDR)
- **Stress response pathways** (e.g., AP-1, HSE, NFkB, Nrf2/ARE, pH2AX, Hif-1/hypoxia, ER stress, real time cytotoxicity/viability, mitochondrial membrane potential, acetylcholinesterase)
- **Developmental pathway** (e.g., retinol signaling, hedgehog/Gli, SBE/Smad)
- **GPCR** (e.g., thyroid stimulating hormone receptor, TSHR and thyrotropin-releasing hormone receptor, TRHR)
- **Epigenetics** (e.g., HDAC) and **others** (e.g., luciferase assay)

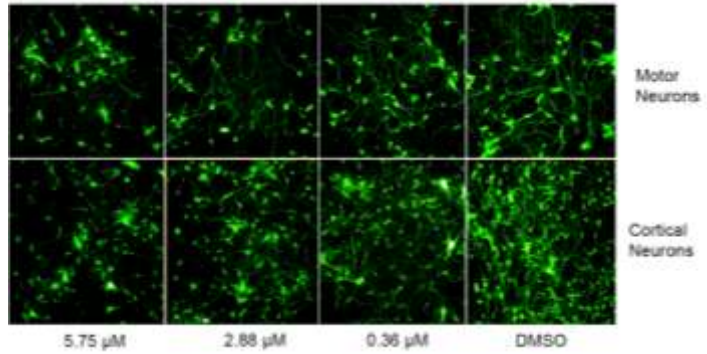


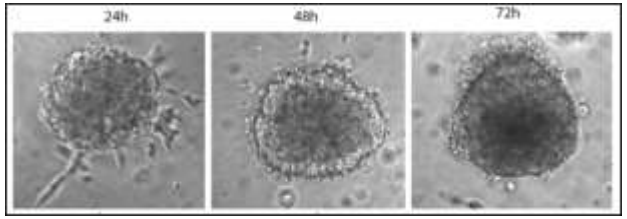
85 Tox21 related scientific articles in **40** journals

37/85 First- or corresponding-author manuscripts

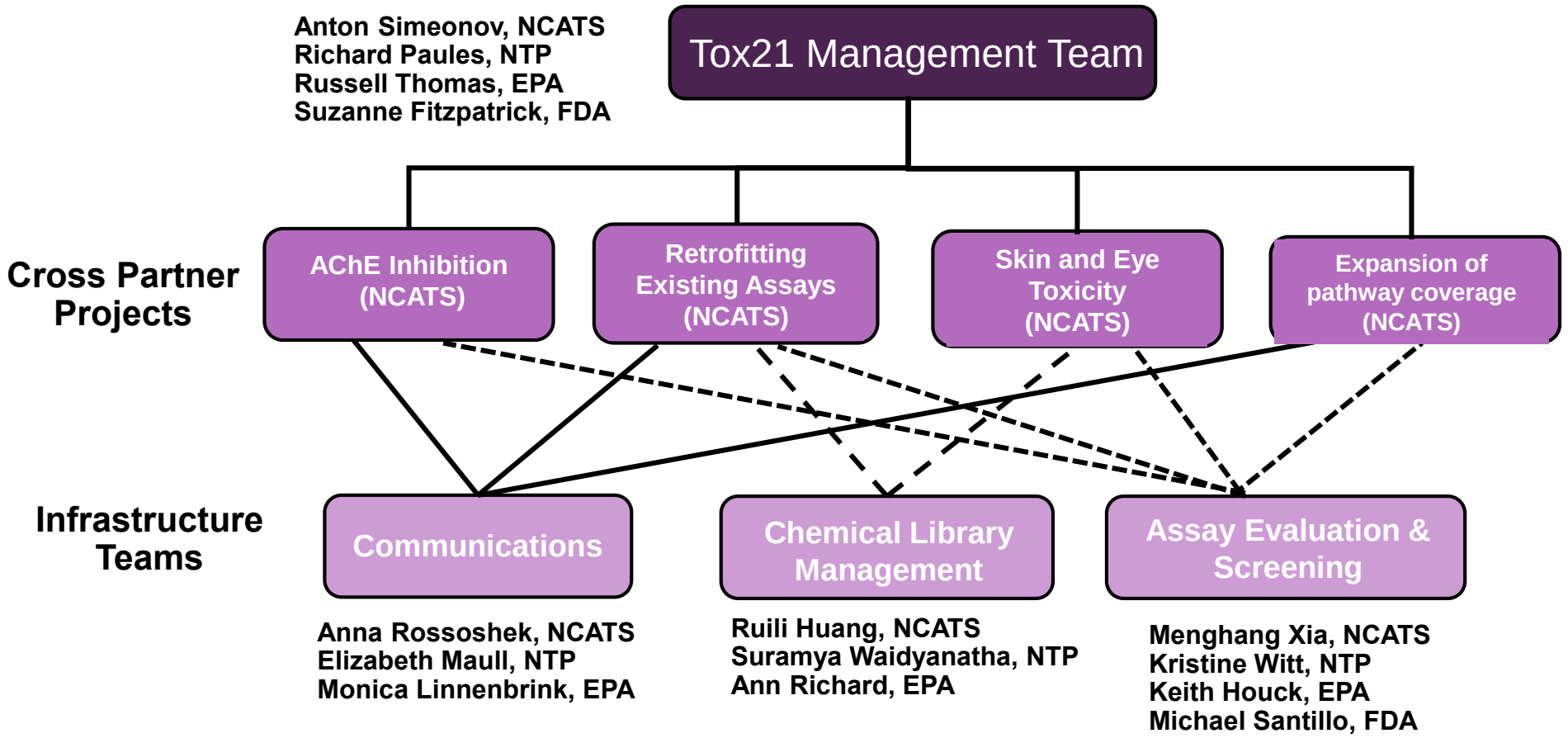
New Tox21 Strategic and Operational Plan

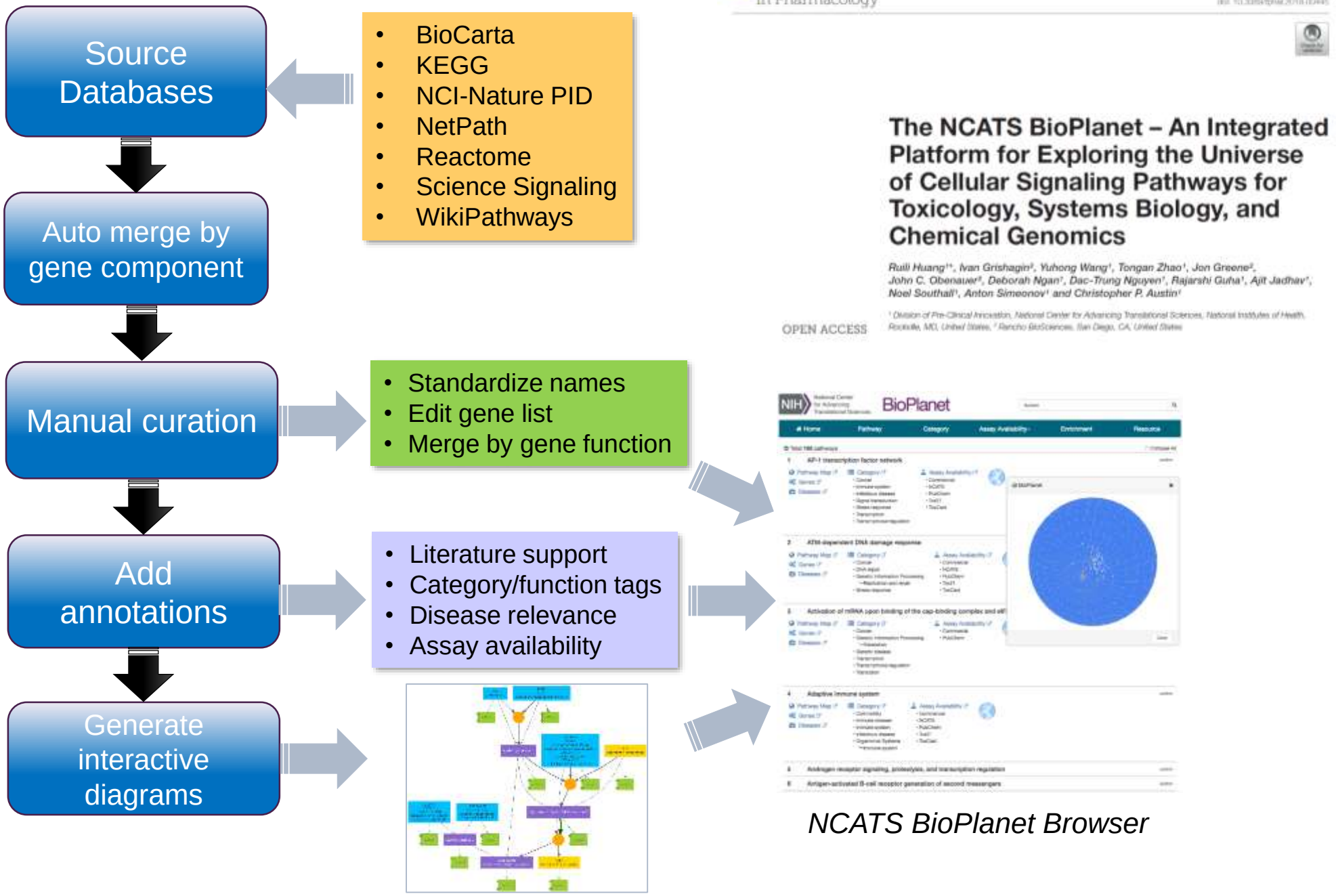
1. Develop innovative test systems that better predict human toxicity
   - Use of primary/iPSC-derived 2D cells, 3D cellular organoids, and in vivo models (e.g., zebrafish)
   - Expanding technological capabilities
     - High-content imaging assays
     - 3D cellular models
   - Assays for molecular events in high priority adverse outcome pathways (AOPs)
   - Chemical-induced changes in the global transcriptome
2. Address key technical limitations of current in vitro test systems
   - Retrofitting existing Tox21 HTS assays with metabolic capability
3. Curate and characterize legacy in vivo toxicity studies to serve as a resource for interpreting Tox21 data
4. Develop framework for efficient validation of Tox21 approaches
5. Refine and deploy in vitro methods for characterizing pharmacokinetics to increase predictivity and reduce uncertainty





