DRUG DISCOVERY & DEVELOPMENT IN NICHD POPULATIONS

Overview

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DIRECTOR, NCATS

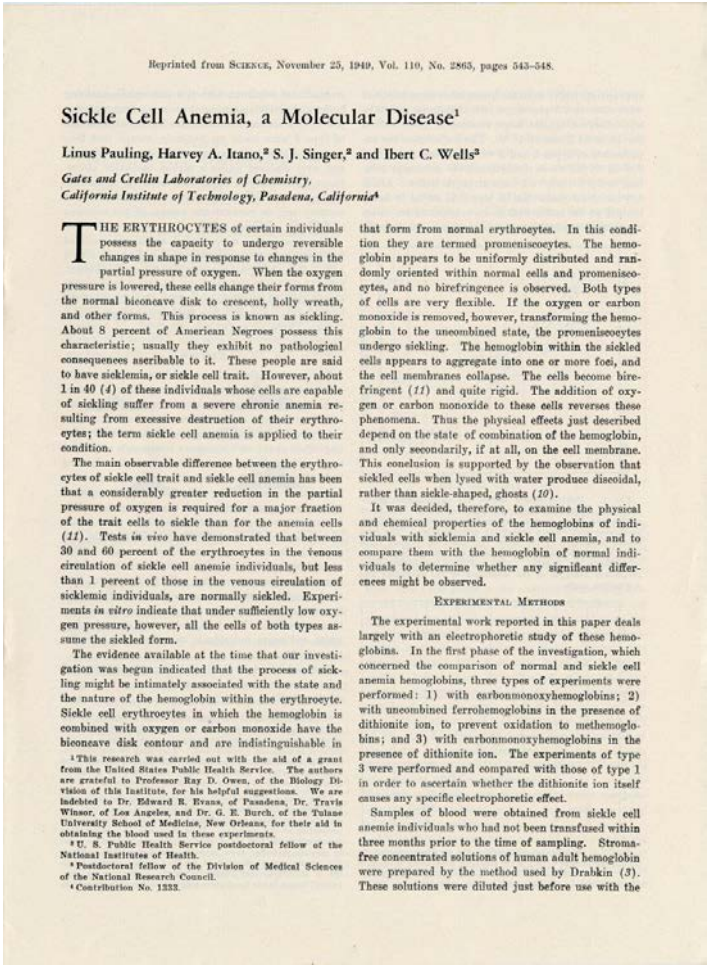
NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
SEPTEMBER 18, 2015

NCATS

Human Conditions with Known Molecular Basis

Source: Online *Mendelian Inheritance in Man*, Morbid Anatomy of the Human Genome

SO….



Reprinted from SCIENCE, November 25, 1949, Vol. 110, No. 2865, pages 543-548.

Sickle Cell Anemia, a Molecular Disease[1]

Linus Pauling, Harvey A. Itano,[2] S. J. Singer,[3] and Ibert C. Wells[3]

Gates and Crellin Laboratories of Chemistry,
California Institute of Technology, Pasadena, California[4]

THE ERYTHROCYTES of certain individuals possess the capacity to undergo reversible changes in shape in response to changes in the partial pressure of oxygen. When the oxygen pressure is lowered, these cells change their forms from the normal biconcave disk to crescent, holly wreath, and other forms. This process is known as sickling. About 8 percent of American Negroes possess this characteristic; usually they exhibit no pathological consequences ascribable to it. These people are said to have sicklemia, or sickle cell trait. However, about 1 in 40 (*4*) of these individuals whose cells are capable of sickling suffer from a severe chronic anemia resulting from excessive destruction of their erythrocytes; the term sickle cell anemia is applied to their condition.

The main observable difference between the erythrocytes of sickle cell trait and sickle cell anemia has been that a considerably greater reduction in the partial pressure of oxygen is required for a major fraction of the trait cells to sickle than for the anemia cells (*11*). Tests *in vivo* have demonstrated that between 30 and 60 percent of the erythrocytes in the venous circulation of sickle cell anemic individuals, but less than 1 percent of those in the venous circulation of sicklemic individuals, are normally sickled. Experiments *in vitro* indicate that under sufficiently low oxygen pressure, however, all the cells of both types assume the sickled form.

The evidence available at the time that our investigation was begun indicated that the process of sickling might be intimately associated with the state and the nature of the hemoglobin within the erythrocyte. Sickle cell erythrocytes in which the hemoglobin is combined with oxygen or carbon monoxide have the biconcave disk contour and are indistinguishable in that form from normal erythrocytes. In this condition they are termed promeniscocytes. The hemoglobin appears to be uniformly distributed and randomly oriented within normal cells and promeniscocytes, and no birefringence is observed. Both types of cells are very flexible. If the oxygen or carbon monoxide is removed, however, transforming the hemoglobin to the uncombined state, the promeniscocytes undergo sickling. The hemoglobin within the sickled cells appears to aggregate into one or more foci, and the cell membranes collapse. The cells become birefringent (*11*) and quite rigid. The addition of oxygen or carbon monoxide to these cells reverses these phenomena. Thus the physical effects just described depend on the state of combination of the hemoglobin, and only secondarily, if at all, on the cell membrane. This conclusion is supported by the observation that sickled cells when lysed with water produce discoidal, rather than sickle-shaped, ghosts (*10*).

It was decided, therefore, to examine the physical and chemical properties of the hemoglobins of individuals with sicklemia and sickle cell anemia, and to compare them with the hemoglobin of normal individuals to determine whether any significant differences might be observed.

EXPERIMENTAL METHODS

The experimental work reported in this paper deals largely with an electrophoretic study of these hemoglobins. In the first phase of the investigation, which concerned the comparison of normal and sickle cell anemia hemoglobins, three types of experiments were performed: 1) with carbonmonoxyhemoglobins; 2) with uncombined ferrohemoglobins in the presence of dithionite ion, to prevent oxidation to methemoglobins; and 3) with carbonmonoxyhemoglobins in the presence of dithionite ion. The experiments of type 3 were performed and compared with those of type 1 in order to ascertain whether the dithionite ion itself causes any specific electrophoretic effect.

Samples of blood were obtained from sickle cell anemic individuals who had not been transfused within three months prior to the time of sampling. Stroma-free concentrated solutions of human adult hemoglobin were prepared by the method used by Drabkin (*3*). These solutions were diluted just before use with the

[1] This research was carried out with the aid of a grant from the United States Public Health Service. The authors are grateful to Professor Ray D. Owen, of the Biology Division of this Institute, for his helpful suggestions. We are indebted to Dr. Edward R. Evans, of Pasadena, Dr. Travis Winsor, of Los Angeles, and Dr. G. E. Burch, of the Tulane University School of Medicine, New Orleans, for their aid in obtaining the blood used in these experiments.

[2] U. S. Public Health Service postdoctoral fellow of the National Institutes of Health.

[3] Postdoctoral fellow of the Division of Medical Sciences of the National Research Council.

[4] Contribution No. 1233.

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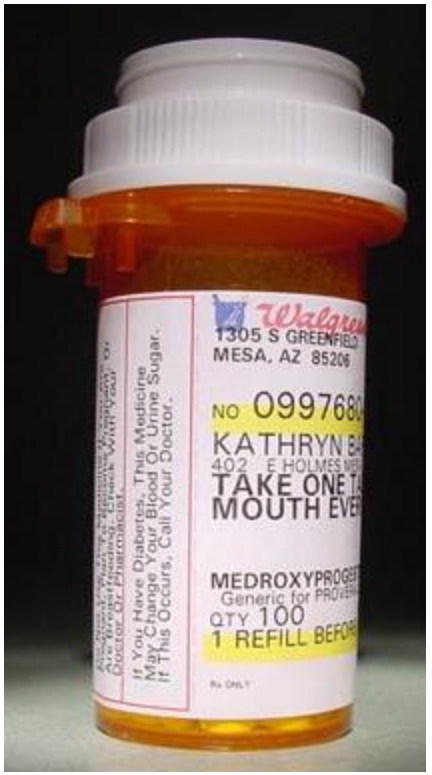

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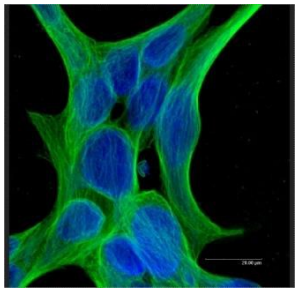
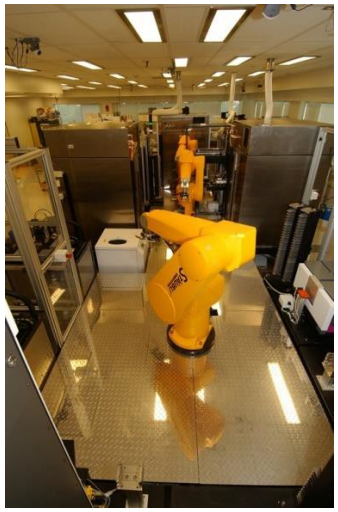
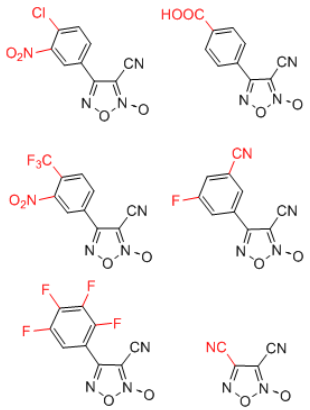
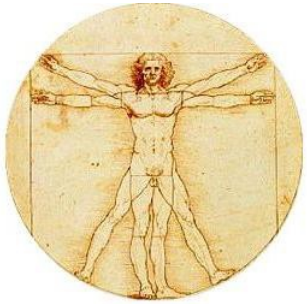
Steps in the drug development process

Identify target → Create testing system (aka, "assay" → Test >100,000 chemicals for activity on target → Make modifications to active chemicals to make suitable for human use → Test in animals for safety, effectiveness → Test in humans for safety, effectiveness









