

Helping Extramural Innovators Reach the Clinic: NCI Developmental Therapeutics Program

PROGRAM

12:30 PM	Welcome Remarks/ Intro to DTP	Rose Aurigemma, PhD
12:40 PM	Funding Opportunities	Sundar Venkatachalam, PhD
12:50 PM	New Drug Development Resources	Rose Aurigemma, PhD
1:00 PM	Stepping Stones Program	Sharad Verma, PhD
1:10 PM	Immuno-oncology Initiatives & Services	Marc Ernstoff, MD
1:20 PM	Q & A	

Welcome Remarks and Overview of the Developmental Therapeutics Program

*Rose Aurigemma, PhD
Associate Director, DTP, DCTD, NCI*

Division of Cancer Treatment and Diagnosis (DCTD), NCI

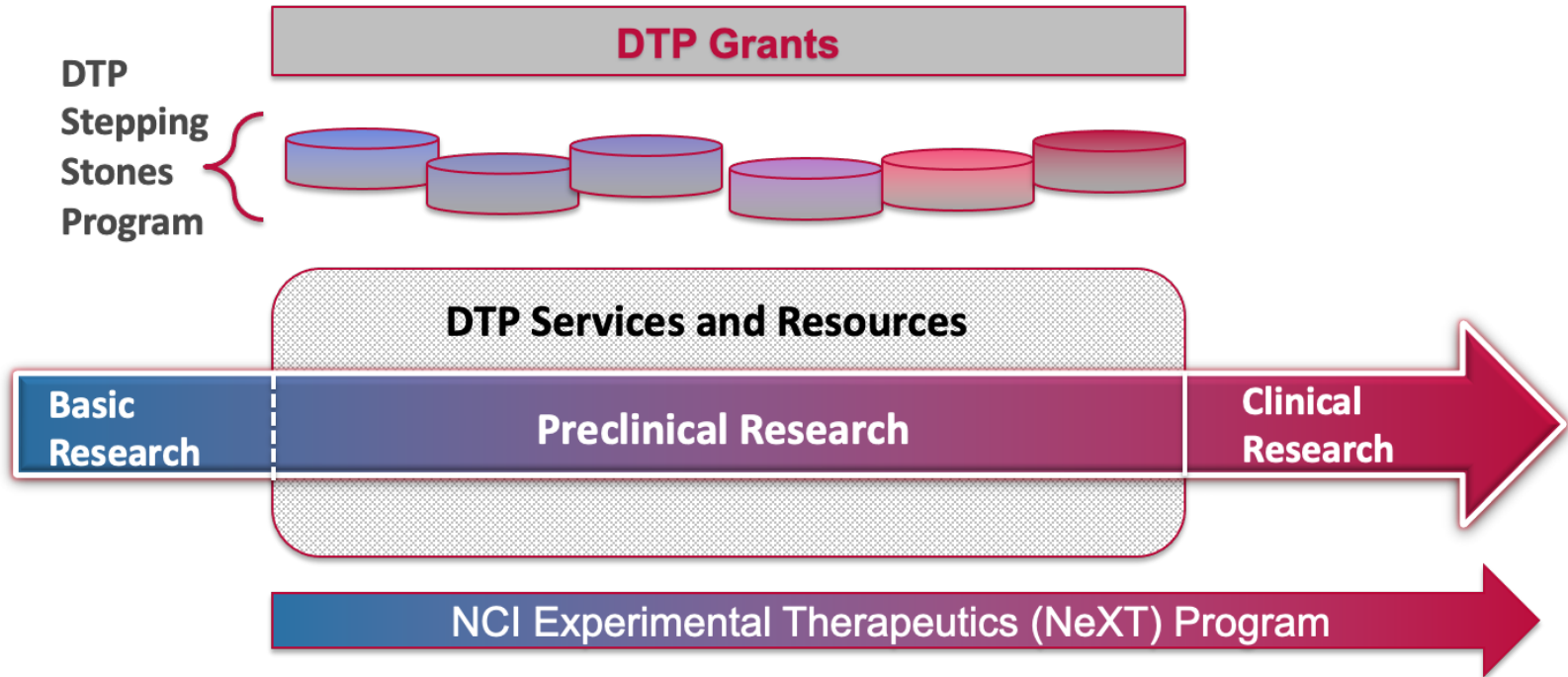
- Biometrics Research Branch (BRB)
- Cancer Diagnosis Program (CDP)
- Cancer Imaging Program (CIP)
- Cancer Therapy Evaluation Program (CTEP)
- **Developmental Therapeutics Program (DTP)**
- Radiation Research Program (RRP)
- Developmental Therapeutics Clinic (DTC)
- Translational Research Program (TRP)
- Office of Cancer Complimentary and Alternative Medicine (OCCAM)

DTP Mission: Support and assist the Extramural Community to advance New Cancer Therapies toward Clinical use

Overview of DTP Extramural Support Mechanisms

- 1. Grant funding:** Over 900 funded awards pertaining to drug discovery and development of small molecules, natural products, biopharmaceuticals, etc.
- 2. Repositories:** Collections of small molecules, pre-fractionated natural products, biologics, tumor models, and data are available to the public
- 3. Access to Discovery and Development Services:** DTP maintains drug discovery and development facilities at Frederick National Laboratory for Cancer Research (FNLCR) as well as contracted resources (CROs)
- 4. Expertise:** Staff with multidisciplinary expertise provide consultations along the critical path of discovery and development (all extramural - academic, non-profit, pharma)

Overlapping Support for Discovery and Development



DTP Branches: Provide Funding, Repositories and Services

Preclinical Therapeutics Grants Branch

Grants: Small Molecule, Natural Product, drug targets, discovery & development of novel therapeutic concepts

Immuno-oncology Branch

Grants: Immuno-oncology
Canine Immunotherapy Network
Pediatric Immunotherapy Network
Cancer Adoptive Cell Therapy (CanACT)

Biological Resources Branch

Grants: Biopharmaceutical discovery & development

Services: Development of clinical grade biologics, adoptive cell therapies, analytical testing (at FNLCR)

Repository: Biologics (MAbs, cytokines)

@ FNLCR

Information Technology Branch

Repository/Resources: Extensive databases of compounds, activity/efficacy, computational tools (COMPARE, ALMANAC)

Natural Products Branch

Repository: Large pre-fractionated library; collections of extracts (marine, plant, soil, fungi)

Services: Natural product chemistry

@ FNLCR

Drug Synthesis & Chemistry Branch

Repository: NCI Compound Repository

Services: Synthetic chemistry, route optimization, scale-up

@ FNLCR

Molecular Pharmacology Branch

Services: NCI-60 tumor cell screen
Patient-derived models screen, target validation, combinatorial screening

@ FNLCR

Biological Testing Branch

Repository: Tumor repository, Patient Derived Tumor Models repository, immunodeficient & immunocompetent

Services: Model development, efficacy, dose schedule, MTD

@ FNLCR

Toxicology & Pharmacology Branch

Services: Non-GLP and GLP PK & toxicology, ADME, *in vitro* tox assays

Investigative Toxicology

Laboratory: develop *in vitro* assays for discovery, development

@ FNLCR

Pharmaceutical Resources Branch

Services: Large scale GMP manufacture bulk API, analytical testing, dose formulation development, stability studies for final drug product

DTP Services Span Critical Path for Discovery and Development

- In vitro screening: NCI-60, Patient Derived Models
- Target characterization, Target validation
- Analog synthesis, route optimization
- Natural product chemistry

- Efficacy: model development, dose schedule, MTD
- Nonclinical: PK, ADME, Toxicology (GLP and non-GLP)
- CMC: Process optimization, scale up, formulation, non-GMP and GMP manufacturing, final drug product
- Regulatory: Assistance with IND submissions

Basic
Research

Preclinical Research

Clinical
Research

The Developmental Therapeutics Program (DTP)

Drug Discovery/Development – Anti-cancer activity screening and proof-of-concept studies *in vitro* and *in vivo* and support for product development through all phases of the critical path toward clinical use from medicinal chemistry through safety testing and cGMP manufacturing

Stepping Stones Program – Discrete drug development studies for grantees

Consultation Service – Helping innovators to meet standards required for early-phase clinical trials via **NeXT**

Repositories – Tumors, cell lines, patient-derived models, chemicals, natural products, and biological reagents

NCI-60 Human Tumor Cell Lines Screens – Unique cell killing dose response screens across 60 human tumor cell lines allowing response patterns to be analyzed by algorithms (**COMPARE**)



Databases & Tools – including data search tools, bulk data download, COMPARE analysis, NCI-ALMANAC, and ROADMAPS datasets

Grants Funding – FOAs:

RFA-CA-22-028: Can-ACT Adult

RFA-CA-22-29: Can-ACT Pediatric

NOT-CA-21-101: Advancing tumor site-activated small molecules

PAR-22-216: NCI Clinical and Translational Studies

PAR-20-271: Assay development and screening

dtp.cancer.gov

Grants Portfolio & Funding Opportunities

Sundar Venkatachalam, PhD

Preclinical Therapeutics Grants Branch (PTGB)

- **Overview of the grants portfolio**
- **Information on current and upcoming funding opportunities**

