Division of Cancer Treatment and Diagnosis (DCTD)

Presented By: Michael Difilippantonio, Ph.D.

NIH NATIONAL CANCER INSTITUTE

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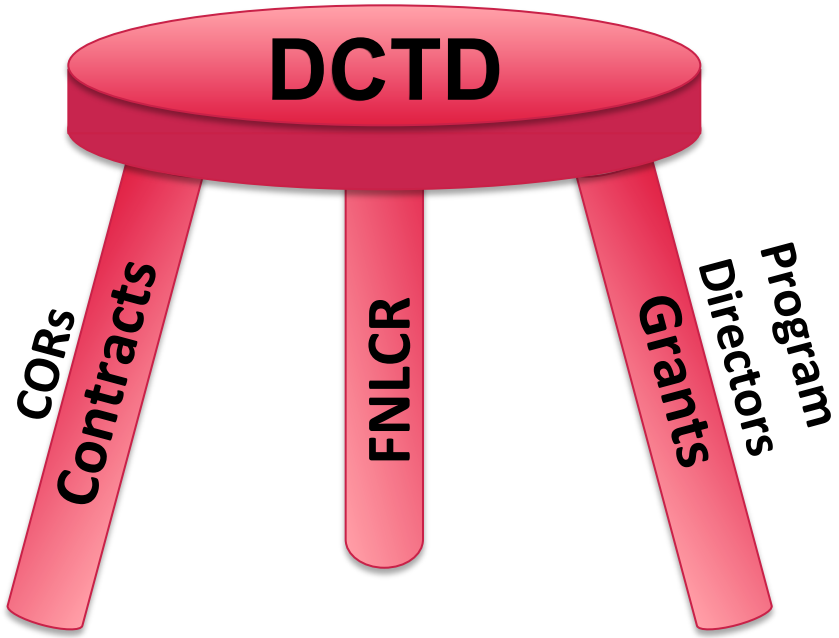
Overview of DCTD

Mission and Purpose

To improve the lives of cancer patients by enabling the scientific transition from basic research to advanced clinical studies of cancer diagnostics and therapeutics.



Division of Cancer Treatment and Diagnosis (DCTD)

James Doroshow, MD – Director
Toby Hecht, PhD – Deputy Director

Biometrics Research Program (BRP) – Richard Simon, D.Sc.

- ***Biostatisticians, Clinical Trial Design, Data Analysis***

Cancer Diagnosis Program (CDP) – Barbara Conley, MD

- ***Clinical Assays (diag., prog., stratification), Biospecimens***

Cancer Imaging Program (CIP) – Paula Jacobs, PhD

- ***Imaging Modalities (PET, SPEC, NMR, etc)***
- ***Applications (diag., surgical margins, Tx response, drug targeting)***

Cancer Therapy Evaluation Program (CTEP) – Jeff Abrams, MD

- ***Phase 1 – Phase 3 clinical trials, invest. agents, new indications, combination studies***

Division of Cancer Treatment and Diagnosis (DCTD)

Developmental Therapeutics Program (DTP) – Jerry Collins, PhD

- ***Drug discovery, pre-clinical development (pharm., ADMET, chem., formulation, PD, Natural Products, biologics, etc)***

Radiation Research Program (RRP) – Norman Coleman, MD

- ***Technical advances, radiation / drug synergy***

Translational Research Program (TRP) – Toby Hecht, PhD

- ***SPORE Grants***

Office of Cancer Complimentary and Alternative Medicine (OCCAM) – Jeffrey White, MD

- ***Traditional Chinese medicine (TCM), herbal, yoga, meditation, etc.***

DCTD Contributions to FDA Approved Drugs

FDA Approved Therapeutics Developed with Assistance from NCI in the Past 15 Years