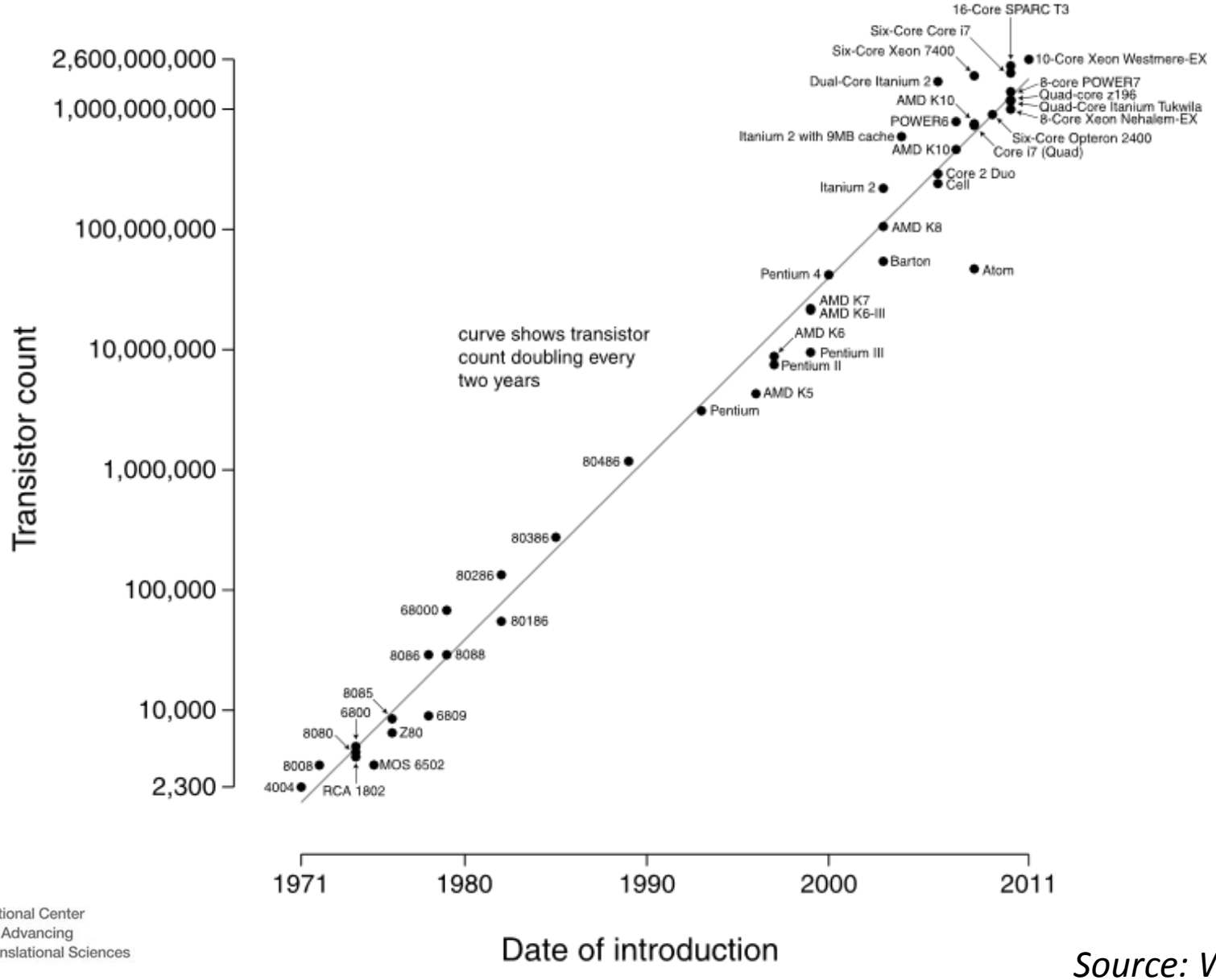
Assay Development | *HTS* | *Medicinal Chemistry* | *Preclinical Development* | *Clinical Development*

Basic research | **Discovery** | **Preclinical and early clinical** | **Late clinical**

$50-100K | $500K-1M | $5-10M | $50-100M

(Per project cost)

Moore's Law



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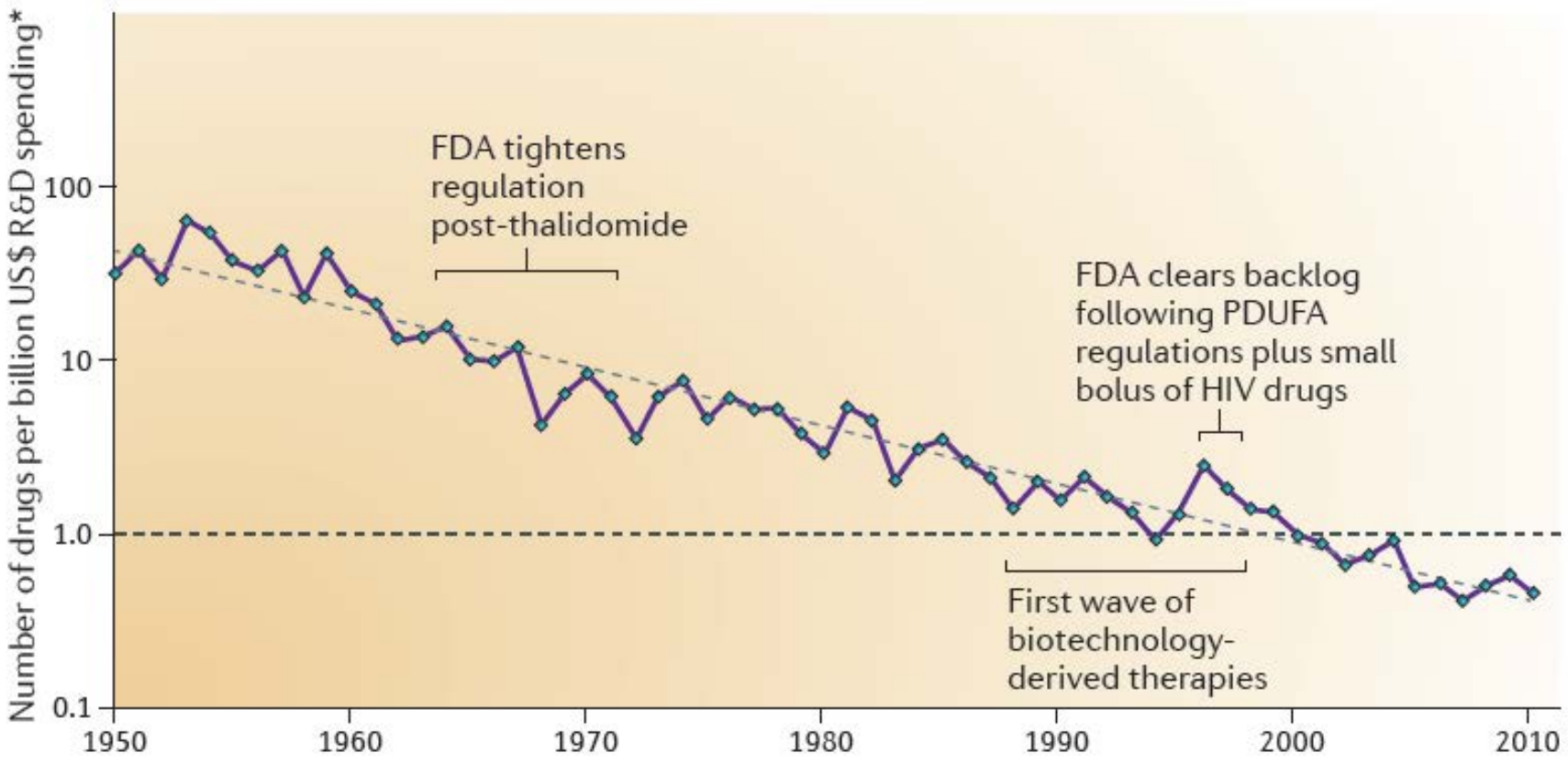
Source: Wikipedia

Eroom's Law



The number of new drugs approved by the FDA per billion US dollars (inflation-adjusted) spent on research and development (R&D) has halved roughly every 9 years since 1950.

