Director's Report

NCATS Advisory Council and CAN Review Board

CHRISTOPHER P. AUSTIN, M.D.
DIRECTOR, NCATS
JUNE 18, 2015

NCATS

New Format for Director's Report

- Council requested more discussion time
- NCATS successes have multiplied → comprehensive accounting of progress in presentation form impractical
- Current presentation features selected highlights only
- Details and more complete accounting of progress since last Council/CAN Board meeting in packet in front of you
  - Access document electronically (entitled "NCATS Activity Summary") via the agenda in ECB
- I'll briefly run through some of these summary items and then return to my highlight presentation
- Feedback welcome

Happy Retirement, EO Janis Mullaney!

As of June 1, 2015

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Outgoing CAN RB/Council Members

Thank you!

- Alta Charo, J.D.
  Warren P. Knowles Professor of Law and Bioethics
  University of Wisconsin Law School
  University of Wisconsin School of Medicine and Public Health

- Sue Seigel, M.S.
  CEO
  healthymagination
  General Electric Co.

- Paul Yock, M.D.
  Martha Meier Weiland Professor
  Departments of Bioengineering and Medicine, Program of Biodesign
  Stanford University

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New NCATS Website Unveiled
May 1, 2015

- In April, based on internal and external input and feedback launched new website
- Items of note:
  - » Prominence of "Work with Us" headline on the home page
  - » Completely reorganized site to provide a better user experience and improve access to NCATS resources/programs
- New content in:
  - » Clinical Research Toolbox – will continue to add resources;
  - » Pre-Clinical Innovation – better showcase of capabilities and expertise;
  - » About Translation – featuring new graphic of spectrum.

Check it out!

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May 1, 2015

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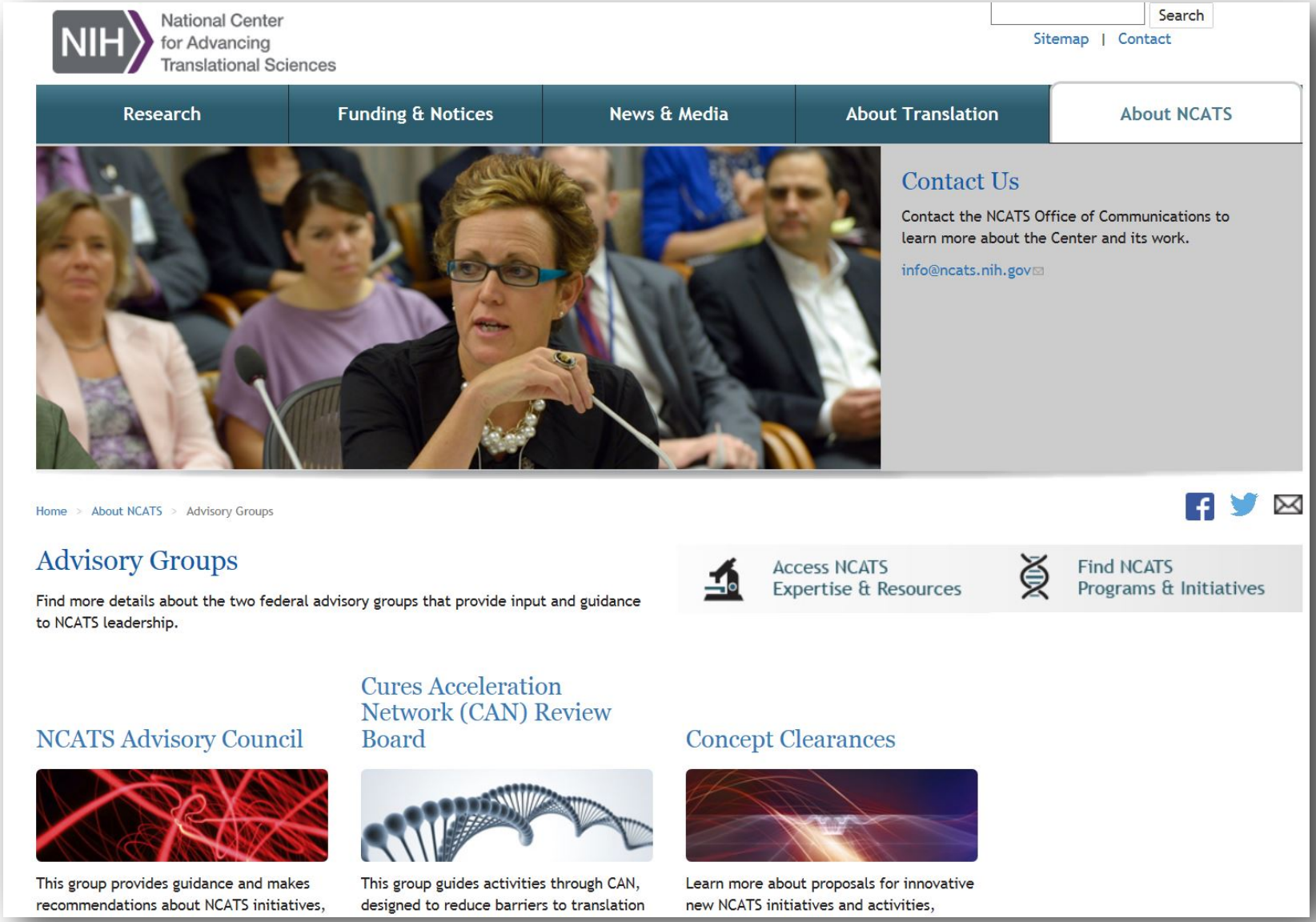

