NCI DTP Resources and the Stepping Stones Program

NCI Drug Development Workshop
Session IX. NCI Translational Resources and Programs
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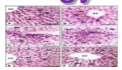
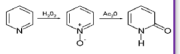
DTP: Ten Branches Supporting Discovery & Development

Molecular Pharmacology:
NCI-60, 2D, 3D
Target validation & screening

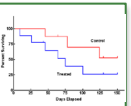



Drug Synthesis & Chemistry:
Chemical Repository
Synthetic Chemistry

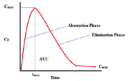


Natural Products:
Collection & Repository
Pre-fractionated library
Screening & identification


Biological Testing:
PDX Repository
Model development & testing
Tumor Repository


Toxicology & Pharmacology:
Nonclinical and GLP studies
Investigative Toxicology lab

Immuno-oncology:
Grant portfolio:
Immuno-oncology, immunotherapy
Canine Immunotherapy


Biological Resources:
GMP biologics, analytics
Biologics Repository
Grant portfolio:
Biotechnology innovation

Pharmaceutical Resources:
GMP manufacture API,
Analytical testing, Dose formulation


Information Technology:
COMPARE, ALMANAC,
Structure-based Medicinal Chemistry

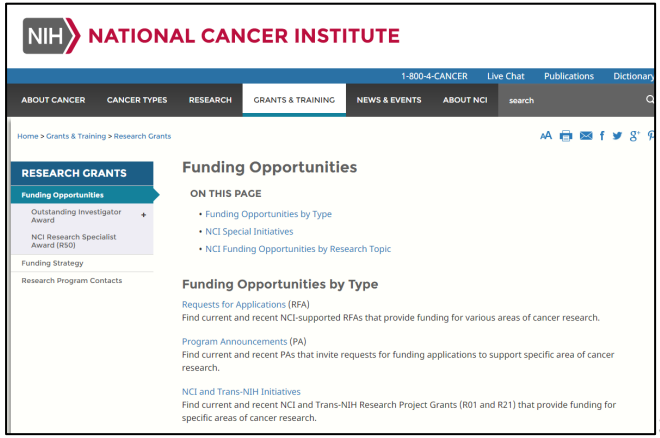
Preclinical Therapeutics Grants:
Grant portfolio for Small Molecule Therapeutics discovery & development

Extramural Support: Grant Funding

- **Preclinical Therapeutics Grants Branch** (Small molecule, natural product, nanotechnology; discovery and development)
- **Biological Resources Branch** (Biotechnology, biopharmaceuticals)
- **Immuno-oncology Branch** (Immunotherapy)
  - DTP funds therapeutics discovery and preclinical development
  - Portfolio of ~ 850 active awards (R01, R21, P01, U01; no SBIR/STTR)

Contact Program Officials:

https://dtp.cancer.gov



Extramural Support: Drug Synthesis & Chemistry Branch

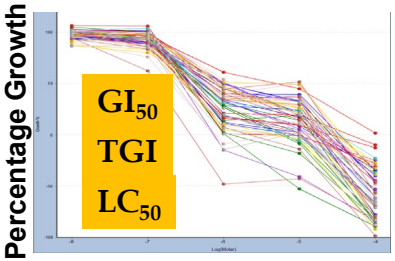
- **NCI Chemical Repository**: >200,000 open compounds
  - Acquire, Synthesize and Distribute Chemical Samples for Research
  - Plated sets: Diversity, Mechanistic, Approved Oncology Drug Sets
- Synthetic and Medicinal Chemistry Resource and Expertise
- Continued acquisition of clinical and pre-clinical investigational oncology agents, bringing the total collection to 935 drugs, representing more than 60 target mechanisms

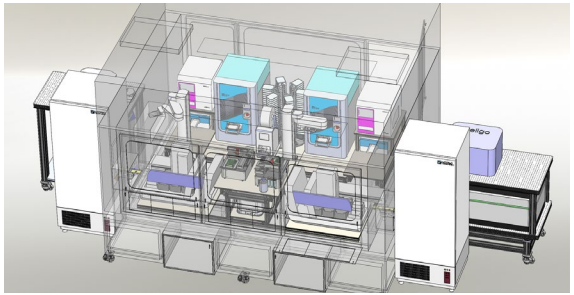
NCI 60 *in vitro* screening submission URL:

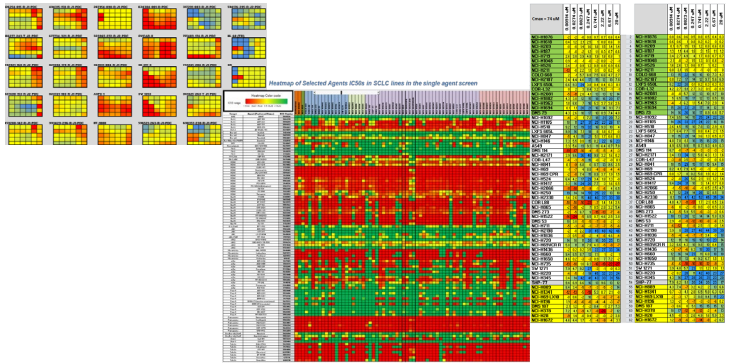
https://dtp.cancer.gov/organization/dscb/compoundSubmission/default.htm

Extramural Support: Molecular Pharmacology Branch

- **NCI 60 Cell Screen**: 60 human tumor cell lines representing leukemia, melanoma and cancers of the lung, colon, brain, ovary, breast, prostate, kidney; data can be assessed in pattern recognition algorithms (COMPARE)
- Functional Genomics, Target Validation and Screening
- DTP Databases: **https://dtp.cancer.gov/databases_tools/bulk_data.htm**
- **Future:** Patient Derived Model 3D cultures screening, HTS in 384 well platform







Extramural Support: Natural Products Branch

Prefractionated natural product extracts

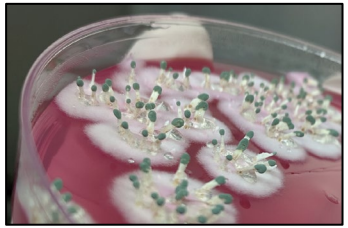
- >485,000 natural product fractions have been produced so far
- First 326,000 fractions released to the public

Acquisition to expand breadth of libraries available to community

- >21,000 U.S. soil fungi/~6700 Australian marine microbes obtained
- >70 requests from screening centers for NPNPD fractions
- 32 MTAs completed for fraction library, 52 additional MTAs for extracts
- ~4,800,000 samples total shipped to screening centers worldwide.

Collaborations yielded >1,900 bioactive hit fractions processed in FY2020

Information on NPB Repositories:
https://dtp.cancer.gov/organization/npb/introduction.htm



Extramural Support: Biological Testing Branch

- Efficacy Testing of Drugs in Cancer Models
- Pharmacokinetic Profiling, Dosage Testing, MTD
- Extensive Tumor Repository for Distribution
- **Patient Derived Models Repository (PDMR)**

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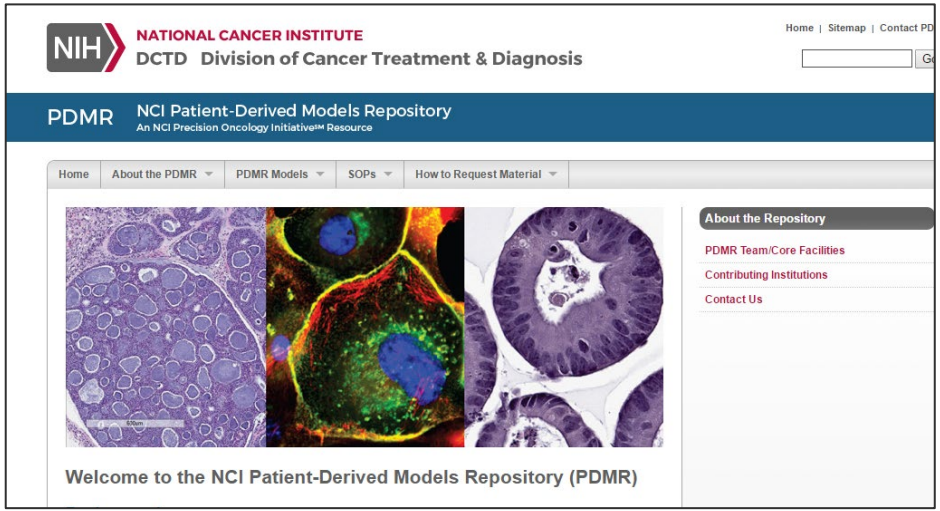
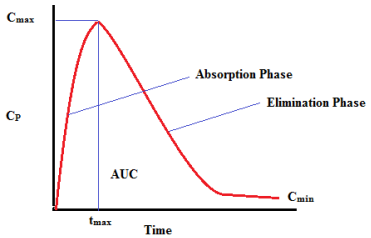
PATIENT-DERIVED MODELS REPOSITORY