DTP Preclinical Therapeutics Grants Branch (PTGB): Areas of Focus

Basic Research

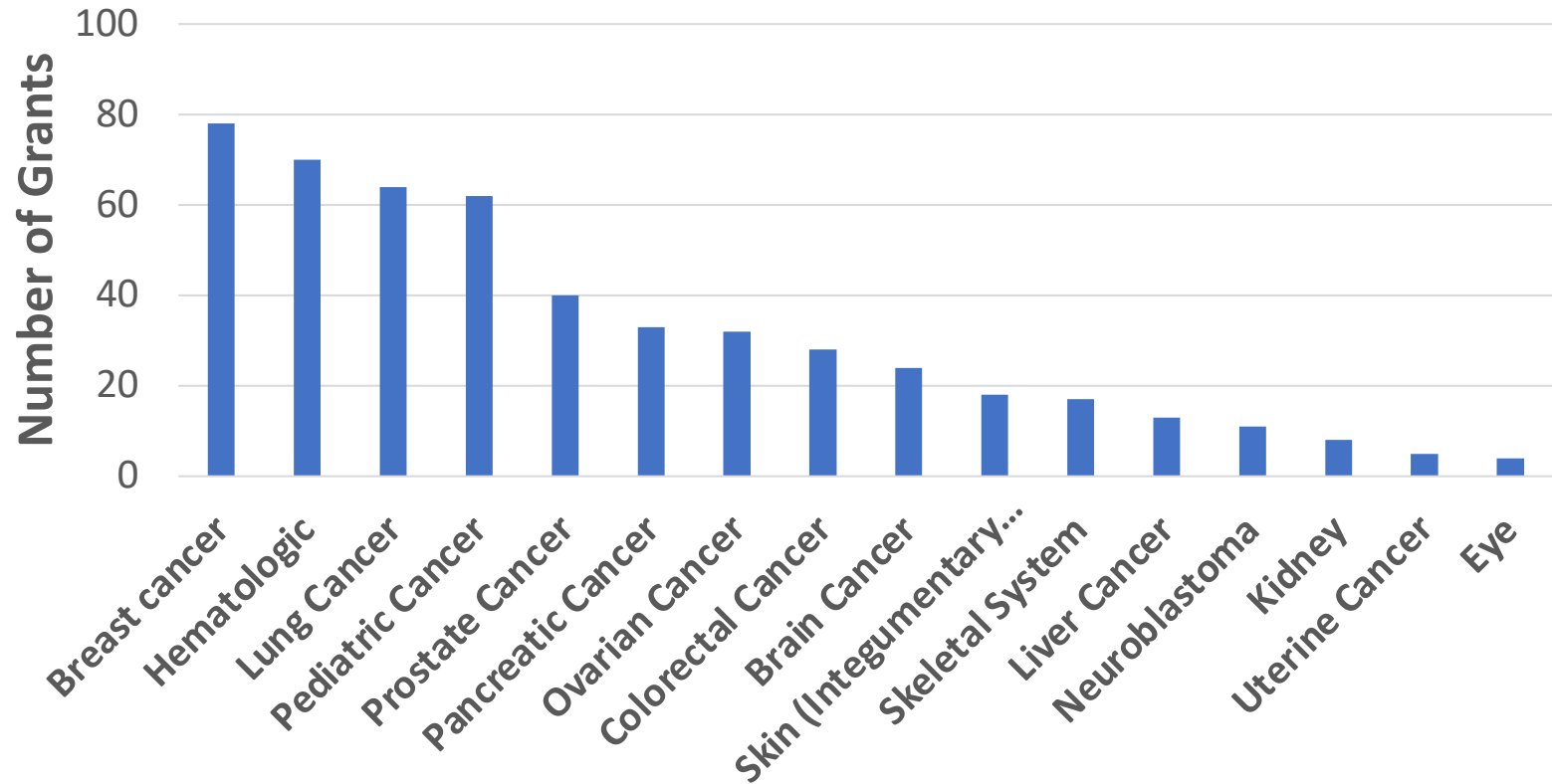
Preclinical Research

Clinical Research

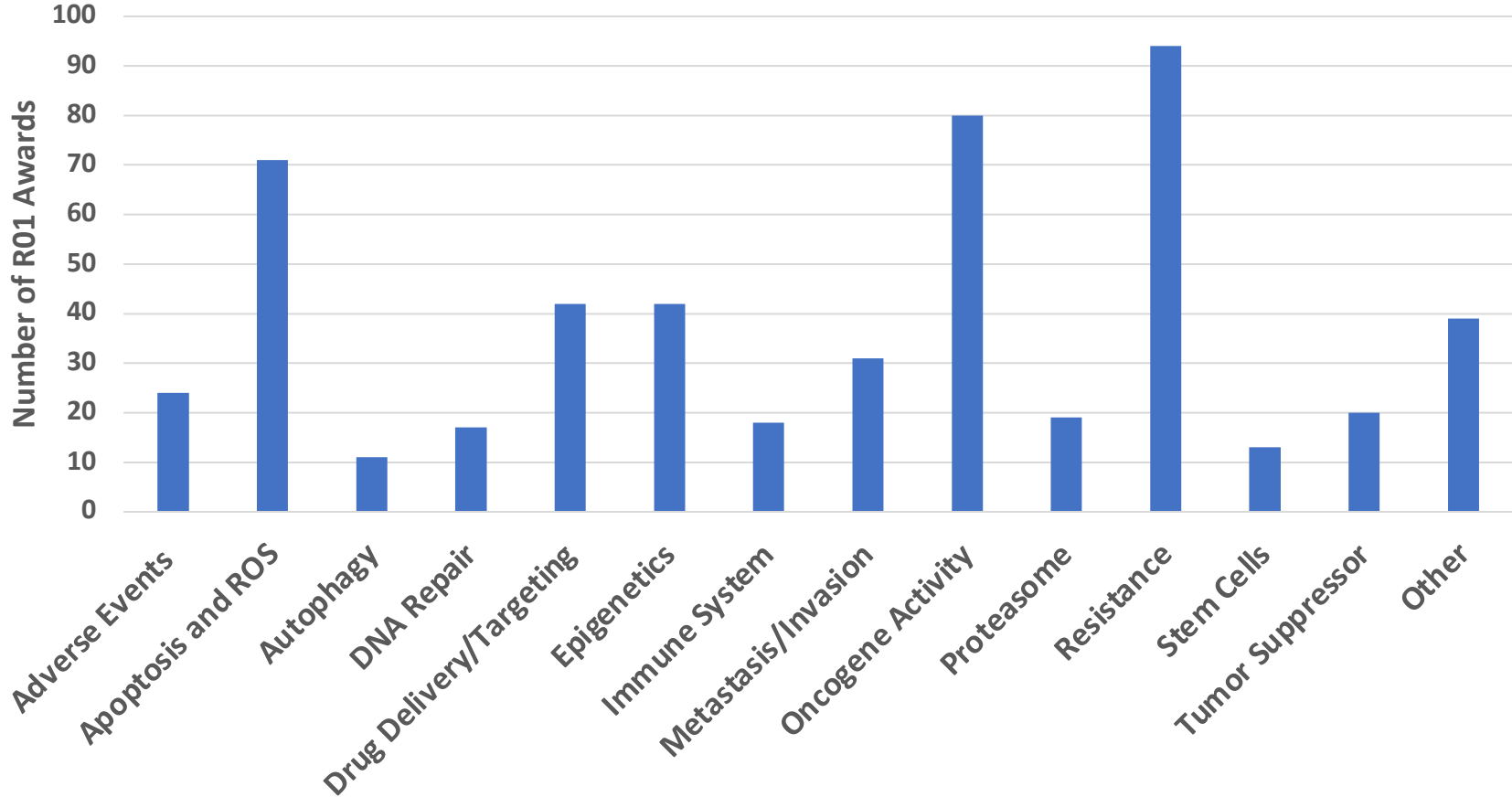
Preclinical therapeutics research up to but not including clinical trials

- Discovery, development and evaluation of **small molecules** (synthetic or natural product origin) for cancer therapy
- Drug delivery using various enabling technologies (e.g. ADC, nanotechnology)
- Validation of cancer drug targets: extracellular or intracellular processes (excluding immune interactions)
- Studies on mechanism(s) of action of therapeutic agents, drug resistance, rational drug combinations, novel preclinical models, drug efficacy, drug pharmacology, and drug toxicology

