



STAFF HIGHLIGHT - Jerry Collins, PhD



Jerry Collins, PhD

After four decades of distinguished government service at NIH and FDA, Dr. Jerry Collins, Associate Director, Developmental Therapeutics Program (DTP), DCTD, retired at the end of December 2020. Jerry is widely recognized as an internationally renowned expert in the field of cancer drug pharmacokinetics (PK) and metabolism, and one of the foremost cancer clinical pharmacologists in the world. While his retirement creates a critical gap for us, we are deeply grateful that he continues to offer his expertise to NCI as a Special Volunteer in DCTD. In his own words below, Jerry describes his research career and the path that led him to NCI.

In 1968, I was hired by the FDA Bureau of Science as a chemist-in-training, measuring herbicides in vegetables - a cousin of PK. I received a Ph.D. in chemical and biochemical engineering from the University of Pennsylvania in 1976, the Bicentennial Year. I measured and modeled flux of inert gases in human and animal subjects. One of the gases, nitrous oxide, is still in use as part of anesthesia cocktails.

My next move was to Johns Hopkins University for a postdoc in PK. The Division of Clinical Pharmacology had active research programs in both clinical and nonclinical research. They also wanted more assistance with analysis of the data. In 1977, my appointment at Hopkins was expanded.

I was initially appointed as a Visiting Researcher and then as a career employee in 1980 at NIH's Chemical Engineering Section (currently, part of NIBIB). These arrangements included research in the Toxicology Lab at the Division of Cancer Treatment (DCT), a predecessor of DCTD, and projects in the DCT Clinical Pharmacology Branch in the Clinical Center. These projects began life-long associations with the next generations of leadership in cancer therapeutics. From the start, it was clear that these folks were scholarly and very energetic. In particular, I was warned not to block the hallway where Gershon Locker and Jim Doroshov were constantly on the move.

In 1983, I was appointed as the first Chief of the Pharmacokinetics

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Section in DCT. These multiple joint appointments were highly productive, and I published 100 papers in my first 10 years at NIH. My work included assisting Vince DeVita on intraperitoneal chemotherapy (“belly bath”), and it expanded into intra-arterial drug delivery models and drug distribution among brain compartments. I led the “Blood Level Working Group,” which developed a clear approach to comparing clinical and preclinical toxicology. In addition to these cancer clinical trials, the PK lab worked with the first class of useful therapies for patients with HIV/AIDS. We had the privilege of analyzing plasma samples from the first two patients in the world to receive AZT (zidovudine). My continued interest in halogenated pyrimidines as radiosensitizers and cytotoxics began in this timeframe.

In 1988, I received an offer from FDA that I could not refuse. My first assignment was to create a Clinical Pharmacology Lab of 20 persons in new space. Within 2 years, I was promoted to Director of the Office of Research Resources in the Center for Drug Evaluation at FDA. This organization included more than 200 federal staff and close involvement in Regulatory Policy in various areas. After 5 years in that position, I had the opportunity to return to the Clinical Pharmacology Lab. My administrative work was reduced, so I was able to write the first Regulatory Guidance on the use of metabolism in guiding early drug development as a tool to reduce the rising numbers of adverse drug-drug interactions. As an example, our lab at FDA offered to help NCI with metabolic issues for paclitaxel as it was getting close to an NDA filing. We identified the structure of the primary metabolite, determined that it had far less total bioactivity than paclitaxel itself, and corrected the misconception that CYP3A was the dominant pathway. Combined with our collaborative clinical PK studies with NCI, we established that there was no probable need for genotyping. I also had a major role in creating the first Regulatory Guidance on first-in-human studies in a framework of reduced regulatory requirements for first-in-human. Subsequently, this work became one of the pillars of the concepts known as “phase zero” clinical trials.

