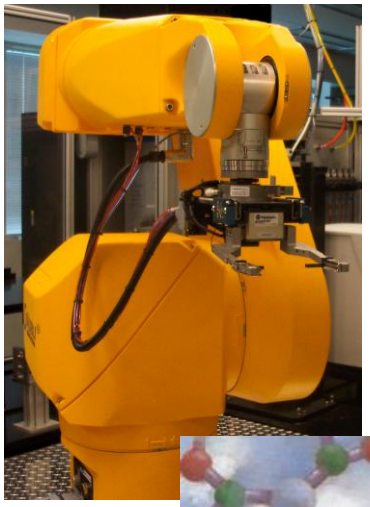
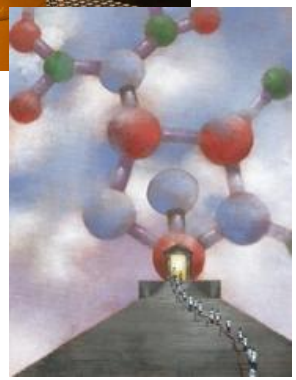




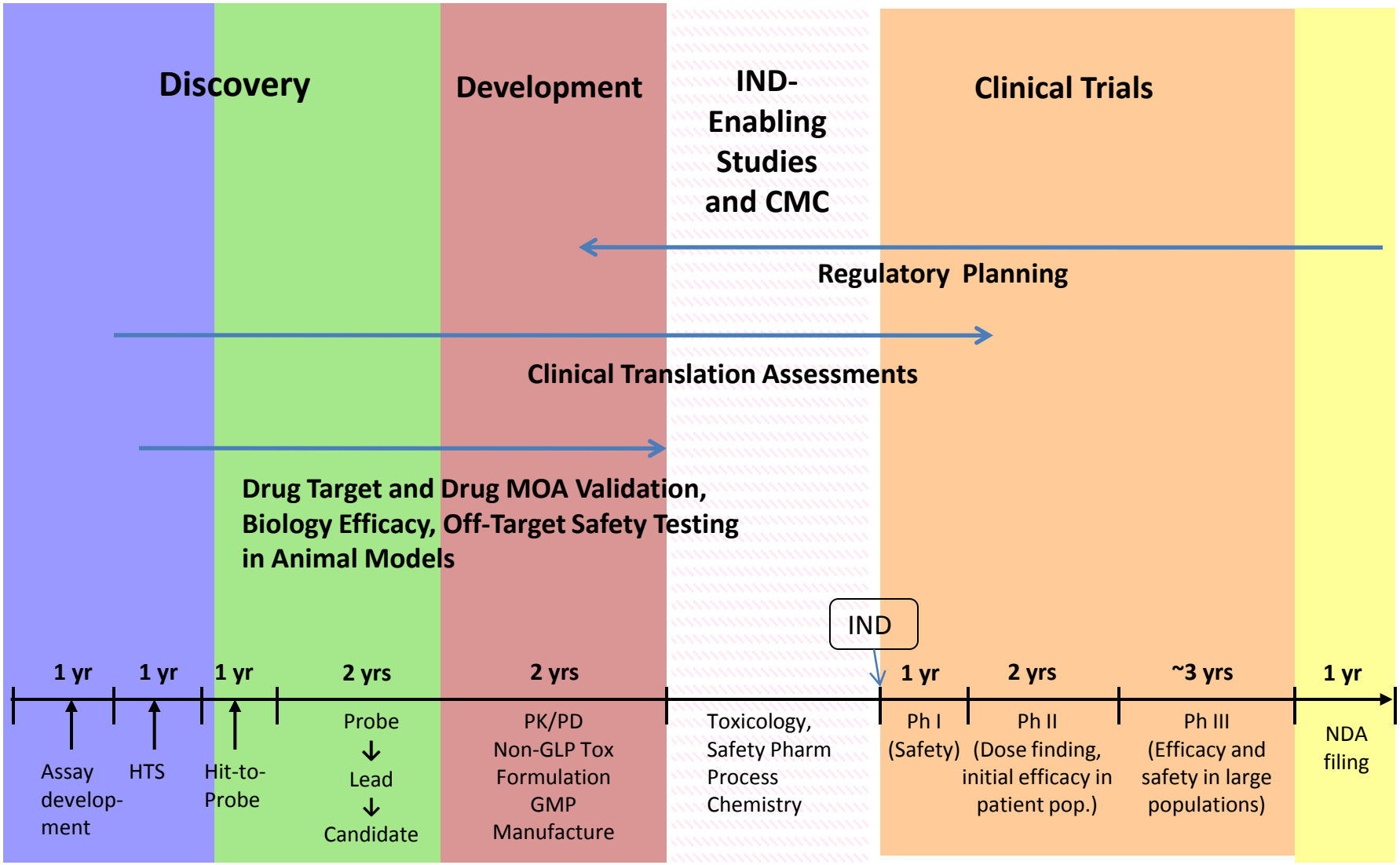
Bridging the Gap: Defining and Understanding the Necessary NIH Capabilities and Infrastructure