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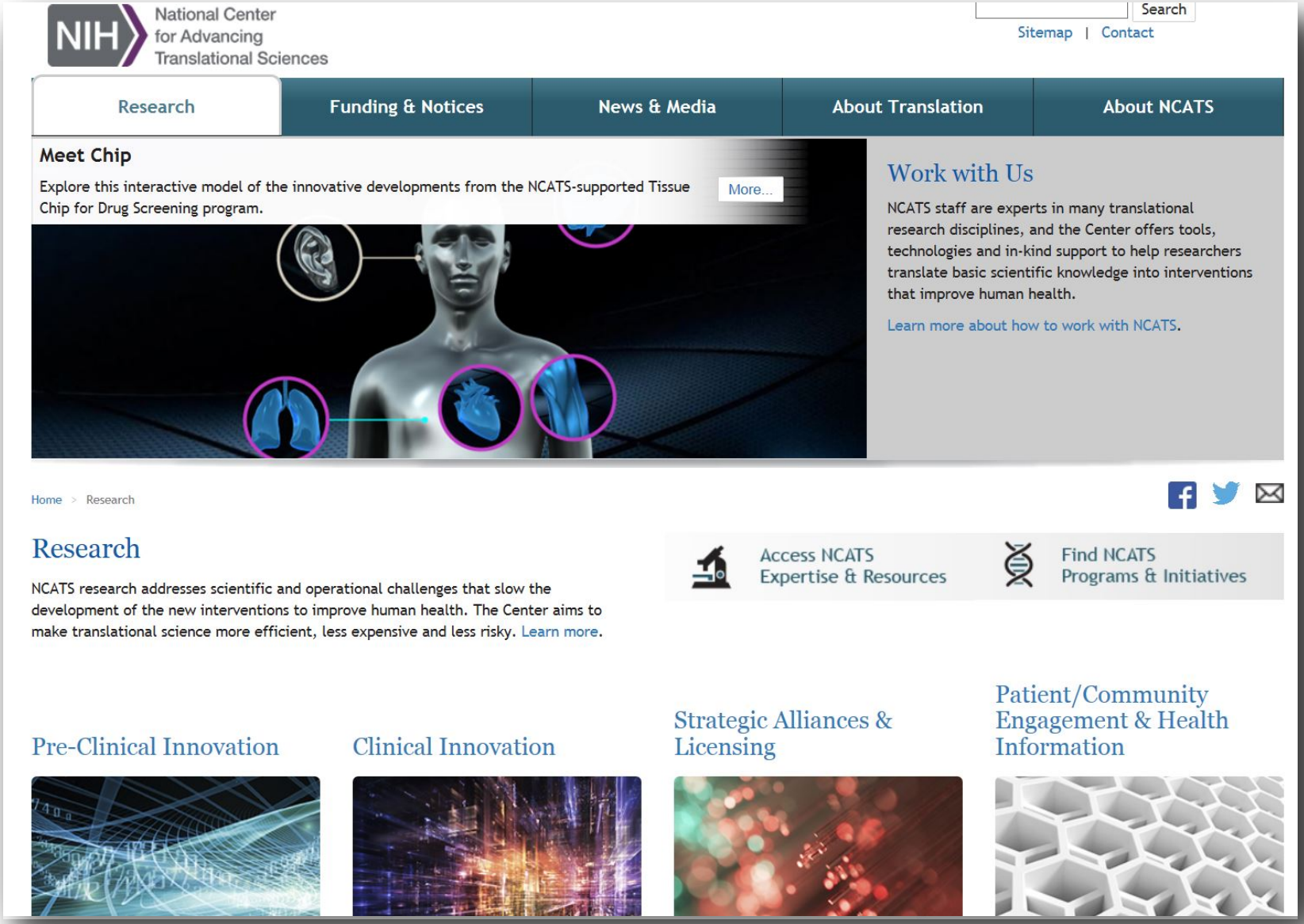