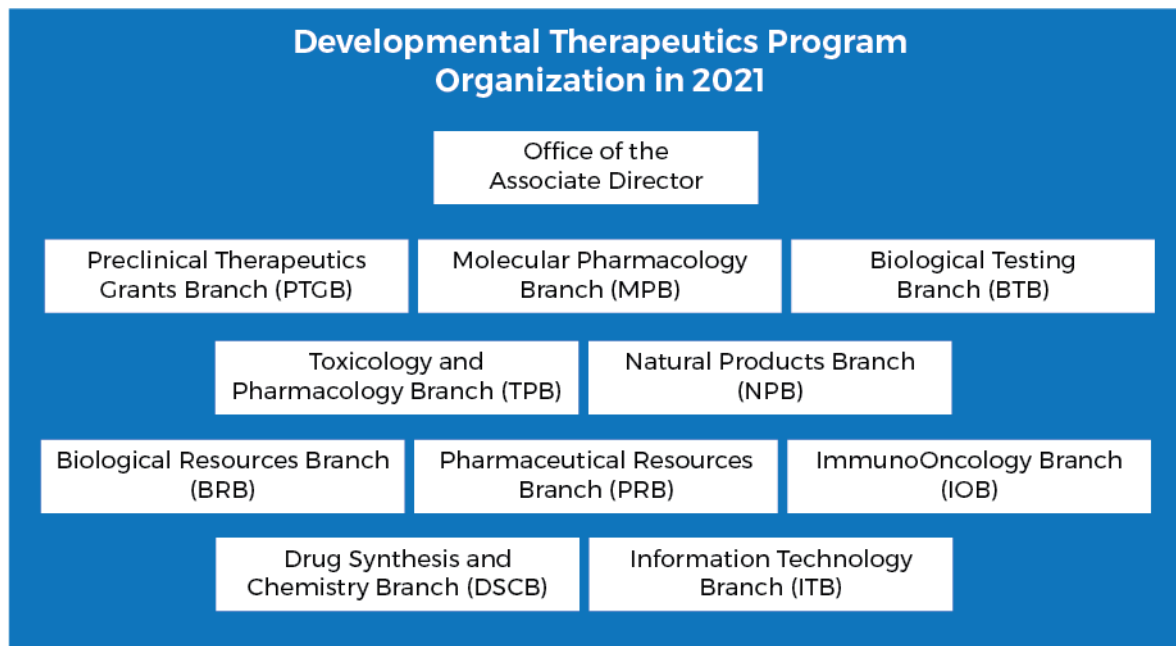
Although I am not attracted to full-time academic work, it is very stimulating to have interactions with faculty and students. Thus, I surely learned as much from my adjunct appointments as the audience learned from me. Georgetown, Johns Hopkins, George Washington, and Uniformed Services University form a distinctive range of environments for these part-time experiences.

As time flew by, my colleagues and family would occasionally ask if I was evaluating any other jobs. Usually, I just said “no” because I thought that was the most likely to succeed. However, in deeper conversations with my family, I said that “there is one other possibility.” Based upon my experience at both FDA and NCI, I thought that the Associate Director (AD) of DCTD was the one position in my varied background where I might be able to contribute the most – but I noted that AD positions do not turn over very often, and there would be many factors related to timing.

Sure enough, the vacancy occurred, and I was appointed as DTP’s AD in 2005. After 15 years, I have never regretted this decision; however, I am less able to effectively cover the ever-growing non-scientific tasks. I know that various papers could be written if I had more time, so due to the steady e-mail queue and my desire for a change, I am retiring as AD, DTP. I am strongly supportive of scientists who can also work in administration, but after 35 consecutive years as a manager, it is time for others to manage.

There is one important caveat of my retirement - there is no chance that I want to leave NCI. I will serve as a “Special Volunteer” not only to write the papers that are a couple of years behind, but also to continue to contribute to the ongoing work of the PK lab, the DCTD Developmental Therapeutics Clinic, DTP’s Natural Products Branch, and those development project teams in the NCI Experimental Therapeutics (NExT) Program for which I could be useful. I can also continue to serve as a member of various FDA advisory committees. *This will not be a passive retirement.*

SPOTLIGHT - The Developmental Therapeutics Program: The Last 15 Years and the Future of Cancer Drug Discovery and Development



The retirement of Dr. Jerry Collins in December 2020 marks a big change for the [Developmental Therapeutics Program \(DTP\)](#). Dr. Collins was appointed as DTP's Associate Director in 2005 and oversaw the growth of the program over the past 15 years.

When Dr. Collins joined DTP, the program consisted of nine branches, with an emphasis on supporting the development of small molecules and biologics as anticancer therapeutics. Since then, DTP's organization and focus have evolved, with the addition of two new branches, expanded capabilities for distribution and screening of natural products, and the establishment of the Patient-Derived Models Repository for the identification of active anticancer agents.