NIH Chemical Genomics Center and Therapeutics for Rare and Neglected Diseases

Susan E. Old, Ph.D.
Special Advisor
Acting Deputy Director
NIH Center for Translational Therapeutics
National Institutes of Health

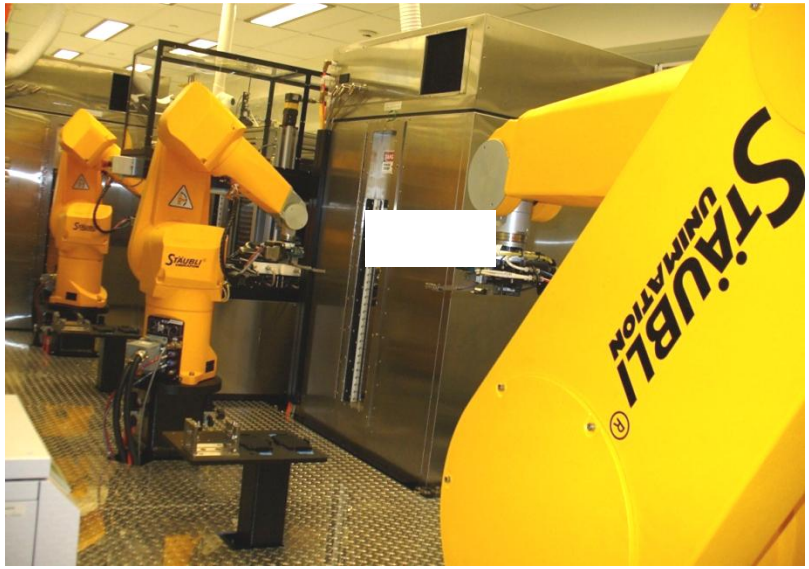
Science and Management Review Board
September 14, 2010

Therapeutic Development Pipeline



NIH Chemical Genomics Center

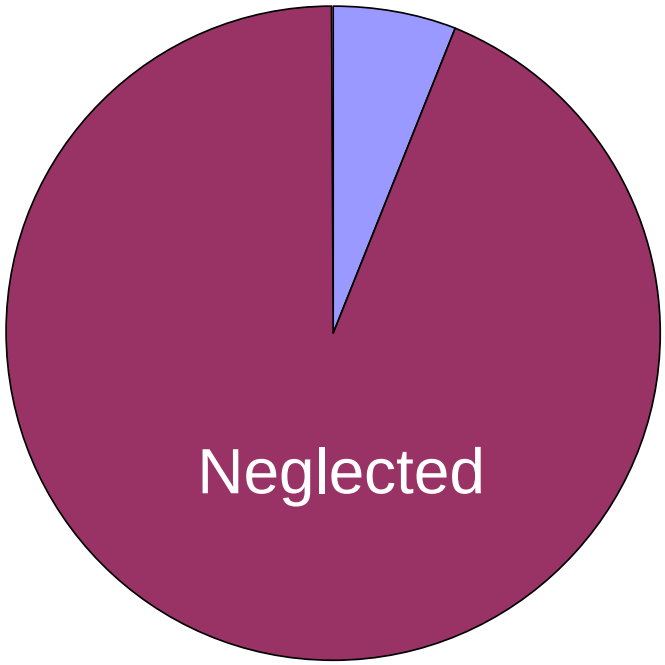
- Founded as part of Roadmap – *Molecular Libraries Program*
- 75 scientists
- > 100 collaborations with investigators worldwide
  - 75% NIH extramural
  - 15% Foundations, Research Consortia, Pharma/Biotech
  - 10% NIH intramural
- Focus on novel targets, rare/neglected diseases
- Produces
  - chemical probes/leads
  - new paradigms for assay development, screening, informatics, chemistry