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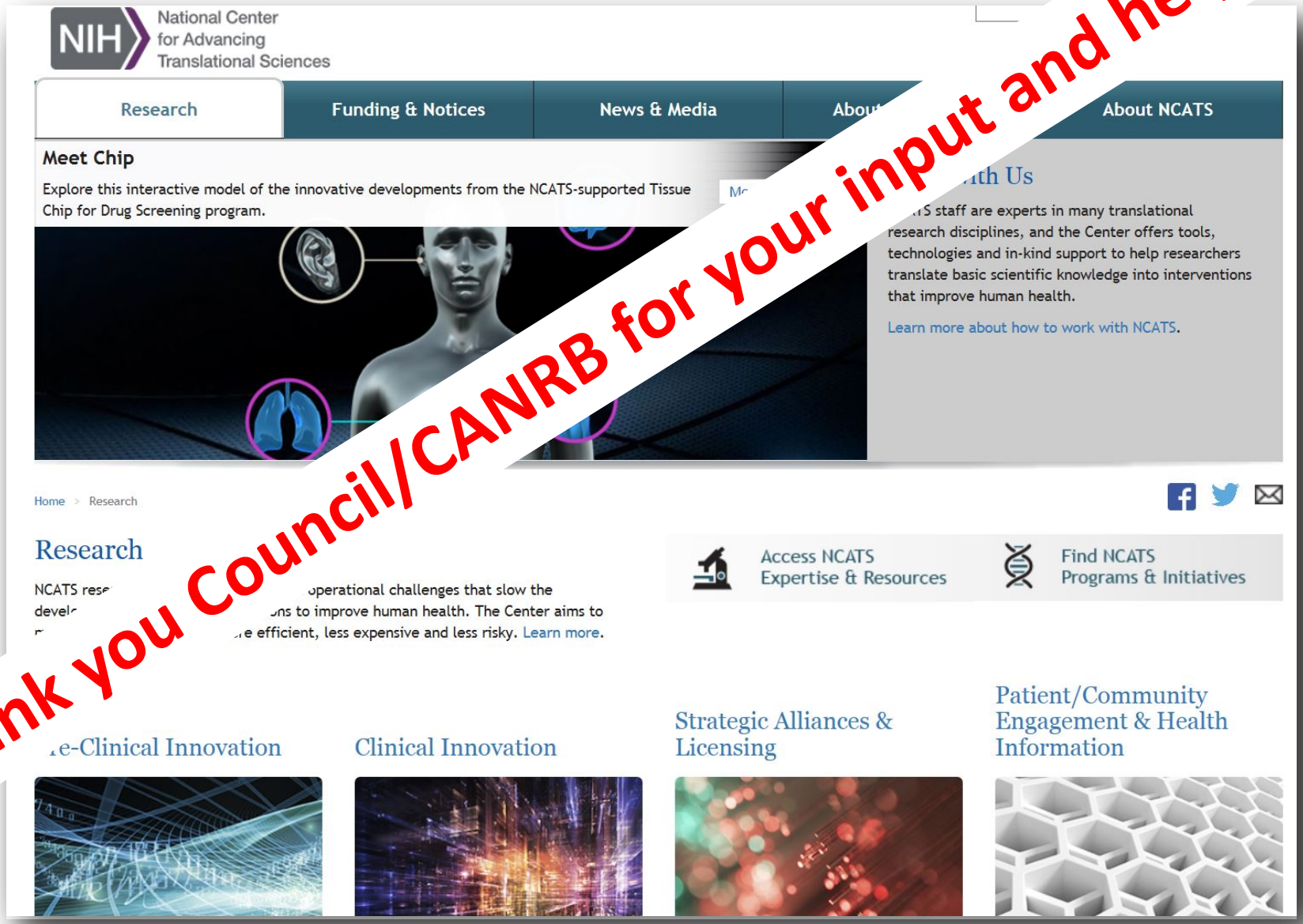

Thank you Council/CANRB for your input and help!

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Selected Translational Innovation Highlights

- *Early-stage translation:* chemical probe/lead development for target validation and therapeutic hypothesis testing
- *Mid-stage translation:* preclinical development to first-in-human studies
- *Late-stage translation:* large-scale studies in humans

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U.S. Department of Health and Human Services
Innovation Ventures Fund Award

- One of three teams selected for an DHHS Ventures investment
- Collaborative Use Repurposing Engine (CURE)
  - » FDA-NCATS collaboration to build a repository that captures and centralizes the global clinical experience of "repurposing" – using existing medical products in new ways
  - » Web-based platform to enable crowdsourcing of medical information from healthcare providers to facilitate and guide new interventions for neglected diseases
- Team members:
  - » Heather Stone, FDA/CDER/Office of Medical Policy
  - » Rose Tiernan, FDA/CDER/OMP
  - » Leonard Sacks, FDA/CDER/OMP
  - » Tim Sheils, NIH/NCATS
  - » Noel Southall, NIH/NCATS

HHS IDEA LAB

U.S. Department of Health and Human Services
Green Champion Award

Awarded to NCATS DPI
HTS Plate Saving Initiative Team

- Sam Michael
- Lili Portilla
- Mohan Viswanathan
- Kyle Brimacombe
- Anna Rossoshek
- Cordelle Tanega

- 97% decrease in plastic waste generation
  - » Kept >50,000 plates out of landfills
- > $500,000 in savings, and counting…