New Tox21 Organizational Structure

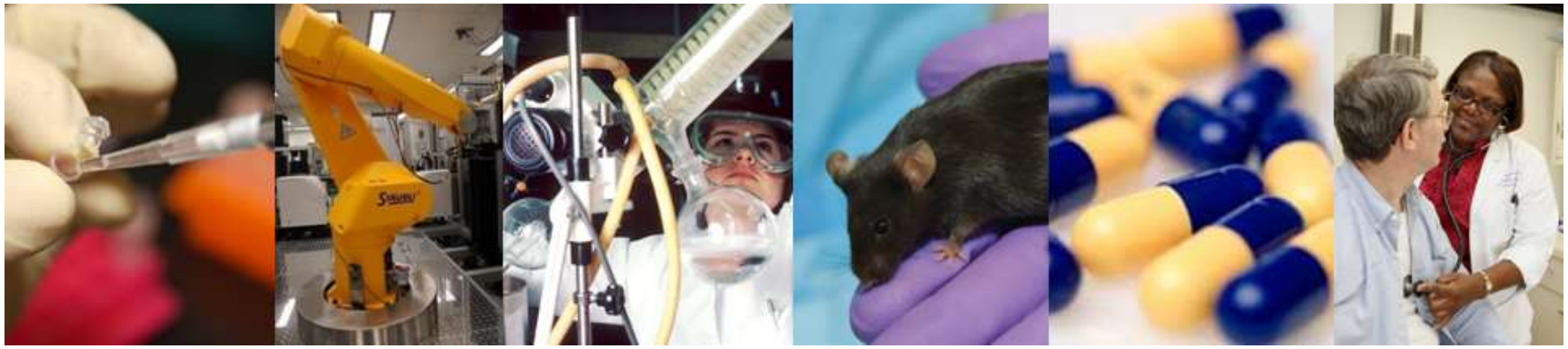




NCATS BioPlanet Browser

National Center for Advancing Translational Sciences

NCATS Mission

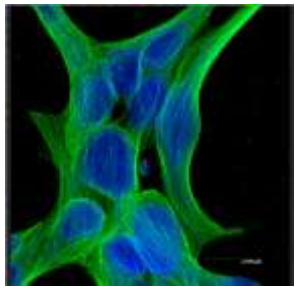


To catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

NCATS Preclinical Programs to Accelerate Translation

Identify disease mechanism → Create testing system → Test chemicals in system → Modify (chemistry) for human use → Test in animals → Test in humans

Basic Research

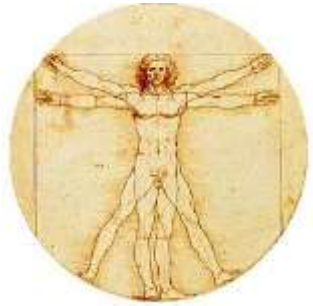


Assay Development

Screening

Medicinal Chemistry

Preclinical Development



Clinical Development

Division of Preclinical Innovation

Cures Acceleration Network (CAN)

Bioprinting **Translator** **Tissue Chips**

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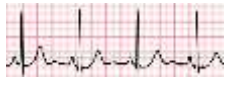
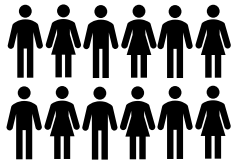
NCATS Clinical Programs to Accelerate Translation

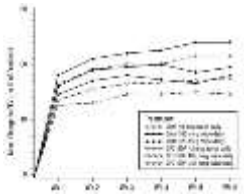
Preparing for clinical trials → Assess safety in humans → Assess multiple doses vs. effectiveness in small # humans → Assess effectiveness in large # humans *(Controlled setting)* → Assess effectiveness in "real world" *(Medical practice setting)* → Assess effectiveness in populations *(Public health setting)*

Registries
Natural History

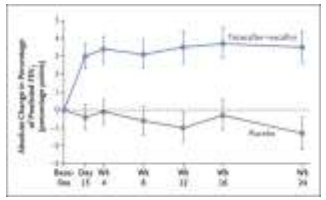




Phase 1
Clinical Trial



Phase 2
Clinical Trial



Phase 3
Clinical Trial

Clinical
Implementation

Public Health
Implementation

Clinical and Translational Science Awards (CTSA) Program

RaDaR

New Therapeutic Uses

Rare Diseases Clinical Research Network

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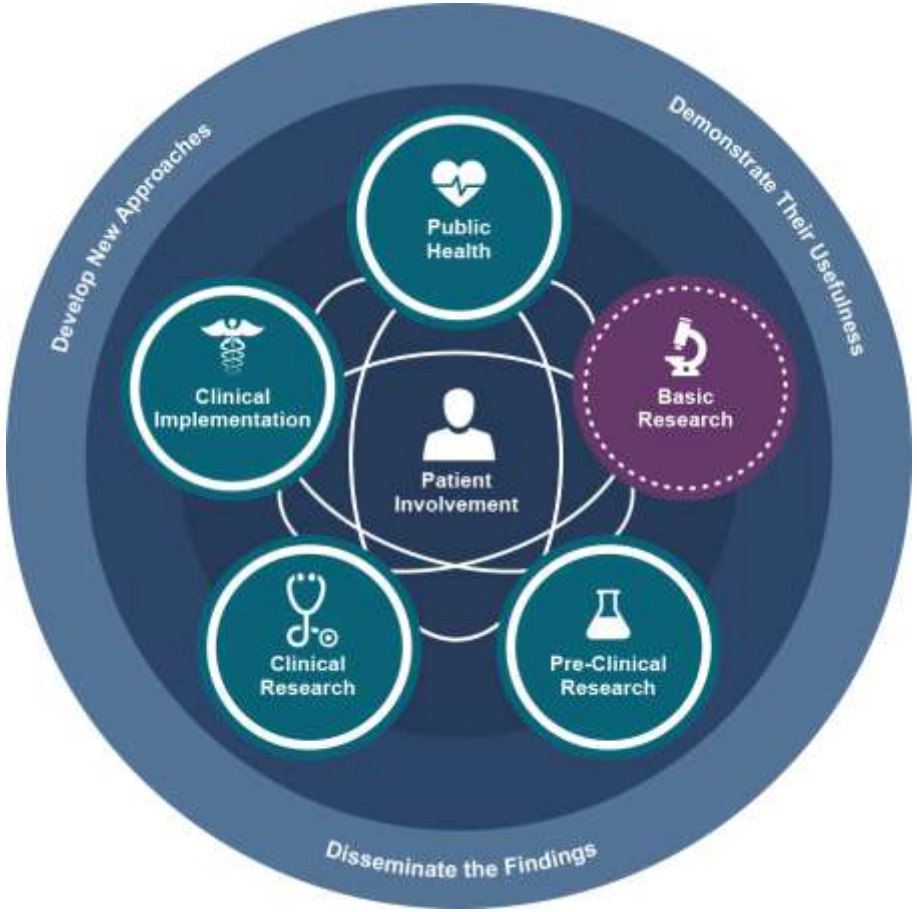
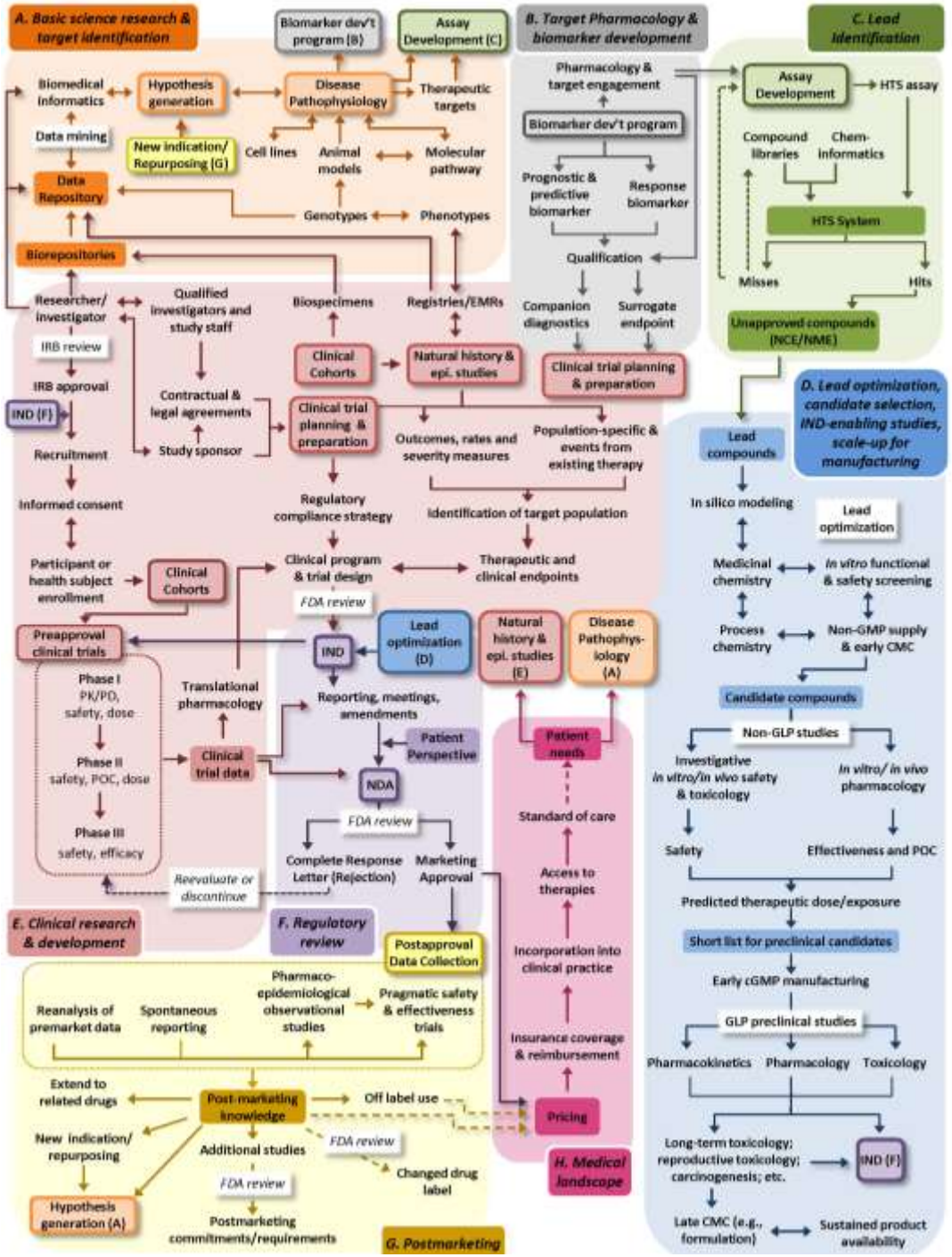
The Translational Science Spectrum



The Drug Discovery, Development and Deployment Map (4DM)