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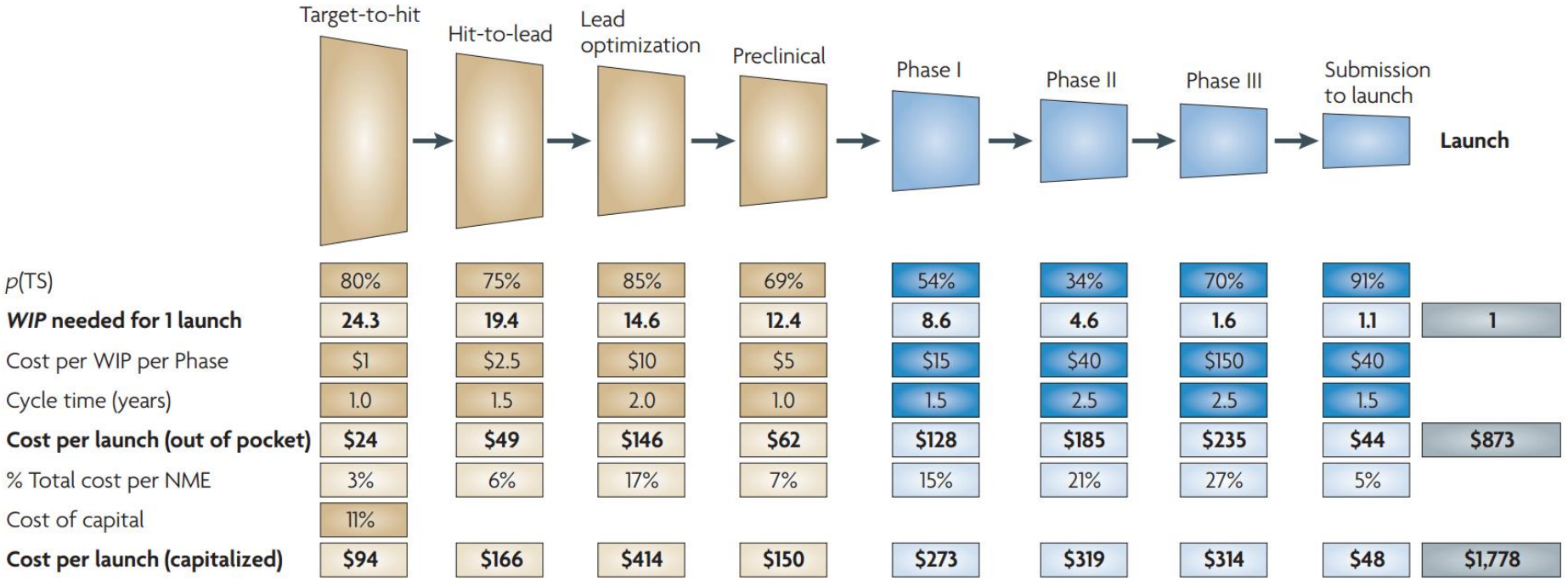
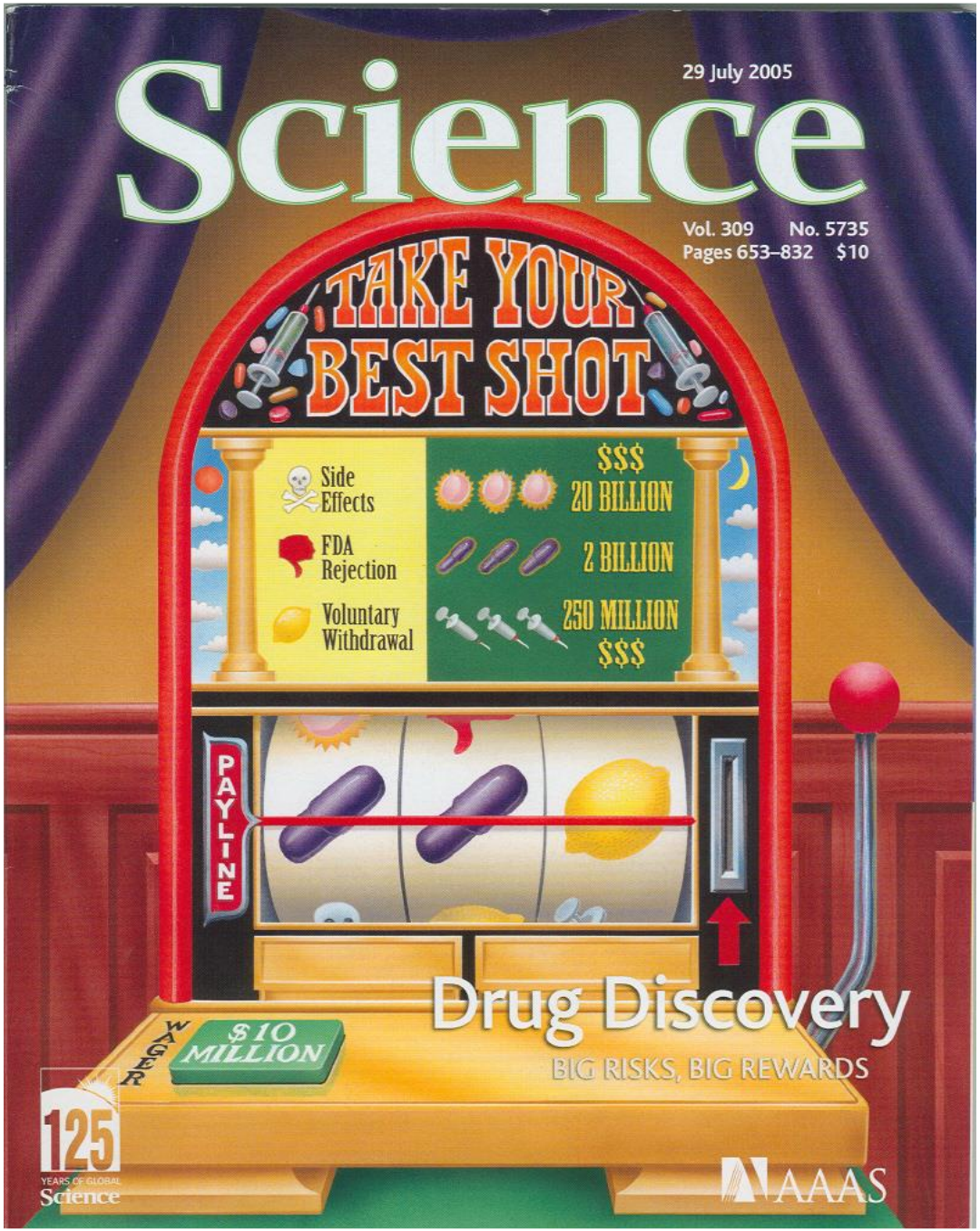
Scannell et al., *Nature Reviews Drug Discovery* 11:191, 2012

Costs and probabilities in drug development



	Target-to-hit	Hit-to-lead	Lead optimization	Preclinical	Phase I	Phase II	Phase III	Submission to launch	Launch
p(TS)	80%	75%	85%	69%	54%	34%	70%	91%	
***WIP* needed for 1 launch**	**24.3**	**19.4**	**14.6**	**12.4**	**8.6**	**4.6**	**1.6**	**1.1**	**1**
Cost per WIP per Phase	$1	$2.5	$10	$5	$15	$40	$150	$40	
Cycle time (years)	1.0	1.5	2.0	1.0	1.5	2.5	2.5	1.5	
Cost per launch (out of pocket)	**$24**	**$49**	**$146**	**$62**	**$128**	**$185**	**$235**	**$44**	**$873**
% Total cost per NME	3%	6%	17%	7%	15%	21%	27%	5%	
Cost of capital	11%								
Cost per launch (capitalized)	**$94**	**$166**	**$414**	**$150**	**$273**	**$319**	**$314**	**$48**	**$1,778**

Paul SM et al., Nature Reviews Drug Discovery 9:203, 2010

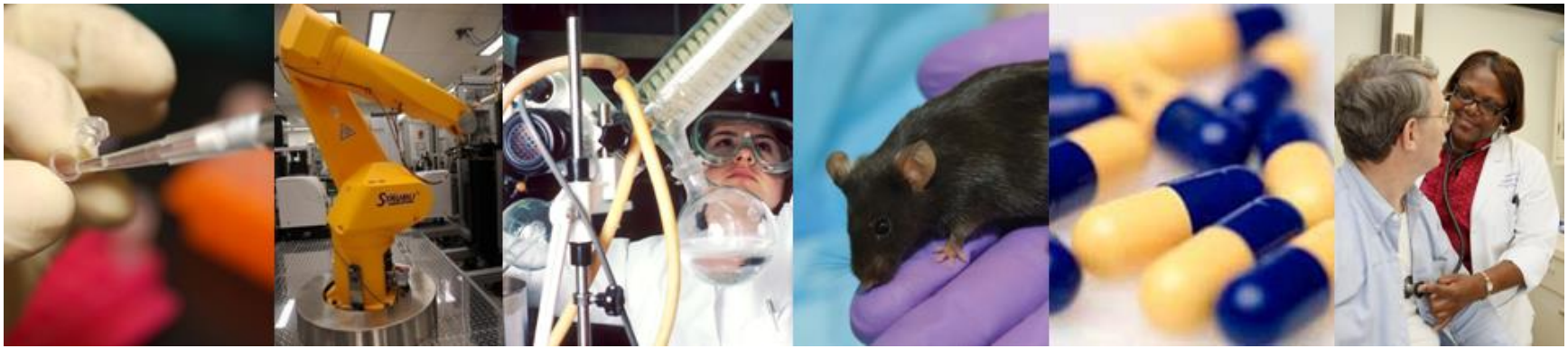


What is Translational Science?

Translational Science is the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process.