Enabling Comprehensive Drug Repurposing

The NCATS 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†

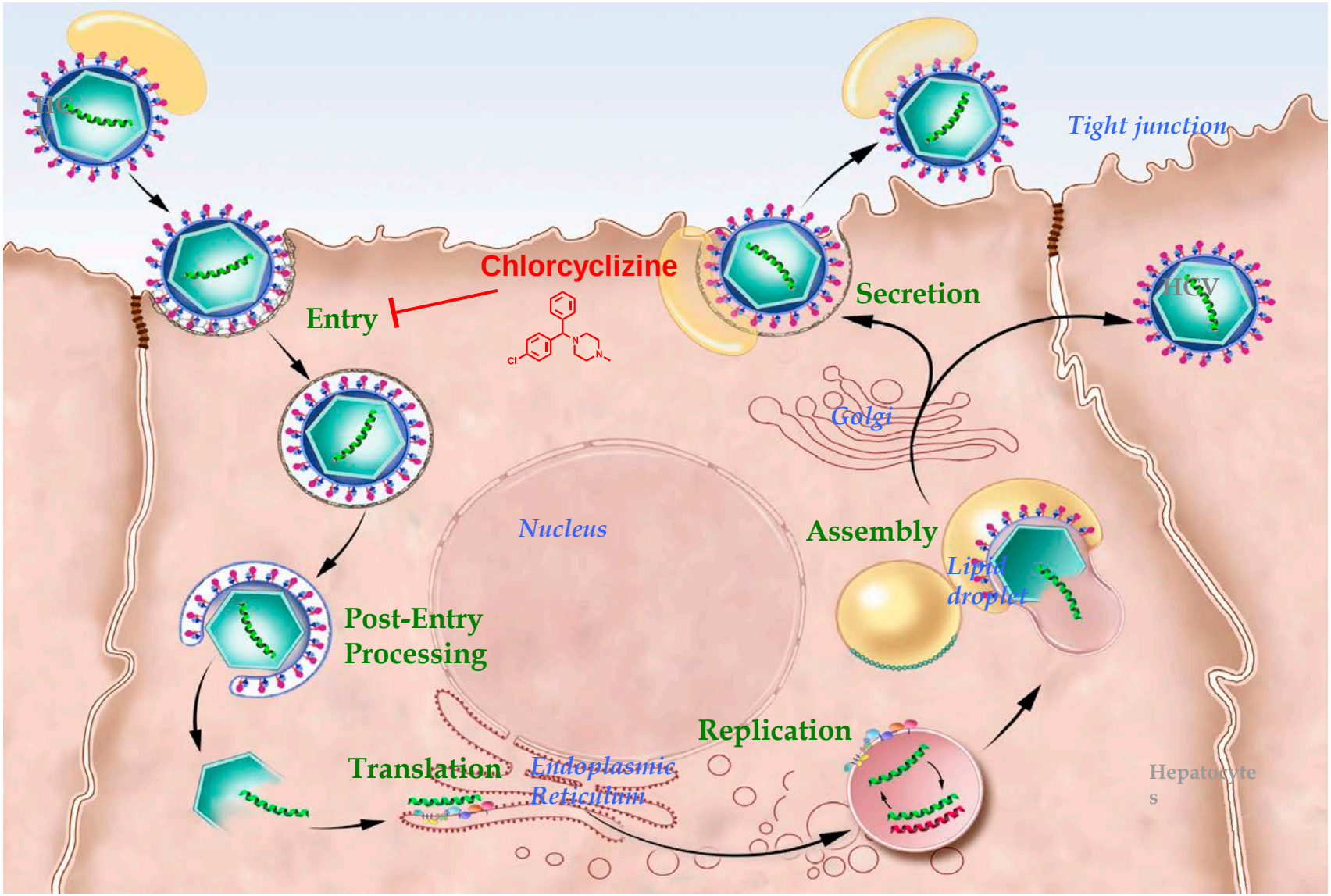
Small-molecule compounds approved for use as drugs may be "repurposed" for new indications and studied to determine the mechanisms of their beneficial and adverse effects. A comprehensive collection of all small-molecule drugs approved for human use would be invaluable for systematic repurposing across 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.

www.ScienceTranslationalMedicine.org 27 April 2011 Vol 3 Issue 80 80ps16

Drug Repurposing for HCV Infection

- Collaborator
  - Jake Liang, NIDDK intramural
- Background
  - HCV infection accelerates development of liver diseases (cirrhosis, liver failure, and hepatocellular carcinoma)
  - New HCV treatments such as Sovaldi (Gilead)
    - Effective but expensive
    - Work via viral RNA polymerase inhibition, so genotype specific
- Project
  - NCATS identified chlorocyclizine (CCZ), a first generation (generic) antihistamine in NPC screen for anti-HCV agents
  - CCZ interacts with host target and prevents infection
  - Combination treatment might reduce costs
  - Rapid initiation of NIDDK-supported clinical trial of CCZ in HCV at NIH Clinical Center

Mode of Action of Chorcyclizine



Chlorcyclizine as an Anti-HCV Drug: Summary

- Potent and selective
- Synergistic with current anti-HCV agents
- Preferential liver distribution
- Inhibits HCV genotype 1b and 2a infections with no clearly emerging resistance in vivo
- Potentially novel host mode of action
- Phase 1b trial for treatment of chronic HCV patients: proof-of-concept study (28 days)

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Unlocking the Secrets of PTSD

LATEST MAGAZINE VIDEOS

Could An Allergy Drug Treat Hepatitis C?

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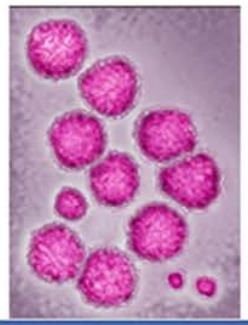
HEALTH MEDICINE

Could An Allergy Drug Treat Hepatitis C?

Alexandra Sifferlin
@acsifferlin
April 8, 2015

A drug that's been around for decades may help find a new solution for an expensive chronic disease

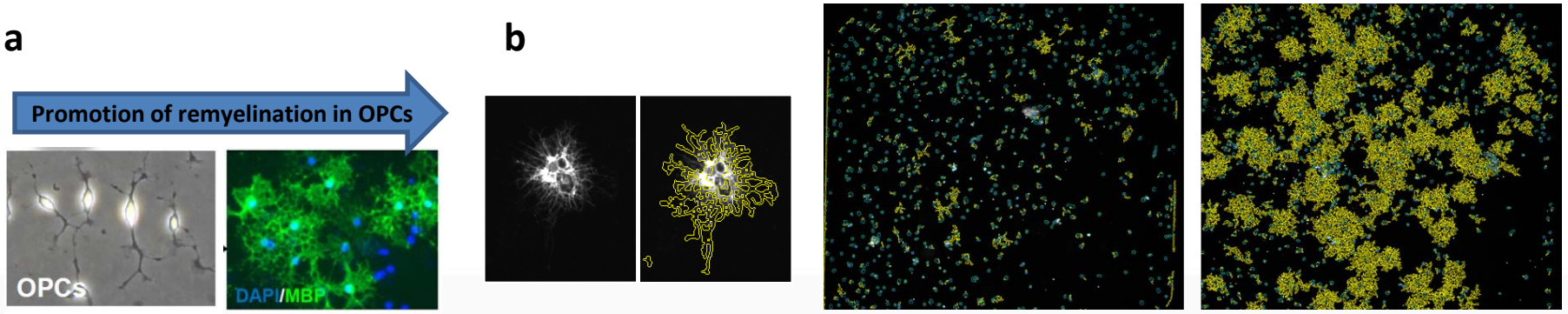
An over-the-counter drug commonly used to treat allergies may one day also contribute to the treatment of hepatitis C, according to new research in mice published in the journal *Science Translational Medicine*.