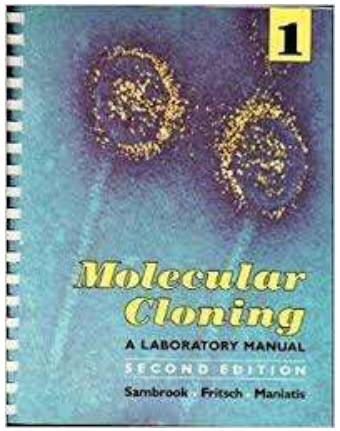
Nature Reviews Drug Discovery 15:150, 2018

https://ncats.nih.gov/translation/maps



The NCATS Assay Guidance Manual

- AGM is a compendium of validated analytical methodologies to test drug-like molecules
- 46 Chapters and 1,338 Printed Pages
- AGM is an eBOOK, dynamically updated regularly
- Provides detailed rationales and protocols for translational methodologies that are
  - Robust
  - Reproducible
  - Consistent
  - High throughput +/- automatable
  - Biologically and translationally relevant



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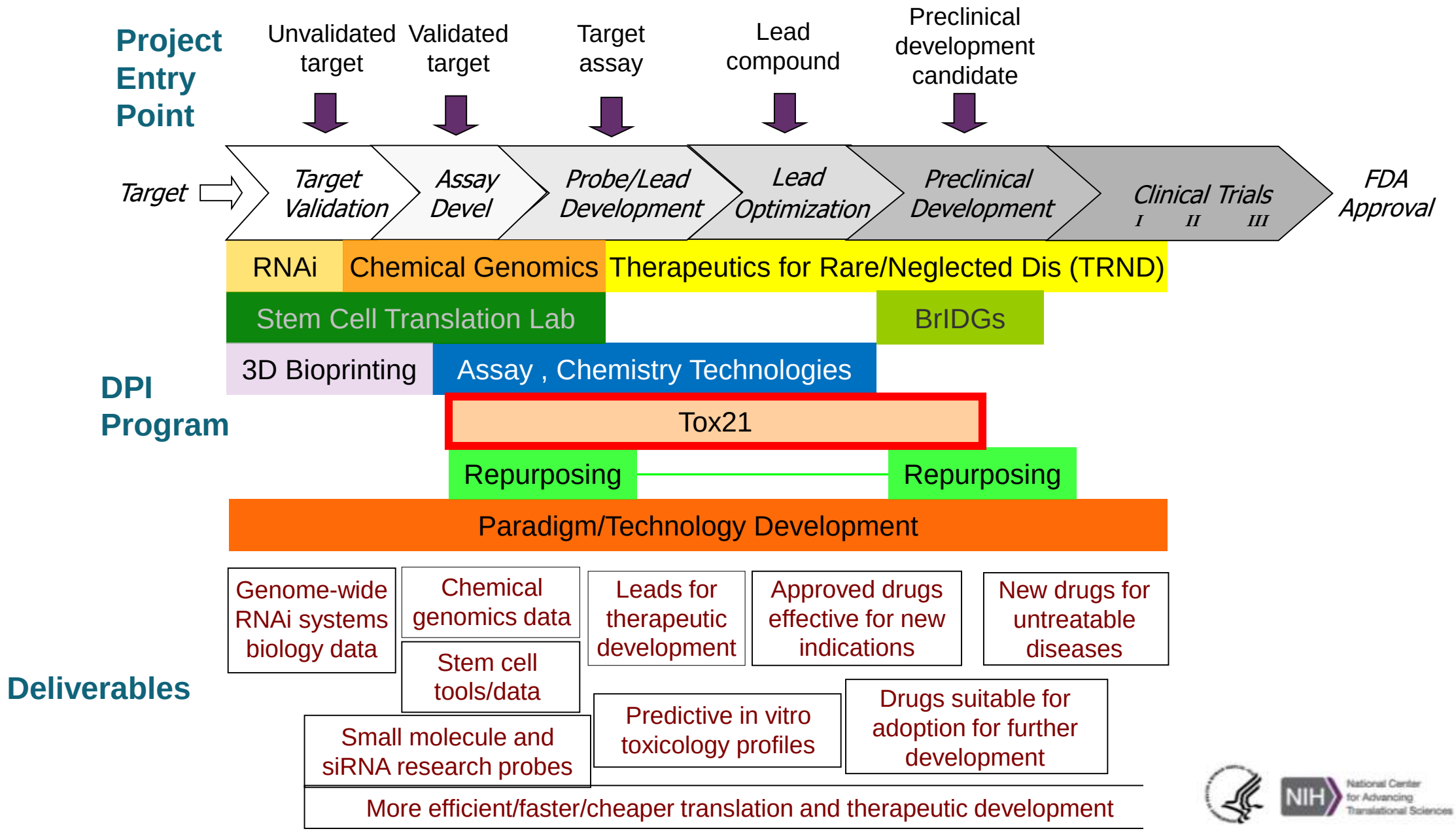
NCATS Division of Preclinical Innovation



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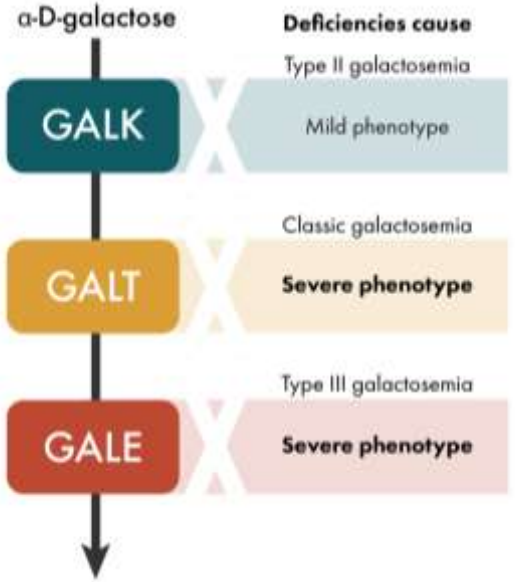
Chemical Probe/Lead Development: First-in-class GALK Inhibitors for Classic Galactosemia

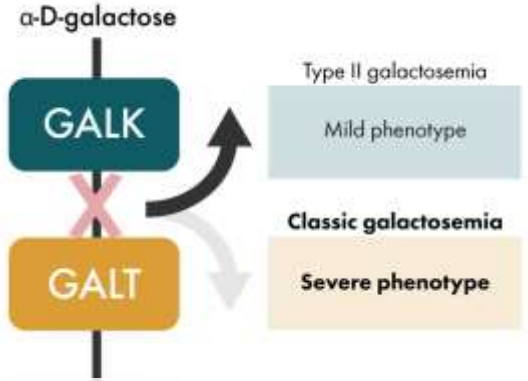
1 Galactosemias: Rare autosomal recessive disorders in which the body cannot properly metabolize galactose



Classic Galactosemia - most common & severe of the galactosemias (~1 in 30,000-60,000 births)

- Results from GALT deficiency
- Lethal without dietary galactose restriction
- Leads to mental deficits, ovarian dysfunction
- No current therapy

2 GALK as a drug target



Type II galactosemics (GALK deficient) do not suffer from same clinical manifestations and long term problems associated with Classic Galactosemia

Hypothesis: GALK inhibition will phenocopy Type II Galactosemia in Classic Galactosemics, leading to milder, more easily manageable disease

3 GALK high-throughput inhibitor screen

Screened 350,000+ compounds for human GALK inhibition → Performed med chem on top active scaffolds → Further refinement to improve ADME/PK

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Hit

GALK IC_{50}: **7.6 uM**
Solubility: **<1 ug/mL**

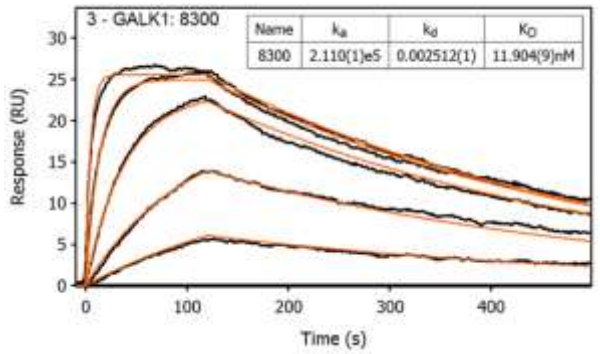
Lead

GALK IC_{50}: **330 nM**
Solubility: **64 ug/mL**

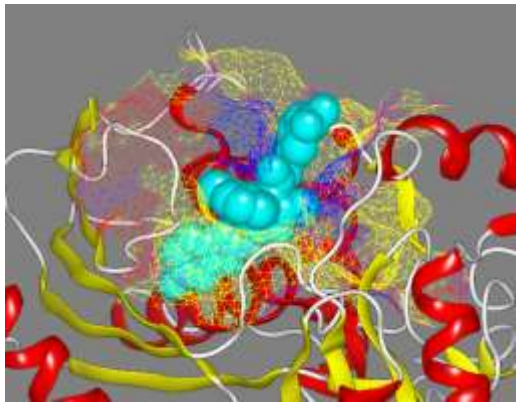
ADME:
Kin. Sol: 64 ug/mL
RLMS $t_{1/2}$: >30 min
MLMS: 93% rem @ 15 min

In vivo PK:
47 mg/kg, IP
$t_{1/2}$: 1.73 hr
Cmax: 226 uM
AUC_{inf} 28,358 h* ng/mL

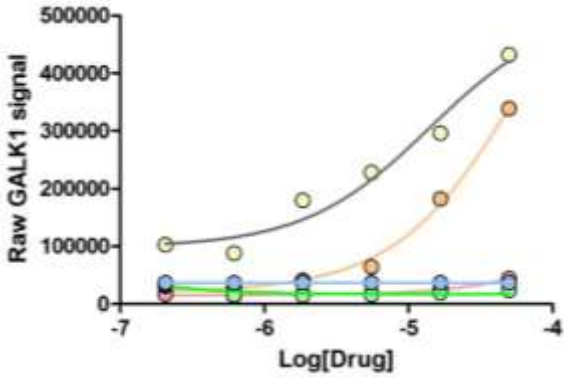
4 Lead characterization & cellular activity