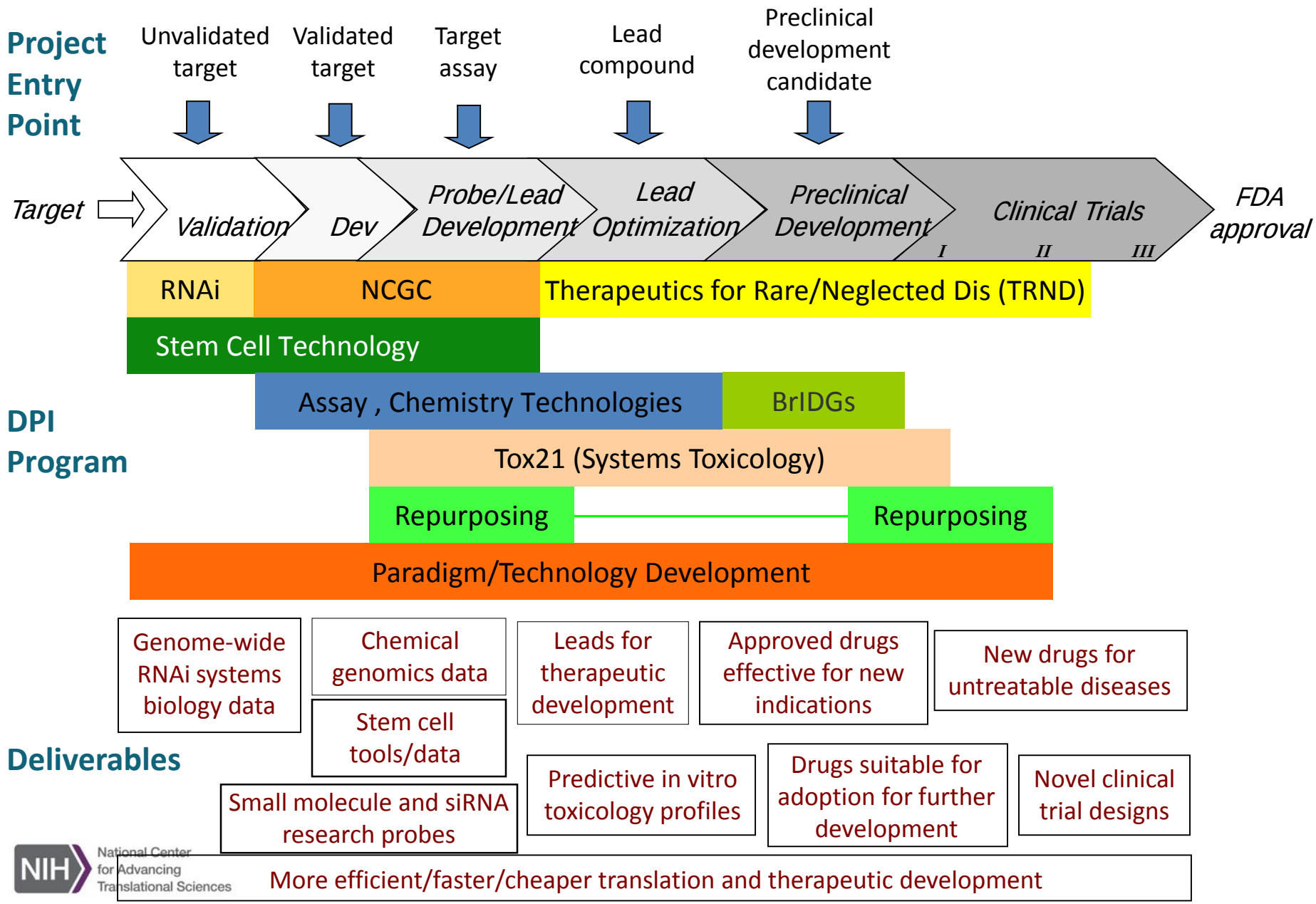
NCATS studies translation as a scientific and organizational problem.

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 Division of Preclinical Innovation



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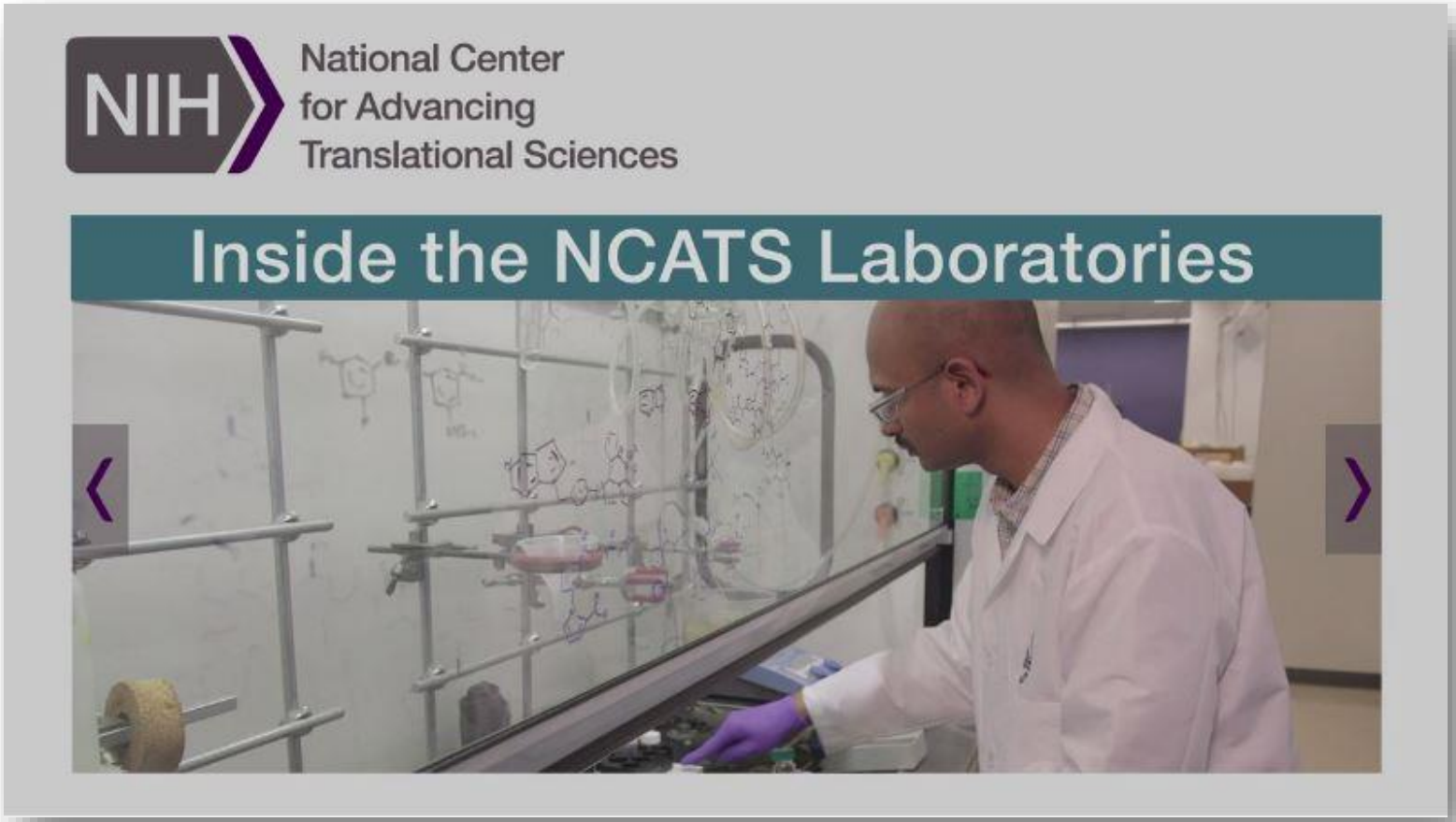
NCATS DPI Staff

Video of NCATS Preclinical Innovation Laboratories



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Developing drugs for Galactosemia

NCATS collaboration with Kent Lai, University of Utah)

Rare autosomal recessive, metabolic disorder caused by GALT deficiency (1 in 60,000)

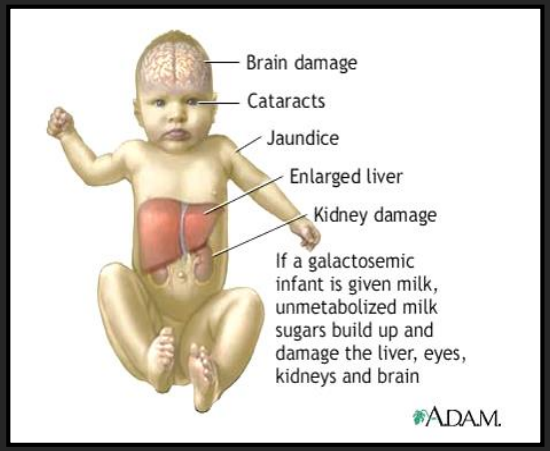
Currently diagnosed by testing newborns for GALT activity and galactose in blood spot test

Only treatment is to restrict galactose & lactose

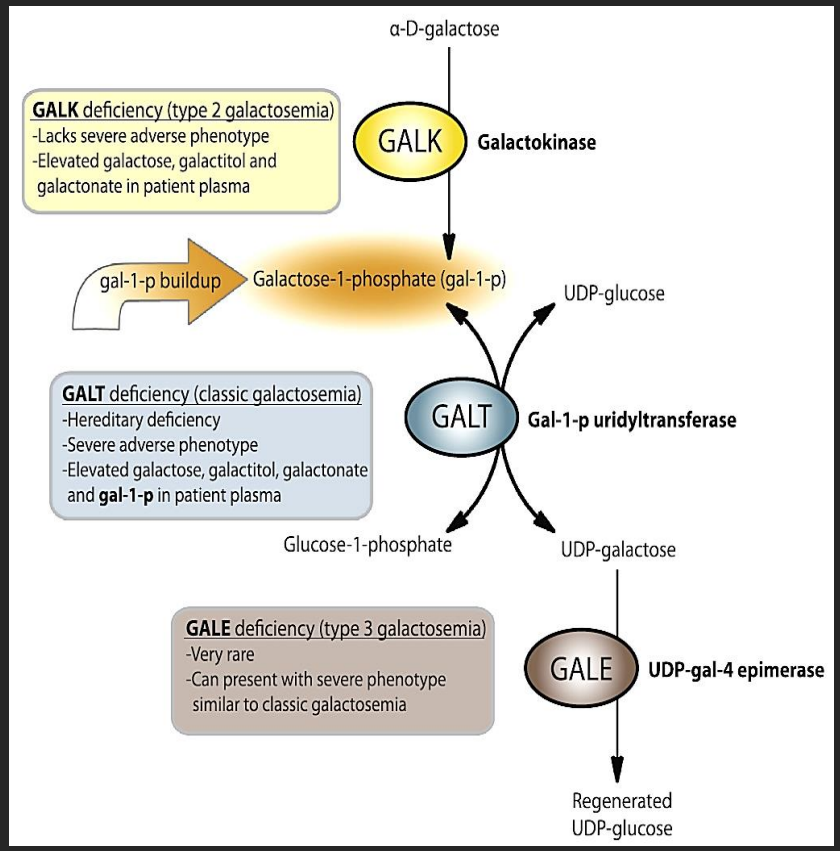
75%

mortality if untreated

Chronic complications



Leloir Pathway



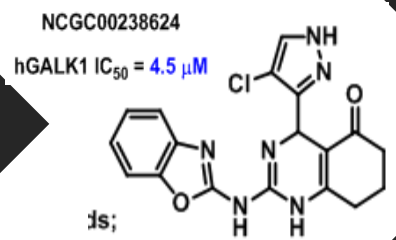
Hypothesis: inhibition of **GALK** could prevent toxic buildup of gal-1-p and improve patient outcomes

