

NCI DTP Resources and the Stepping Stones Program

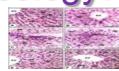
NCI Drug Development Workshop
Session IX. NCI Translational Resources and Programs
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Division of Cancer Treatment and Diagnosis

DTP: Ten Branches Supporting Discovery & Development

Molecular Pharmacology:

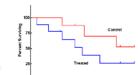
NCI-60, 2D, 3D



Target validation & screening

Biological Testing:

PDX Repository



Model development & testing

Tumor Repository



Pharmaceutical Resources:

GMP manufacture API,

Analytical testing, Dose

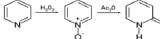
formulation



Drug Synthesis & Chemistry:

Chemical Repository

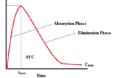
Synthetic Chemistry



Toxicology & Pharmacology:

Nonclinical and GLP studies

Investigative Toxicology lab



Biological Resources:

GMP biologics, analytics

Biologics Repository

Grant portfolio:

Biotechnology innovation



Information Technology:

COMPARE, ALMANAC,

Structure-based Medicinal Chemistry



Natural Products:

Collection & Repository



Pre-fractionated library

Screening & identification



Immuno-oncology:

Grant portfolio:



Immuno-oncology,



immunotherapy

Canine Immunotherapy

Preclinical Therapeutics Grants:

Grant portfolio for Small Molecule

Therapeutics

discovery &

development

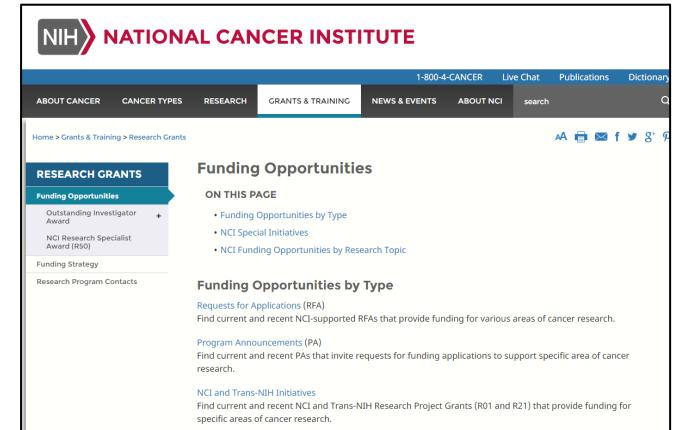


Extramural Support: Grant Funding

- **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>



The screenshot shows the NCI website with a search bar at the top. The main navigation menu includes links for 'ABOUT CANCER', 'CANCER TYPES', 'RESEARCH', 'GRANTS & TRAINING' (which is highlighted in blue), 'NEWS & EVENTS', and 'ABOUT NCI'. Below the menu, a breadcrumb trail shows 'Home > Grants & Training > Research Grants'. On the right side, there is a sidebar with links for 'Funding Opportunities by Type', 'NCI Special Initiatives', and 'NCI Funding Opportunities by Research Topic'. The main content area is titled 'Funding Opportunities' and includes sections for 'ON THIS PAGE' (with links to 'Funding Opportunities by Type', 'NCI Special Initiatives', and 'NCI Funding Opportunities by Research Topic'), 'Requests for Applications (RFA)', 'Program Announcements (PA)', and 'NCI and Trans-NIH Initiatives'.

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

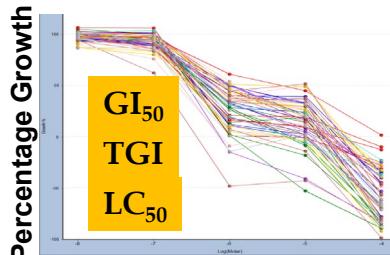
NCI 60 *in vitro* screening submission URL:

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

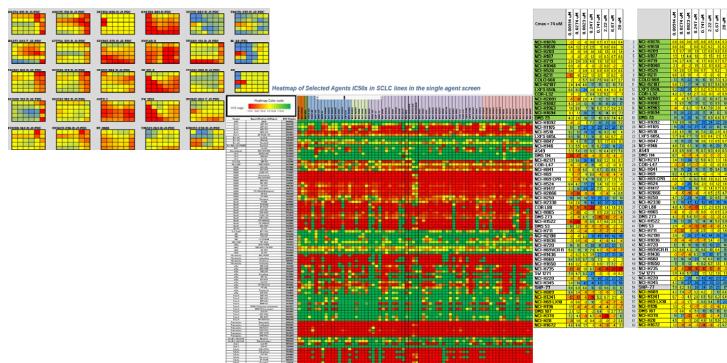
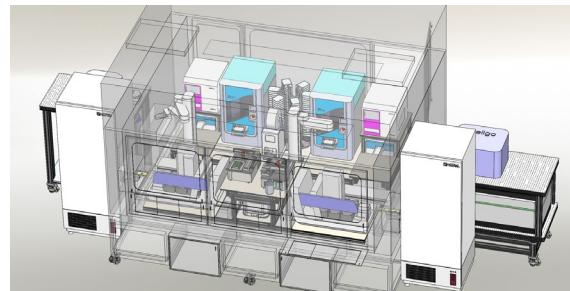