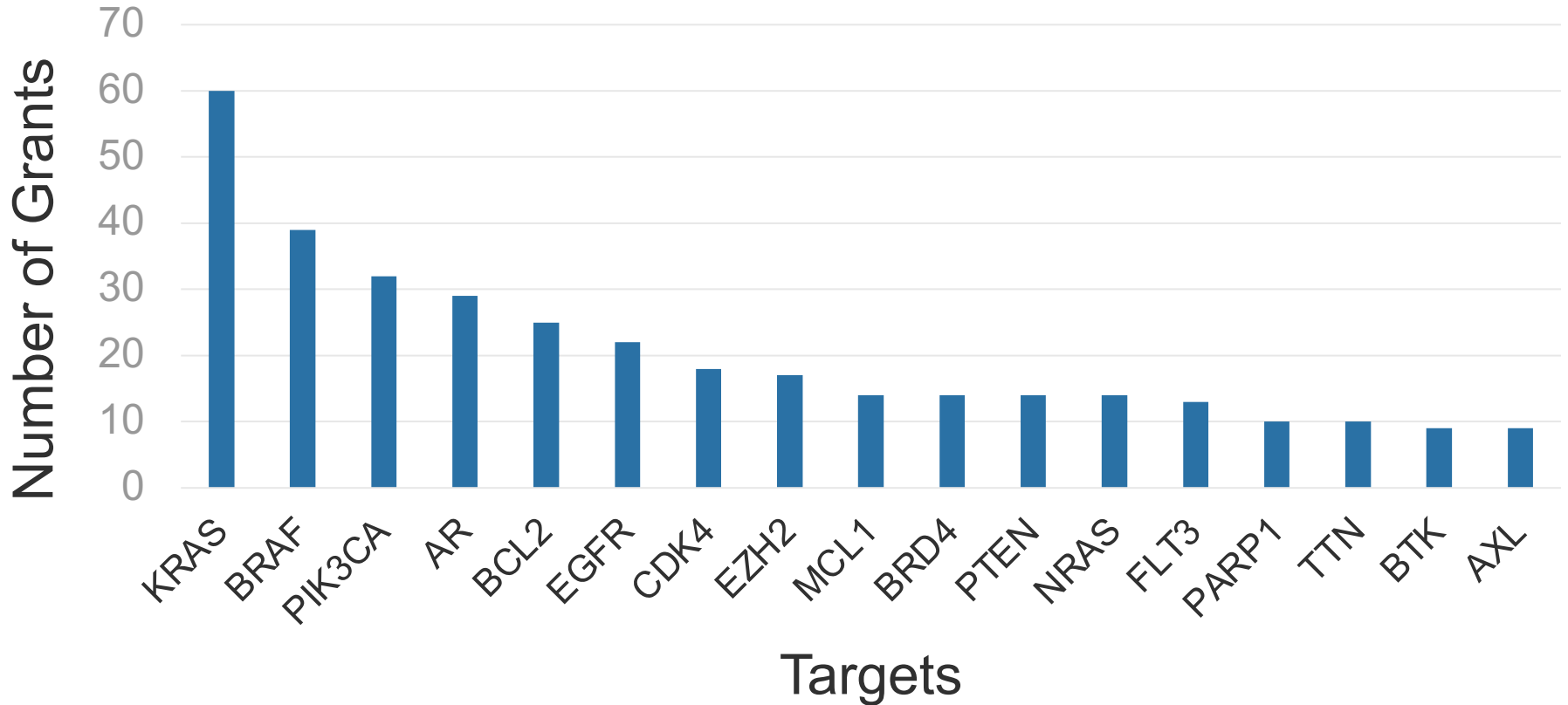
Active Awards by Cancer Site



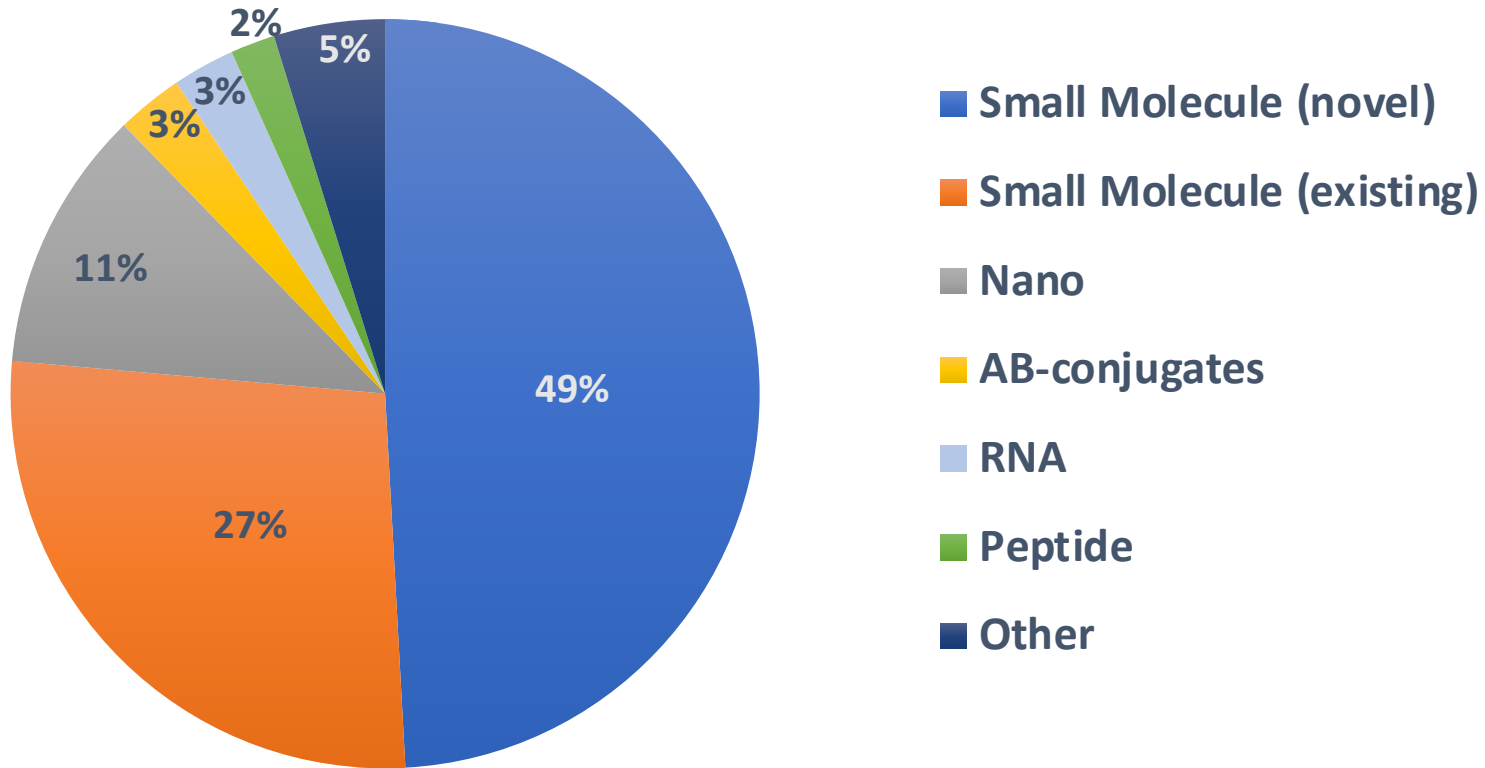
Primary Topic Areas (R01s)



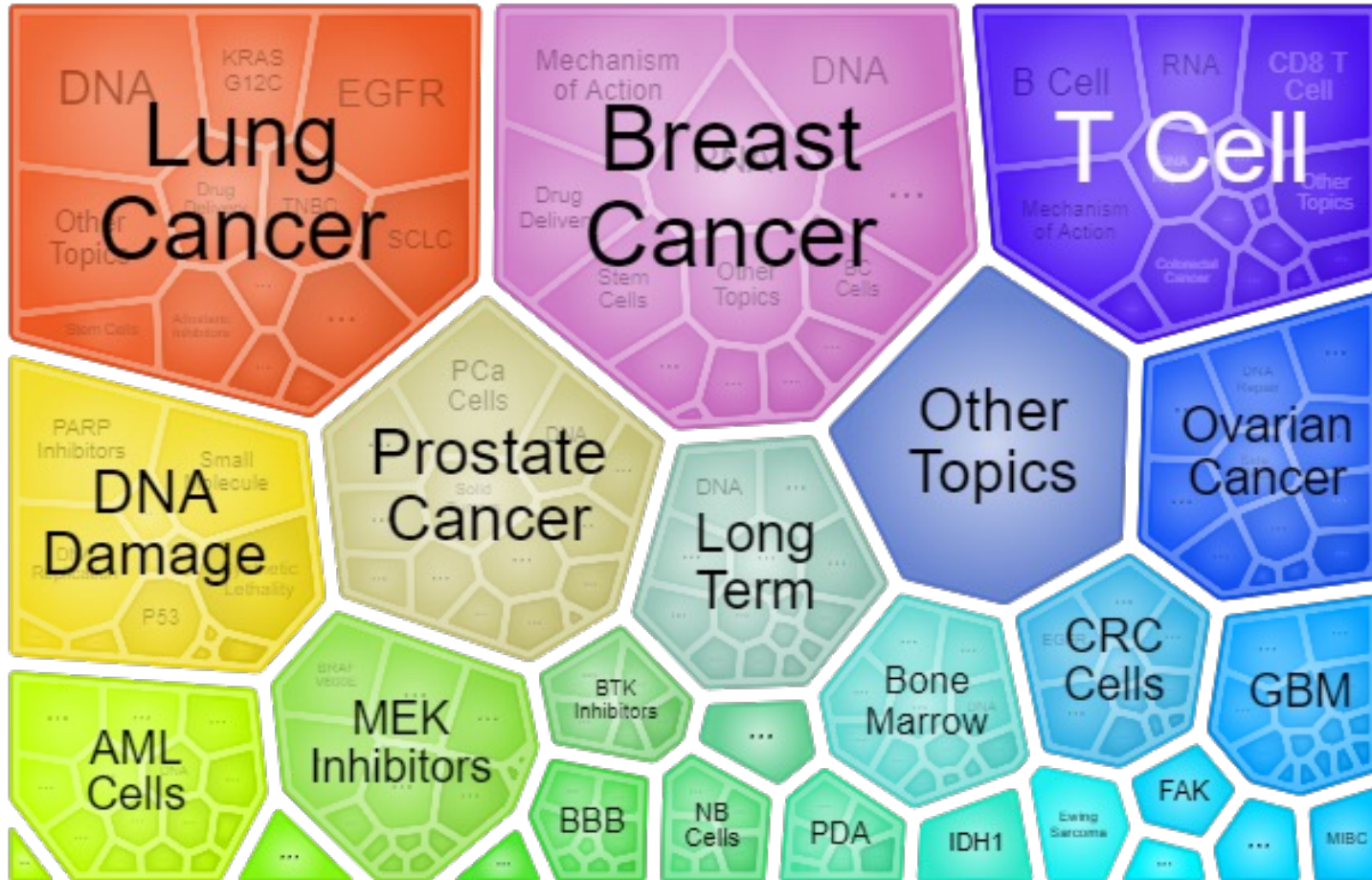
Active Awards - Top Targets



Therapeutic Modalities



Snapshot: Visualization of FY2023 Active Awards

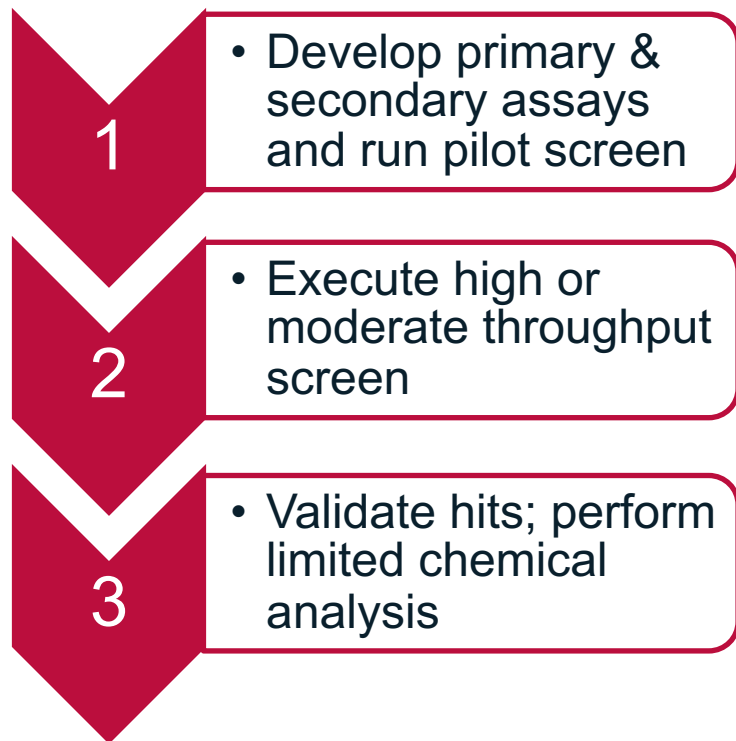


Current DTP - PTGB Funding Opportunities

FOA #	Title
PAR-20-271	Assay development and screening for discovery of chemical probes, drugs or immunomodulators (R01)
NOT-CA-21-101	Advancing the development of tumor site-activated small molecules (R01, R21, R15)
PAR-22-216	NCI Clinical and Translational Exploratory/Developmental Studies (R21 Clinical Trial Optional)
PA-19-056	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)

Stages of discovery research: PAR20- 271

“Assay development and screening for discovery of chemical probes, drugs or immunomodulators”



- A trans-NIH Funding Opportunity focused on small molecules
- The aims of an application may span one or more of the stages
- Flexible “on- and off-ramps” along the discovery pipeline
- Up to 4 years of funding; time and budget should match scope


UPCOMING FUNDING OPPORTUNITY

Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) Network

- Projects to better understand basic mechanisms of fusion-driven oncogenesis
 - **Goal:** Identify novel drug targets and critical dependencies
- Next Generation Chemistry Centers for Fusion Oncoproteins
 - **Goal:** Identify and develop small molecules that disrupt activity of fusion oncoprotein drivers for high-risk solid tumors and brain cancers