DEVELOPMENT OF GALK INHIBITORS

High-throughput screen

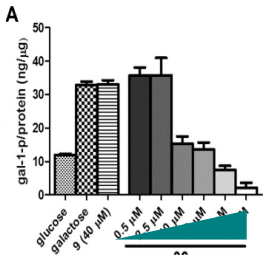
- 280,000+ compounds screened
- Single chemical series identified

Selective GALK inhibition



- Inactive against GALK2
- Clean in Kinome panel

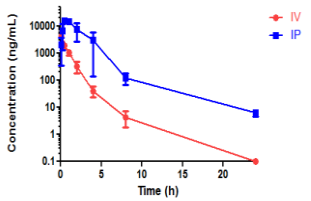
Cellular efficacy



- Decreases gal 1 p levels in patient cells
- No effect on cell viability

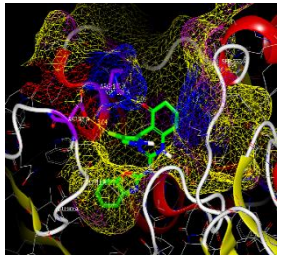
Medicinal chemistry optimization of series (GALK activity, ADME/PK properties)

Pharmacokinetic profiling



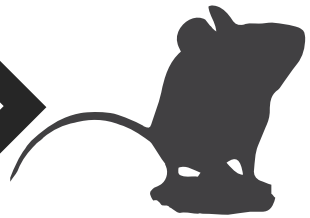
- Single chemical series identified
- Possesses acceptable PK profile

Co-crystal



- Inhibitor/GALK co crystal structure resolved

Galactosemia mouse models



- Only mouse model for galactosemia that closely mimics the human phenotype
- Compounds currently being tested

GOAL: Preclinical development

Patient-driven science

ACS chemical biology

Articles

pubs.acs.org/acschemicalbiology

Identification of Drug Modulators Targeting Gene-Dosage Disease CMT1A

Sung-Wook Jang,[†] Camila Lopez-Anido,[§] Ryan MacArthur,[†] John Svaren,[§] and James Inglese*[,†,‡]

[†]National Center of Advancing Translational Sciences and [‡]National Human Genome Research Institute, National Institutes of Health, Bethesda,

[§]Department of Cc

Cancer Biology & Therapy 14:7, 638–647; July 2013; © 2013 Landes Bioscience

Supporting In

ABSTRACT: T
Schwann cells i
required for pro
adequate expres
myelin protein
resulting from it
been directly ass
Charcot-Marie-T
prevalent type
transcriptional
CMT1A, we de
reporter assays,
(βLac), capable
Each compound
pharmacological
independent counter-screen for cytotoxicity, the design of our orthogon
prioritization of active compounds, among which three drugs (fenretini
of endogenous Pmp22 mRNA and protein. Overall, the findings of this
for gene-dosage diseases such as CMT1A.

Identification of repurposed small molecule drugs for chordoma therapy

Menghang Xia,[1,†,*] Ruili Huang,[1,†] Srilatha Sakamuru,[1] David Alcorta,[2] Ming-Hsuang Cho,[1] Dae-Hee Lee,[3] Deric M Park,[3] Michael J Kelley,[2] Josh Sommer,[4] and Christopher P Austin[1]

[1]NIH Chemical Genomics Center; Nati
[2]Department of Medicine; Duke University;

nature COMMUNICATIONS

Keywords: chordoma, NCGC

ARTICLE

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DOI: 10.1038/ncomms3044

Induction and reversal of myotonic dystrophy type 1 pre-mRNA splicing defects by small molecules

Jessica L. Childs-Disney[1,*], Ewa Stepniak-Konieczna[2,*], Tuan Tran[1,3,*], Ilyas Yildirim[4], HaJeung Park[1], Catherine Z. Chen[5], Jason Hoskins[6], Noel Southall[5], Juan J. Marugan[5], Samarjit Patnaik[5], Wei Zheng[5], Chris P. Austin[5], George C. Schatz[4], Krzysztof Sobczak[2], Charles A. Thornton[6] & Matthew D. Disney[1]

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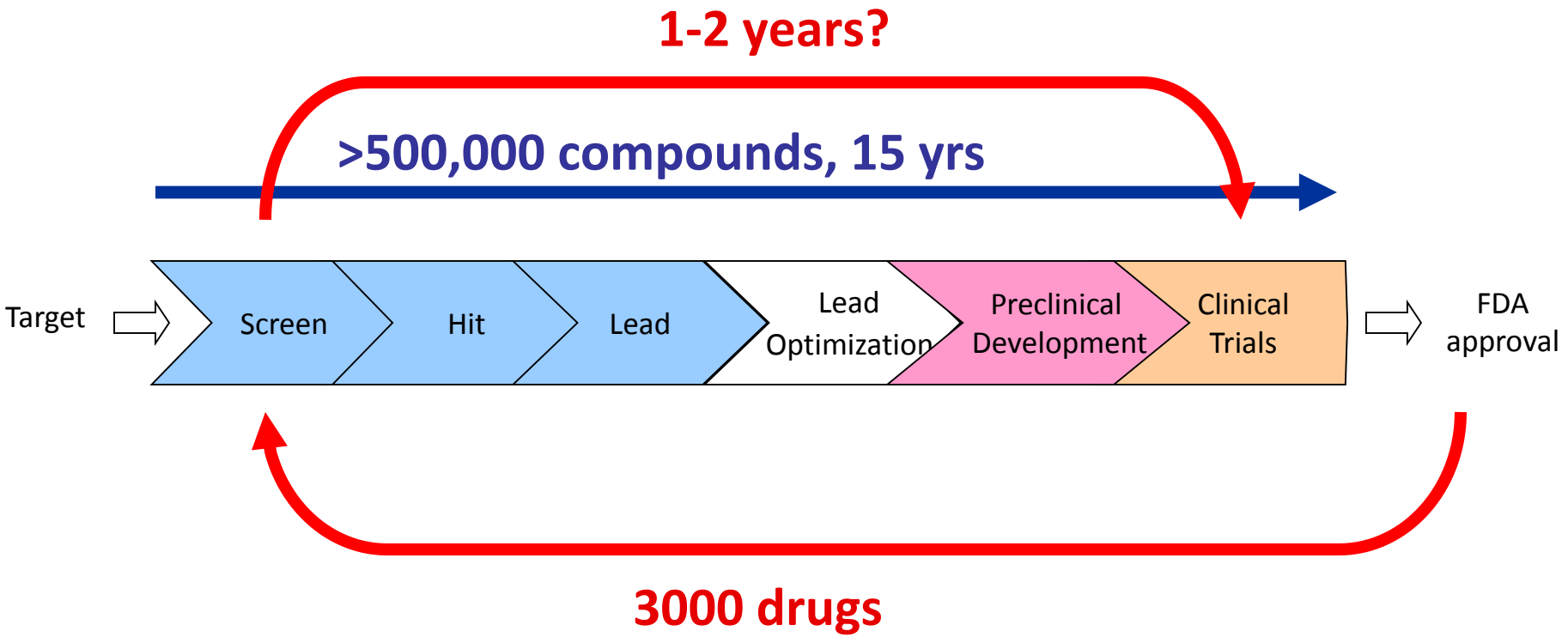
Why Repurposing?



NCATS Comprehensive Repurposing Program
"Systematizing Serendipity"

The NCGC Pharmaceutical Collection: A Comprehensive Resource of Clinically Approved Drugs Enabling Repurposing and Chemical Genomics

Ruili Huang,* Noel Southall,* Yuhong Wang, Adam Yasgar, Paul Shinn, Ajit Jadhav, Dac-Trung Nguyen, Christopher P. Austin†

Small-molecule compounds approved for use as drugs may be "repurposed" for new indications and studied to determine the mechanisms of their beneficial and adverse effects. A comprehensive collection of all small-molecule drugs approved for human use would be invaluable for systematic repurposing across human diseases, particularly for rare and neglected diseases, for which the cost and time required for development of a new chemical entity are often prohibitive. Previous efforts to build such a comprehensive collection have been limited by the complexities, redundancies, and semantic inconsistencies of drug naming within and among regulatory agencies worldwide; a lack of clear conceptualization of what constitutes a drug; and a lack of access to physical samples. We report here the creation of a definitive, complete, and nonredundant list of all approved molecular entities as a freely available electronic resource and a physical collection of small molecules amenable to high-throughput screening.

