

NCI DTP Resources and the Stepping Stones Program

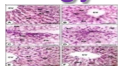
**NCI Drug Development Workshop
Session IX. NCI Translational Resources and Programs
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Division of Cancer Treatment and Diagnosis

DTP: Ten Branches Supporting Discovery & Development

Molecular Pharmacology:

NCI-60, 2D, 3D

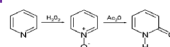


Target validation & screening

Drug Synthesis & Chemistry:

Chemical Repository

Synthetic Chemistry



Natural Products:

Collection & Repository

Pre-fractionated library

Screening & identification

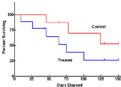


Biological Testing:

PDX Repository

Model development & testing

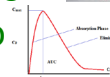
Tumor Repository



Toxicology & Pharmacology:

Nonclinical and GLP studies

Investigative Toxicology lab



Pharmaceutical Resources:

GMP manufacture API,

Analytical testing, Dose

formulation



Biological Resources:

GMP biologics, analytics

Biologics Repository

Grant portfolio:

Biotechnology innovation



Information Technology:

COMPARE, ALMANAC,

Structure-based Medicinal Chemistry



Immuno-oncology:

Grant portfolio:

Immuno-oncology,

immunotherapy

Canine Immunotherapy



Preclinical Therapeutics Grants:

Grant portfolio for Small Molecule

Therapeutics

discovery &

development

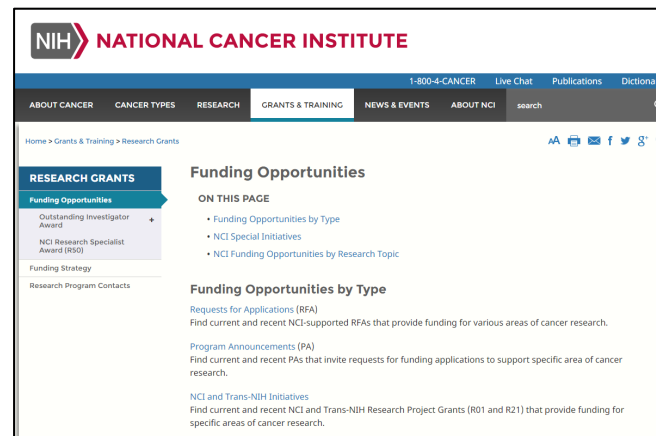
NATIONAL CANCER INSTITUTE DCTD Division of Cancer Treatment & Diagnosis			
Home	Current Research	Funding & Partnerships	Scientific Advances
Funding Opportunities		Funding & Partnerships	
Partnerships		Funding Opportunities	
All Experimental Therapeutics (NET) Program			

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

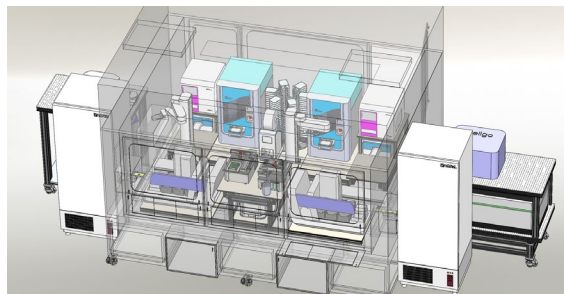
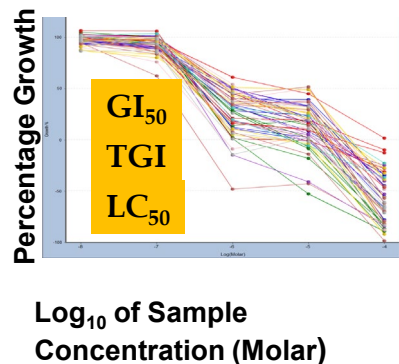
NCI 60 *in vitro* screening submission URL:

<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 NPNDP 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