Establishment of the Molecular Pharmacology Branch (MPB)

MPB was established in 2010 to improve the treatment of recalcitrant, rare, and neglected cancers. MPB works towards this goal by:

- operating several labs with state-of-the-art screening and molecular characterization capabilities at Frederick National Laboratory for Cancer Research (FNLCR)
- identifying novel therapeutic targets, screening new agents, and discovering potential therapeutic combinations

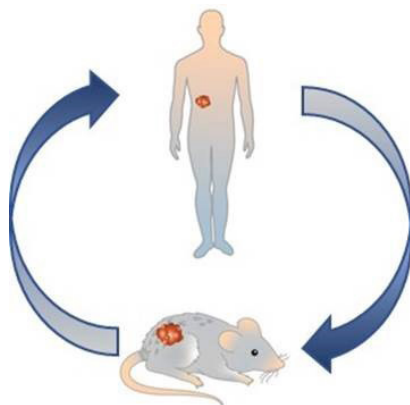
Screening Efforts for Anticancer Agent Discovery

DTP facilitates anticancer drug discovery by maintaining various repositories and screening services.

- MPB operates the [Target Validation and Screening Laboratory](#), which has developed in-house expertise, automation, instrumentation, and information technology infrastructure to carry out screening campaigns on large chemical libraries.

SPOTLIGHT... continued

- BTB has developed the NCI [Patient-Derived Models Repository \(PDMR\)](#), which offers patient-derived xenografts (PDXs) and patient-derived cell cultures (PDCs) to allow for screening of compounds for indications of preclinical efficacy.



- MPB is working to develop an automated high-throughput organoid screen using organoid cultures developed by the PDMR.
- MPB and ITB are collaborating to develop new software (expected in 2021) for the [NCI-60 Screening Lab](#), which will increase the throughput, data collection, storage, and analysis capabilities for a new 384-well based NCI-60 production pipeline.

Establishment of the Immuno-Oncology Branch (IOB)

Recognizing the explosion of growth in the cancer immunotherapy field, DTP established IOB in December 2016 to support immunotherapy-related projects. IOB is responsible for:

- managing an immuno-oncology grants portfolio that focuses on the development and evaluation of therapeutic approaches that utilize the immune system for the treatment of cancer
- developing various immunotherapy resources and funding initiatives to advance immunotherapy-related projects both within NCI and in the extramural research community

Production of GMP Products for Investigators

BRB has produced and released many GMP products for investigators through the Biopharmaceutical Development Program (BDP) at FNLCR, including the following since 2005:

- 30 investigational product lots (20 unique products)
- 13 master/working cell banks
- 7 master virus banks
- 4 product diluent/placebos

Support of Immune Cell Therapy Research

IOB and BRB have collaborated in a major initiative to support the development of cell-based therapies for cancer, including:

- providing [manufacturing of clinical grade vector and cell therapy products](#) through the BDP for intramural and extramural investigators conducting phase 1/2 cell immunotherapy trials
- holding the [2nd NCI Workshop on Cell-Based Immunotherapy for Solid Tumors](#) in December 2020 to discuss challenges in the cell therapy field and identify additional ways in which NCI can support the research community



Establishment of Natural Product Library

NPB launched the [NCI Program for Natural Product Discovery \(NPNDP\)](#) in 2018. This initiative aims to generate pre-fractionated extracts from natural product crude extracts to enable high-throughput targeted screening, while also developing integrated analytical resources for structure elucidation of biologically active natural products. The NPNDP has:

- produced ~440,000 pre-fractionated extracts
- plated ~18,000,000 wells on more than 28,000 384-well plates for distribution
- made 326,000 pre-fractionated natural product samples available to the public
- shipped more than 4,000,000 screening samples to the extramural community

Support of Discovery and Development Projects through the NExT Program

The [NCI Experimental Therapeutics \(NExT\)](#) Program was established in 2009 to provide extramural investigators with access to NCI resources and expertise in therapeutics development. The NExT Program receives support from various DTP branches, including:

- DSCB - provides synthetic and medicinal chemistry resources and expertise for NExT projects
- BTB - performs efficacy testing for NExT drug candidates in preclinical models
- TPB - provides pharmacology expertise and drug safety data to enable clinical trials. TPB supported 15 NExT projects in 2020.