Therapeutics for Rare and Neglected Diseases (TRND) Program

- Model: Collaboration between NIH intramural labs with preclinical drug development expertise and extramural labs with disease-area / target expertise
- Projects:
  - May enter at various stages of development
  - Taken to stage needed to attract external organization to adopt for final clinical development
  - Serve to develop new generally applicable platform technologies and paradigms
- Eligible Applicants:
  - Academic, Non-Profit, Government Lab, Small Business, or Large Biotech / Pharma
  - Ex-U.S. applicants accepted
- Intellectual Property:
  - Partnerships are creative
  - TRND may generate intellectual property

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TRND Portfolio

Therapeutic Area/Disease	Organization Name(s)	Partner Type(s)
Autoimmune pulmonary alveolar proteinosis	Cincinnati Children's Hospital	Academic
Creatine Transporter Defect	Lumos Pharma, Inc.	Biotech
Chronic lymphocytic leukemia	Leukemia & Lymphoma Society, University of Kansas Cancer Center	Disease foundation, academic
Core binding factor leukemia	NHGRI	NIH intramural labs
Fibrodysplasia ossificans progressiva	Massachusetts General Hospital	Academic
GNE Myopathy (Hereditary Inclusion Body Myopathy NIBM)	New Zealand Pharmaceuticals, NHGRI	Biotech and NIH intramural clinical labs
Hemoglobinopathies	Phoenicia Biosciences, Inc.	Biotech
Hypoparathyroidism	Eli Lilly & Co.	Pharmaceutical
LEOPARD syndrome	Beth Israel Deaconess Medical Center	Academic
Malaria	Loyola University Chicago	Academic
Niemann-Pick disease type C	Ara Parseghian Medical Research Foundation, Niemann-Pick Type C Support of Accelerated Research (NPC-SOAR), Einstein College of Medicine, University of Pennsylvania, Washington University, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and National Human Genome Research Institute (NHGRI)	Disease foundation, academic, NIH intramural labs
Retinitis pigmentosa	University of California, Irvine	Academic
Schistosomiasis	CoNCERT Pharmaceuticals	Biotech
Sickle cell disease	Aes-Rx, National Heart, Lung and Blood Institute	Biotech, NIH intramural labs

TRND
Niemann Pick Type C Collaboration

- Drug: Cyclodextrin (HPBCD)
- Collaborators
  - NICHD
    - Denny Porter – Clinical
  - Washington University
    - Dan Ory – Biochemistry, Biomarkers
  - Albert Einstein and UPenn
    - Steve Walkley and Charles Vite - Animal models
  - Johnson & Johnson Pharmaceuticals
- NPC disease foundations involved and facilitating

- Milestones
  - **February 2011:** 2-hydroxypropyl-ß-cyclodextrin (HP-ß-CD) selected by TRND as pre-clinical candidate
  - **December 2012:** IND filed
  - **February 2013:** Phase I initiated and 1st patient dosed
  - **January 2015:** Agreement signed with Vtesse to complete clinical development of HPBCD for NPC and investigate use in other LSDs
  - **September 2015:** Phase I completed
  - ***October 2015**: Phase II start planned*

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Agreement with Vtesse January 7, 2015

Advancing treatments for Lysosomal Storage Disorders

- CRADA: NCATS - NICHD – Vtesse (Gaithersburg, MD)

For Immediate Release: Wednesday, January 7, 2015

NIH teams with industry to d
treatments for Niemann-Pick
disease

Researchers from the National Institutes of Health h
agreement with biotechnology company Vtesse, Inc.,
Maryland, to develop treatments for Niemann-Pick d
and other lysosomal storage disorders.

Lysosomal storage diseases, also known as lipid stor
comprise about 50 rare inherited disorders that usua
Fatty materials accumulate in the cells and tissues o
diseases can result in damage to the brain, peripher
liver, and other organs and tissues; they are often f

Researchers at the National Center for Advancing Tr
National Institute of Child Health and Human Develo
other lysosomal

FierceBiotech
THE BIOTECH INDUSTRY'S DAILY MONITOR

3. Pfizer, NEA orphan drug project launches its first biotech on PhII/III threshold

By John Carroll

Comment | Forward | Twitter | Facebook | LinkedIn

Less than two years after New Enterprise Associates and Pfizer Ventures got together to launch Cydan, an incubator for new orphan disease drug developers, the group is spawning its first new biotech with a $25 million round and a program for Niemann-Pick disease type C ready to go straight into a Phase II/III study.

The venture backing provides enough money to get the pivotal data needed to know whether or not they have a product, says Chris Adams, who runs Cydan out of Cambridge, MA, and is on the board of the newly created Vtesse. The same syndicate that set up Cydan--NEA, Pfizer ($PFE), Lundbeckfond Ventures, Bay City Capital and Alexandria Venture Investments--is also backing the startup, he adds, which is being run by the experienced drug developer Ben Machielse and his small but knowledgeable team.

It's a virtual operation, notes Machielse, but there's also a wide group of investigators at the NIH and elsewhere who have pitched in to get VTS-270--a formulation of 2-hydroxypropyl-beta-cyclodextrin--to the threshold of a pivotal study.

"I actually got approached by Dave (Mott, NEA partner and former MedImmune CEO) in May to actually see if I could help out with this particular opportunity," says Machielse, a MedImmune veteran and former CEO of Omthera, which was acquired by AstraZeneca ($AZN). Vtesse licensed in the program but will continue to work with public investigators to take it the final step in the clinic.

Ben Machielse

"This public/private model is pretty cool," says Machielse, adding that this particular biotech business model should be something that can be replicated in other developers. Machielse is keeping the biotech close to home--and the NIH--in Gaithersburg, MD.

Their lead drug, VTS-270, is designed to clear away the cholesterol that builds up inside the cells of Niemann-Pick patients. But there are also plans to add to the pipeline. Vtesse is starting up with a Cooperative Research and Development Agreement, or CRADA, with the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Center for Advancing Translational Sciences at NIH. Vtesse and NCATS forged a licensing agreement for the current rights held by NIH for the worldwide use of cyclodextrin, delta-tocopherol, and derivatives of tocopherol for lysosomal storage diseases, including NPC.

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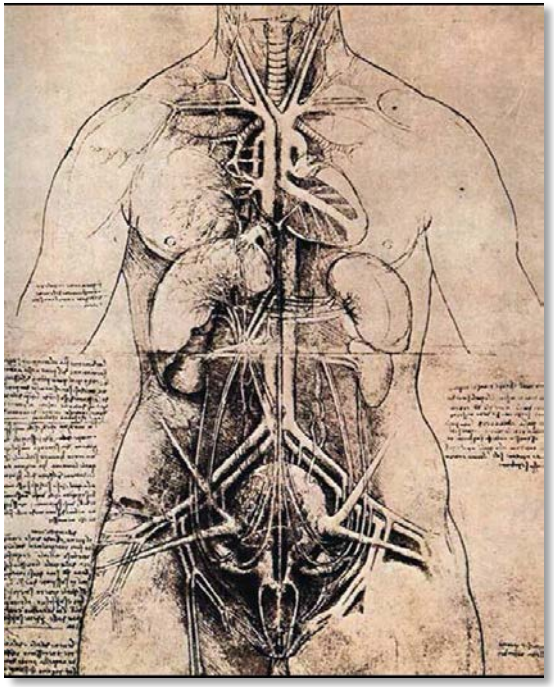
Tissue Chip Program

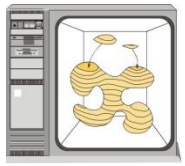
GOAL: Develop an *in vitro* platform that uses human tissues to evaluate the efficacy, safety and toxicity of promising therapies.



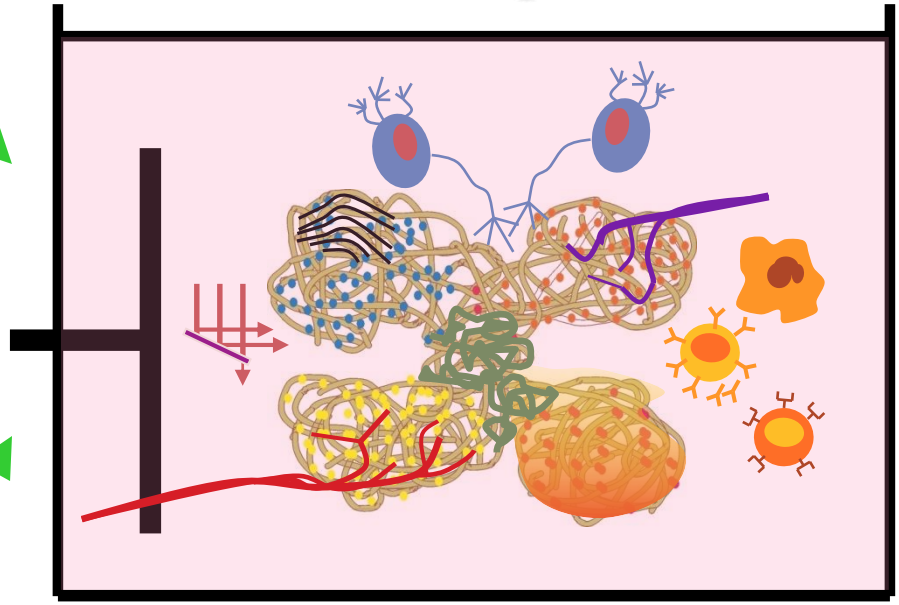
- All ten human physiological systems will be functionally represented by human tissue constructs:
  - Circulatory
  - Endocrine
  - Gastrointestinal
  - Immune
  - Integumentary
  - Musculoskeletal
  - Nervous
  - Reproductive
  - Respiratory
  - Urinary
- Physiologically relevant, genetically diverse, and pathologically meaningful.
- Modular, reconfigurable platform.
- Tissue viability for at least 4 weeks.
- Community-wide access.