SPR demonstrating high affinity GALK binding of lead

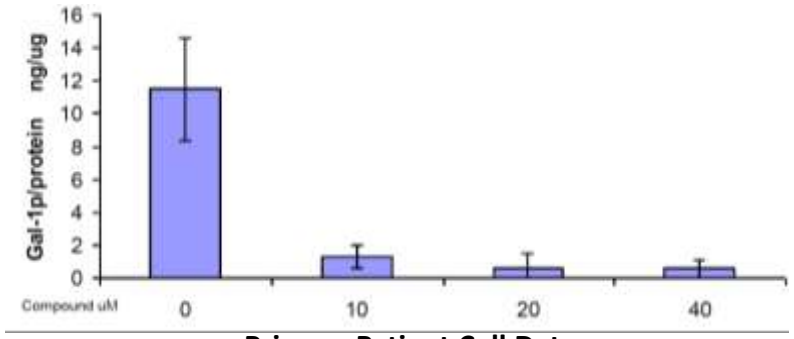


Human GALK co crystal w/ lead



CETSA demonstrating on target binding of GALK in cells

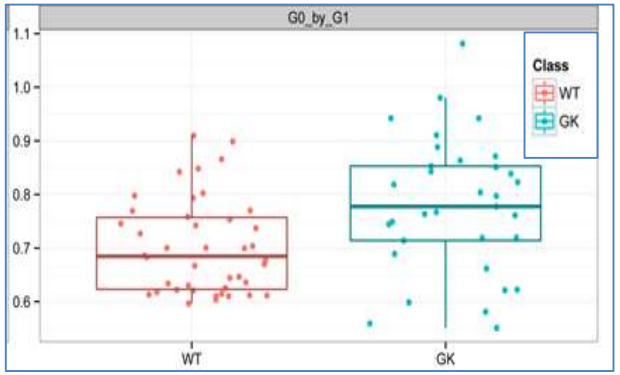
5 Patient cell activity and upcoming *in vivo* models



Primary Patient Cell Data

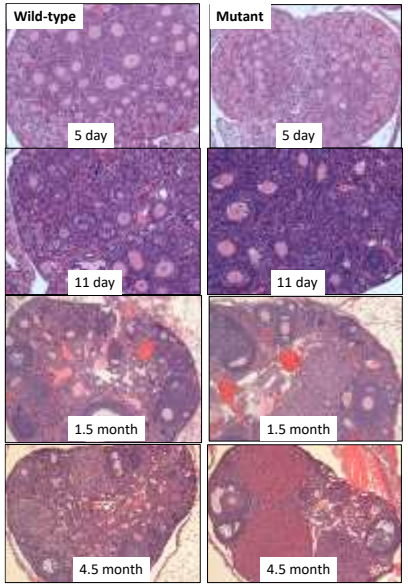
Compounds very effectively lower gal-1-p levels in Classic Galactosemia primary patient fibroblasts with no galactose challenge (clinically relevant assay)

GalT-gene trapped mice



Ratio of non-galactosylated IgG (G0) to mono-galactosylated IgG (G1) in wild type (red boxes) vs GalT-gene trapped (GalT-"knockout") (GK, blue boxes) mice

WT vs mutant mouse ovary histopathology



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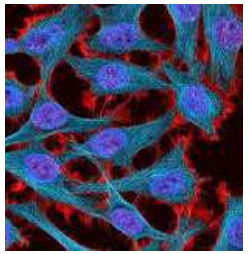
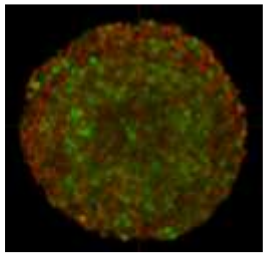
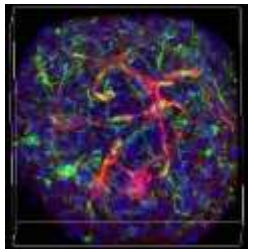
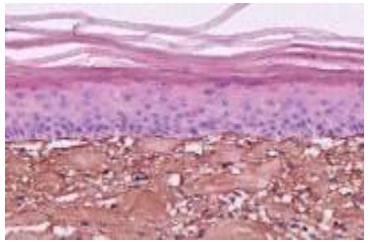
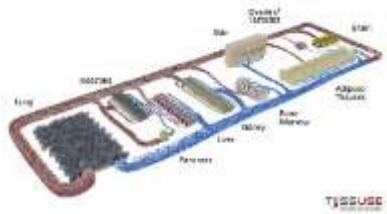
- Medicinal chemistry lead optimization
- Evaluation of functional activity, potency, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy
- Biomarker development
- Definition and optimization of dose and schedule for *in vivo* activity
- Development and implementation of pharmacological assays
- Chemical and biologics process research and development
- Manufacturing of bulk substance (GMP and non-GMP)
- Development of suitable formulations
- Development of analytical methods
- Production and stability studies of dosage forms
- Range-finding initial toxicity
- Investigational New Drug (IND)-directed toxicology, with correlative pharmacology and histopathology
- Planning of clinical trials (Phase 1 and/or Phase 2)
- Regulatory and IND filing support
- Natural history and patient-finding studies

Therapeutics for Rare and Neglected Diseases Program

Collaborations to cross the Valley of Death

Innovation in assay models

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

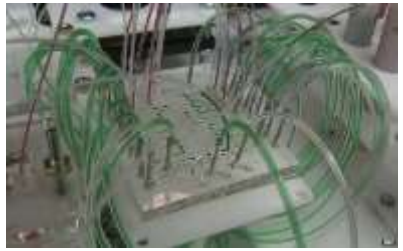






Physiological complexity

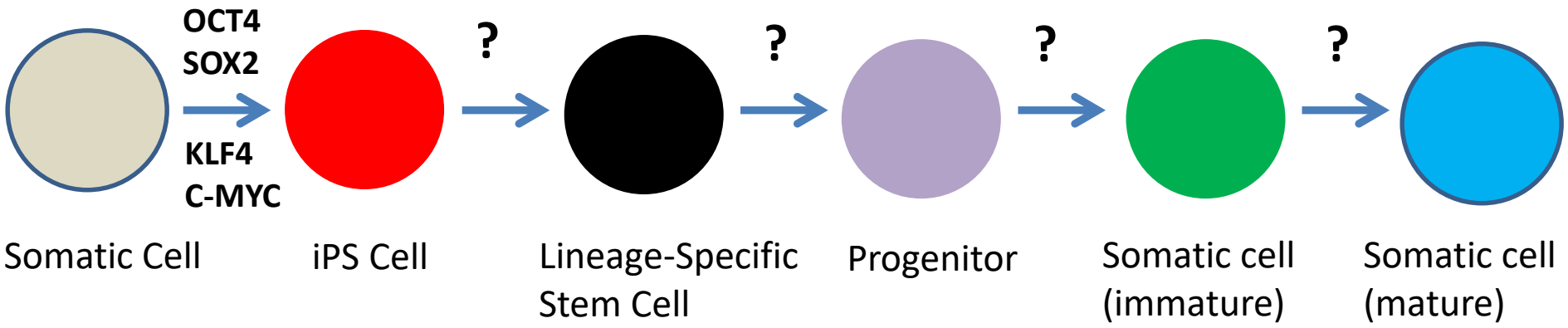
HTS compatibility







How to generate specific cell types from iPSCs?



Pluripotent → **Differentiated**

Feeder-Free
Monolayer
Controlled
Rapid & Scalable
Highly Pure
Amenable for Drug Screening
Cellular Diversity of Organs

Goals of the NCATS Stem Cell Translation Laboratory

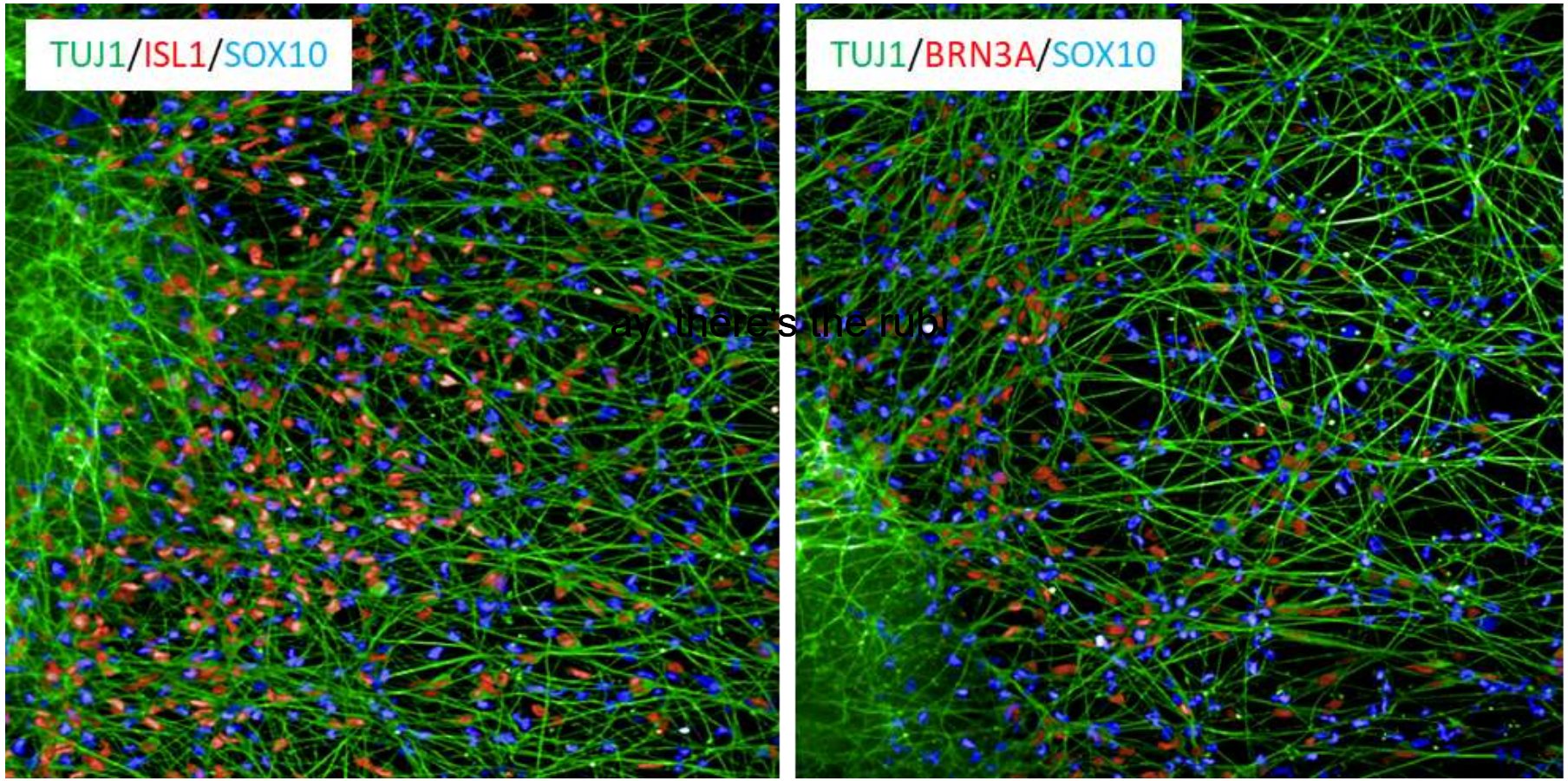
1. Establish QC standards to define pluripotency and differentiated cell types