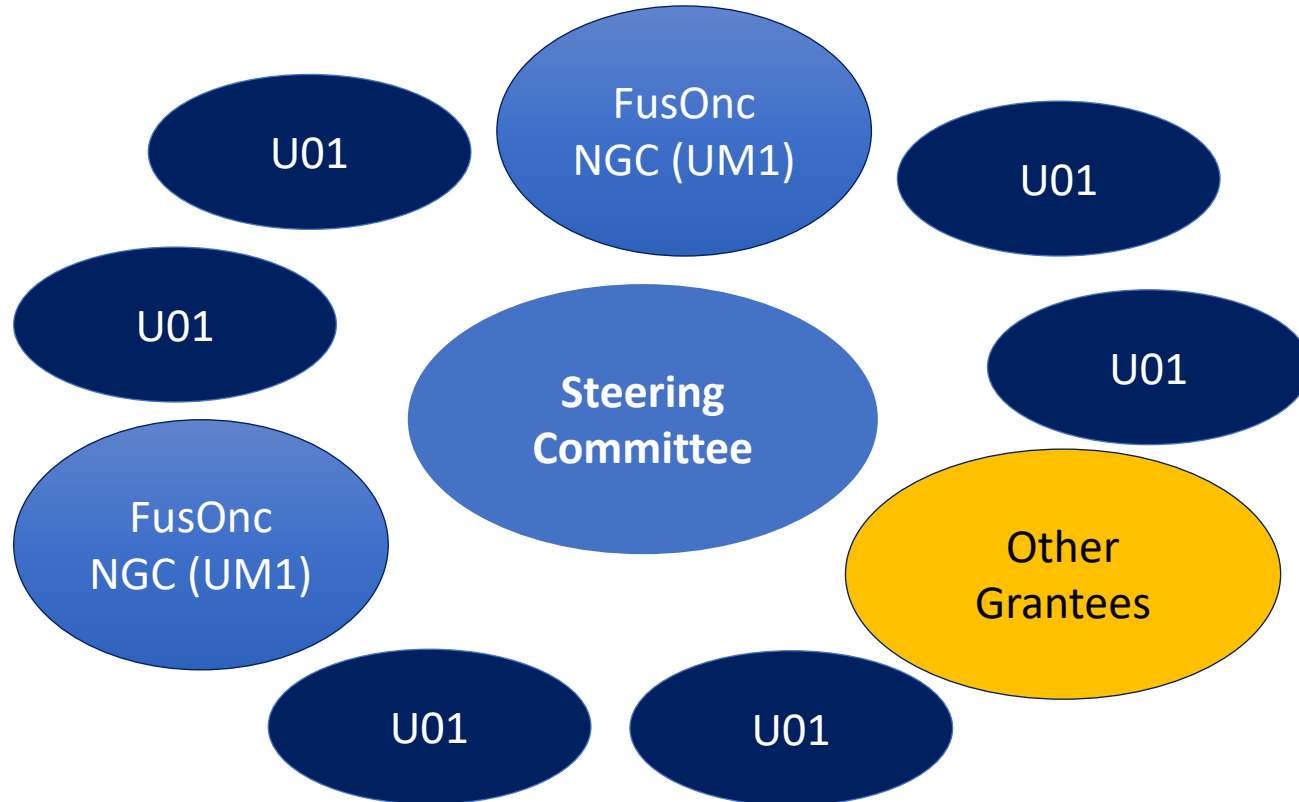


U01



FusOnc
NGCC
(UM1)

Planned Structure of the Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) Network



Notice of Intent to Publish a Funding Opportunity Announcement for Next Generation Chemistry Centers for Fusion Oncoproteins (UM1 Clinical Trial Not Allowed)

Notice Number: NOT-CA-23-058

Key Dates

Release Date: April 05, 2023

Estimated Publication Date of Notice of Funding Opportunity : June 29, 2023

First Estimated Application Due Date: November 17, 2023

Earliest Estimated Award Date: July 01, 2024

**Notice of Intent to Publish a Funding Opportunity Announcement for
Mechanisms of Fusion-Driven Oncogenesis in Childhood Cancers (U01
Clinical Trial Not Allowed)**

Notice Number: NOT-CA-23-057

Key Dates

Release Date: April 05, 2023

Estimated Publication Date of Notice of Funding Opportunity : June 29, 2023

First Estimated Application Due Date: November 17, 2023

Earliest Estimated Award Date: July 01, 2024

NCI Drug Development Workshop II: Specialized Topics in Preclinical Development of Small Molecule Cancer Drugs



Purpose: To help investigators reduce the translational risk of selected candidates during later stages of product development and increase the chances of entering clinical evaluation.

Workshop content: Six webinar sessions addressing specialized topics important for preclinical development of small molecule cancer drugs. Lectures will be 60 - 90 minutes, followed by 15-minute Q&A.

Session I. Considerations for Lead Optimization of Small Molecules (Thursday, June 22, 1 pm – 2:45 pm, ET)

Session II. Considerations for Advancing to Late Preclinical Development (Friday, June 23, 1 pm – 2:45 pm, ET)

Session III. Safety and Toxicity Studies for Small Molecules (Thursday, July 13, 1 pm – 2:15 pm, ET)

Session IV. Formulation of Small Molecules (Friday, July 14, 1 pm – 2:45 pm, ET)

Session V. Nanoparticle Delivery of Cancer Drugs (Thursday, July 27, 1 pm – 2:45 pm, ET)

Session VI. Good-to-know IP Knowledge (Friday, July 28, 1 pm – 2:15 pm, ET)

Target Audience: Scientists who are interested in preclinical drug development for cancer

Registration is **free** and open to the public: www.events.cancer.gov/dctd/drugdevelopment
(scan QR code to register)

Contact: Weiwei.Chen@nih.gov; Sundar.Venkatachalam@nih.gov; or, Jason.Yovandich@nih.gov

PTGB Members

- Joseph Agyin, Ph.D.
- Weiwei Chen, Ph.D.
- Suzanne L. Forry, Ph.D.
- Yali Fu, Ph.D.
- Sudhir B. Kondapaka, Ph.D.
- Morgan O'Hayre, Ph.D.
- Sundar Venkatachalam, Ph.D.

New Drug Development Resources

Rose Aurigemma, PhD

Molecular Pharmacology Branch

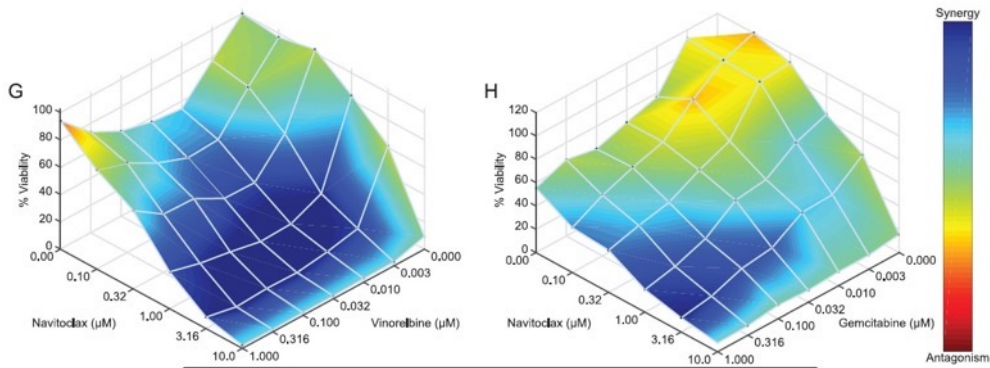
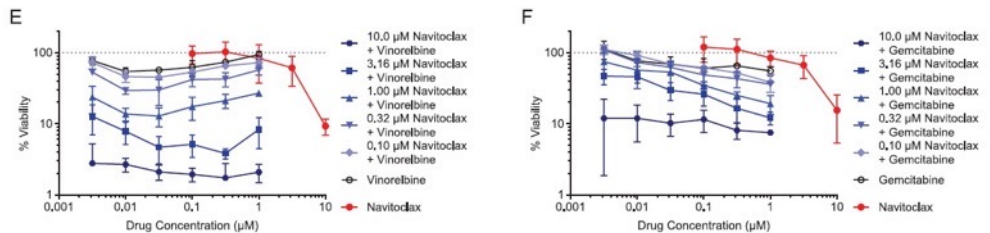
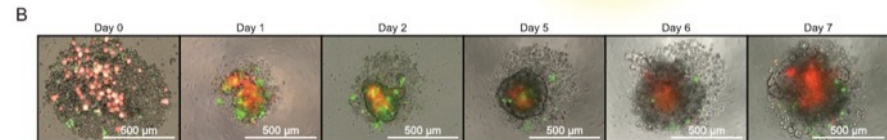
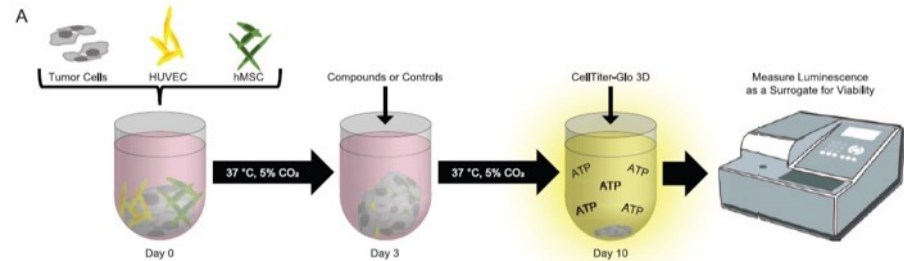
Chief: Bev Teicher, PhD

GOAL: Provide HTS platform and 3D cultures to provide more innovative drug screening, molecular pharmacology data

> *SLAS Discov.* 2021 Dec;26(10):1298-1314. doi: 10.1177/24725552211038362. Epub 2021 Nov 12.

Complex Tumor Spheroids, a Tissue-Mimicking Tumor Model, for Drug Discovery and Precision Medicine