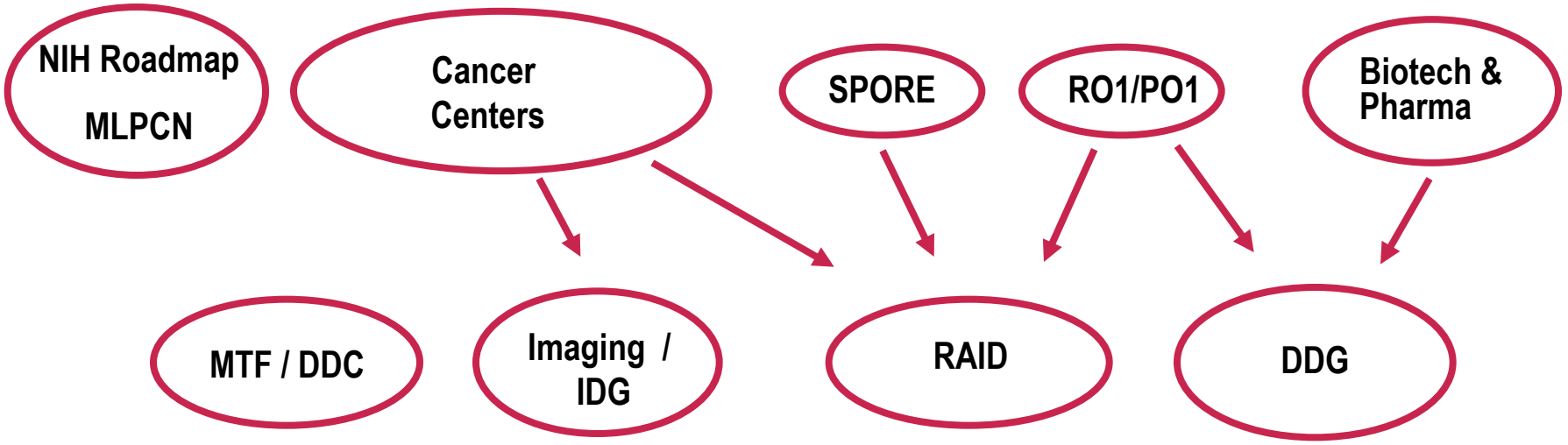
Year	Agent	Role of NCI	Mechanism of Support
2015	Dinutuximab (ch14.18 ab)	Produced antibody; conducted pivotal trials	FNLCR biologics facility; NCI Cooperative Grant
2010	Sipuleucel (Provenge®)	Oversaw production	National Cooperative Drug Discovery Grant
2010	Eribulin	Natural product discovery; screening; formulation of clinical product; animal efficacy testing; clinical candidate selection; first-in-human trial	FNLCR labs; Analytical, Formulation, PK, Toxicology contracts; RO1 grant; U01 grant
2009	Pralatrexate	RAID project; NCI produced GMP bulk drug	GMP bulk drug mfg. contract
2009	Romidepsin (Depsipeptide)	Developed safe human dosing schedule in large animals; PK and Tox; produced drug; conducted first-in-human trials in NIH CC	FNLCR animal facilities; Pharmacology, Toxicology, Drug Production contracts
2004	Cetuximab	Produced first lots for imaging and chimeric clones	Contracts; Cooperative Drug Discovery Grant
2004	5-Azacytidine	Pre-clinical molecular pharmacology; produced pre-clinical / clinical drug supply; conducted pivotal trial	FNLCR Labs; Contracts; U01 Grants
2003	Bortezomib	Extensive analog screening; MOA and PD studies; PK & Tox; clinical formulation	FNLCR Labs; Formulation, PK, Toxicology contracts
2000	Temozolomide	Scale up synthesis and clinical formulation	Bulk drug and Formulation contracts

Pivotal NCI/CTEP-sponsored Group Trials Contributing to FDA Approved Indications for New Oncology Agents

Year	Agents	Group	Company
2009	Depsipeptide (Istodax®)	ECOG, Intergroup	Gloucester Pharmaceuticals, Inc.
2007	Lapatininb (Tykerb®) Deoxycoformycin (Pentostatin®)	NCCTG, CALGB, Intergroup	GSK Bedford Labs
2006	Dasatinib (Sprycel®) Sunitinib (Sutent®) Pegaspargase (Oncaspar®)	SWOG, Intergroup ECOG, Intergroup	BMS Pfizer Enzon
2005	Lenalidomide (Revlimid®) Nelarabine (Arranon®) Sorafenib (Nexavar®)	ECOG, Intergroup COG, CALGB ECOG, Intergroup	Celgene GSK Bayer / Onyx
2004	5-Azacytidine (Vidaza®) Bevacizumab (Avastin®) Erlotinib (Tarceva®) Taxotere (Doxetaxol®)	CALGB ECOG. Intergroup NCCTG, Intergroup SWOG	Celgene Genetech Genentech / OSI Sanofi-Aventis
2002	Oxaliplatin (Eloxitin®)	NCCTG, Intergroup	Sanofi-Aventis
2001	Imatinib mexylate (Gleevec®) Letrozole (Femara®)	COG, SWOG NCIC, Intergroup	Novartis Novartis
2000	Arsenic trioxide (Trisenox®)	CALGB	Cell Therapeutics