2. Develop methods to assess heterogeneity in iPSC-derived cells using multi-omics technologies (bulk culture & single cell level)

3. Develop standardized methods to produce mature cells meeting the QC standards above

4. Discover, validate, and disseminate small molecule reagents to replace expensive recombinant proteins, xenogeneic material, and undefined media components in cell differentiation protocols

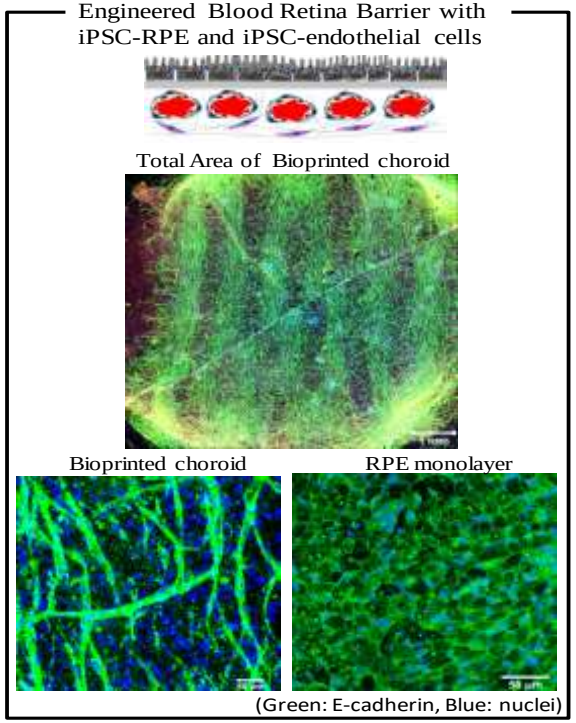
Human Sensory Neurons Derived From iPSCs Under Defined Conditions



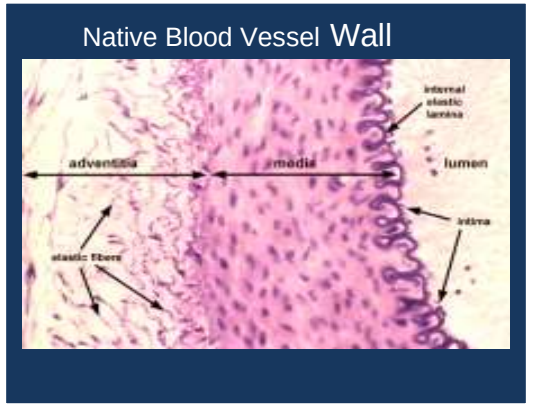
ay, there's the rub!

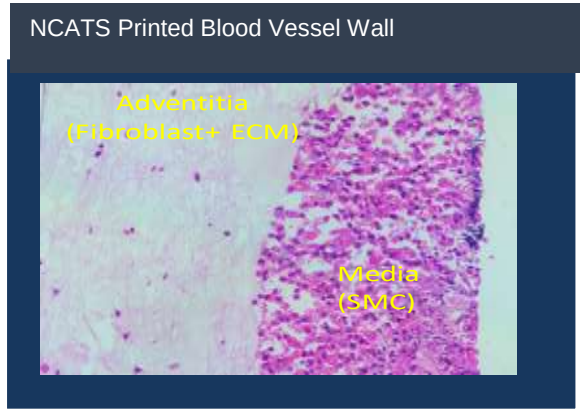
3D Bio-Printing Projects

7 June 2019

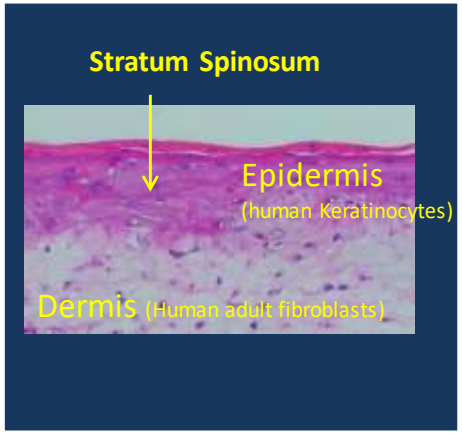


Retina (Kapil Bharti, National Eye Institute)





Blood vessel wall (Kan Cao, U of Maryland)



Skin (Angela Christiano, Columbia University)

Microphysiological Systems Program 1.0
"Tissue Chips for Drug Screening"

AstraZeneca

Pfizer

NIH National Institutes of Health

gsk GlaxoSmithKline

IQ International Consortium for Innovation & Quality in Pharmaceutical Development

Platform and cell resources development

Functional Validation, training set of compounds, multi-organ integration

2012 13 | 2013 14 | 2014 15 | 2015 16 | 2016 17

$75 M over 5 years – cell source, platform development, validation and integration (NCATS, CF, NIBIB, NIEHS, NICHD, ORWH, NCI)

DARPA

$75 M over 5 years - development of 10-organ platforms

FDA

****FDA provides insight and expertise throughout the program**

Publications: over 600 original and review articles published in top tier journals, including *Nature Medicine, Nature Communications, Nature Materials, PNAS, Science, Science Translational Medicine, etc.*

Phased award and milestone-driven

NIH National Center for Advancing Translational Sciences

Tissues-on-Chips

Scaffold

Cells

Structure

Spatial and Temporal Patterning

Perfusion

Bioreactor

Innervation

Host Response

Functional Readout

Computational Design

- Microfluidic cell culture devices
- Created with microchip manufacturing methods
- Contains continuously perfused chambers
- Seeded by human derived cells
- Cytoarchitecture mimics tissue and organ level physiology
- High resolution, real time imaging and in vitro analysis of biochemical, genetic and metabolic activities

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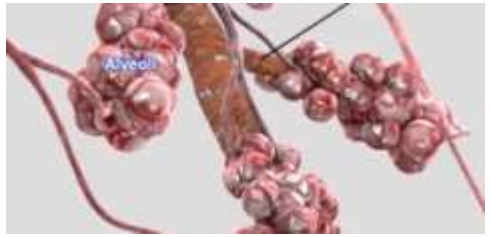
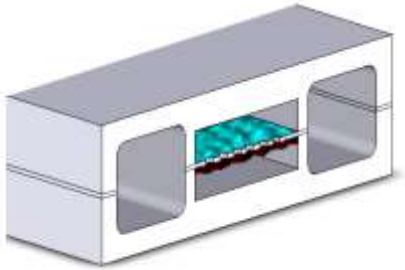
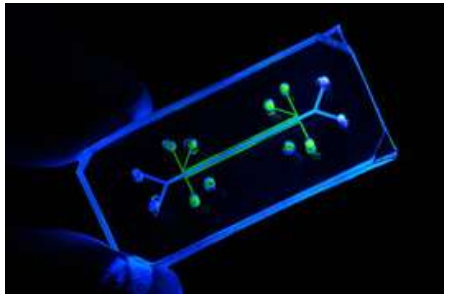
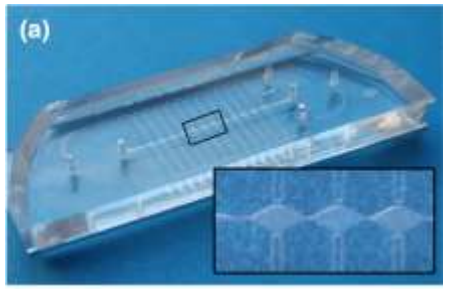
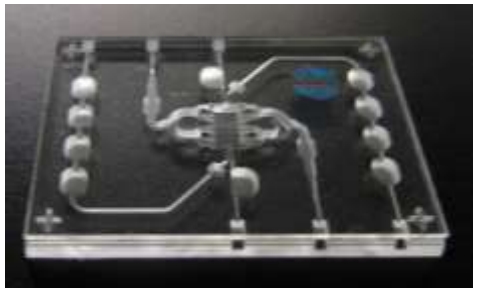
Microphysiological Systems: *In Vitro* Mimics of Human Organ Function