Drug Repurposing for Remyelination

- **Collaborators**
  - Paul Tesar & Fadi Najm (Case Western Reserve University)
- **Background**
  - Multiple sclerosis and other demyelinating disorders lead to irreversible disability
- **Project**
  - NPC screen identified two approved drugs (clobetasol and miconazole) as promotors of remyelination via oligodendrocyte precursor activation
  - Effects recapitulated *in vivo*
  - Publication in *Nature* April 20, 2015

    Najm FJ et al, Drug-based modulation of endogenous stem cells promotes functional remyelination in vivo. *Nature* 522:216-20. doi: 10.1038/nature14335



NIH News Release
Multiple Sclerosis

Health Information | Grants & Funding | News & Events | Research & Training | Institutes at NIH | About NIH

NIH Home > News & Events > News Releases

NEWS & EVENTS

News & Events

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- Events
- Videos
- Images
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NIH News in Health

NIH Research Matters

NIH Record

For Immediate Release: Monday, April 20, 2015

Drugs that activate brain stem cells may reverse multiple sclerosis

NIH-funded study identifies over-the-counter compounds that may replace damaged cells

g+1 34

Two drugs already on the market – an antifungal and a steroid – may potentially take on new roles as treatments for multiple sclerosis. According to a study published in Nature today, researchers discovered that these drugs may activate stem cells in the brain to stimulate myelin producing cells and repair white matter, which is damaged in multiple sclerosis. The study was partially funded by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health.

Institute/Center

National Institute of Neurological Disorders and Stroke (NINDS)

National Center for Advancing Translational Sciences (NCATS)

Contact

Barbara McMakin
301-496-5751

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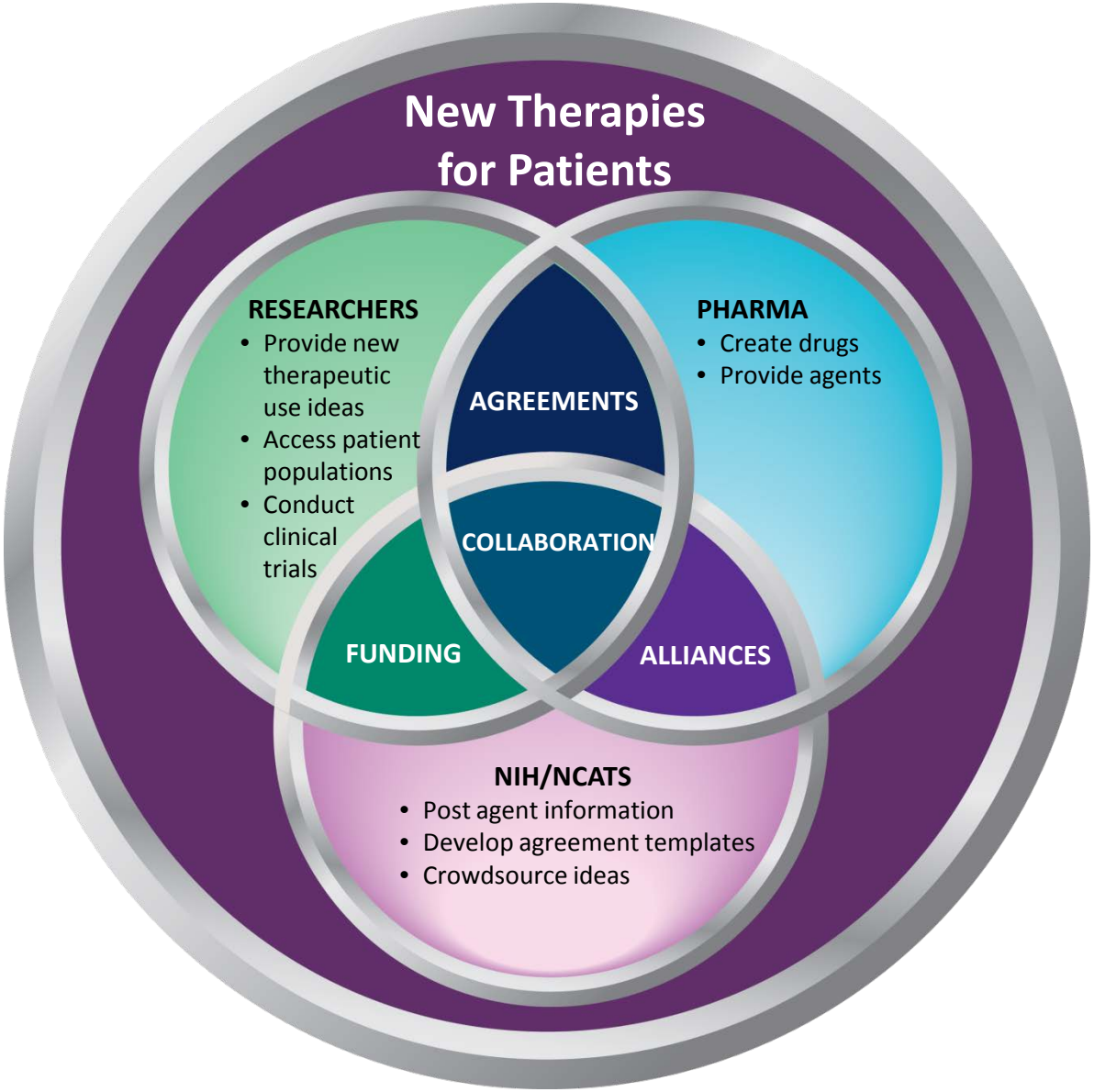
New Therapeutic Uses Program