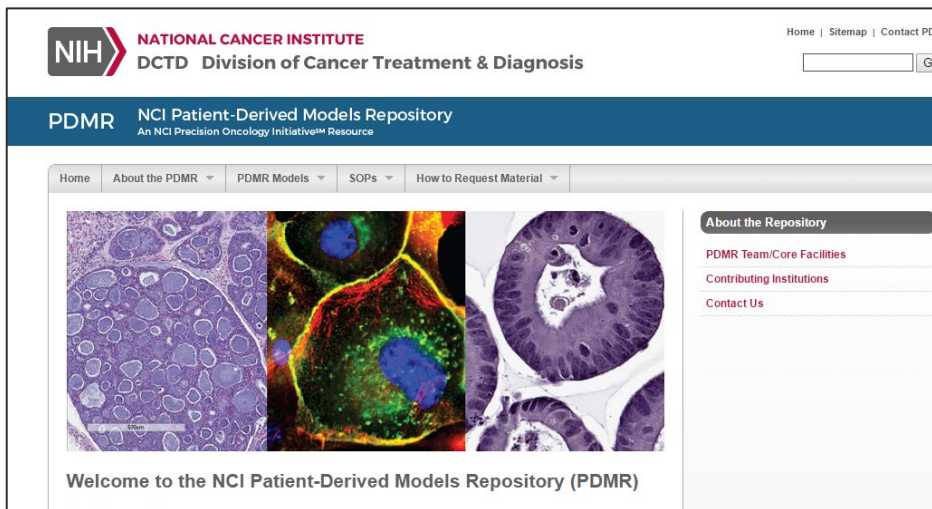
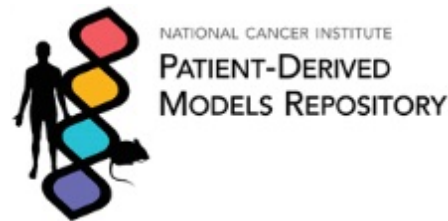
Information on NPB Repositories:

<https://ntp.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)**

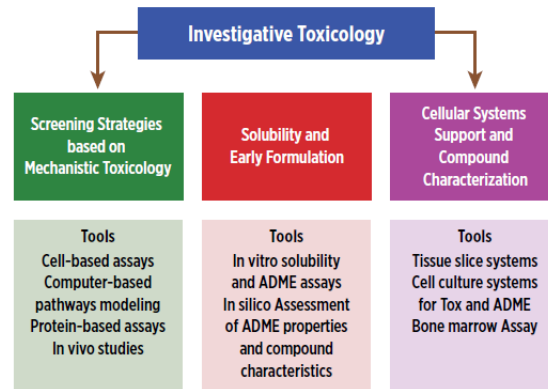
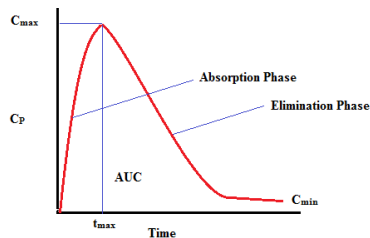