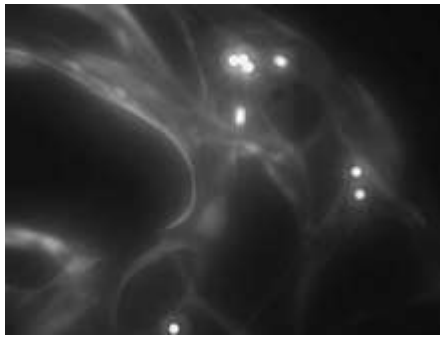


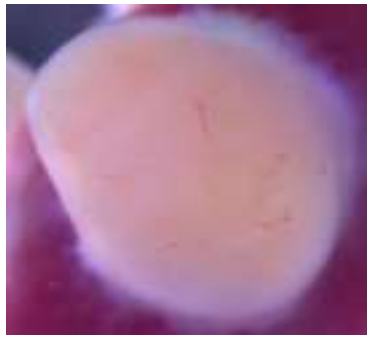


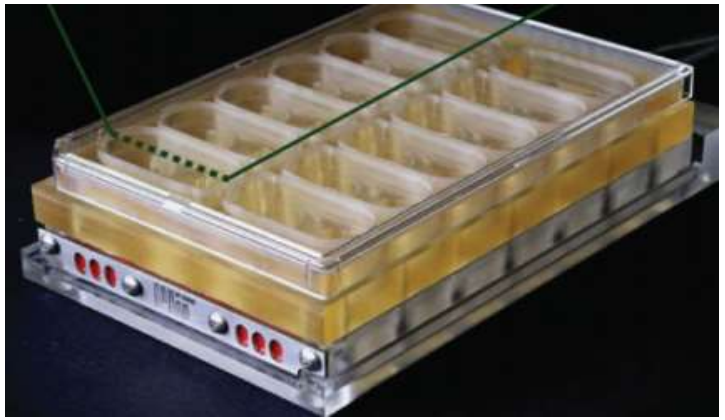


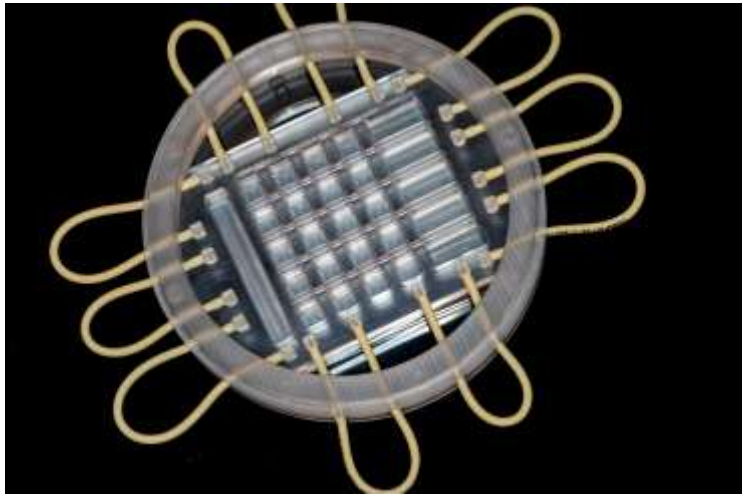


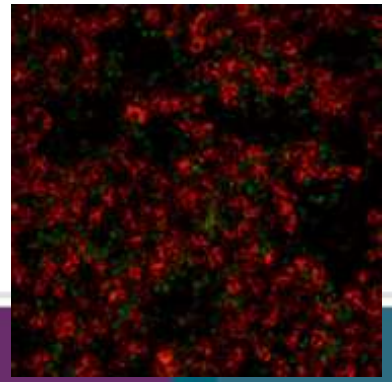












Tissue Chip Program 2.0

Validation Centers

MIT
Murat Cirit, PI

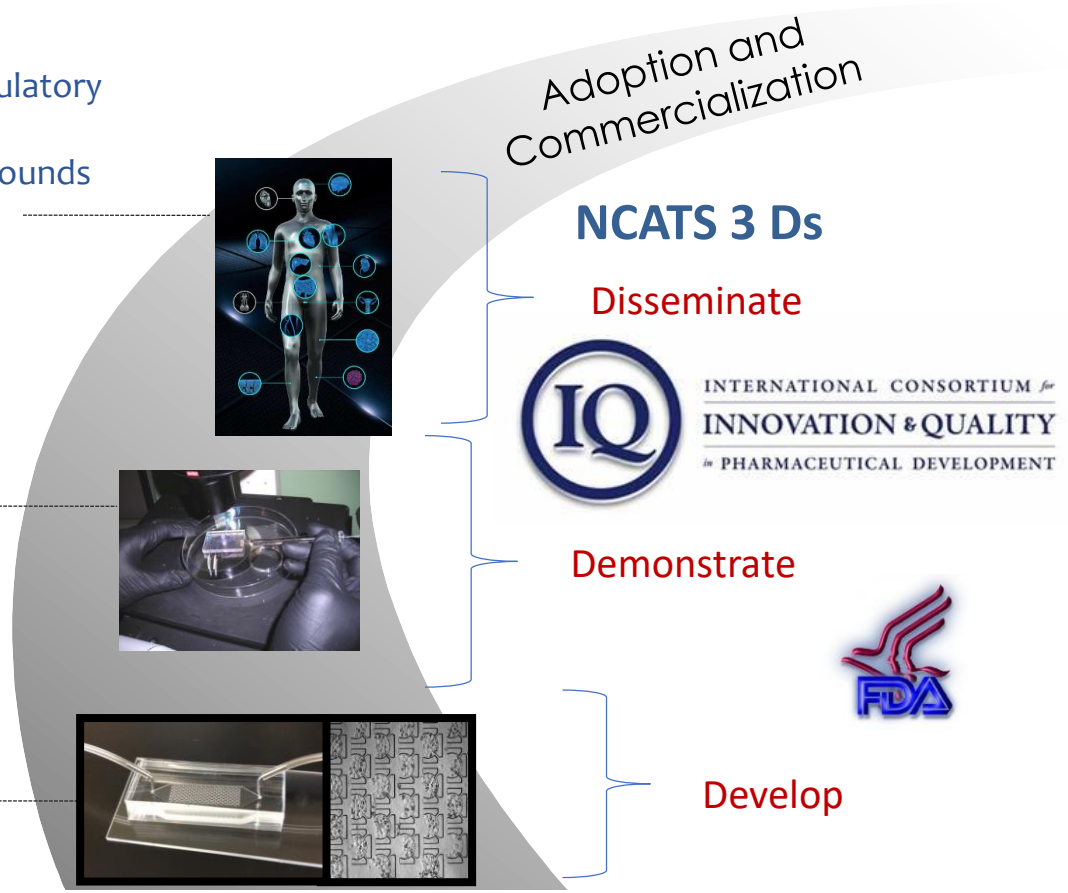
TEX-VAL
Ivan Rusyn, PI

MPS Database
Mark Schurdak, PI

3) Industrial
- Use by industry and regulatory agencies
- Proprietary set of compounds
- CRO-type environment

2) Analytical
- Independent: robustness, reproducibility, rigor
- Validation set of compounds
- TC Testing Centers

1) Physiological
- Organ function and structure
- Training set of compounds
- TC developers



Comput Struct Biotechnol J.(2016) 14: 207–210.

https://ncats.nih.gov/tissuechip/projects/centers

National Center for Advancing Translational Sciences

NIH Tissue Chips 2.0: Disease Modeling and Efficacy Testing

Kam Leong, Columbia U
Proteus Syndrome and DiGeorge Syndrome

Danielle Benoit, Lisa Delouise, Catherine Ovitt, U Rochester
Radiation-induced xerostomia

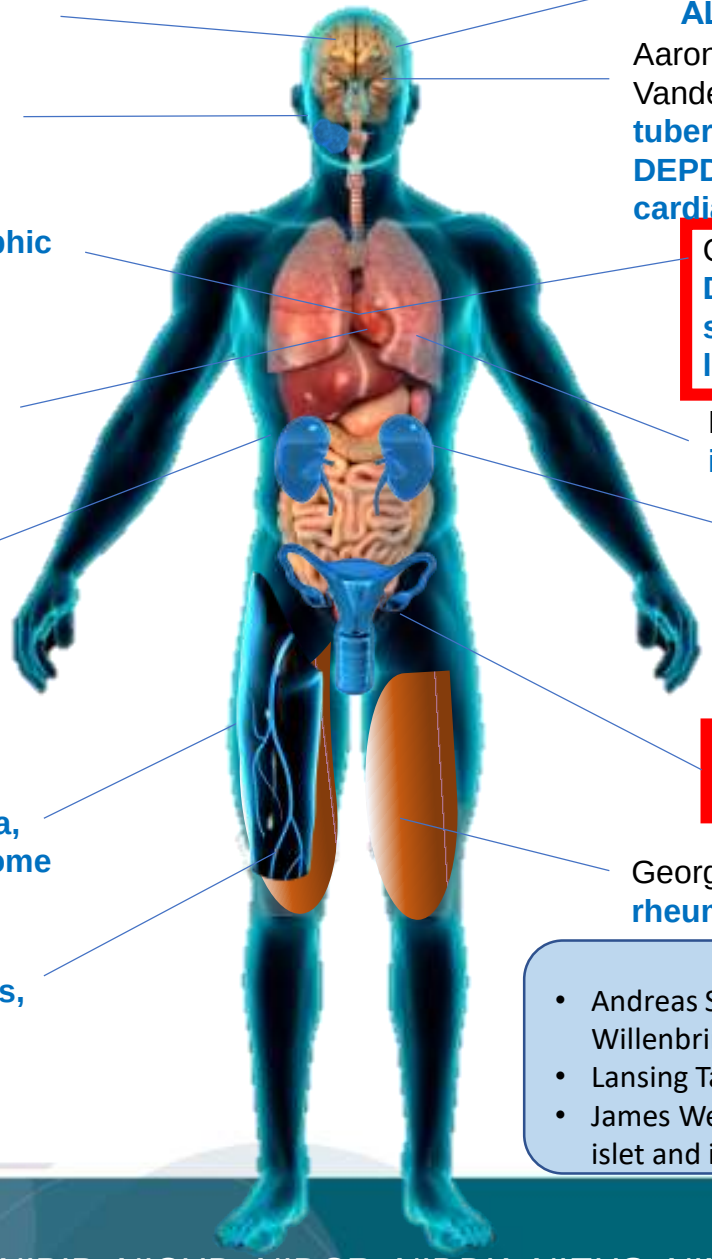
Kevin Kit Parker, William Pu, Harvard U
Barth syndrome, catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic cardiomyopathy

Steven George, David Curiel, Stacey Rentschler, UC Davis and WashU **atrial fibrillation**

Joseph Vincent Bonventre, Luke Lee, Brigham and Women's **autosomal dominant/recessive models of polycystic kidney disease, Focal segmental glomerulosclerosis**

Christopher Hughes, UC Irvine
Hereditary hemorrhagic telangiectasia, Port Wine stain, Sturge-Weber syndrome

Rocky Tuan, U Pittsburgh
Osteoarthritis, inflammatory arthritis, adipose-mediated diabetic joint complications



Clive Svendsen, Cedars-Sinai
ALS; Parkinson's Disease

Aaron Bowman, Kevin Ess, John Wikswo, Vanderbilt U
tuberous sclerosis complex (TSC) epilepsy, DEPDC5-associated epilepsy, & associated cardiac dysfunction

Gordana Vunjak-Novakovic, Columbia U
Dox induced cardiomyopathy; multi-system pathologies involving heart, liver, skin, bone and vasculature

Donald Ingber, Harvard U
influenza infection, COPD

Jonathan Himmelfarb, U Washington
apolipoprotein L1 mediated kidney disease, drug induced and host-pathogen interaction induced renal thrombotic microangiopathies

Teresa Woodruff, Northwestern U
Polycystic Ovarian Syndrome

George Truskey, Duke U
rheumatoid arthritis, atherosclerosis

Type-2 Diabetes Mellitus

- Andreas Stahl, Kevin Healy, Matthias Hebrok, Edward Hsiao, Holger Willenbring, UC Berkeley - Pancreatic islet, liver, adipose
- Lansing Taylor, U Pittsburgh – Vascularized liver and pancreatic islets
- James Wells, Moo-Yeal Lee, Cincinnati Children's Hospital - Liver, pancreatic islet and intestine

NCATS, NHLBI, NIAMS, NIBIB, NICHD, NIDCR, NIDDK, NIEHS, NINDS, ORWH

NIH National Center for Advancing Translational Sciences

Chips in Space

Launch dates to date: December 5, 2018 (SpaceX CRS-16)
May 4, 2019 (SpaceX CRS-17)

- Biomedical research using tissue chips aboard the International Space Station
- Opportunities to study the effects of a micro-gravity environment on the human body re muscle deterioration osteoporosis, cardio-pulmonary function, and immune deficiency.
- Studies under reduced gravity will contribute to our understanding of the process of aging and could reveal molecular targets that can slow that process.