Only a small % of genome-encoded targets and diseases are being addressed for drug development

Current drug targets:

Well understood proteins

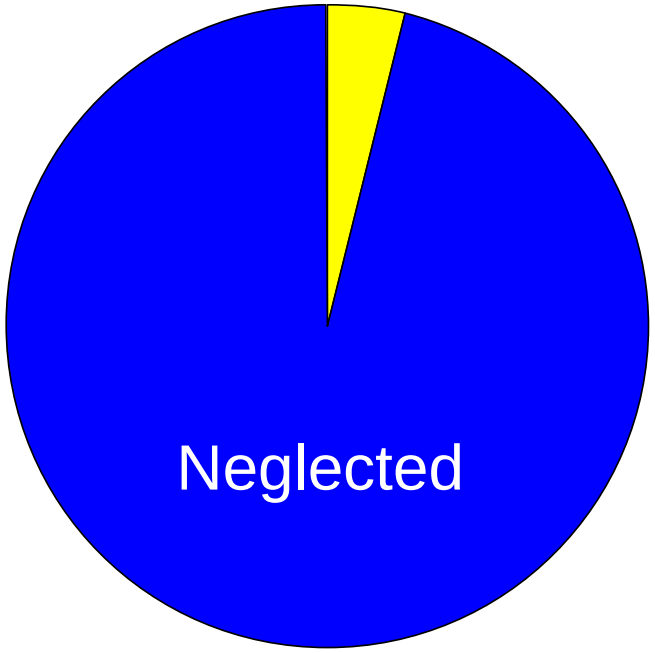


Human Genome

20,000 genes

Current targeted diseases:

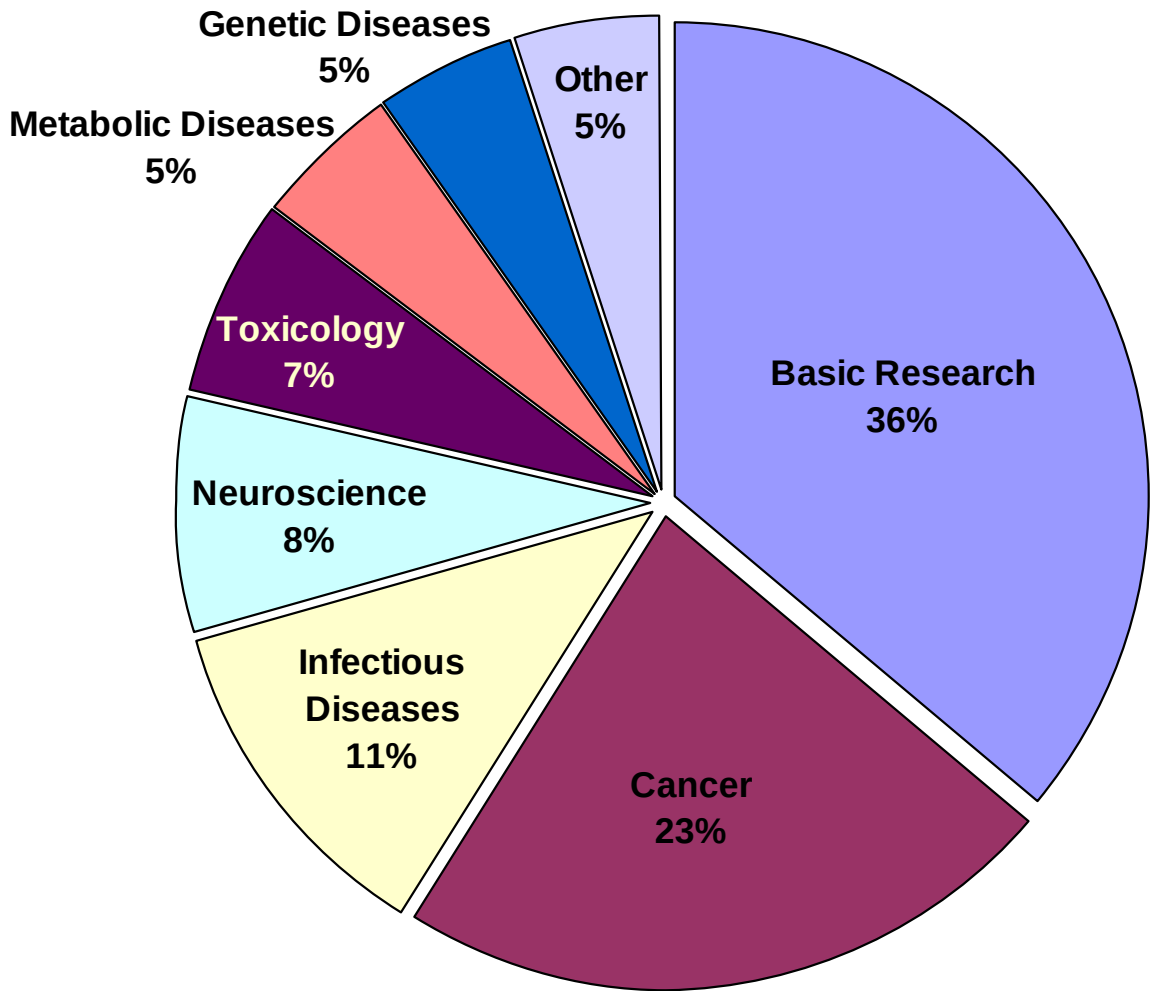
Prevalent diseases that affect developed world