Microphysiological Systems from Common Building Blocks

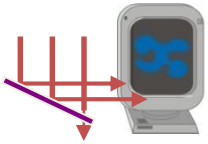
Computational Design
- systems integration
- multi-scale modeling
- simulation
- feedback



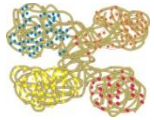
Scaffold
- purified ECM
- synthetic polymers
- composites



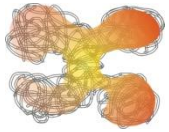
Functional Readout
- real-time, label-free, non-destructive sensing
- imaging



Cells
- stem/progenitor
- differentiated
- mixed cell types

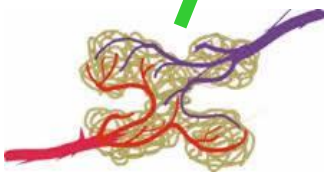


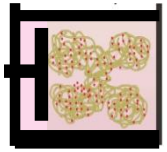
Structure
- porosity
- topography
- stiffness



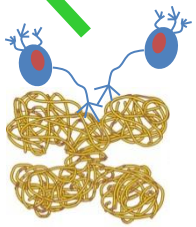
Spatial/Temporal Patterning
- cytokine gradients
- controlled release

Perfusion
- embedded channels
- vascularization

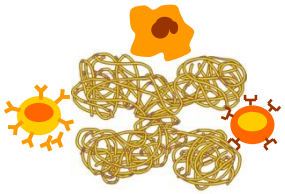




Bioreactors
- optimized culture conditions
- biomechanical properties
- blood mimetics



Innervation
- signal propagation
- coordinated response



Host Response
- generalized inflammation
- specific immunity

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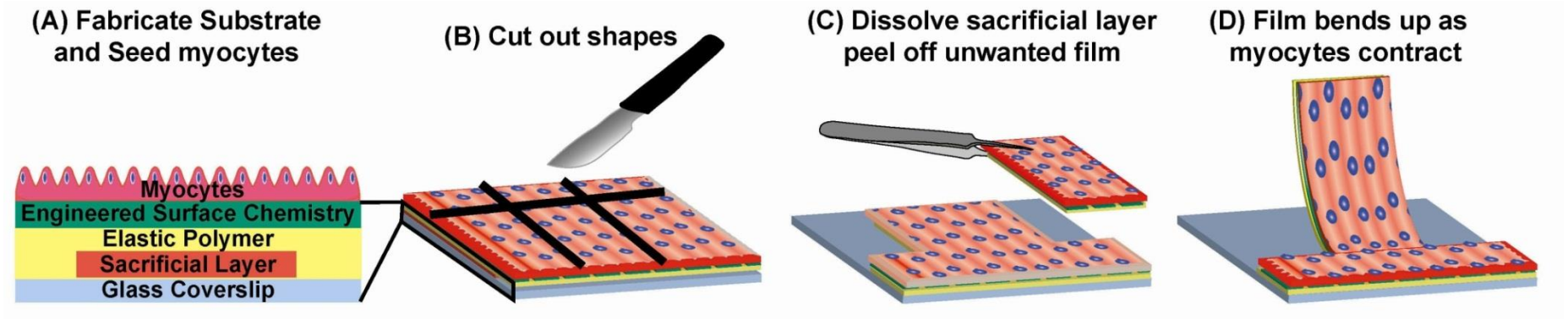
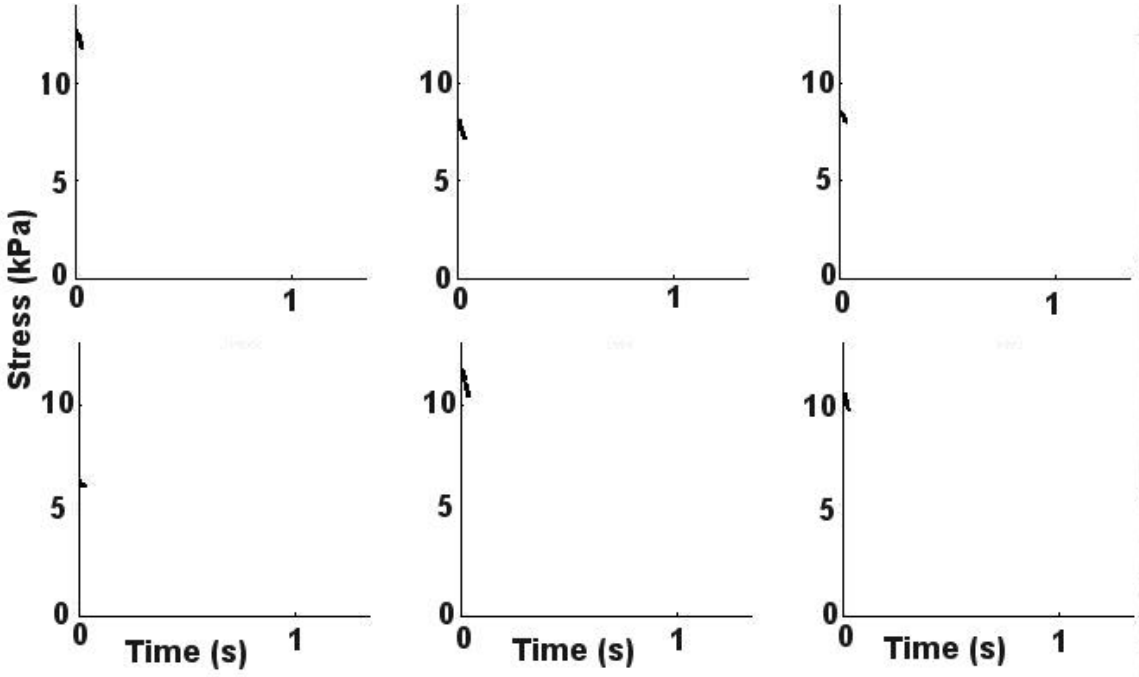
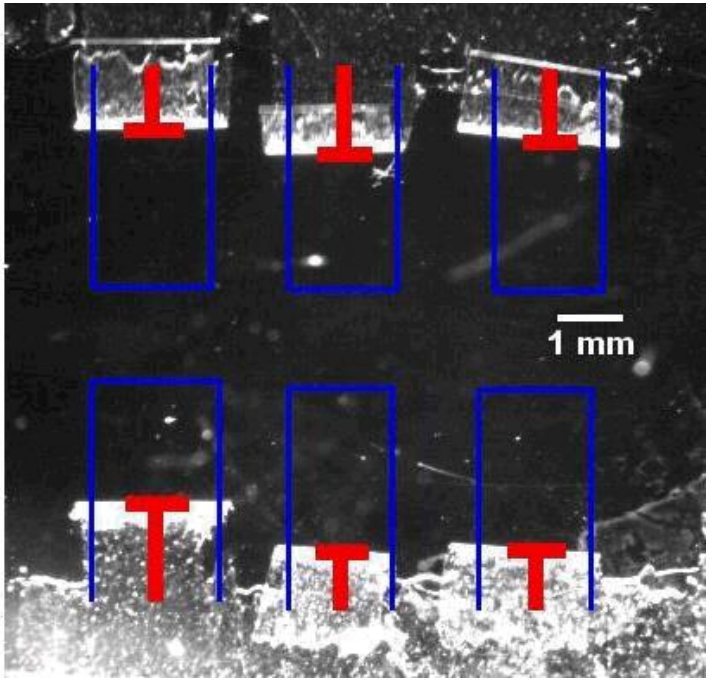
Engineered Cardiac Muscular Thin Films







Film length
Automatic projection tracking

Data provided by Dr. Kit Parker, Wyss Institute

National Center for Advancing Translational Sciences

Science 2007;317:1366
Lab Chip 2011;11:4165

Biomaterials 2010;31:3613
J Pharm Tox Methods 2012;65:126

What is Barth Syndrome?

Barth syndrome (BTHS; OMIM #302060) is a rare, life-threatening genetic disorder primarily affecting males around the world. It is caused by a mutation in the *tafazzin* gene (*TAZ*, also called G4.5), resulting in an inborn error of lipid metabolism.

Though not always present, cardinal characteristics of this multi-system disorder often include combinations and varying degrees of:

- **Cardiomyopathy**
  (Usually dilated with variable myocardial hypertrophy, sometimes with left ventricular noncompaction and/or endocardial fibroelastosis)
- **Neutropenia**
  (Chronic, cyclic, or intermittent)
- **Underdeveloped skeletal musculature and muscle weakness**
- **Growth delay**
  (Growth pattern similar to but often more severe than constitutional growth delay)
- **Exercise intolerance**
- **Cardiolipin abnormalities**
- **3-methylglutaconic aciduria**
  (Typically a 5- to 20-fold increase)

Devin (age 9) and Henry (age 5).

Important Clinical Problems May Include (in varying severity):

- Congestive heart failure
- Life-threatening bacterial infection
- Gross motor delay
- Risk of stroke
- Short stature in the early years, followed by accelerated growth in mid- to late puberty
- Extreme fatigue
- Diarrhea and/or constipation
- Feeding problems (*e.g.*, difficulty sucking, swallowing, or chewing; aversion to some food textures; selective or picky eating)
- Recurrent mouth ulcers
- Risk of thrombosis
- Diminished capacity for exercise
- Hypoglycemia, including fasting hypoglycemia (especially in the newborn period)
- Chronic headache, abdominal pain, and/or body aches (especially during puberty)
- Osteoporosis
- Some mild learning disabilities

Will (age 27) and John (age 31) at BSF's 2012 Conference.