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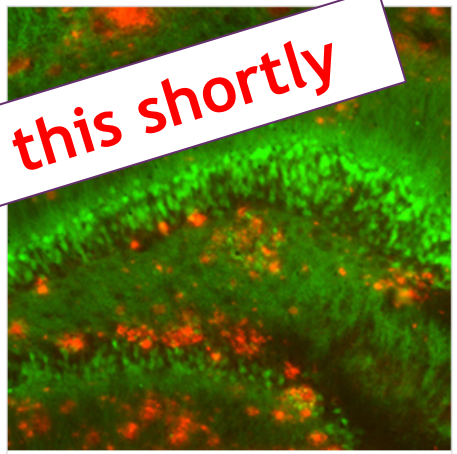
NCATS Support Leads to Clinical Trial to Test Repurposed Cancer Treatment as Alzheimer's Therapy

As Baby Boomers get older, the number of people with age-related conditions such as cancer and Alzheimer's disease continues to grow. Alzheimer's disease is the most common form of dementia, a group of disorders that cause progressive loss of memory and other mental processes. About 5 million Americans have Alzhei... disease, and current drug therapies can only e... disease without stopping its progres... called disease-modifying ... Alzheimer's by ...

...tic success is the costly, complex ...elopment. The average length of time from ... of a therapeutic target to approval of a new drug is about 14 years. The failure rate during this process exceeds 95 percent.



In a mouse model of Alzheimer's disease, amyloid beta clusters (red) build up among neurons (green) in a memory-related area of the brain. (Strittmatter Laboratory, Yale University Photo/Adam Kaufman)

NCATS is addressing these translational bottlenecks through programs such as the Discovering New Therapeutic Uses for Existing Molecules (New Therapeutic Uses) program. Launched in 2012, this initiative matches academic researchers with pharmaceutical industry assets that have undergone significant research and development to accelerate the process of finding new therapies.

Now, NCATS is celebrating one of the first promising results from the New Therapeutic Uses program: Center-supported scientists at Yale University School of Medicine have found that an experimental compound originally developed as a cancer therapy potentially could be used to treat Alzheimer's disease. The compound successfully reversed brain problems in mouse models of the condition, and now the researchers are testing it in humans. The results of the animal study were published for early view on March 21, 2015, in the *Annals of Neurology*. Read the NIH news release.

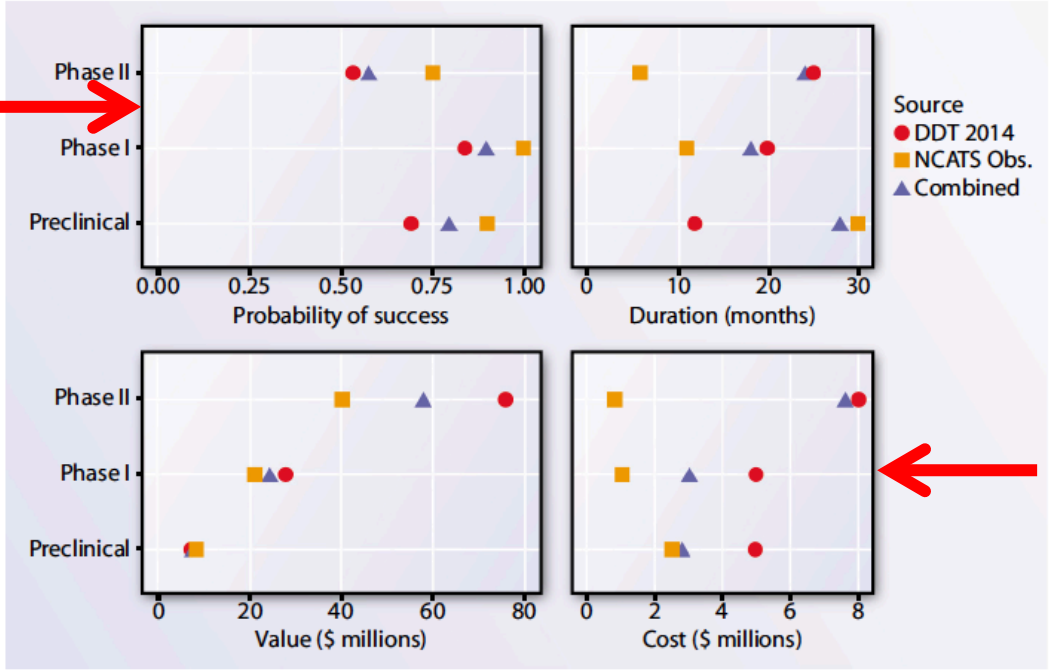
Science Translational Medicine 7: 276ps3, 26 Jan 2015

FUNDING

Financing translation: Analysis of the NCATS rare-diseases portfolio

David E. Fagnan,[1,2]* N. Nora Yang,[3]* John C. McKew,[3]† Andrew W. Lo[1,2,4,5]‡

Success rates higher



Costs lower

Fig. 2. Simulation calibration. Shown are weighted averaging of parameter estimates based on NCATS rare-disease portfolio, valuation panel, and literature estimates (*4*), using prior belief weights (methodological details are provided in the supplementary materials).