<https://pdmr.cancer.gov/>



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

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/#/preclinicalRepository>

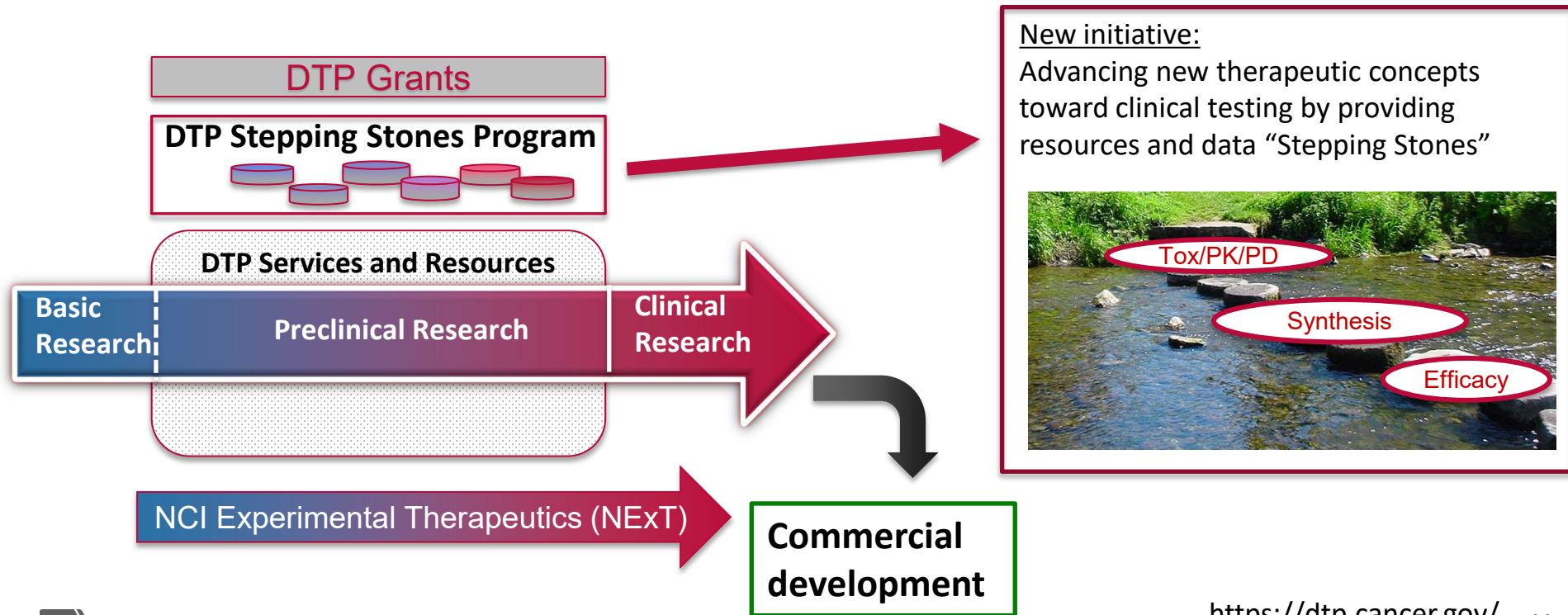


NCI Biopharmaceutical
Development Program
at the
Frederick National Laboratory



Development Support: Stepping Stones

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



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

The screenshot shows the NIH National Cancer Institute (NCI) DCTD Division of Cancer Treatment & Diagnosis website. The main header is "DTP Developmental Therapeutics Program". The left sidebar lists "DTP Branches and Offices" including the Office of the Associate Director, Preclinical Therapeutic Grants Branch, Molecular Pharmacology Branch, Biological Testing Branch, Toxicology and Pharmacology Branch, Drug Synthesis and Chemistry Branch, Natural Products Branch, Biological Resources Branch, Pharmaceutical Resources Branch, Information Technology Branch, and Immunology Branch. The main content area is titled "About the Stepping Stones Program" and features a diagram of the "Stepping Stones Initiative". The diagram shows a path from "Discovery" to "Clinical Development" through several "stepping stones": PK/PD, Synthesis, Efficacy, Toxicity, Formulation, and CMC. A large red arrow points from the "Discovery" box to the "Clinical Development" box. The text below the diagram states: "The Stepping Stones Program provides critical resources to advance innovative anti-cancer therapeutics toward clinical development. This initiative is intended to augment grant-supported programs with access to NCI/DCTD/DTP drug development capabilities to fill knowledge and data gaps, thus enabling these programs to advance and procure additional resources for development toward clinical testing. The goals are:" followed by a bulleted list: "Support peer-reviewed anti-cancer product development", "Facilitate access to federal resources for preclinical product development", and "Fill the NCINExT pipeline with innovative therapeutic candidates".

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*****

The screenshot displays the NCI NExT website. At the top, the NIH logo is on the left, and the text 'NATIONAL CANCER INSTITUTE', 'DCTD Division of Cancer Treatment & Diagnosis', and 'CCR Center for Cancer Research' is on the right. A search bar is in the top right corner. Below this is a blue header with 'NExT NCI Experimental Therapeutics Program'. A navigation bar contains links: Home, About NExT, How NExT Works, How To Apply, NExT Resources, and Chemical Biology Consortium. On the left, a sidebar menu lists: Main, Discovery, Development, and Drug Development Consultation (which is highlighted). The main content area is titled 'NExT Resources' and 'Consultation on Development of Experimental Cancer Drugs'. It includes a paragraph about the service, a list of five bullet points describing the consultation process, and a 'Request Consultation' section with input fields for 'Name of Investigator' and 'Institution'.

NIH NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis
CCR Center for Cancer Research

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NExT NCI Experimental Therapeutics Program

Home About NExT How NExT Works How To Apply NExT Resources Chemical Biology Consortium

Main
Discovery
Development
Drug Development Consultation

NExT Resources
Last Updated: 03/13/18

Consultation on Development of Experimental Cancer Drugs

A focused consultation service provided by staff from the DCTD **Developmental Therapeutics Program** and **Cancer Imaging Program**

DTP and CIP staff have extensive experience in preclinical development of small molecule, biological or imaging drugs for cancer. Investigators from academia or small biotech companies can request this consultation service, which may help them to develop:

- A carefully designed drug discovery strategy for hit-to-lead
- A tailored approach to nonclinical safety studies guided by sound scientific principles
- An acceptable plan for Good Manufacturing Practices (GMP) production and other aspects for the clinical grade drug substance and drug product
- An Investigational New Drug (IND) filing plan with data-supported rationale
- A better strategy for communication with the Food and Drug Administration (FDA)
- A more refined application to **NExT** - the primary route for extramural scientists to access NCI's preclinical and clinical development resources

Request Consultation

Name of Investigator *

Institution *

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

<https://dtp.cancer.gov>



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