NCI Experimental Therapeutics (NExT) Program: One Goal, Several Mechanisms

Transformation of the NCI Therapeutics Pipeline



The NCI Experimental Therapeutics (NExT) Pipeline:
Target discovery through early stage clinical trials

Drug Discovery | **Early Drug Development**

Harmonize Activities into Single Pipeline

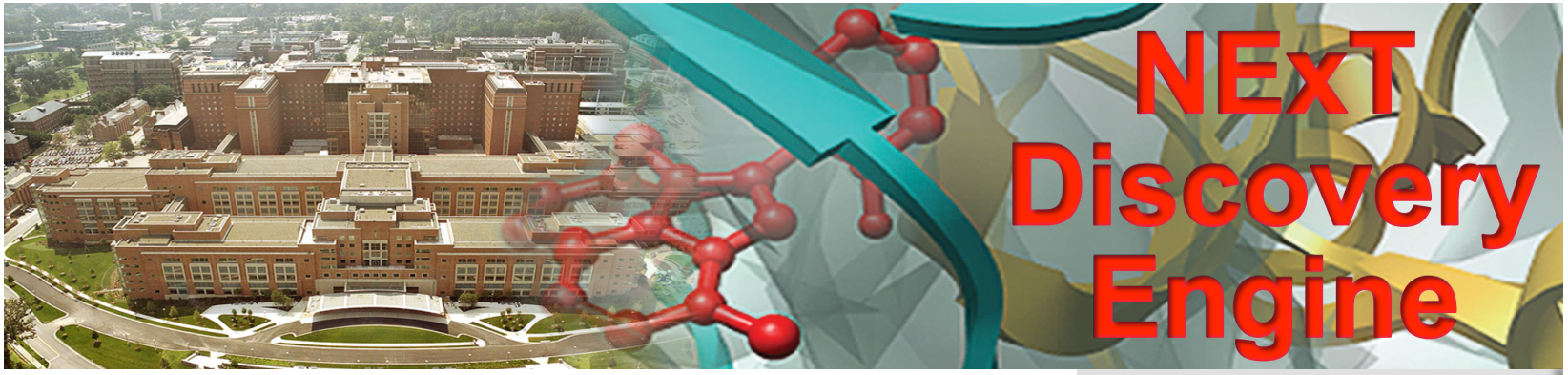
NOT A GRANT PROGRAM

- ***Clear path to clinic/patient benefit***
- ***Provides access to NCI resources and drug development expertise***
- ***Integrates a variety of prior decentralized and uncoordinated programs***
- ***Simple application***
- ***Applicant PI is actively involved since it is their project***

NExT Resources Currently Support

- ***Investigational drugs, biologics and NP's***
- ***Investigational imaging agents***
- ***Academic, biotech, pharma and government projects***
- ***HTS, Hit-to-Lead, Lead Optimization, Clinical Candidate, Phase 0, 1 and 2 clinical trials***