"The Barth Syndrome Foundation has saved my life due to some clinical information that was shared through the organization. Beyond the clinical impact that the BSF has had on my life, the foundation has also been a haven of understanding and social support as well as providing a built-in group of friends."
~ Will, age 27, Affected Individual

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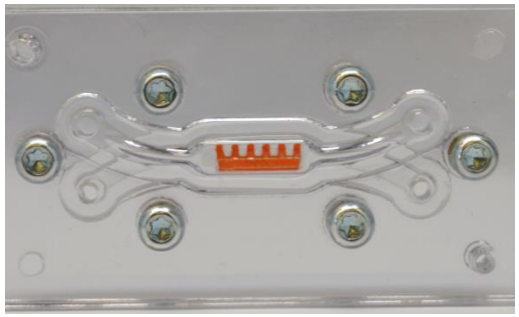
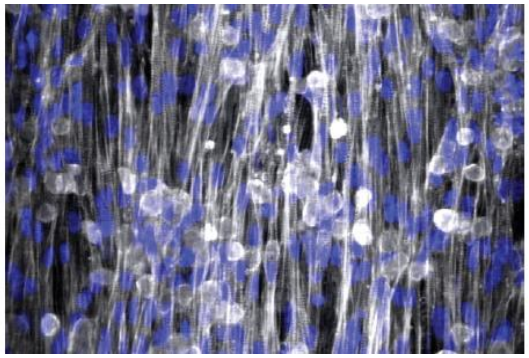
Heart on a Chip Barth Model

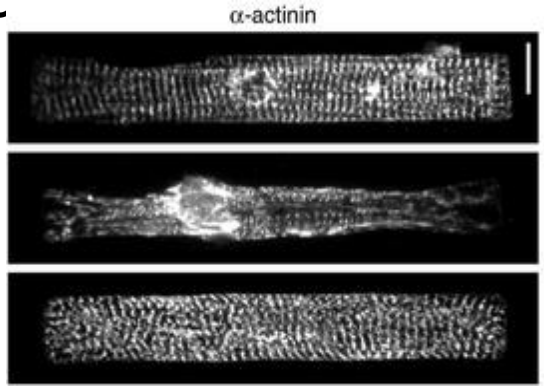
A



B



C



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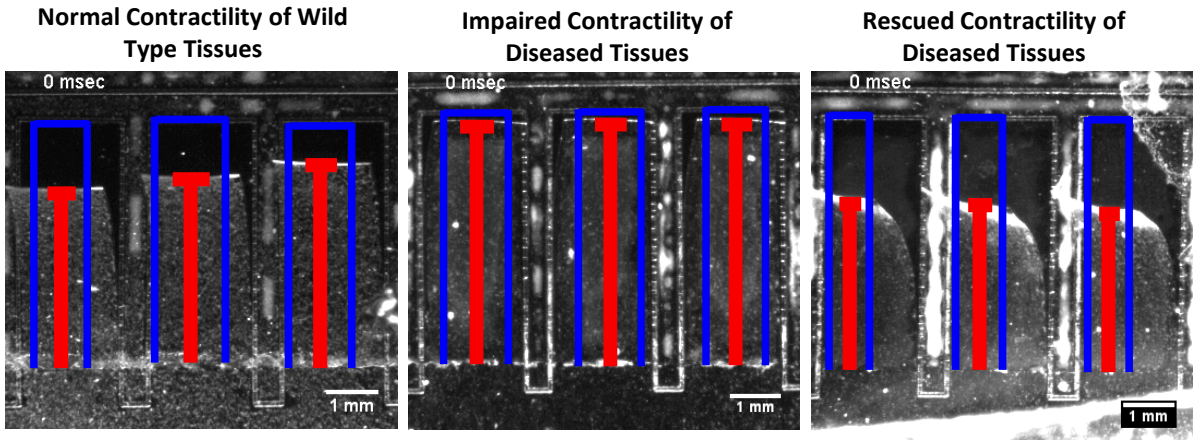

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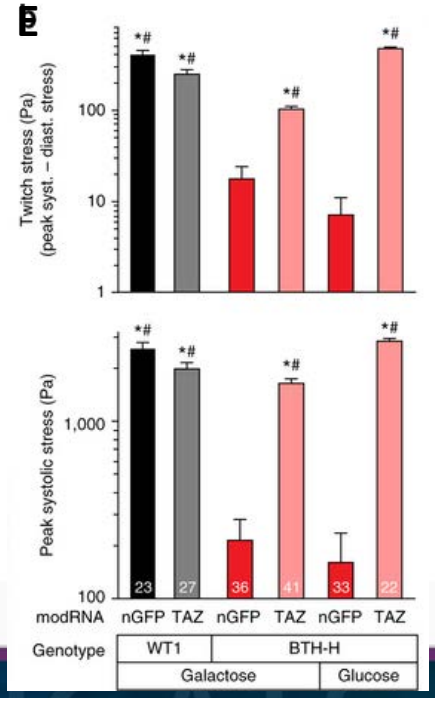

Dr. Kevin Parker, Harvard University:
http://diseasebiophysics.seas.harvard.edu

Modeling the mitochondrial cardiomyopathy of Barth syndrome with induced pluripotent stem cell and heart-on-chip technologies

Gang Wang[1,14], Megan L McCain[2,14], Luhan Yang[2,3], Aibin He[1], Francesco Silvio Pasqualini[2], Ashutosh Agarwal[2], Hongyan Yuan[2], Dawei Jiang[1], Donghui Zhang[1], Lior Zangi[1], Judith Geva[1], Amy E Roberts[1,4], Qing Ma[1], Jian Ding[1], Jinghai Chen[1], Da-Zhi Wang[1], Kai Li[1], Jiwu Wang[5,6], Ronald J A Wanders[7], Wim Kulik[7], Frédéric M Vaz[7], Michael A Laflamme[8], Charles E Murry[8–10], Kenneth R Chien[11], Richard I Kelley[12], George M Church[2,3], Kevin Kit Parker[2,13] & William T Pu[1,13]

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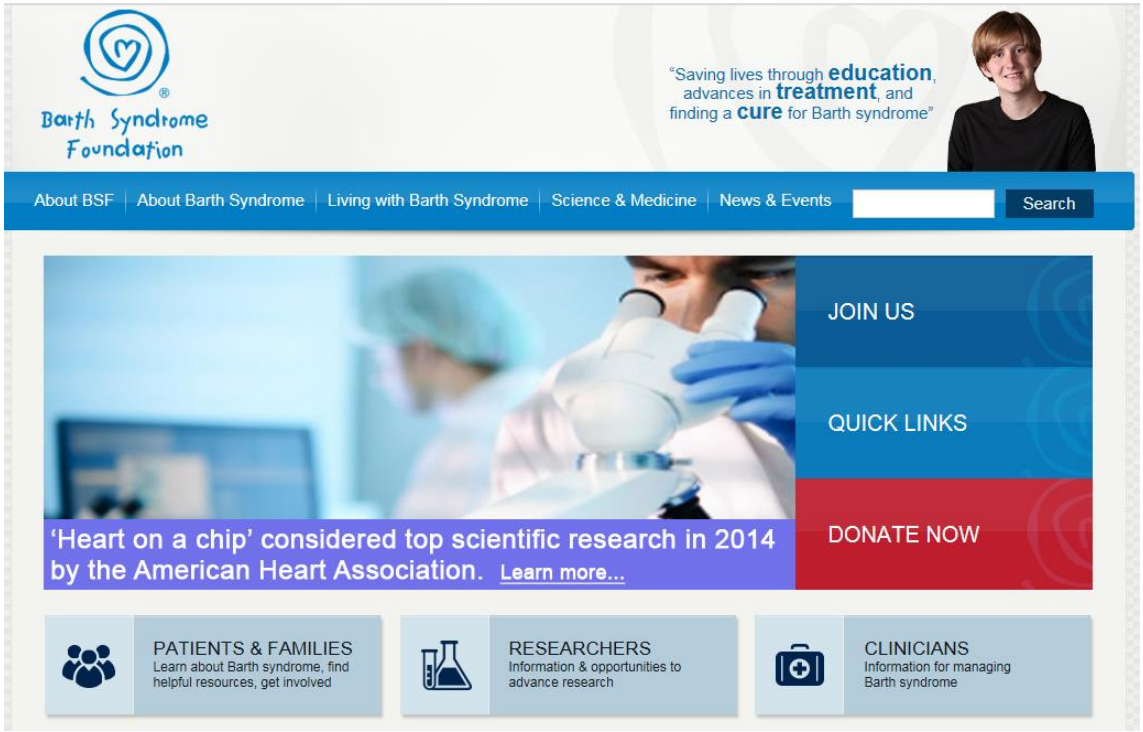

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Modeling the Female Reproductive Tract in 3-D: The Birth of EVATAR™

Science fiction and gaming enthusiasts are familiar with the concept of an avatar, the digital character a user creates to navigate a virtual world. Now, NIH-funded researchers are turning science fiction into scientific reality by building one. EVATAR™ is a miniaturized 3-D representation of the female reproductive tract and liver on a handheld, interconnected platform. The team of scientists from Northwestern University, Charles Stark Draper Laboratory and the University of Illinois at Chicago (UIC) is designing the model for use in drug testing and to study the basic biology of female reproduction.

Too often, laboratory and animal tests used by scientists in the early phases of research fail to predict a therapy's effectiveness or potential side effects in humans. Use of inaccurate models can result in many years and millions of dollars being wasted while patients wait for effective treatments. Researchers need scientifically valid alternatives for predicting treatment effectiveness and safety.

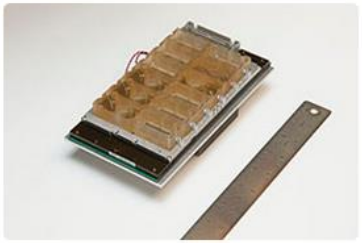
Another issue is consideration of sex as a biological variable. Although women now comprise roughly half the participants in NIH-funded clinical trials, the same is not true for pre-clinical research. More often than not, pre-clinical research conducted to date has involved mostly male-derived cells and male animals. These practices have resulted in a lack of information about female physiology and women's health.

To address these and other drug development challenges, NCATS, along with the Defense Advanced Research Projects Agency and the Food and Drug Administration, developed the Tissue Chip for Drug Screening program. Program funding is used to support scientists developing 3-D platforms with living human tissues and cells, called tissue chips or organs-on-chips. These devices are designed as accurate models of the structure and function of human organs and systems, such as the lung, liver, heart and, in this case, female reproductive tract.

A Team Effort

The EVATAR™ team at Northwestern University. (Northwestern University Photo)

Tissue Chip in Action: EVATAR™



EVATAR™, the female reproductive tract and liver tissue chip. (Northwestern University Photo)

The 3Ds of NCATS: Multi-Organ-Chip Platforms

Develop 3-D chip platforms with multiple human organsto improve pre-clinical research beyond currently available methods

Demonstrate the usefulness and accuracy of the chips using individual organ models and integrated systems

Disseminate the chip technology to the scientific community, enabling others to build similar models and create innovative approaches to answering biological questions

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https://ncats.nih.gov/pubs/features/evatar

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