Extramural Support: Molecular Pharmacology Branch

- **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



Percentage Growth
 \log_{10} of Sample
Concentration (Molar)



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

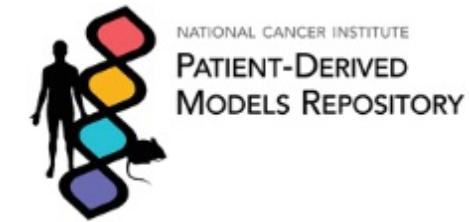
Information on NPB Repositories:

<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)**

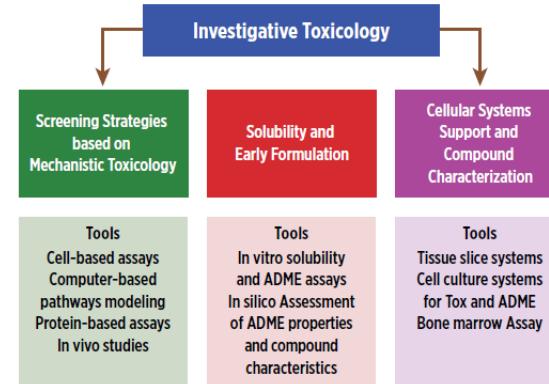
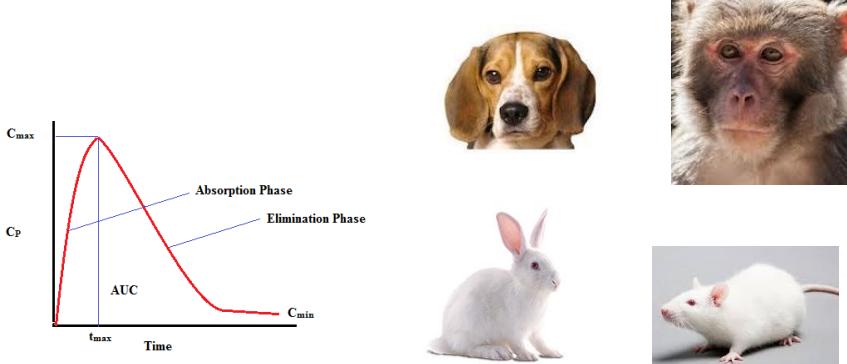


<https://pdmr.cancer.gov/>



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



NCI Biopharmaceutical Development Program at the Frederick National Laboratory



Repository of Biological Reagents:

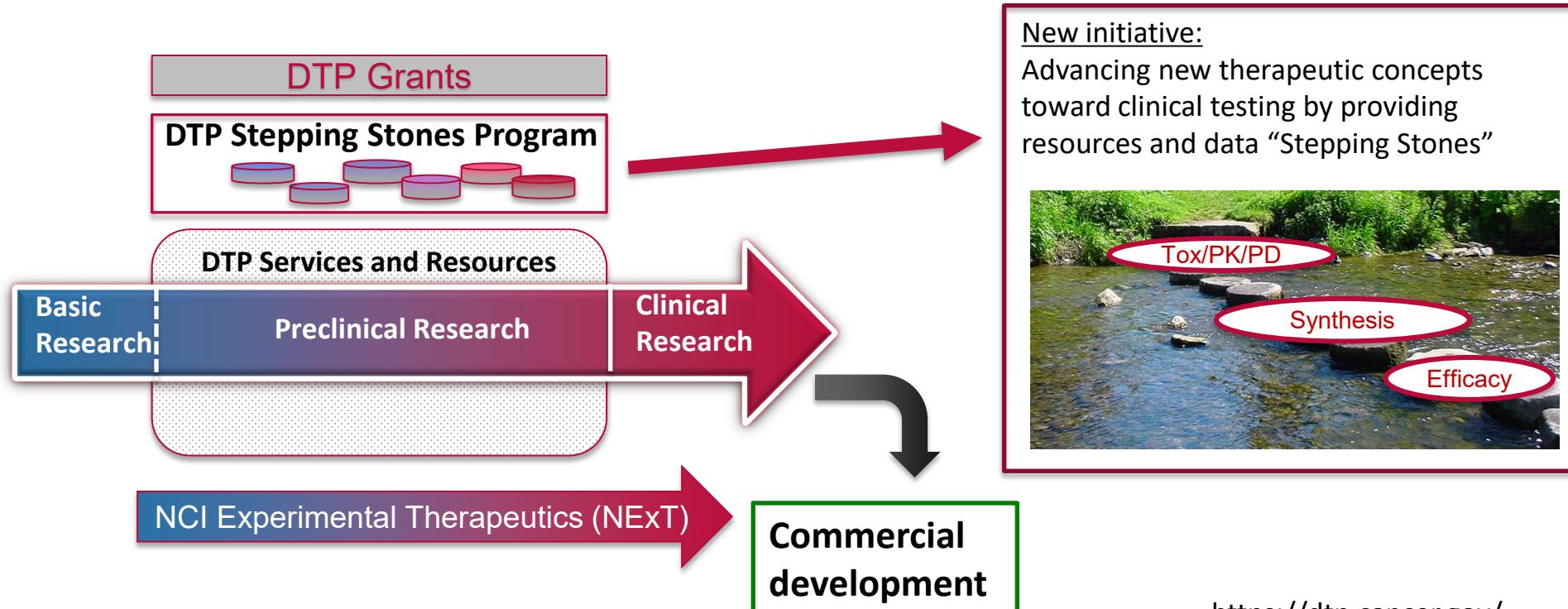
- Monoclonal Abs, Murine & Human Cytokines, Growth Factors, Interferons & Interleukins