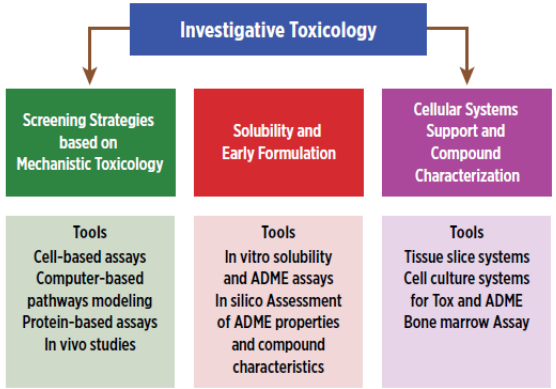


https://pdmr.cancer.gov/

Extramural Support: Toxicology & Pharmacology Branch

- Pharmacokinetic and toxicological profile; MTD and clinical dose setting
- **Investigational Toxicology Laboratory:** Development of special target organ toxicity assays (e.g. screening CIPN protectants)
- IND-directed toxicology studies including toxicokinetics
- Documentation for IND filing
- Access via **NExT** and **Stepping Stones**





Pharmaceutical Resources Branch

- **Active Pharmaceutical Ingredients and/or Clinical supplies to support ongoing trials**
- **Analytical testing for product release and stability programs during clinical trials**

Examples: GMP synthesis, formulation and Final Drug Product projects not yet in clinical trials

ATTM	Maintenance treatment for tNBC. Capsules for Phase 3 trials.
Rocaglamide/DDR	Inhibitor of eIF4A. Preclinical stage - Scaleup and GMP synthesis
Novobiocin	Pol Q inhibitor for treatment of Ovarian Cancer - Capsule Manufacturing
Isopure 2-KG	Imaging agent- Development of GMP synthesis
TAK-243	E1 ligase UAE inhibitor. Manufacture of sterile injectable

Extramural Support: Biological Resources Branch

NCI Biopharmaceutical Development Program at the Frederick National Laboratory

Biopharmaceutical Development Program

- Cell banking MCB and WCB production, testing and release
- Process development to optimize expression and purification
- GMP manufacturing, various bioreactor and fermentation platforms
- Analytical methods for product release and stability program

NEW: Adoptive cell therapy, lenti and retrovirus vector manufacturing, CRISPR-based editing of cell therapies

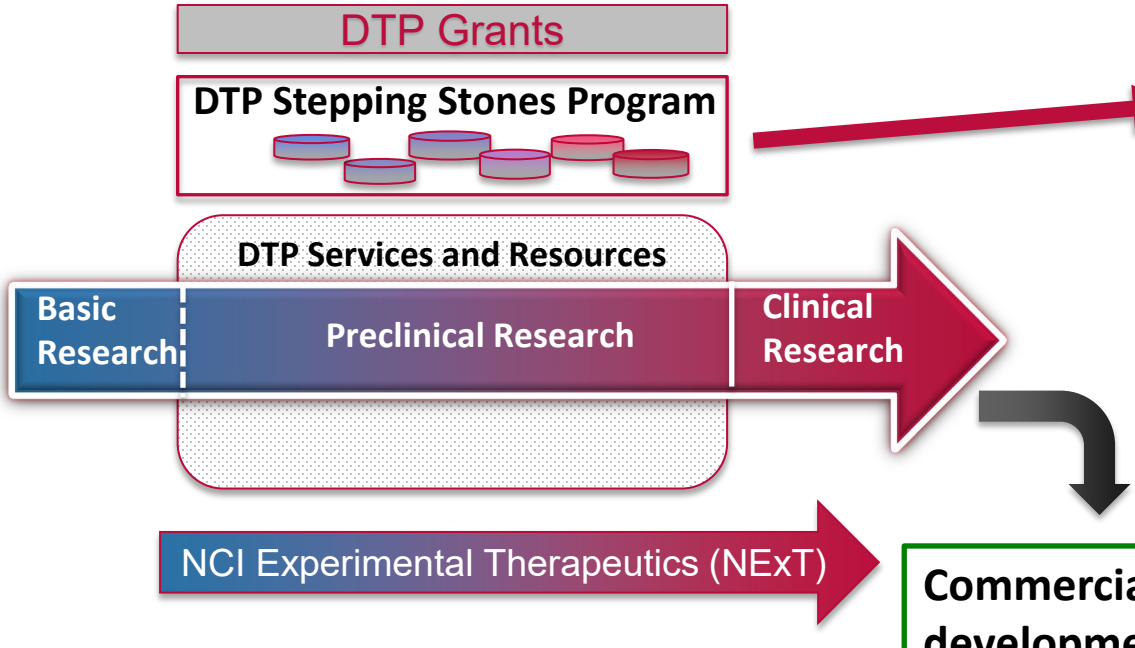
Repository of Biological Reagents:

- Monoclonal Abs, Murine & Human Cytokines, Growth Factors, Interferons & Interleukins

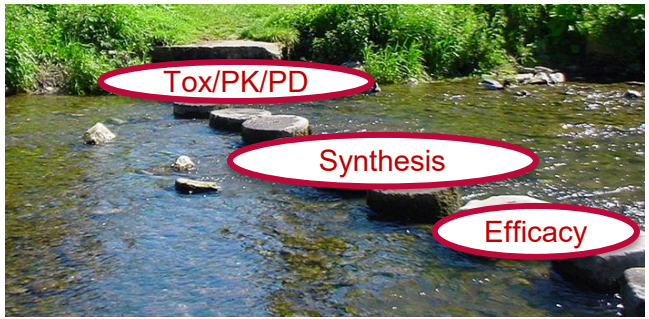
https://frederick.cancer.gov/resources/repositories/Brb/#/preclinical Repository

Development Support: Stepping Stones

- Open to active grantees
- Provides discreet gap-filling studies for small molecules



New initiative:
Advancing new therapeutic concepts toward clinical testing by providing resources and data "Stepping Stones"



Development Support: Stepping Stones Program

Support investment in the NCI therapeutics grants portfolio

- Augments data package for gaining access to other resources (NExT, VC, SBIR/STTR)
- Provide critical data that PI can't easily obtain or isn't covered by funding (synthesis, solubility, early PK, etc.)

https://dtp.cancer.gov/discovery_development/stepping_stones/default.htm

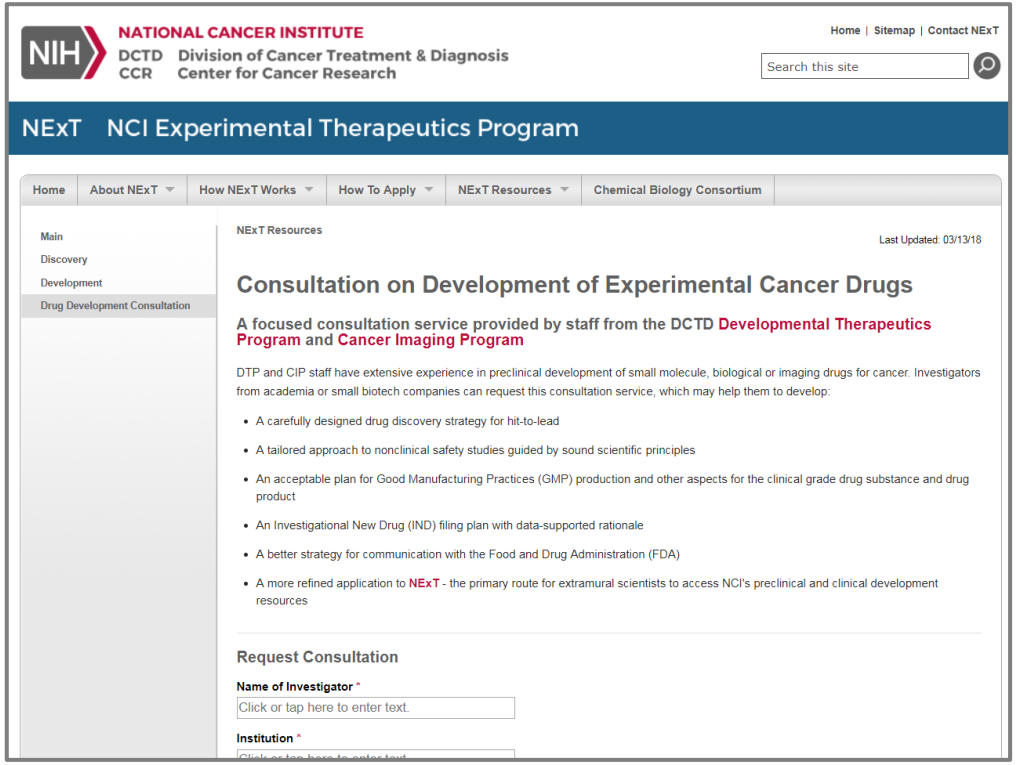
Drug Development Consultation Service

- Open to all innovators
- Confidential
- Assess critical path for product development

DTP expertise:

- chemistry, tox/pharm, molecular pharm, biology, manufacturing, regulatory

*****Introductory step for Stepping Stones*****



https://next.cancer.gov/experimentalTherapeutics/form.htm

https://dtp.cancer.gov

www.cancer.gov

www.cancer.gov/espanol