Gurmeet Kaur¹, David M Evans², Beverly A Teicher¹, Nathan P Coussens³



Molecular Pharmacology: 384-well NCI60 and Organoids HTS

Assay Plate Set Information

Filter By: All Plan Gates

Plan Date: 06/30/2022

Experiment: 22064776

Cell Line: 254851-301-R-V2-organoid

Buttons: Edit, Cancel, Release

Previous: 254851-301-R-V2-organoid Next: 1768371

3-Dose Compounds

1768190

1768185

1768188

1768141

1768142

1768145

254851-301-R-V2-organoid

22064776

Time Zero: 458,854 835,414

Vehicle Control: Low 461,714 341

Mean: 606,368 423,828

High: 787,334 391,134

K8 Control: Low 1,876 761

Mean: 1,717 5,441

High: 2,361 11,463

Disabling Time: 187 134

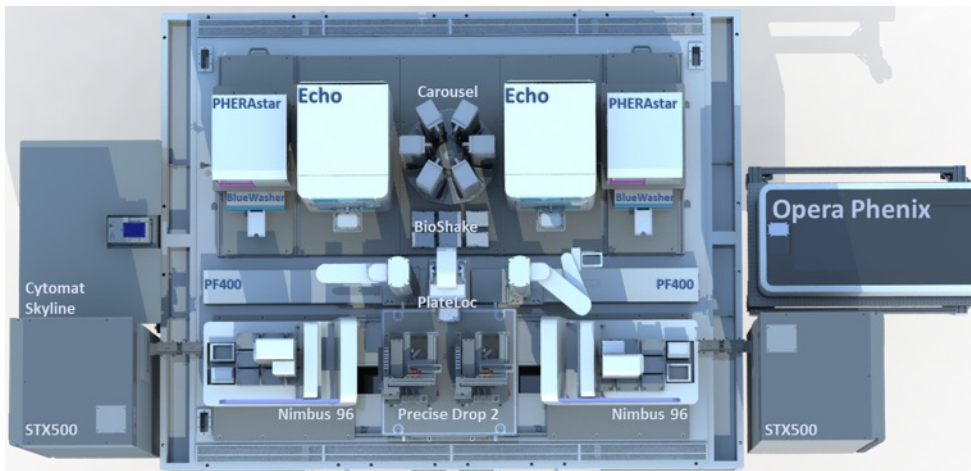
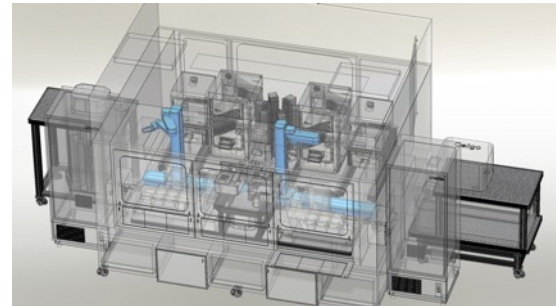
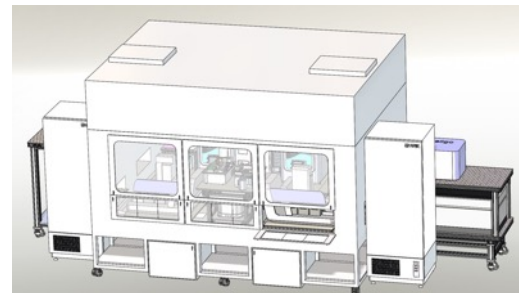
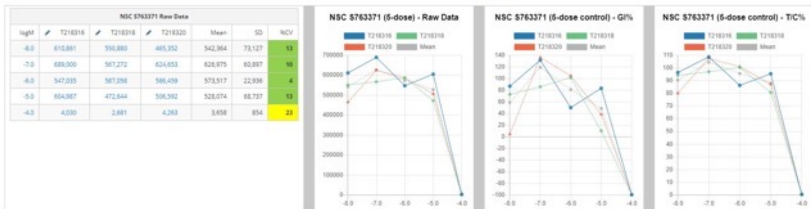
Z Factor: 0.628 0.536

9128127-050

9128127-036

Code Color Key - QC's

- NCV +30% - Action recommended
- NCV +20% - Review data
- NCV +20% - Pass
- Z Factor <0.5 - Action recommended
- Z Factor <0.5 - Pass
- Raw Value +2SD from Mean
- Raw Value +3SD from Mean
- Well not used in calculations - cancelled



Biological Testing Branch

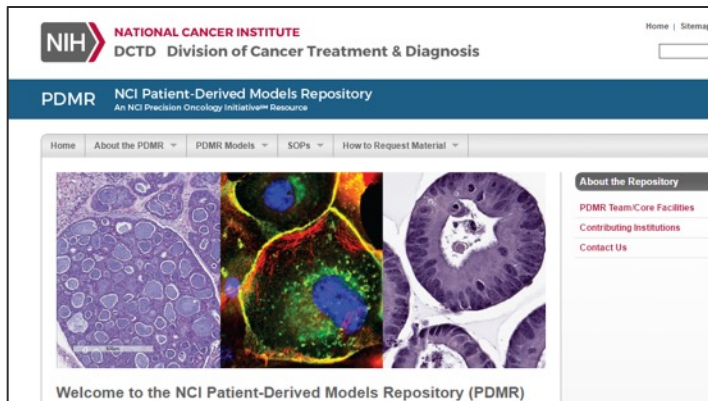
Chief: Melinda Hollingshead, DVM, PhD

GOAL: Provide quality-controlled human tumor models derived from fresh patient samples that are genetically characterized and

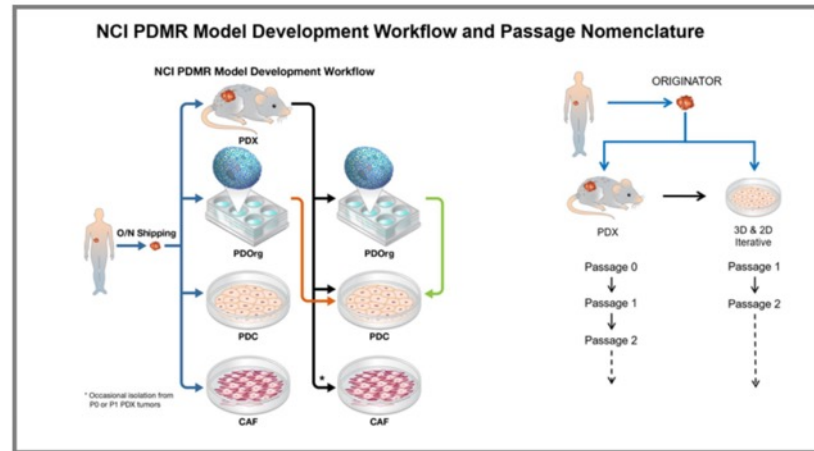
Patient-Derived Models Repository – now distributing internationally

- Over 600 PDX tumor models now publicly available
- 429 cancer associated fibroblast lines, 384 tumor cell lines, 87 paired sets of tumor & fibroblast, and 397 organoid cultures are available for distribution

Collaboration with Advanced Development and Research Directorate, Frederick National Laboratory for Cancer Research



dmr.cancer.gov/



AACR: Molecular Pharmacology and Biological Testing Resources

ORAL presentation 5720 - Combination therapies in matched 3D in vitro and in vivo preclinical models of rare and recalcitrant cancers from the National Cancer Institute's Patient-Derived Models Repository

April 18, 2023, 3:22 PM - 3:37 PM Room W414 Thomas Dexheimer, PhD FNLCR

Oral presentation 5776 - Advancing a screening platform with panels of patient-derived organoid models for drug discovery and development
Annamaria Rapisarda, PhD FNLCR

April 18, 2023, 3:22 PM - 3:37 PM Room W304 A-D Annamaria Rapisarda, PhD, FNLCR

POSTER Session PO.ET05.02 - Anticancer Approaches Targeting Signal Transduction Pathways

4884 / 27 - Targeted investigational oncology agents (IOA) in the NCI60: a phenotypic systems-based resource

April 18, 2023, 1:30 PM - 5:00 PM Section 13 Mark Kunkel, PhD, DTP

POSTER Session PO.TB05.01 - 3D and Tissue Recombinant Models

4555 / 6 - Aryl-hydrocarbon receptor inhibitors in combination with anticancer agents, especially proteasome pathway inhibitors, in a complex spheroid screen using patient-derived cell lines can result in greater-than additive cytotoxicity

April 18, 2023, 1:30 PM - 5:00 PM Section 2 Beverly Teicher, PhD, DTP

AACR: Molecular Pharmacology and Biological Testing Resources

CTD

POSTER Session PO.TB05.02 - Novel Models of Human Cancer

40 / 8 - NCI patient derived models repository: PDX, organoid and cell lines from the same patient - bridging the translational pipeline

April 16, 2023, 1:30 PM - 5:00 PM

Section 2

Yvonne Evrard, PhD FNLCR

POSTER Session PO.TB05.02 - Novel Models of Human Cancer

36 / 4 - Comparing twenty-two matched patient-derived cell lines developed from either patient, PDX, or organoid tumor cell material

April 16, 2023, 1:30 PM - 5:00 PM

Section 2

Cindy Timme, PhD, FNLCR

POSTER Session PO.ET02.02 - Chemotherapeutic Combinations

2665 / 1 - Biochemical inhibition profiles of 370 wild type human kinases provide a basis for selecting alternative combinations of EGFR and VEGFR inhibitors

April 17, 2023, 1:30 PM - 5:00 PM

Section 14

Nathan Coussens, PhD, FNLCR

POSTER Session PO.MCB08.02 - Multi-omics Tumor Profiling

6072 / 12 - Chromosomal aneuploidy, whole-genome doubling and mutational signatures in NCI PDMMR models

April 19, 2023, 9:00 AM - 12:30 PM

Section 12

Li Chen, PhD FNLC

Natural Products Branch

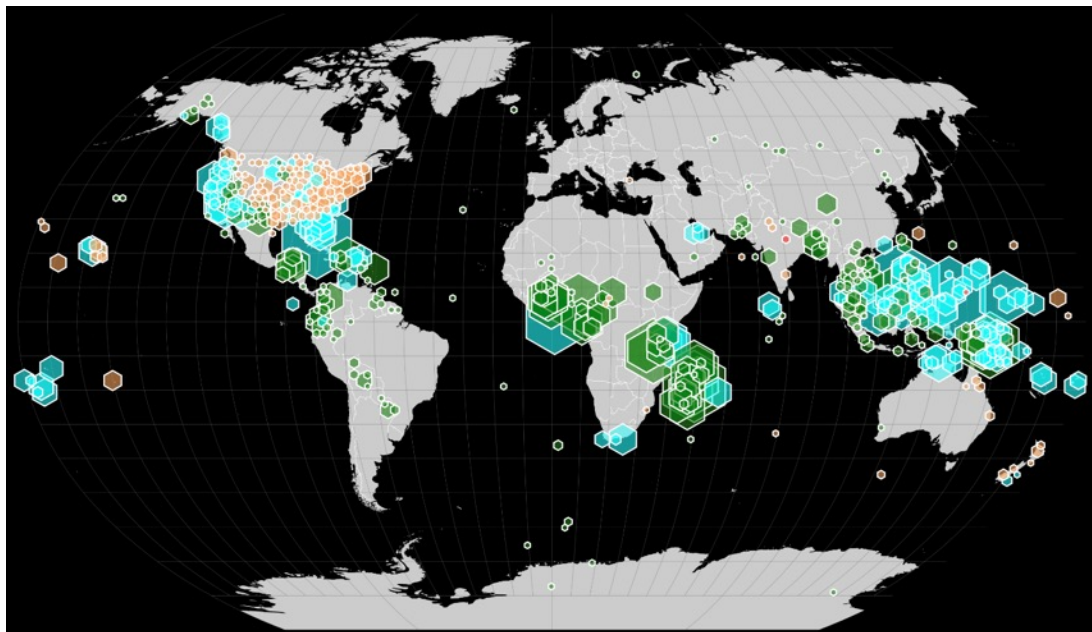
Chief: Barry O'Keefe, PhD



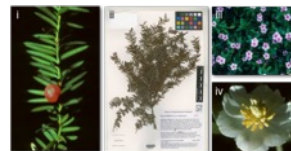
Director, Molecular Targets Program, Center For Cancer Research, and Chief, Natural Products Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, USA

NCI Natural Product Repository

GOAL: Prepare prefractionated, plated samples from NCI's extensive collection of natural product extracts (>230,000 crude extracts) to allow more accessible screening and identifying of active compounds



Plant Extract Library



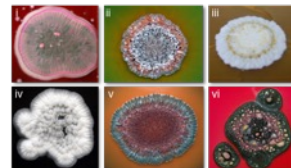
- ~161,000 extracts (organic + aqueous)
- ~44,000 plants, including 81,400 raw materials (leaves, roots, fruit, etc.) collected from Africa and Madagascar; North, Central and South America; and Southeast Asia.