New Tissue Chip Video

Selected Translational Innovation Highlights

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Rare Disease Day

27 February 2015

Patients and Researchers, Partners for Life!

- Organized by NCATS and CC
- Featured speakers included
  - Congressman Leonard Lance (R-NJ 7th District)
    - *Co-chair of Congressional Rare Disease Caucus*
  - NIH Children's Inn CEO Jennie Lucca
  - NGLY1 President Matt Might
  - Voyager Therapeutics, Inc. Vice President of Production Robert Kotin
- Reached >1,000 people
- View the videocast at http://1.usa.gov/1EdL3QM

Evolving the CTSA Program to Transform Clinical Translational Science

CTSA Hubs

TIC:
Trial Innovation Centers
Central IRB
Contracting
Budgeting
Other support PRN

RIC:
Recruitment Innovation Centers
Feasibility Assessment
Recruitment Plan and Implementation

Multi-site Study funded by NIH IC or others

Clinical Lead

Stats/Data Management

No need to re-build trial components each time

Summary of Recent CTSA Program FOAs

- Two new funding opportunity announcements (FOAs) for **Collaborative Innovation Awards**
  - Designed to stimulate team-based research across the CTSA consortium
  - Released April 2, 2015
  - PAR-15-172 & PAR-15-173
- **Recruitment Innovation Center (**
  - Focus on:
    - Data for trial
    - ility analysis, and site selection
    - Recru ng and implementation
  - Re 15, 2015
  - RFA TR-15-004
- **Trial Innovation Center (TIC)** FOA
  - Focus on:
    - Innovation to increase the efficiency and quality of clinical trials
  - Released June 5, 2015
  - RFA-TR-15-002

You will be hearing more on this shortly

Policy and Legislative Updates

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FY 2016 Budget Request

- On February 2, 2015, President Obama released the FY 2016 budget
  - NIH: request for $31.3B, increase of $1B over FY15
  - NCATS: request for $660.1M, increase of $27.4M over FY 2015
  - NCATS' Congressional Justification (CJ) and appropriation status is available at: https://ncats.nih.gov/about/center/budget
- Congressional Appropriation Subcommittee Hearings
  - House: March 3, 2015, Senate: April 30, 2015
- House Appropriations bill released June 16; awaiting Senate Appropriations bill

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U.S. House of Representatives "21st Century Cures" Effort

- Bipartisan effort led by Representatives Fred Upton (R-MI) and Diana DeGette (D-CO) with numerous hearings in 2014
- Purpose:
  - Accelerate discovery, development, and delivery of treatments and cures for disease
- Unanimously reported out of the House Energy and Commerce Committee in May

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21st Century Cures
Highlights

- Reauthorizes NIH
- Establishes "Innovation Fund"
  - Authorizes $2 billion each year for five years
    - $500 M toward Accelerating Advancement Program
    - ~35% remaining funds for Early Stage Investigators
    - ~20% remaining funds for High-Risk, High-Reward Research
    - No more than 10% remaining funds for Intramural Research
- Requires NIH Strategic Plan
- NCATS-specific provisions:
  - Allows to support clinical trial activities through phase IIB and rare disease conditions through phase III
  - Removes CAN's Other Transaction Authority (OTA) restriction that no more than 20% of CAN funds may be used for OTA

Senate HELP Committee Biomedical Innovation Efforts

- "Innovation for Healthier Americans"
  - Released by Sens. Lamar Alexander (R-TN) and Richard Burr (R-NC) in January
- Hearings held in March and April
  - April 28, 2015: "Continuing America's Leadership: The Future of Medical Innovation for Patients"
  - Attendees:
    - Christopher Austin
      NIH/NCATS
    - Roderic Pettigrew
      NIH/NIBIB
    - Janet Woodcock
      FDA/CDER
    - Jeffrey Shuren
      FDA/CDRH

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Congressional Visit to NCATS

- **Senator Barbara Mikulski (D-MD)**
  - Visited NCATS Chemical Genomics Center on March 21, 2015 with Dr. Collins and Dr. Austin
  - Introduction to NCATS Programs
  - Dr. Collins announced NTU advance in Alzheimer's disease
  - Press Conference:
    - *Senator called for a 10 percent increase in NIH budget this year, with subsequent increases to grow the NIH budget to $45 billion by 2020*

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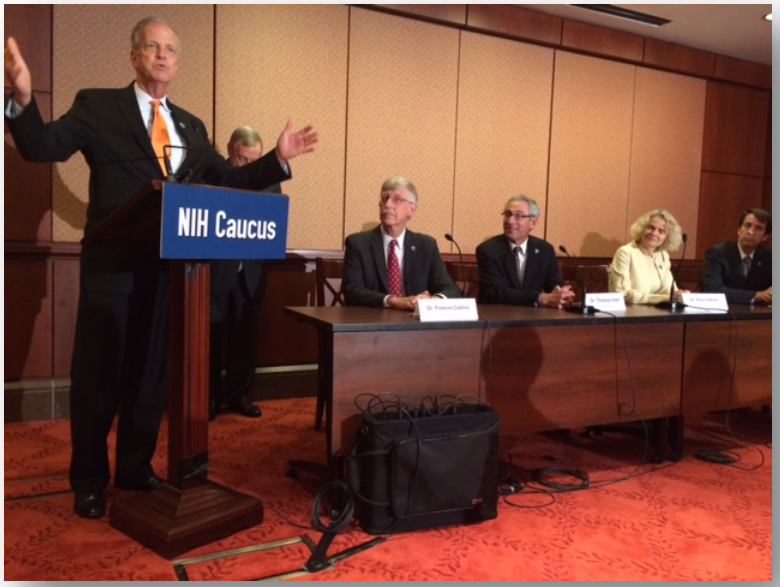
New Senate NIH Caucus