- PRB - manufactures NExT drug candidates for early-stage clinical trials. There are currently 10 clinical products in the PRB portfolio.
- BRB - manufactures antibodies and other biologics in the NExT portfolio for preclinical and early-stage clinical studies

The DTP Grant Portfolio

DTP's extramural grants portfolio covers various aspects of the discovery and development of small molecule and biologic anticancer therapeutics, such as drug discovery screens, medicinal chemistry, mechanism of action studies, and testing in preclinical models. DTP supported over 800 active awards in FY 2020.

- The PTGB portfolio included 635 active awards in FY 2020, the largest portion of DTP grants. PTGB supports discovery, development, and evaluation of anticancer agents, with an emphasis on small molecules.
- PTGB staff have also led or co-led specific topics within the [NCI Provocative Questions initiative](#) during the past four years, with targeted funding opportunities for topics such as treatment-induced cell lineage plasticity and adverse effects of cancer therapy.
- IOB and BRB grant portfolios focus on the development and evaluation of immunotherapeutic strategies and other biologic therapies.

NEWS ABOUT DCTD PROGRAMS AND ACTIVITIES

Program Updates

The Cancer Imaging Program (CIP) Joins the Cancer Diagnosis Program (CDP) to Support Cancer Moonshot Biobank



The Biorepositories and Biospecimen Research Branch (BBRB) of CDP launched the [Cancer MoonshotSM Biobank](#) in September 2020 with the goal of accelerating research on cancer drug resistance and sensitivity through the collection of donated biospecimens and data from over 1,000 patient participants. Biospecimens and

medical information will be collected from patients at multiple timepoints over the course of their cancer treatment to help researchers better understand why some drugs work, or do not work, over time.

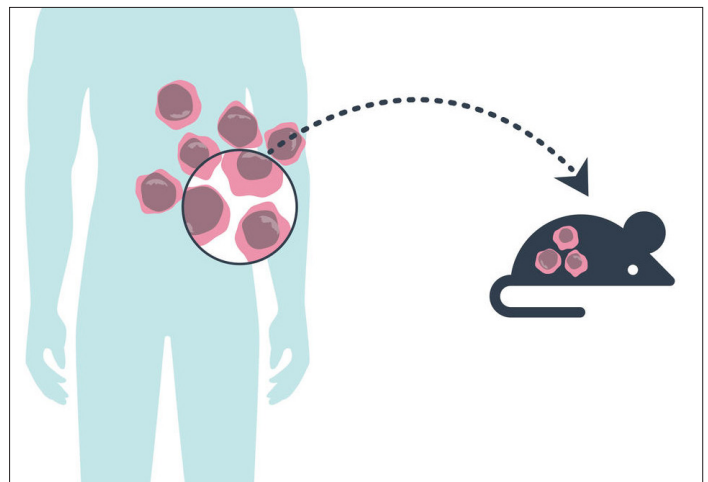
Radiological and digital pathology images will also be collected and hosted with support from CIP, which is coordinating the collection through services from the Imaging and [Radiation Oncology Core](#) of the NCTN and [The Cancer Imaging Archive \(TCIA\)](#). TCIA will host the imaging data and provide direct links to view the images from the Biobank's online catalog. The imaging data managed by CIP will add valuable information to the biospecimens and clinical data, making the Biobank an important resource for the cancer research community. Information on the Biobank is available in both [English](#) and [Spanish](#).

The Patient-Derived Xenograft Network (PDXNet) Publishes Research on Genomic Integrity of PDX Models

Crucial new research published in *Nature Genetics* ([Woo, 2021](#)) confirms that patient-derived xenograft (PDX) mouse models largely retain the genetic integrity of the original patient tumor. This collaborative study from the Cancer MoonshotSM-supported [Patient-derived Xenograft Network \(PDXNet\)](#) provides evidence to support the use of PDX models in cancer research studies.

PDXNet comprises five U.S. research institutions and aims to coordinate large-scale development and preclinical testing of targeted therapeutic agents in PDX models to advance precision medicine. Read more about the recent publication and its impact on cancer research in this [NCI Cancer Currents blog](#),

including input from Jeff Moscow, CTEP, related to the contribution of PDX models to cancer drug development.