Marine Extract Library



- ~41,000 extracts (organic + aqueous)
- ~20,500 organisms collected from the Indo-Pacific region.

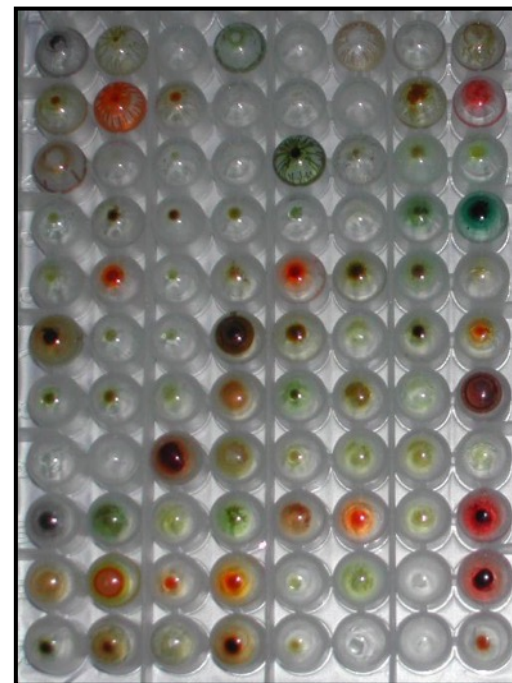
Microbial Extract Library



- ~30,000 extracts (organic + aqueous)
- ~26,000 organisms collected from US
- **New Collection:** 20,000 Fungal strains from USA (Univ. of Oklahoma)

Why Have Natural Products Not Been Included in HTS?

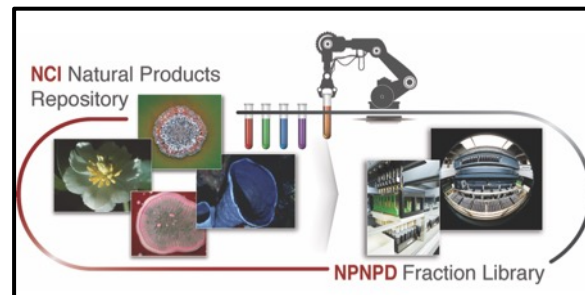
- Extracts are difficult to screen in their crude form
- Contain numerous compounds at different concentrations
- Purification and structure elucidation of active compounds was time consuming; did not mesh with HTS screening schedules
- Need to address these challenges to efficiently access the unique chemical diversity in natural products



Natural Product Extract Pre-fractionation Plans and Progress

PLAN:

- Create a library of ~1,000,000 semi-pure natural product fractions more amenable to modern screening technologies
- Supply the library of chemical diversity to researchers for free
- Open use for all screening labs, against all disease targets
- Method development:
 - Purification based on polarity
 - Optimized for mass, compound separation, biological activity



PROGRESS:

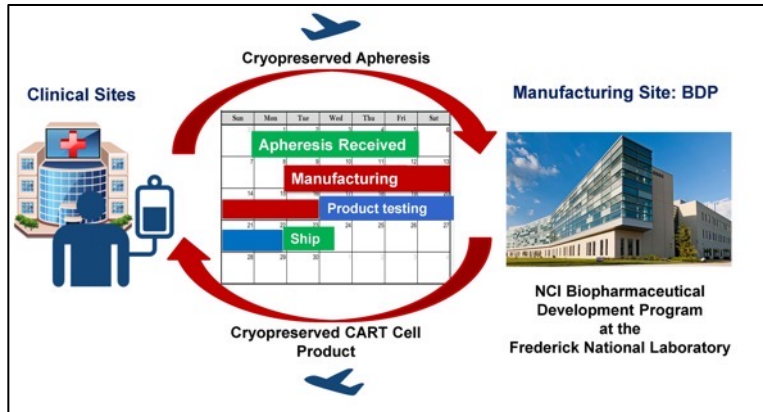
- >580,000 fractions produced
- First 500,000 fractions released to the public
- >25,000,000 wells of fractions plated in 384-well plates for shipping, stored in repository
- >5,000,000 samples shipped to screening centers worldwide
- New, marine aqueous pre-fractionated library in production

Biological Resources Branch

Chief: Jason Yovandich, PhD

Goal: Provide resources to manufacture clinical-grade adoptive cell therapy products to accelerate research in the extramural community

- Expanded to 5 GMP suites for cell therapy and vector manufacturing
- Established expertise and capability to support multi-center cell therapy clinical trials
 - Active: Anti-CD33 CAR T for pediatric AML
 - Active: Anti-GD2 CAR T for pediatric sarcoma and neuroblastoma
- CRISPR/cas-based editing capability (near completion)



Collaboration with
Biopharmaceutical Development
Program, Frederick National
Laboratory for Cancer Research



Stepping Stones Program

Sharad K. Verma, PhD

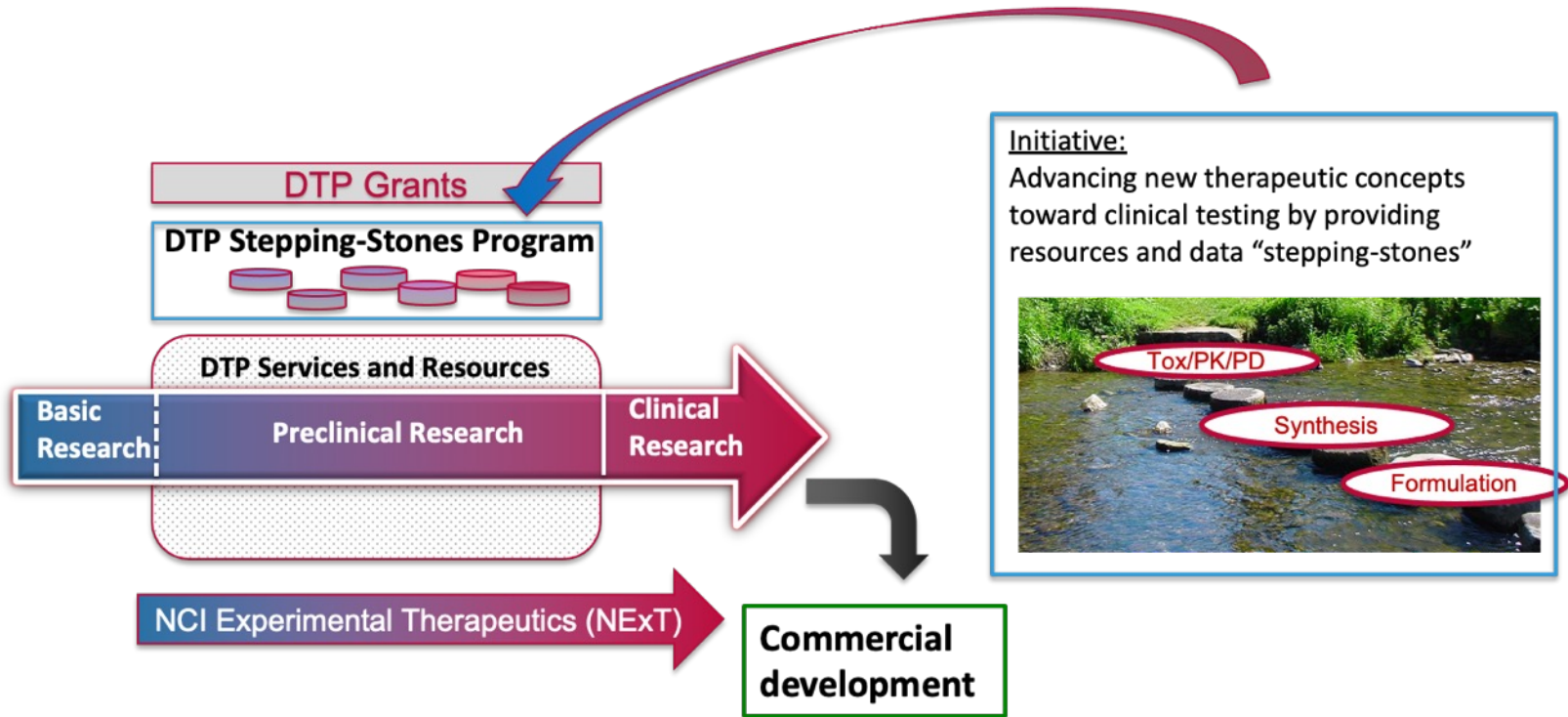
Supporting and Assisting the Extramural Community to Advance New Therapeutic Concepts toward Clinical Use

Product Development Stepping-Stones



Program manager: Dr. Morgan O'Hayre (morgan.o'hayre@nih.gov)

Leverage Extramural R&D



Stepping-Stones Mission

Assist academic innovators with critical data gaps

- Limited access to full range of development resources
- Academic funding may not cover iterative/routine product development tasks
- Unavailable expertise in full range of regulatory critical path steps toward IND

Support NCI investment in the grant portfolio

- Limited to NIH-funded therapeutic concepts
- Small investment (<\$100K) to advance promising lead **candidates**
- **Provide critical data** a PI can't easily obtain or not covered by funding (e.g. formulation work, synthesis optimization, discrete DMPK/ADME studies, etc.)
- **Improves chances for gaining other resources** (NExT, VC, SBIR/STTR)
- Special emphasis on area of unmet need and institutions with fewer resources

Examples of Stepping-Stones Project Support

Formulation Development

- Enabled PI to produce an orally available drug formulation
 - PI continuing with startup and received STTR Ph I and II funding
- Unable to achieve sufficient bioavailability (few projects)
 - PIs considering other analogs, formulation options

Synthesis and PK studies

- Synthesis improvements, multi-gram quantities of non-GMP API, and salt-forms
- PK studies (mouse, rat) to characterize bioavailability
 - 2 PIs continuing and plan to apply to NExT and/or SBIR

Biomarker studies

- Connected to resources for pilot PD studies
 - PI continuing with startup and aiming to file IND in 2024

In Vitro ADME and safety studies

- De-risking and ID of liabilities early (CYP, UGT, metabolic stability, hERG, etc)

Stepping-Stones has supported NIH-funded projects targeting a variety of malignancies with a focus on areas of unmet need

- Uveal Melanoma
- Pancreatic Cancer
- Melanoma
- K-Ras (G12D) mutant cancers
- Glioblastoma multiforme (GBM)
- Castration Resistant Prostate Cancer (CRPC)
- Acute Myeloid Leukemia (AML)
- Triple Negative Breast Cancer (TNBC)
- Chemotherapy Induced Peripheral Neuropathy (CIPN)

With more to come to help patients!