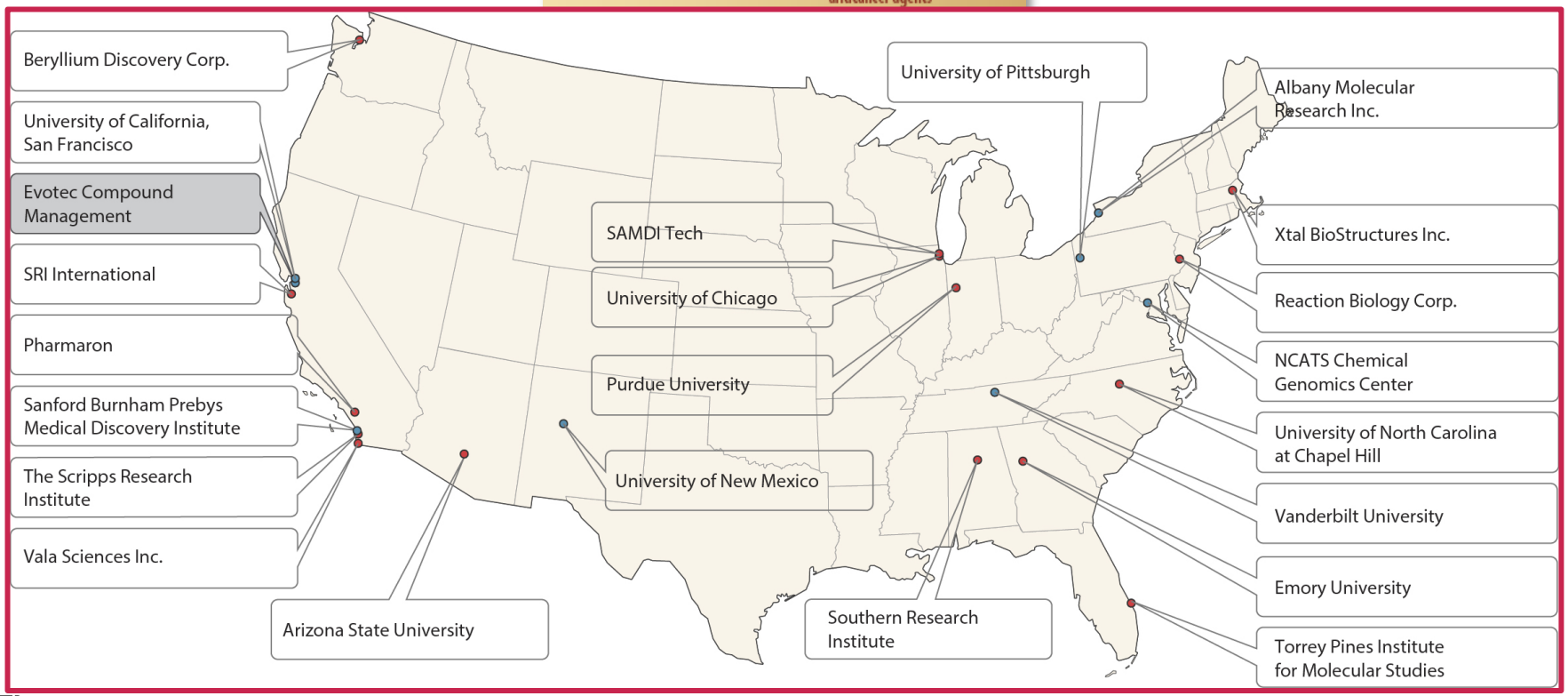
NOT basic research

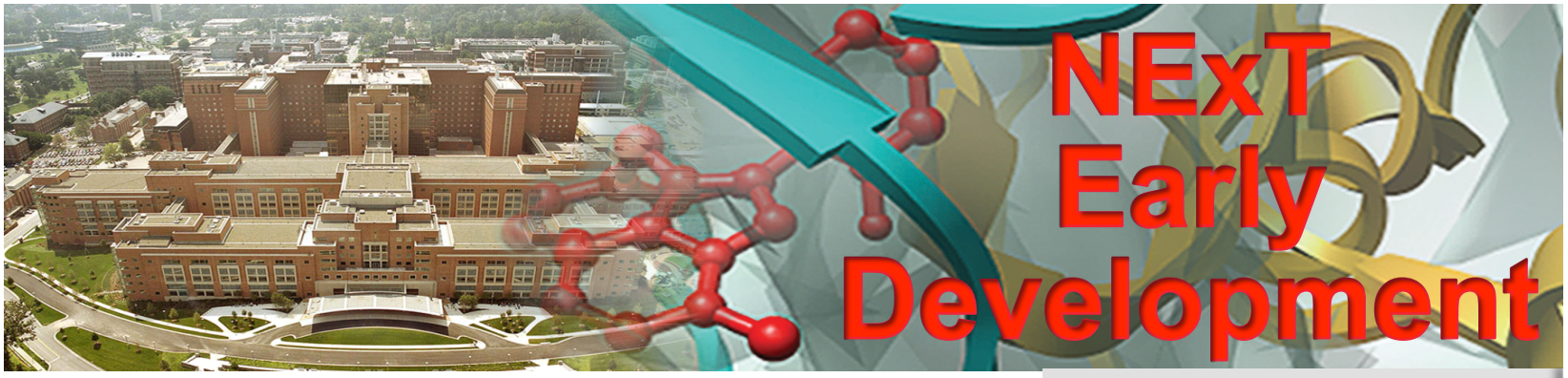


FNLCR sub-contracts

Chemical Biology Consortium

Accelerating the discovery and development of new anticancer agents



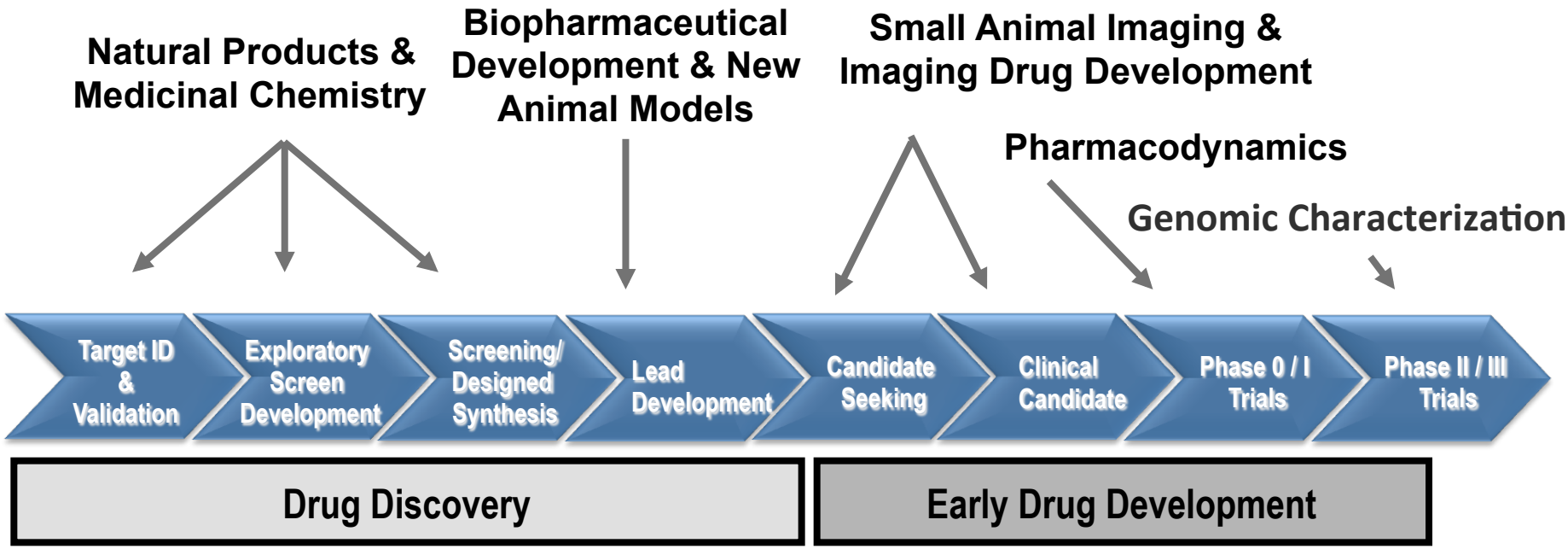


NCI contracts

- *PK/PD Modeling*
- *Tox/Safety Pharmacology*
- *GMP Scale-Up*
- *Imaging supported by Cancer Imaging Program*
- *Development and validation of PD assays during preclinical stages is supported by the Pharmacodynamics Assay Development & Implementation Section (PADIS) and during clinical stages by the National Clinical Target Validation Laboratory (NCTVL).*
- *Clinical Assay Development Program (CADP) development and validation of clinical assays (including diagnostic).*

- *Currently sponsors over 100 INDs*
- *Approx. 11,000 registered investigators at over 3,300 institutions*
- *Over 750 active protocols*
- *150-250 new protocols/year*
- *Approx. 30,000 patients accrued/year*
- *Over 80 collaborative agreements (CRADAs, CTAs, and CSAs) with pharmaceutical companies (Collaborators)*

Role of FNLCR in NCI Therapeutics Development Program



Targets

- High risk targets
- Investigational imaging agents
- Investigational drugs, biologics, natural products
- Unmet medical needs (rare cancers, pediatric tumors)
- Academic & Biotech & Pharma projects

Therapeutics

What are we looking for?

- ***Program Directors (pre-clinical development)***
  - ***Immunotherapy***
  - ***Molecular Pharmacology***
- ***Program Directors (clinical development)***
  - ***Clinical Assays***
  - ***Clinicians***

**** Supervisory and non-supervisory positions available***

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