NASA

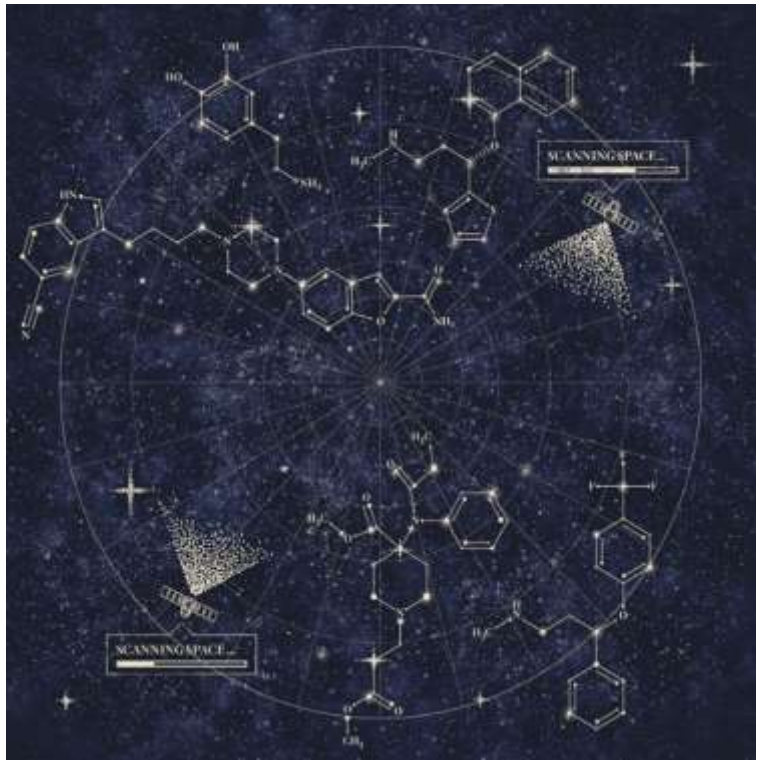
CASIS™

NIH National Center for Advancing Translational Sciences

A Specialized Platform for Innovative Research Exploration (ASPIRE)

Defining biologically active chemical space:
A key translational challenge

- 95% of human diseases have no regulatorily approved treatment
- 90% of biological space (“targets”) is currently undrugged
- Vast chemical space: 10^{60} potential “drug-like” small molecules
  - » Only 10^{7} of these have been made in the entire history of synthetic chemistry
- Current approach to exploring chemical space is inefficient



Mullard A. *Nature*, 2017 Sep 26; 549 (7673): 445-447.

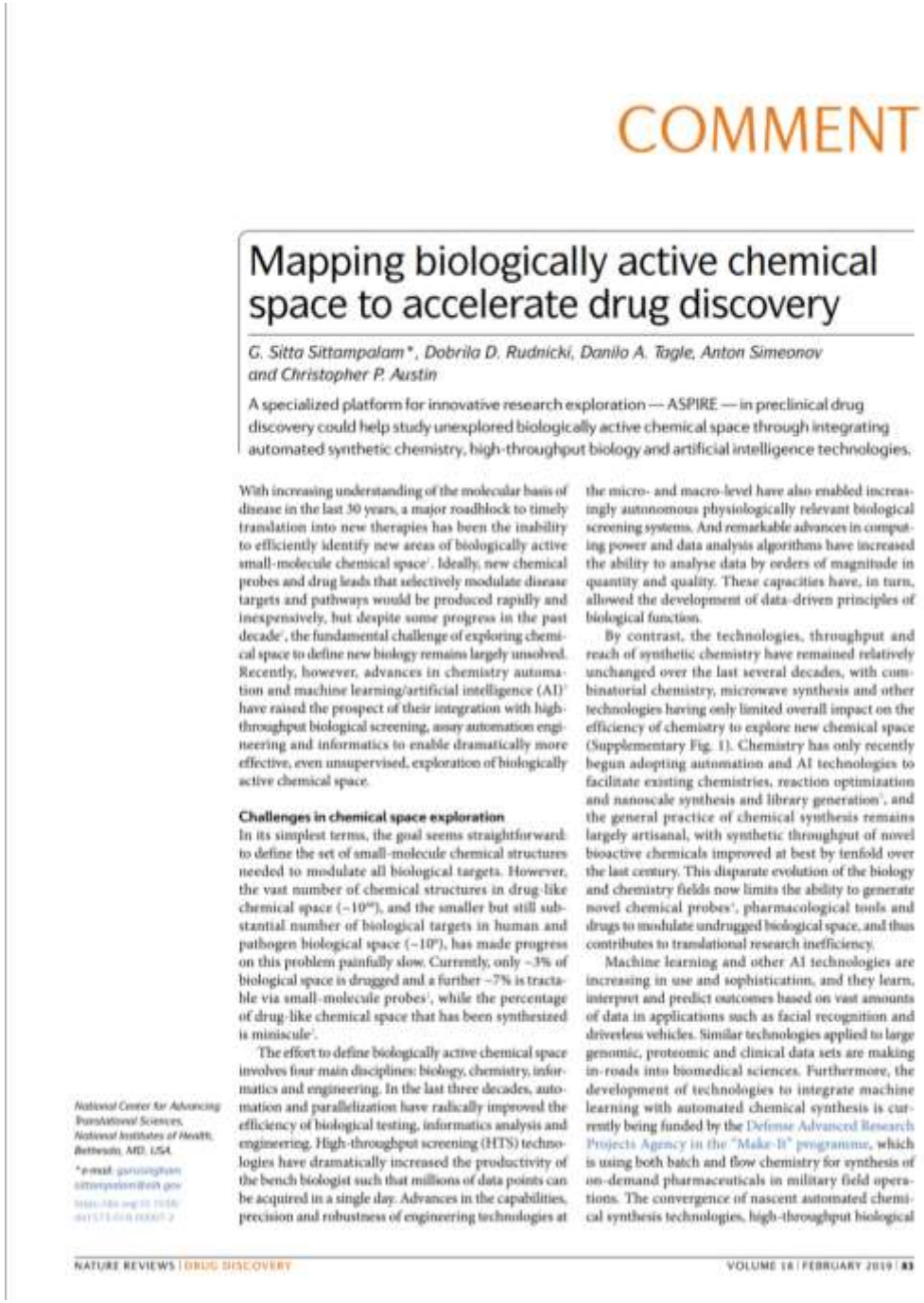
National Center for Advancing Translational Sciences

ASPIRE Work Flow

Figure by Kyle Brimacombe, NIH/NCATS

[Sittampalam, G. S. et al, *NRDD*, 2019]

National Center for Advancing Translational Sciences



COMMENT

Mapping biologically active chemical space to accelerate drug discovery

G. Sitta Sittampalam, Dobrila D. Rudnicki, Danilo A. Tagle, Anton Simeonov and Christopher P. Austin*

A specialized platform for innovative research exploration — ASPIRE — in preclinical drug discovery could help study unexplored biologically active chemical space through integrating automated synthetic chemistry, high-throughput biology and artificial intelligence technologies.

With increasing understanding of the molecular basis of disease in the last 30 years, a major roadblock to timely translation into new therapies has been the inability to efficiently identify new areas of biologically active small-molecule chemical space[1]. Ideally, new chemical probes and drug leads that selectively modulate disease targets and pathways would be produced rapidly and inexpensively, but despite some progress in the past decade[2], the fundamental challenge of exploring chemical space to define new biology remains largely unsolved. Recently, however, advances in chemistry automation and machine learning/artificial intelligence (AI)[3] have raised the prospect of their integration with high-throughput biological screening, assay automation engineering and informatics to enable dramatically more effective, even unsupervised, exploration of biologically active chemical space.

Challenges in chemical space exploration

In its simplest terms, the goal seems straightforward: to define the set of small-molecule chemical structures needed to modulate all biological targets. However, the vast number of chemical structures in drug-like chemical space ($\sim 10^{60}$), and the smaller but still substantial number of biological targets in human and pathogen biological space ($\sim 10^{9}$), has made progress on this problem painfully slow. Currently, only ~3% of biological space is drugged and a further ~7% is tractable via small-molecule probes[1], while the percentage of drug-like chemical space that has been synthesized is miniscule[2].

The effort to define biologically active chemical space involves four main disciplines: biology, chemistry, informatics and engineering. In the last three decades, automation and parallelization have radically improved the efficiency of biological testing, informatics analysis and engineering. High-throughput screening (HTS) technologies have dramatically increased the productivity of the bench biologist such that millions of data points can be acquired in a single day. Advances in the capabilities, precision and robustness of engineering technologies at the micro- and macro-level have also enabled increasingly autonomous physiologically relevant biological screening systems. And remarkable advances in computing power and data analysis algorithms have increased the ability to analyse data by orders of magnitude in quantity and quality. These capacities have, in turn, allowed the development of data-driven principles of biological function.

By contrast, the technologies, throughput and reach of synthetic chemistry have remained relatively unchanged over the last several decades, with combinatorial chemistry, microwave synthesis and other technologies having only limited overall impact on the efficiency of chemistry to explore new chemical space (Supplementary Fig. 1). Chemistry has only recently begun adopting automation and AI technologies to facilitate existing chemistries, reaction optimization and nanoscale synthesis and library generation[3], and the general practice of chemical synthesis remains largely artisanal, with synthetic throughput of novel bioactive chemicals improved at best by tenfold over the last century. This disparate evolution of the biology and chemistry fields now limits the ability to generate novel chemical probes[4], pharmacological tools and drugs to modulate undrugged biological space, and thus contributes to translational research inefficiency.