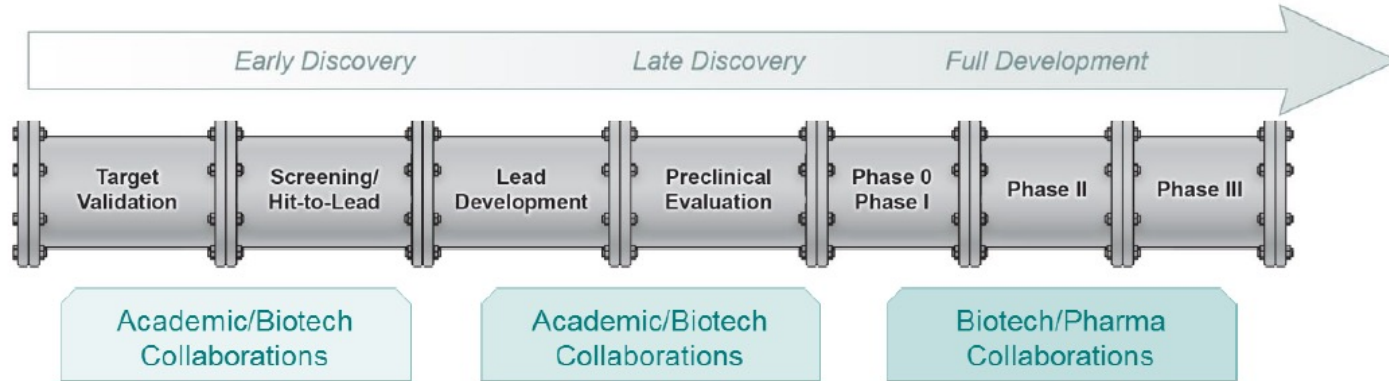
Drug Development Consultation Service

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

- Open to all innovators
- Confidential
- Assess critical path for product development
- **On-ramp for Stepping-Stones**
- Expert advice for:
 - chemistry and synthesis, tox/pharm, molecular pharmacology, biology, immunooncology, biological products, natural products, *in vivo* models and testing, manufacturing and formulations

The screenshot displays the NCI NExT website interface. At the top, the NIH logo and 'NATIONAL CANCER INSTITUTE' are visible, along with the DCTD and CCR divisions. A search bar is present in the top right. The main header reads 'NExT NCI Experimental Therapeutics Program'. Below this is a navigation menu with options like 'Home', 'About NExT', 'How NExT Works', 'How To Apply', 'NExT Resources', and 'Chemical Biology Consortium'. The left sidebar contains a menu with 'Main', 'Discovery', 'Development', and 'Drug Development Consultation' (which is highlighted). The main content area is titled 'NExT Resources' and features the heading 'Consultation on Development of Experimental Cancer Drugs'. The text describes a focused consultation service provided by staff from the DCTD Developmental Therapeutics Program and Cancer Imaging Program. It lists several key areas of expertise: drug discovery strategy, nonclinical safety studies, GMP production, IND filing plans, FDA communication, and access to NCI's preclinical and clinical resources. At the bottom, there is a 'Request Consultation' section with input fields for 'Name of Investigator' and 'Institution'.

NCI Experimental Therapeutics (NExT) Program



- Projects can enter at any stage of discovery or development
- Applications are peer reviewed by NExT Special Emphasis Panels
- Submission deadlines: February 15, June 15 and October 15
- NExT program provides resource, not funding or money, for approved studies
- Applicants retain ownership of intellectual property that they bring to the program

To learn more about NExT, please join the following Meet-the-Expert (MTE) lecture:

“NCI Experimental Therapeutics (NExT) Program: A Government, Academic, Industry Partnership for Cancer Drug Discovery and Development” **Tuesday April 18, 3:00pm ET @ the NCI Kiosk**

Immuno-oncology Initiatives and Services

Marc Ernstoff, MD

Immuno-Oncology Branch (IOB)

Marc S. Ernstoff, MD

Chief, ImmunoOncology Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, USA

Biological Resources Branch (BRB)

Jason Yovandich, PhD

Chief, Biological Resource Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, USA

**American Association for Cancer Researcher Annual Meeting
April 14-19, 2023
Orlando, Florida**

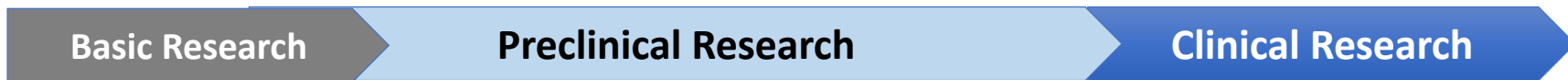
Today's Topics

- I. ImmunoOncology (IO) and Biological Resource (BR) Branches
 - Who we are and what we do

- II. Programs in IOB
 - K9CIN, PIN, Can-ACT
 - Opportunities

- III. Resources Available in BRB
 - Reagents
 - Consultation Services
 - Production Services

DTP ImmunoOncology Branch (IOB) established Dec 2016: Areas of Focus



Preclinical therapeutics research up to but not including clinical trials

- Discovery, development and evaluation of Immunotherapeutic agents and approaches (humoral, cellular, genetically modified cells, TME regulators)
- Guidance on preclinical and clinical PK/PD, toxicology, drug formulation and production, and IND-directed regulatory requirements for IO agents.
- Coordination within DCTD by identifying new immunotherapeutic agent candidates to recommend for development.
- Identification of scientific gaps and opportunities.

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

IOB Members

Program Officers

Connie Sommers, PhD

Anju Singh, PhD

Marco Cardone, PhD

Zhang Zhi Hu, MD

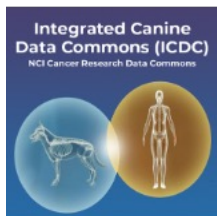
Program Specialist

Monica Cooper

IOB RFAs as of 2023

- RFA-21-050 Canine Cancer Immunotherapy Network (K9CIN)
- RFA-21-051 Coordinating Center for Canine Cancer Immunotherapy Network (K9CIN)
 - goal** – to perform cancer immunotherapy clinical trials and correlative studies in pet dogs to inform potential treatments for human cancer
- RFA 22-016 Pediatric Immunotherapy Network (PIN)
 - goal** – to develop novel immunotherapies for children and adolescents with solid tumors including brain tumors
- Cancer Adoptive Cellular Therapy Network (Can-ACT) for Adult Cancers (UG3/UH3)
- Cancer Adoptive Cellular Therapy Network (Can-ACT) for Pediatric Cancers (UG3/UH3)
- Cancer Adoptive Cellular Therapy Network (Can-ACT) Coordinating Center (U24)
 - goal** – to advance new cell therapy for cancer strategies into clinical testing for the treatment of solid tumors in adult and pediatric cancer patients

PRECINCT/K9CIN Network Structure



Frederick
National
Laboratory
for Cancer Research

The logo for PRECINCT Canine Trials features a stylized orange and blue figure of a person and a dog. Text includes "PRE-medical Cancer Immunotherapy Network for PRECINCT Canine Trials".

**PRE-medical
Cancer
Immunotherapy
Network for
PRECINCT Canine
Trials**

The logo for the University of Pennsylvania, featuring a shield with a book and a star.

Penn
UNIVERSITY OF PENNSYLVANIA
Coordinating Center
**N. Mason
Q. Long**

The logo for the National Cancer Institute, featuring the text "NATIONAL CANCER INSTITUTE" in a stylized font.

**NATIONAL
CANCER
INSTITUTE**

**T. Hecht (DCTD)
C. Sommers (DCTD)
Z. Hu (DCTD)
A. LeBlanc (CCR)**

The logo for Mayo Clinic, featuring a shield with a cross and a caduceus.

**MAYO
CLINIC**

**S. Naik
J. Modiano**

The logo for the University of Minnesota, featuring a red and white "M" with a gold outline.

**UNIVERSITY
OF MINNESOTA**

The logo for North Carolina State University, featuring a red square with "NC STATE UNIVERSITY" in white.

**NC STATE
UNIVERSITY**

**D. Zaharoff
P. Hess**

The logo for Purdue University, featuring a gold "P" on a white background.

**PURDUE
UNIVERSITY**

D. Knapp

The logo for the University of Pennsylvania, featuring a shield with a book and a star.

Penn
UNIVERSITY OF PENNSYLVANIA

N. Mason

The logo for Tufts University, featuring a blue shield with a tree and a book.

**Tufts
UNIVERSITY**

**C. London
G. Richmond**

The logo for the University of Massachusetts Medical School, featuring a blue shield with a white "M" and a caduceus.

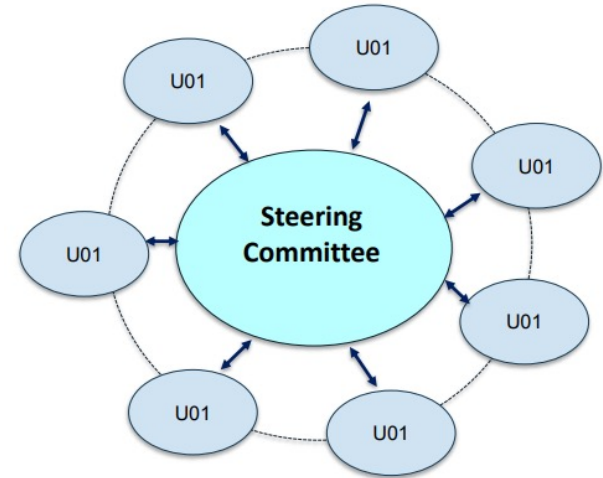
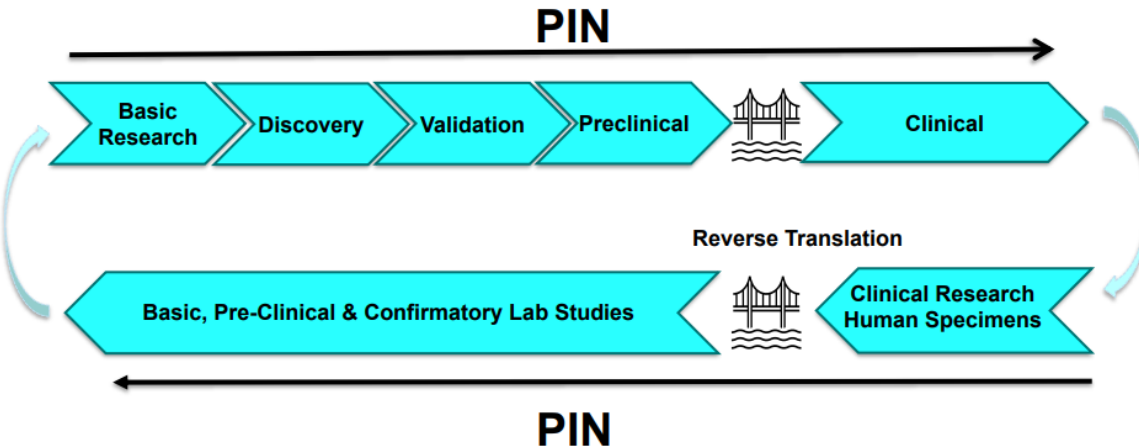
**UMASS
MEDICAL
SCHOOL**