Updates on NCI's Initiative to Stimulate CAR T-Cell Production and Immunotherapy Research



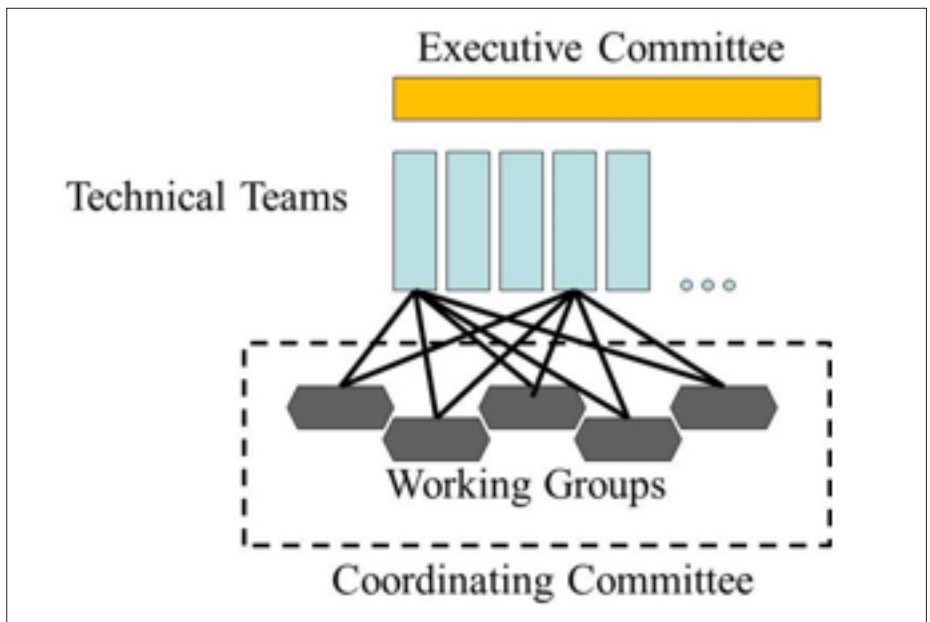
for use in multi-site clinical trials. Some background information on this initiative is provided in a comprehensive [Cancer Currents blog post](#), a [DCTD News story](#) on how investigators can request cell therapy and viral vector production at NCI, and a summary of the [2nd NCI Workshop on Cell-based Immunotherapy for Solid Tumors](#), which convened last December to understand challenges and future directions in the cell therapy field. Now, NCI has a new video entitled ["Manufacturing CAR T Cells to](#)

The Developmental Therapeutics Program, the Center for Cancer Research, and the Frederick National Laboratory for Cancer Research are collaborating to manufacture CAR T-cells

[Accelerate Cancer Immunotherapy Research"](#) to explain the process and current and future efforts in CAR T-cell therapy.

The 2021 Quantitative Imaging Network Annual Meeting

The Quantitative Imaging Network (QIN) promotes research, development, and clinical validation of quantitative imaging tools and methods for the measurement or prediction of tumor response to therapies in clinical trial settings. The QIN's overall goal is to facilitate clinical decision making. The Cancer Imaging Program held its Annual Meeting of the QIN in January. This year's meeting focused on translation of developed quantitative imaging tools and methods into clinical trials. [See the meeting agenda and summary.](#)



Publications and Outreach

Publications

Xiao Y, Roncali E, Hobbs R, et al. [Toward Individualized Voxel-Level Dosimetry for Radiopharmaceutical Therapy](#). *Int J Radiat Oncol Biol Phys*. 2021 Mar 15;109(4):902-904.

Monjazeb AM, Giobbie-Hurder A, Lako A, et al. [A Randomized Trial of Combined PD-L1 and CTLA-4 Inhibition with Targeted Low-Dose or Hypofractionated Radiation for Patients with Metastatic Colorectal Cancer](#). *Clin Cancer Res*. 2021 Feb 10. Online ahead of print.

Buchsbaum JC, Coleman CN, Espey MG, et al. [FLASH Radiotherapy: New Technology Plus Biology Required](#). *Int J Radiat Oncol Biol Phys*. 2021 Feb 3. Online ahead of print.

Herrick WG, Kilpatrick CL, Hollingshead MG, et al. [Isoform- and Phosphorylation-specific Multiplexed Quantitative Pharmacodynamics of Drugs Targeting PI3K and MAPK Signaling in Xenograft Models and Clinical Biopsies](#). *Mol Cancer Ther*. 2021 Feb 3. Online ahead of print.

Wang L-B, Karpova A, Gritsenko MA, et al. [Proteogenomic and Metabolomic Characterization of Human Glioblastoma](#). *Cancer Cell*. 2021 Feb 2. Online ahead of print.