Human Diseases

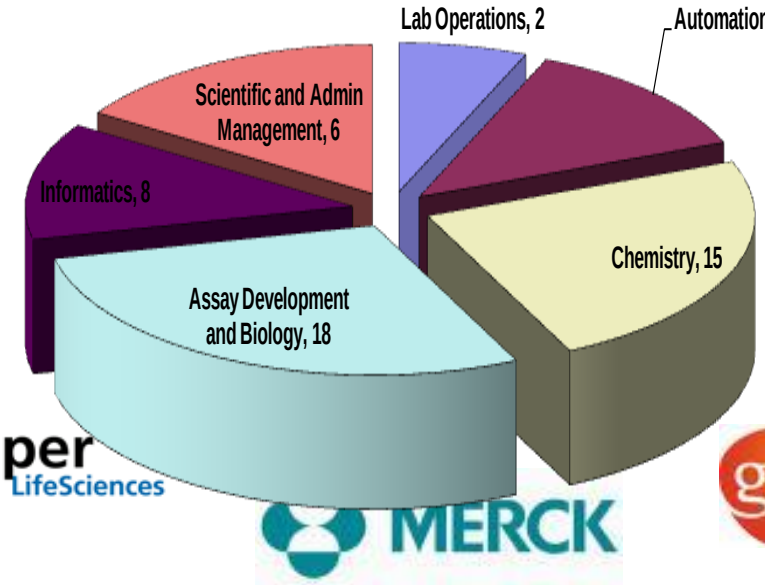
7000 diseases

Disease areas of NCGC assays



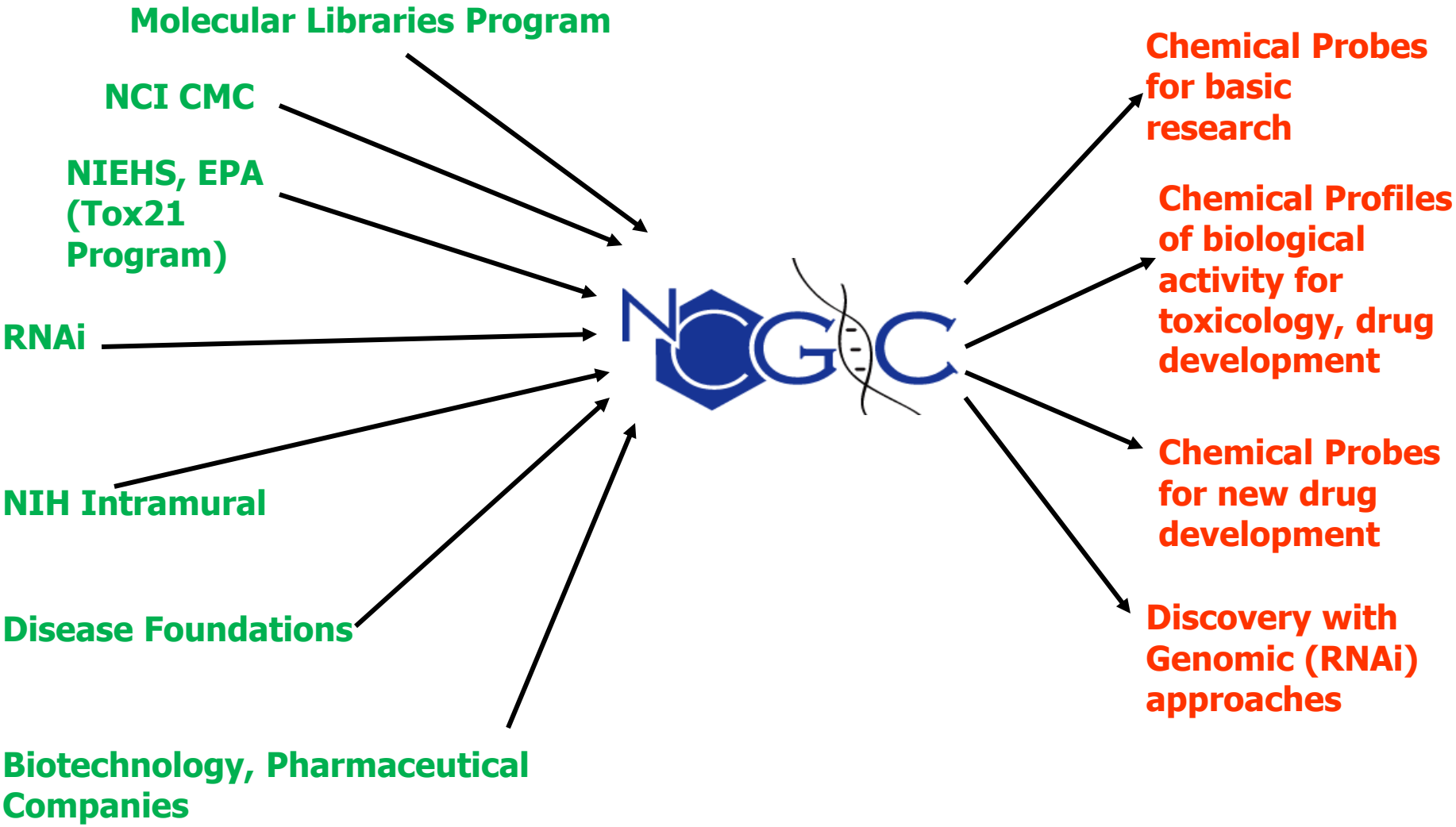
NIH Chemical Genomics Center

NCGC Staff



Amphora
Lilly
LARGE SCALE BIOLOGY
CELERA
an Applera Corporation Business
Pfizer
HGS
NORTHROP GRUMMAN
DEFINING THE FUTURE
AMGEN
ArQule
Caliper LifeSciences
MERCK
Johnson & Johnson
gsk GlaxoSmithKline
Pharmacopeia
BD
BD Biosciences
Lexicon pharmaceuticals
NCGC
NIH Chemical Genomics Center

The NCGC: Facilitating Drug Discovery



The long pathway to drug development

Basic and Clinical Research

NCGC, Molecular Libraries Initiative

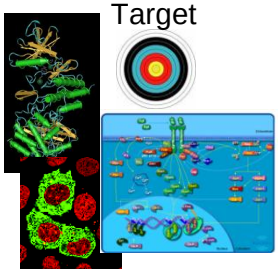
"Valley of Death"

Pharmas, Biotechs NIH Clinical Center, Academic Clinical Centers

FDA

IND

Indefinite	3 yrs	4 yrs	1 yr	2 yrs	~3 yrs	1 yr
Identify Target	Identify chemical starting point for drug	Make many chemical modifications to give drug beneficial effect without side effects	Ph I	Ph II	Ph III	Review	Patient Use



NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

Creating a Drug Development Pipeline at NIH

- Congressionally-mandated effort to speed development of new drugs for rare and neglected diseases
- Administration and governance at NIH
  - Governance/oversight by Office of Rare Diseases Research
  - Administered by NHGRI
- Operations: collaboration between intramural and extramural labs with appropriate expertise
- Projects will:
  - Enter TRND at a variety of stages of development
  - Be taken to phase needed for external organization to adopt for clinical development

NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

Distinguishing features

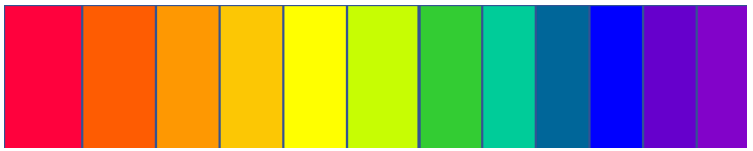
- Collaboration / Partnerships (not service center)
  - Government, Academics, Non-Profit, For-Profit collaborations
- Building the laboratory and expertise infrastructure at NIH
- Disease agnostic, take advantage of cross-cutting mechanisms
- *Science* of preclinical drug development
- Technology/paradigm development (20% of effort, toward improving success rates)
- Large-scale systematic repurposing

Project-specific activities

- Medicinal chemistry, efficacy, pharmacology, absorption, distribution, metabolism, and excretion (ADME), toxicology, pharmacokinetics/pharmacodynamics (PK/PD)
- Chemical Manufacturing and Controls (CMC), Compound scale-up, formulation
- First in Human or Proof of Concept clinical trials as needed for project

NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

- FY09: infrastructure (May 2009)
- FY10: infrastructure and pilot projects (June 2009)
  - Budget $24M
  - Focus: governance, hiring, research community outreach, pilot projects
- **FY11:** infrastructure and project solicitation
  - **President's budget recommends $50M**
  - **Solicitation of projects in Sept 2010 to begin in April 2011; 3-5 projects**
- FY12: fully operational
  - Laboratories completed Early 2012
  - Work on several new projects per year
  - Average project should take ~3 years
  - Projects will be monitored closely for progress



TRND Pilot Projects

Chosen to establish processes in advance of solicitation, with diversity of project stage, type of disease and collaborators

Disease	Type	Pathology	Collaborators	Compound type	Stage
Schistosomiasis, Hookworm	Neglected	Infectious parasite	Extramural	NME	Early (lead optimization)
Niemann Pick C	Rare	CNS, liver/spleen	Disease Fnd, Extramural, Intramural	Repurposed approved drug	Mid-stage
HIBM	Rare	Muscle	Biotech, Intramural	Intermediate replacement	Pre-IND
Sickle Cell Disease	Rare	Blood	Nonprofit, Intramural, Extramural	NME	Mid-stage
Chronic Lymphocytic Leukemia	Rare	Cancer	Disease Fnd, Extramural	Repurposed approved drug	Pre-IND

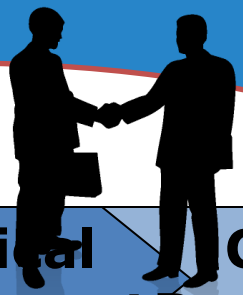
NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

Pilot Program Discoveries

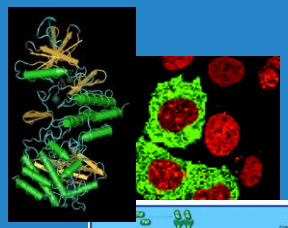
- **Funding Collaborators**
- **Collaboration Agreements**
- **Intellectual Property**
- **Project Management**
- **Expert Advice: inside and outside**
- **Excitement and Anticipation**

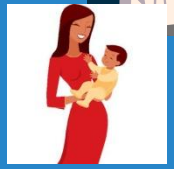
Filling the Gaps Between Discovery and Product

Partnerships and Collaborations



Discovery → Target ID & Validation → Preclinical Development → Clinical Development → Licensed Product





Therapeutic Development Pipeline