[https://frederick.cancer.gov/resources/repositories/Brb/#/preclinical Repository](https://frederick.cancer.gov/resources/repositories/Brb/#/preclinicalRepository)



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 NCI DTP Stepping Stones Program website. The header includes the NIH logo, the National Cancer Institute logo, and the text 'DCTD Division of Cancer Treatment & Diagnosis'. The main navigation bar has links for Home, Discovery & Development Services, Repositories, Databases & Tools, Grants, Our Organization, Consultation, and Contact Us. The 'Discovery & Development Services' dropdown is open, showing 'Stepping Stones' as the selected option. The 'About the Stepping Stones Program' section features a large red arrow pointing from 'Discovery' to 'Clinical Development', with intermediate steps labeled 'PK/PD', 'Synthesis', 'Efficacy', 'Toxicity', 'Formulation', and 'CMC'. The text describes the program as advancing innovative therapeutics toward clinical development by providing resources and data "stepping stones". A sidebar on the right lists various DTP branches and offices, including the Office of the Associate Director for Therapeutic Grants Branch, Molecular Pharmacology Branch, Biological Testing Branch, Toxicology and Pharmacokinetics Branch, Drug Synthesis and Chemistry Branch, Natural Products Branch, Biologics Resources Branch, Pharmaceutical Resources Branch, Information Technology Branch, and ImmunoOncology Branch. The footer contains a 'Last Updated: 09/27/18' timestamp and a list of goals for the program.

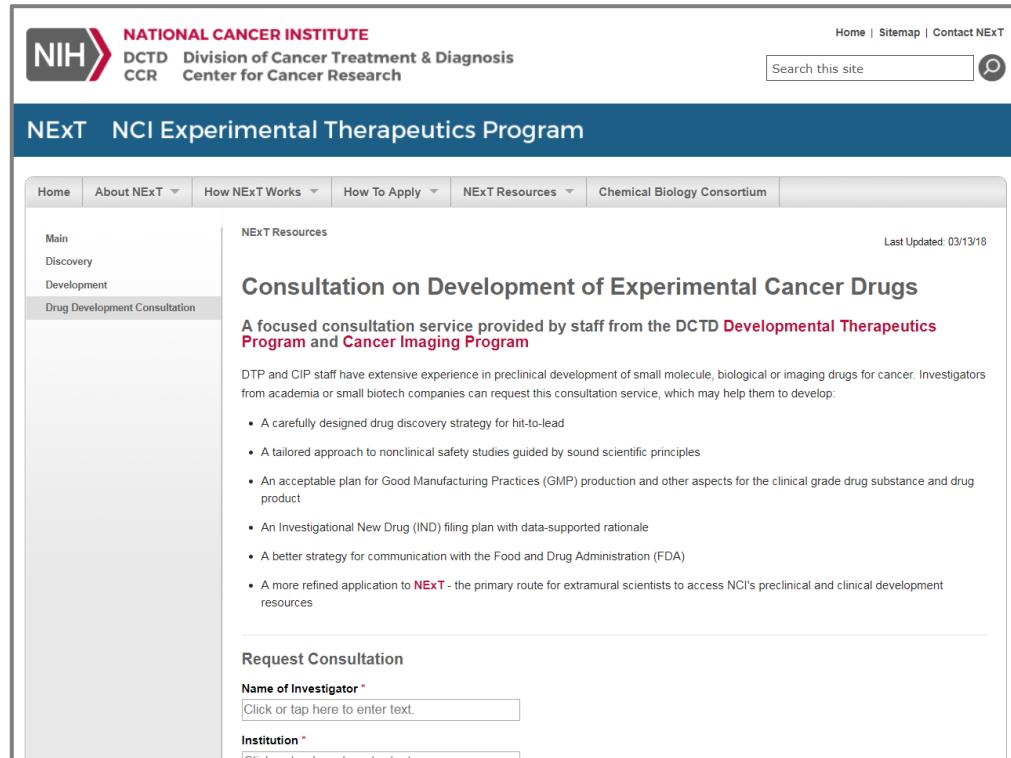
Drug Development Consultation Service

- 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*****



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 *

Click or tap here to enter text.

Institution *

Click or tap here to enter text.

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

<https://dtp.cancer.gov>



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