Machine learning and other AI technologies are increasing in use and sophistication, and they learn, interpret and predict outcomes based on vast amounts of data in applications such as facial recognition and driverless vehicles. Similar technologies applied to large genomic, proteomic and clinical data sets are making in-roads into biomedical sciences. Furthermore, the development of technologies to integrate machine learning with automated chemical synthesis is currently being funded by the Defense Advanced Research Projects Agency in the "Make-It" programme, which is using both batch and flow chemistry for synthesis of on-demand pharmaceuticals in military field operations. The convergence of nascent automated chemical synthesis technologies, high-throughput biological

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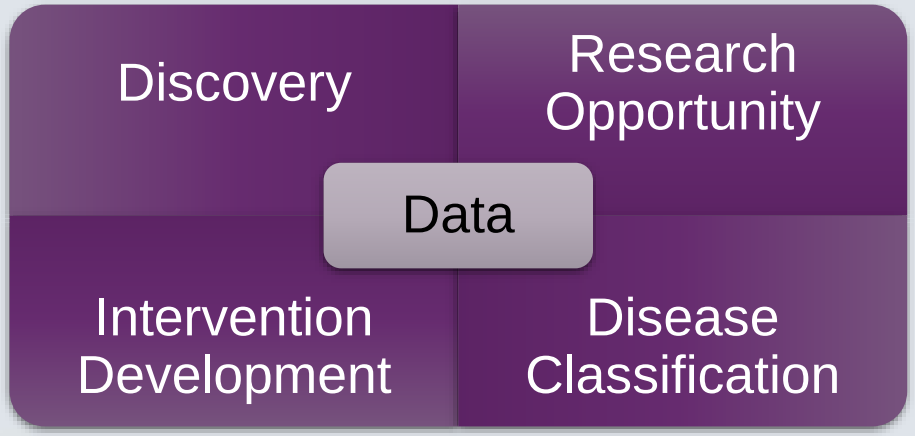
National Center for Advancing Translational Sciences

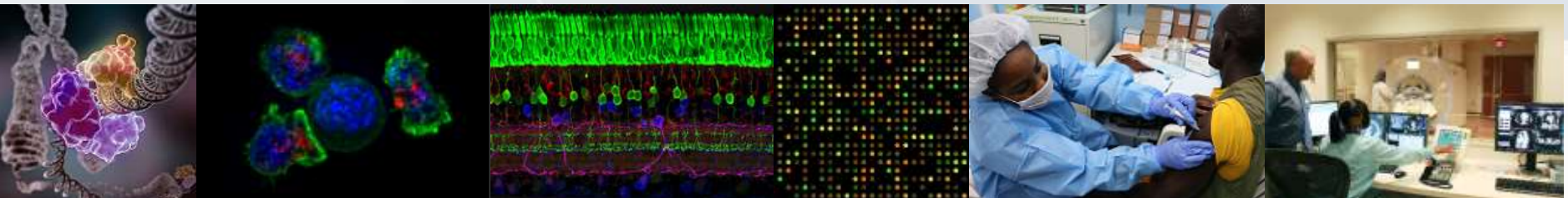
"ASPIRE aims to address two challenges of the current era in biomedical research: to harness new technologies to accelerate understanding of living systems and to fulfill the promise of science to improve the lives of the many patients with untreatable or poorly treatable diseases.

Much like other types of space exploration, ASPIRE is an ambitious vision that we hope will spawn new technologies, excite a generation of aspiring scientists and produce solutions to heretofore intractable challenges in science and medicine."

The NCATS Biomedical Data Translator Program

Revealing new connections among existing data





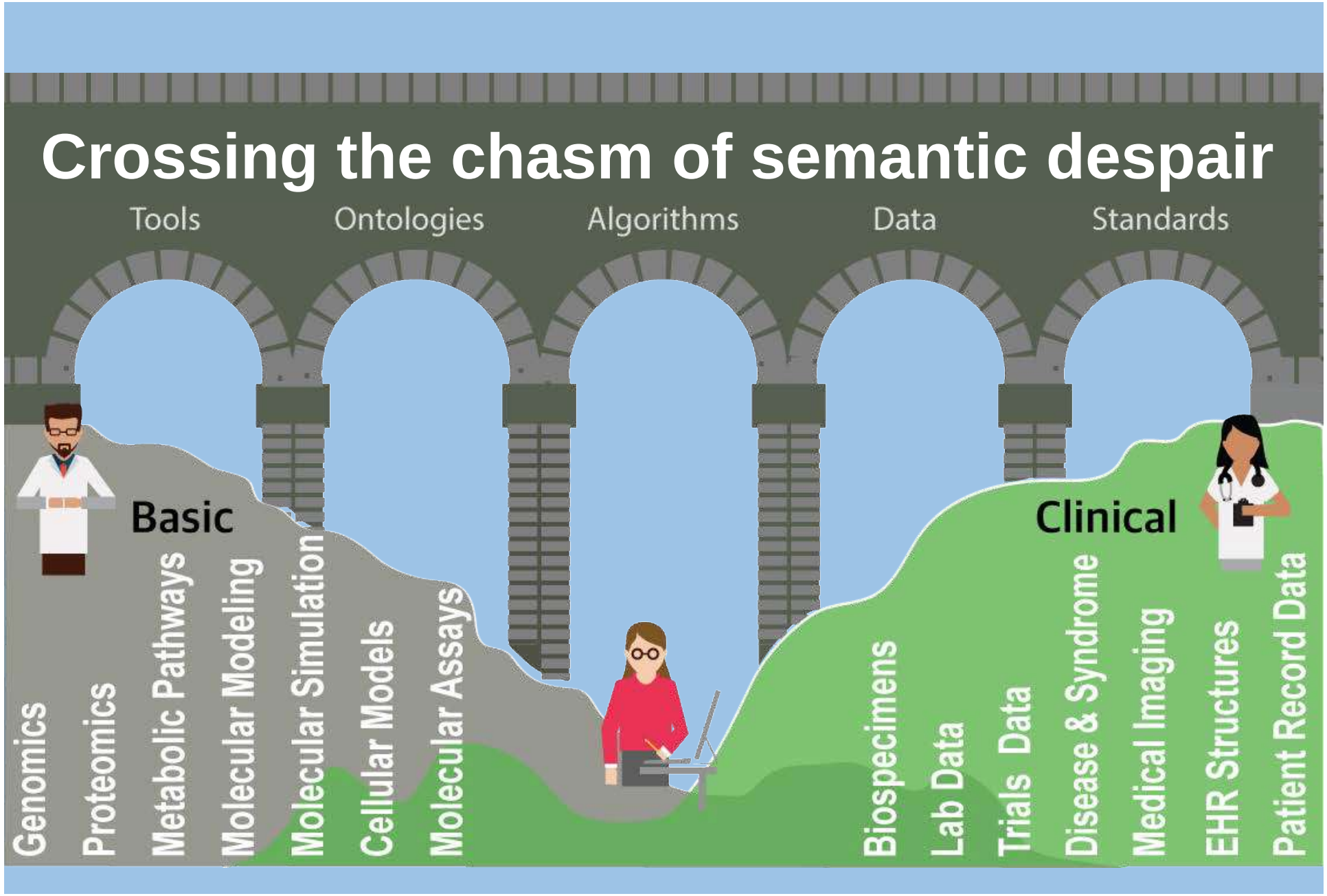
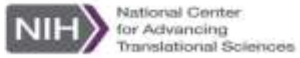
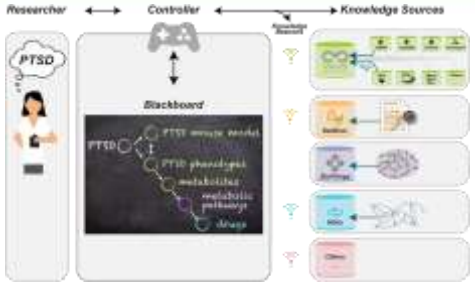


Figure courtesy of Julie McMurry & Chris Chute

The Broad Institute of MIT and Harvard

Initial Participating Institutions





Sep 16

Oct 16

First Face-to-Face Meeting

Notice of Awards Issued

Nov 16

Funds Released

Jan 17

Blackboard/ Architecture Meeting

May 17

Adapt Knowledge Sources to Interact with Blackboard Meeting

Sep 17

Reasoning Tool FOA Released

Oct 17

Open Meeting/ Hackathon

Reasoning Tool Initial Awards issued

Jan 18

Hackathon

May 18

Hackathon

Sep 18

Hackathon

Dec '18

CAN Review Board Meeting

Mar 19

Hackathon

How We Got Here

Volume 12, Issue 2
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Pages 85-85

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Deconstructing the Translational Tower of Babel

Christopher P. Austin, Christine M. Colvis, Noel T. Southall

First published: 09 November 2018 | https://doi.org/10.1111/cts.12595

Citation: Clin Transl Sci (2019) 12, 85; doi:10.1111/cts.12595

EDITORIAL

Deconstructing the Translational Tower of Babel

Christopher P. Austin*, Christine M. Colvis and Noel T. Southall

A principal stumbling block in translation is the compartmentalized nature of data—from biomedical research, disease classifications, health records, clinical trials, and adverse event reports—across diseases and disciplines. These silos impede discovery of commonalities across diseases, and the distinct languages that each discipline uses impede the cross-discipline understanding that is required for efficient translation from basic to clinical to public health science.

By contrast, imagine a world in which researchers had a way to easily access and interrelate these data and languages. Such a tool would accelerate hypotheses about, e.g., which drugs have the potential to treat diseases, the impact of environmental exposures on the onset or worsening of disease; what might be causing illness in patients for whom existing approaches have failed to identify the origin of their symptoms; and better understand the relationships between rare and common diseases. This is the vision of the Biomedical Data Translator: to bridge the current symptom-based diagnosis of disease with research-based molecular and cellular characterizations through an informatics platform that enables interrogation of relationships across the full spectrum of data types, from disease names, clinical signs and symptoms, to organ and cell pathology, genomics, and drug effects.

When we committed to this vision in 2016, we were well aware of its ambitious scope. We, therefore, designed the program to be different in virtually every way from how National Institutes of Health (NIH) research projects are typically competed, supported, and managed, and have taken an explicitly flexible and staged approach to its construction. For the last 24 months, the National Center for Advancing Translational Sciences (NCATS) has been funding a feasibility assessment phase of the Translator, focused on identifying data integration and inclusion barriers and exploring inferential or predictive models that would provide new insights into biology, health, and disease. It was assumed that we did not understand all requirements or needed capabilities when we started, and the platform is being built in an agile way with frequent modifications driven by data from pressure testing using research questions that have been difficult to address by other means. Operationally, the NCATS supports the Translator through a flexible research authority called Other Transactions within the Center's Cures Acceleration Network. The flexibility of Other Transactions to expand, contract, add, discontinue, or modify activities based on data as the program is built has changed the usual ways that we, as funders, interact with research teams and they interact with each other. This too was an experiment: could we entice over a dozen high-performing research teams from diverse backgrounds to become fully miscible with each other and with us to make the Translator vision possible? At the end of the feasibility phase, the NCATS will assess whether the scientific, operational, and cultural experiments have been successful enough to warrant ramping up to build a fully functional Translator that finds and connects existing data, provides previously unknown insights into diseases and possible treatments, and is able to make inferences and predictions even when data are missing. The early results are in, and they are encouraging, as you will read in the articles from the investigators.[1,2]

Two hundred years ago, chemists created a comprehensive enumeration of the elements and systematic relationships among them. This Periodic Table transformed chemistry by placing it on firm scientific footing. We envision the Translator doing the same for translational science.

Funding. No funding was received for this work.

Conflict of Interest. The authors declared no competing interests for this work.

1. The Biomedical Data Translator Consortium. Toward a universal biomedical data translator. Clin. Transl. Sci. 12, 86–90 (2019).
2. The Biomedical Data Translator Consortium. The Biomedical Data Translator program: conception, culture, and community. Clin. Transl. Sci. 12, 91–94 (2019).

[Correction updated on November 23, 2018; after initial online publication: Reference section has been updated.]

NIH National Center for Advancing Translational Sciences

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