- Created by Senators Lindsey Graham (R-SC) and Richard Durbin (D-IL)
  - *"a bipartisan strategy to restore the purchasing power that NIH has lost and provide steady, predictable growth for biomedical research in the future."*
- 21 other members (19 Ds & 4 Rs)
- Initial Capitol Hill briefing on May 19, 2015



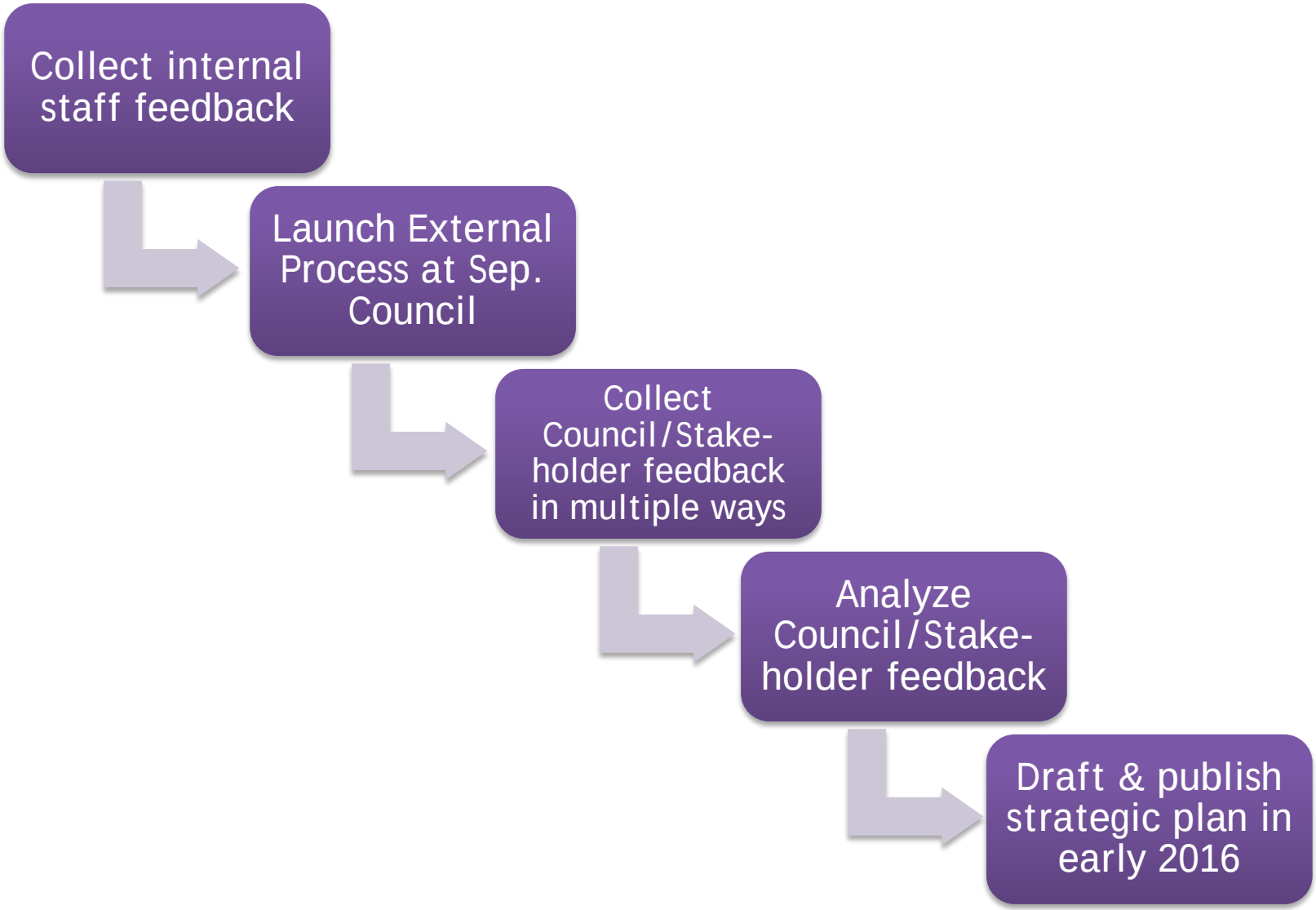
Source: Talk Radio News Service

Senator Jerry Moran (R-KS) at kickoff briefing for Senate NIH Caucus

NIH Strategic Planning Process

- CRomnibus and 21st Century Cures mandate an NIH Strategic Plan by end of 2015
- NIH is currently engaged in an internal planning process to create a guide for the development of a Strategic Plan
- Public comment period and engagement with stakeholder groups regarding the planning process will take place over the course of the Summer
- IC Advisory Councils will be updated on progress at Fall Council meetings

NCATS Strategic Planning Process



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Discussion