Kalinsky K, Hong F, McCourt CK, et al. [Effect of Capivasertib in Patients with an AKT1 E17K-Mutated Tumor: NCI-MATCH Subprotocol EAY131-Y Nonrandomized Trial](#). *JAMA Oncol*. 2021 Feb 1;(2):271-278.

Huang C, Chen L, Savage SR, et al. [Proteogenomic Insights into the Biology and Treatment of HPV-negative Head and Neck Squamous Cell Carcinoma](#). *Cancer Cell*. 2021 Jan 7. Online ahead of print.

Quinn DI, Tsao-Wei DD, Twardowski P, et al. [Phase II Study of the Histone Deacetylase Inhibitor Vorinostat \(Suberoylanilide Hydroxamic Acid; SAHA\) in Recurrent or Metastatic Transitional Cell Carcinoma of the Urothelium - an NCI-CTEP Sponsored: California Cancer Consortium Trial, NCI 6879](#). *Invest New Drugs*. 2021 Jan 6. Online ahead of print.

Kunos CA, Mankoff DA, Schultz MK, et al. [Radiopharmaceutical Chemistry and Drug Development-What's Changed?](#) *Semin Radiat Oncol*. 2021 Jan; 31(1):3-11.

Woo XY, Giordano J, Srivastava A, et al. [Conservation of Copy Number Profiles During Engraftment and Passaging of Patient-derived Cancer Xenografts](#). *Nat Genet*. 2021 Jan;53(1):86-89.

Nielsen TO, Leung SCY, Rimm DL, et al. [Assessment of Ki67 in Breast Cancer: Updated Recommendations from the International Ki67 in Breast Cancer Working Group](#). *J Natl Cancer Inst*. 2020 Dec 28. Online ahead of print.

NCI Cancer Currents Blog Posts

[PDX Mouse Models Are Reliable Stand-Ins for Human Tumors, Study Finds](#); Jeff Moscow, MD, CTEP; February 2, 2021.

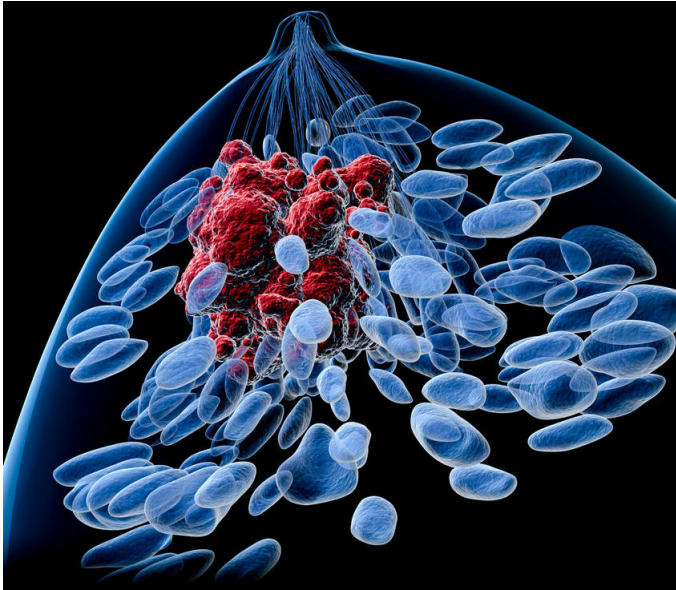
[Trial Tests Abemaciclib As New Option for Early-Stage Breast Cancer](#); Larissa Korde, MD, MPH, CTEP; January 6, 2021.

Interviews and Press

[Are COVID-19 Vaccines Safe for Cancer Patients? Here Is What Cancer Experts Say](#); CNN Health; Elad Sharon, MD, MPH, CTEP; February 9, 2021.

[Use of Commercial Genomic Testing for Prostate Cancer 'Highly Variable' in the United States](#); Lyndsay Harris, MD, CDP; January 12, 2021.

[Some Postmenopausal Women with Breast Cancer May Forgo Chemotherapy](#); NCI Press Release; Larissa Korde, MD, MPH, CTEP; December 9, 2020.



New DCTD Funding Opportunity and Funding Information

Title	Announcement Number	Open Date	Expiration Date	Activity Code
Notice of Special Interest (NOSI): Administrative Supplements to Support Collaborations with the NCI-supported Drug Resistance and Sensitivity Network (DRSN)	NOT-CA-21-034	April 4, 2021	April 5, 2021	Admin Supp