Additional participants
-Former PRECINCT PIs
-PIs with canine cancer RO1s
-other canine cancer researchers

goal – to perform cancer immunotherapy clinical trials and correlative studies in pet dogs to inform potential treatments for human cancer

PIN Network Structure

- The RFA had one round of competition and is completed (2/14/2023 review)
- Sites under consideration



Patient advocates and additional NIH-funded pediatric immunotherapy researchers will be added as associate members

goal – to develop novel immunotherapies for children and adolescents with solid tumors including brain tumors

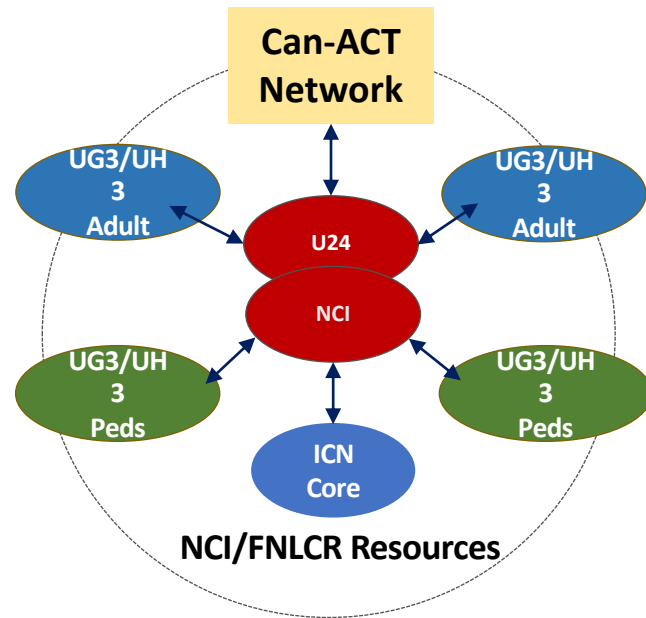
Can-ACT Network Structure

The goal of Can-ACT RFAs is to foster innovation and promote **early-stage clinical testing** of novel **cell-based immunotherapies for solid tumors** in adult and pediatric patients and leverage NCI resources to support the cell therapy community.

- Can-ACT for **Adult** Cancers (RFA-CA-22-028) – UG3/UH3
- Can-ACT for **Pediatric** Cancers (RFA-CA-22-029) – UG3/UH3
- Can-ACT **Coordinating** Center (RFA-CA-22-030) – U24

The RFAs have two rounds of competition:

- Round 1 is completed (3/2/2023 review meeting)
- Round 2 submission due June 30, 2023
- The U24 Coordinating Center has only one round



Current Funding Opportunities

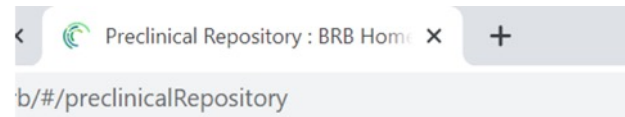
FOA #	Title
RFA-22-028 RFA-22-029	Cancer Adoptive Cellular Therapy Network (Can-ACT) for Adult Cancers Cancer Adoptive Cellular Therapy Network (Can-ACT) for Pediatric Cancers (UG3/UH3 Clinical Trial Required)
RFA-22-050	NCI Cancer Moonshot Scholars Diversity Program (R01 Clinical Trial Optional)
PAR-22-085 PAR-22-086	Microbial-based Cancer Imaging and Therapy – Bugs as Drugs (R01) Microbial-based Cancer Imaging and Therapy – Bugs as Drugs (R21)
PAR-20-284 PAR-22-071	Innovative Research in Cancer Nanotechnology (R01) Toward Translation of Nanotechnology Cancer Interventions (R01)
PAR-22-216	NCI Clinical and Translational Exploratory/Developmental Studies (R21 Clinical Trial Optional)
PA-20-185	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)

Biological Resources Branch

Repository of Biological Reagents:

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

<https://frederick.cancer.gov/resources/repositories/Brb/#/preclinicalRepository>



Reagents Available

Human Cytokines and Growth Factors

Abbreviation	Reagent Name	Reagent Size	Agreement
IL-2	Interleukin-2	1 x 10 ⁶ units	* MTA Required
IL-7 (Glycosylated)	Interleukin-7	213 µg/3 ml vial	* MTA Required
IL-15 (E. coli)	Interleukin-15	150 µg (0.5 mg/ml in 0.3 ml volume/3ml vial)	* MTA Required
IL-1 alpha	Interleukin-1 alpha	10 µg	* MTA Required
IL-1 alpha	Interleukin-1 alpha	100 µg	* MTA Required
rHU IL-6	Interleukin-6	200 µg	* MTA Required

Monoclonal Antibodies - Anti-Human

Abbreviation	Reagent Name	Reagent Size	Agreement
HeFi-1	Anti-Human-CD30	5 mg	* MTA Required

NCI Biopharmaceutical Development Program at the Frederick National Laboratory for Cancer Research



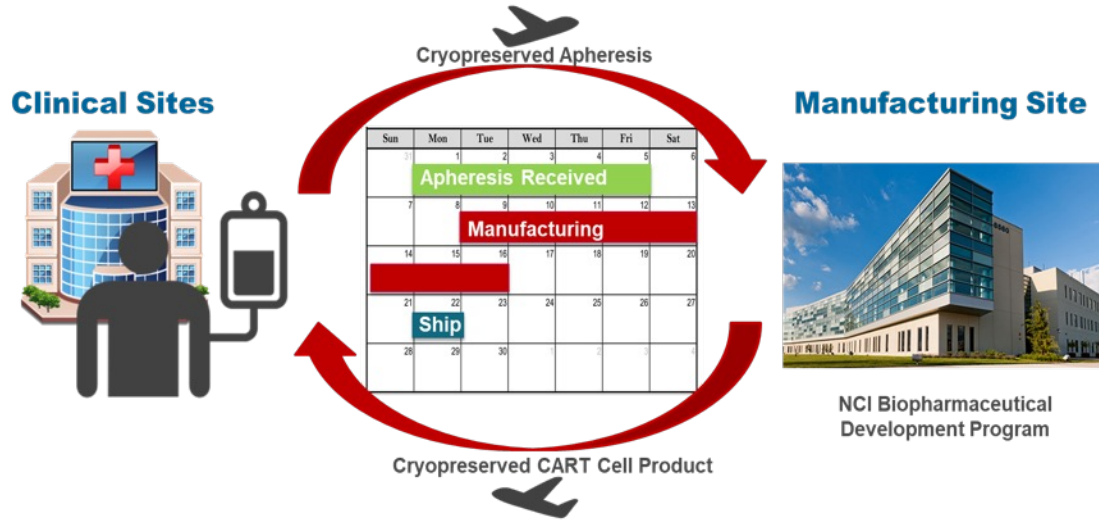
NCI established the BDP (formerly MARP) in 1993 to:

- Provide specialized and unique technical expertise and services
- Perform feasibility studies of novel candidates
- Develop manufacturing processes and assays
- Conduct GMP manufacturing, filling, testing, and release
- Generate and submit FDA and international regulatory filings
- Conduct technology transfer to commercial entities

BDP Website – <https://frederick.cancer.gov/Science/Bdp/>

- >300 SOPs, manufacturing, testing, quality system, and training documents FREE to download
- *Sponsors Guide to Regulatory Submissions for an Investigational New Drug* FREE to download

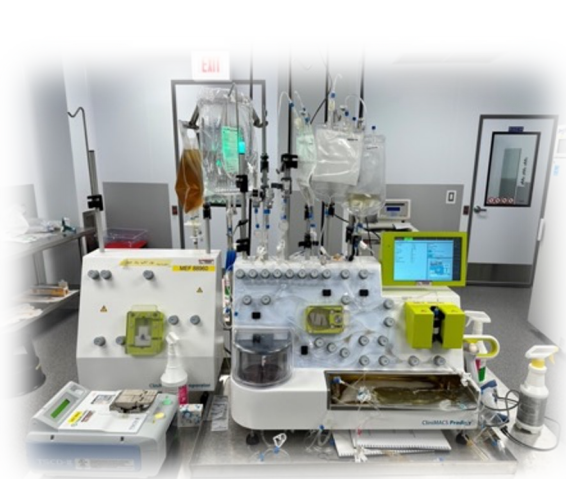
NCI Leverages BDP to Address Cell Therapy Manufacturing Challenges



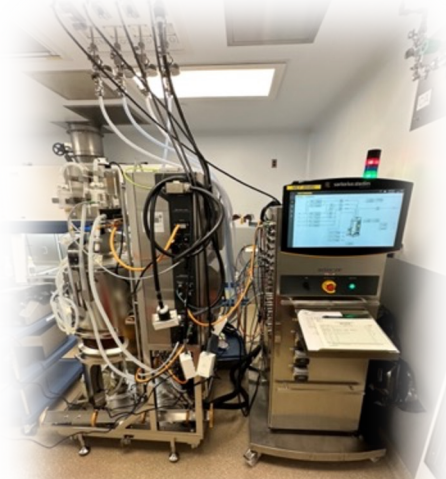
- Closed manufacturing systems
- Aseptic process qualification / validation
- cGMP lenti- and retroviral production
- Standardized product testing and rapid product release
- Shipping validation and product chain logistics to support multi-center trials

Cell Therapy GMP Expansion at the Frederick National Lab

FUTURE ADDED TECHNOLOGY	ADDED FACILITY	ADDED CAPACITY
<ul style="list-style-type: none">• G-Rex (disposable flask) and Wave manufacturing platforms• CRISPR-based gene editing	<ul style="list-style-type: none">• 3 new GMP suites: Q2 2023• Freezer farm: Q1 2023	~ 12 cell therapy products/month ~ 8 virus vector campaigns/year <ul style="list-style-type: none">• Controlled storage for cell and virus products



Prodigy System



**Vector production
bioreactor**



**Biobubble with Wave
bioreactor**

QUESTIONS FOR OUR TEAM

Funding Opportunities

New Drug Development Resources

Stepping Stones Program

Immuno-oncology Initiatives & Services

Sundar Venkatachalam, PhD
Chief, Preclinical Therapeutics Grant Branch

Rose Aurigemma, PhD
Associate Director, DTP, DCTD, NCI

Sharad Verma, PhD
Special Assistant to the Associate Director

Marc Ernstoff, MD
Chief, ImmunoOncology Branch



**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol