NIH NATIONAL CANCER INSTITUTE

pipeline news

February 2019

DCTD Division of Cancer Treatment and Diagnosis

Staff Highlight: Barbara Mroczkowski, PhD

Barbara Mroczkowski, PhD, Special Assistant to the Director, Division of Cancer Treatment and Diagnosis, Head, NCI Experimental Therapeutics (NExT) Program

What is your research background, and how did it influence your decision to work at NCI?

I have devoted my career in medical research to leveraging knowledge from basic science to provide insights into disease pathogenesis and have focused on translating these insights into improved treatments for human disease. I received my PhD in Genetics from the University of Connecticut and did postdoctoral work with Dr. Stanley Cohen, Distinguished Professor and Nobel Laureate, at Vanderbilt School of Medicine. This was an exciting time in science because the field of oncogenes was just starting to thrive, and I was working on the epidermal growth factor receptor (EGFR) and tyrosine kinases. As a faculty member in the Department of Biochemistry at Vanderbilt School of Medicine, I participated in seminal studies in the field of signal transduction that led to the elucidation of the pivotal role of protein kinases in signal transduction and as targets for therapeutic intervention. I left academia in 1993 to join a small start-up company, Agouron Pharmaceuticals. We learned how to do everything at this drug discovery biotech – structure-based drug discovery, cloning targets, etc. At Agouron, we developed Viracept, one of the first HIV protease inhibitors approved by the FDA. I led a productive team of scientists that advanced targeted agents into early phase clinical trials, many of which received FDA approval. After Agouron Pharmaceuticals was acquired by Pfizer, I worked there as part of the multi-site oncology team and was the project lead on tyrosine kinase inhibitors that were commercially viable. It was a valuable experience and a great learning opportunity because I saw the drug discovery to development transition at a large pharmaceutical company.

My time in industry was productive and gratifying in many ways, but I wanted more freedom to take scientific risks to address unmet medical needs, especially in

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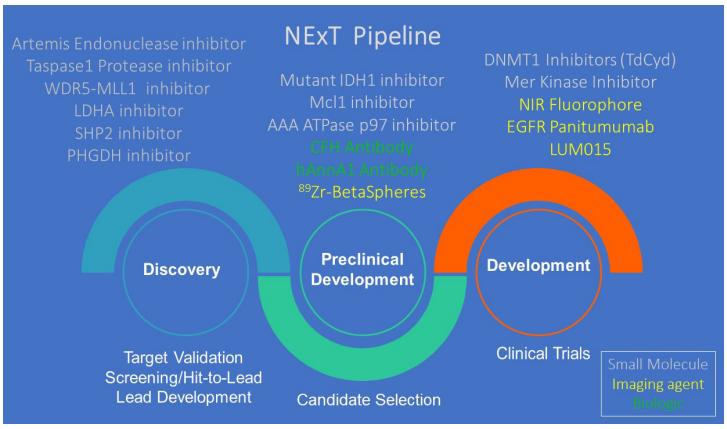
diseases with no monetary value. In 2007, NCI offered me the opportunity to participate in the conceptualization and implementation of a pharma/biotech pipeline that was not constrained by business decisions and that was not risk-averse. The NCI Experimental Therapeutics (NExT) Program, which was launched in the Fall of 2009, was the result of a two-year implementation effort to consolidate all drug discovery and development resources and expertise in DCTD into a single pipeline.

What is the mission of the NExT Program, and how does NExT work?

The mission of the NExT Program is to advance clinical practice and bring improved therapies to patients with cancer by supporting the most promising new drug discovery and development projects. NExT provides resources to domestic and international researchers in academia, non-profit, government, and industry for projects focused on developing therapies for unmet needs that are not adequately addressed by the private sector.



The NExT Program combines DCTD's extensive expertise in cancer treatment with the dynamic intramural research resources of the Center for Cancer Research and the NIH Clinical Center. The discovery engine of the program is the Chemical Biology Consortium (CBC), which is a collaborative network of specialized and comprehensive screening and chemistry centers. The CBC has grown from 11 centers at its inception to 23 currently, with a broad range of capabilities that includes high-throughput screening, bioinformatics, medicinal chemistry, and structural biology to support early-stage drug discovery. Subsequent late-stage, IND-enabling studies leading to first-in-human clinical trials of promising new chemical and biological entities utilize the resources of NCI's Developmental Therapeutics Program. The NExT Program also develops molecular imaging agents with support from the NCI Cancer Imaging Program and proof-of-mechanism pharmacodynamic assays through the efforts of DCTD's Pharmacodynamic Assay Development and Implementation Section (PADIS) for application in early-phase clinical trials. These coordinated activities incorporate cutting-edge technologies into every step of the NExT drug discovery and development continuum, increasing the potential for successful clinical evaluation of new target- and mechanism-based therapies.

What is your current role in the NExT Program?

One of my responsibilities is to ensure that NExT remains closely aligned with DCTD's vision of consolidating all drug discovery and development resources into a single pipeline with extramural and intramural oversight. I also oversee the expansion and evolution of the program to ensure that it is aligned with NCI's mission to support the translation of promising research into clinical applications in areas of unmet need not adequately addressed by industry or academia. Since its inception, the NExT program has received more than 700 applications with an overall 20% acceptance rate.

What are some examples of NExT projects?

We've recently advanced a novel class of DNA methyltransferase inhibitors into first-in-human clinical trials at NCI, and a CBC MCL1 project in collaboration with Stephen Fesik was recently out-licensed by Vanderbilt University to Boehringer-Ingelheim. We also had

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a longstanding program that identified small molecule inhibitors of mutant IDH-1, which was recently out-licensed. We're excited to see the program gain momentum.

What makes the NExT Program unique?

The mission is important, and the staff is smart and dedicated - that's why I'm here. A lot of the projects we bring in to NExT are ones that pharmaceutical companies won't do, sometimes because the drugs may target small patient populations, or they are risky projects, so we do have a unique role.

Another unique element of NExT is the collaborative approach to research, which is the vision of Dr. Jim Doroshow. We collaborate extensively with outside experts, which is wonderful. It's exciting that we can attract people with unique expertise to join the team as needed; I don't think this happens anywhere else. We run like a project team or a small biotech, and the team makes all the scientific decisions. I believe it's about getting the smartest people in the room to help us - discovering and developing drugs is difficult, so having as many smart people to help you along the way is essential.

In Memoriam: Andrew Hruszkewycz, MD, PhD

Andrew Hruszkewycz, MD, PhD, a beloved and respected Program Officer with the Translational Research Program, died unexpectedly on December 16, 2018. Andrew earned his master's degree in physiology at the Ohio State University and his MD/PhD at Case Western Reserve University. He completed postgraduate training at the University of California, Los Angeles, Temple University, and George Washington University, and he volunteered at Johns Hopkins University as a visiting scientist. Early in his career, he published scientific papers on lipid peroxidation, oxidative stress, and molecular diagnostics and received several awards. He used his clinical training to supervise the development, administration, and monitoring of clinical trials in the prevention of prostate, bladder, and other cancers. Andrew had strong interest in biomarkers that later became one of his major contributions to the current conduct of clinical research and standard of care.

Andrew joined NCI's Organ Systems Branch 16 years ago to help administer the Specialized Programs of Research Excellence (SPOREs), a program managed, in those days, by NCI's Office of the Director. Andrew had already spent ten years at NIH, five of those years at NCI. He began at the Frederick Cancer Research and Development Center, continued at the Department of Clinical Pathology of the Intramural Program, and then joined the Division of Cancer Prevention. During this period, he interacted with SPORE investigators who would eventually become his grantees, and he became familiar with the mission of the SPORE program that resonated so well with his personal goals. Andrew appreciated the importance of integrating teams of basic scientists, clinical investigators, and population scientists for the common goal to translate scientific discoveries into clinical practice. The SPORE program was a perfect fit for him.

As a program officer in the Translational Research Program, Andrew managed translational research of the highest quality and significantly shaped the prostate cancer SPORE program. He was a dedicated, creative thinker who had the ability to bring together the brightest minds in cancer research to solve intricate problems. Under his guidance, Prostate Cancer SPOREs became the leading scientific teams in the world, which brought many diagnostic tools and therapeutic agents to patients. Andrew spearheaded the December 2018 scientific meeting on Lineage Plasticity

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and Androgen Receptor-Independent Prostate Cancer that brought to the NCI world experts tackling a clinical and biological problem spanning many cancers. Andrew helped to create a culture of camaraderie and kindness among his colleagues, while always focusing on how best to deliver the results of his work to benefit cancer patients. Besides these scientific aspects, he was a generous and kind person with a terrific sense of humor, and he will be missed by his friends and colleagues.

Spotlight – Updates from the Cancer Imaging Program (CIP)

caNanoLab: CIP's Nanodelivery Systems and Devices Branch Hosts a Novel Database

caNanoLab is a one-of-a-kind data repository designed for the unique needs of the cancer nanomedicine community. Hosted by CIP's Nanodelivery Systems and Devices Branch and NCI's Center for Biomedical Informatics & Information Technology (CBIIT), caNanoLab is a cornerstone of the US nanoinformatics landscape and the primary informatics arm of the NCI Alliance for Nanotechnology in Cancer program.

caNanoLab Details

- Provides a unique nanotechnology resource that facilitates data sharing in the community to expedite and validate the use of nanomaterials in medicine
- Contains annotations of nanomaterials with composition information and physico-chemical, *in vitro*, and *in vivo* characterizations
- Provides access to information on samples, protocols, and publications originating from a broad biomedical nanotechnology community
- Provides the nanotechnology community with a specifically tailored data sharing platform
- Expanding its reach to include one-of-a-kind support for synthetic protocols
- Focusing efforts on increasing interoperability in 2019

New Content on the CIP Website

The reformatted and updated "Clinical Trials" section of CIP's website provides clinical investigators with information on the NIH Clinical Trial Policy, specifically regarding how the NIH Clinical Trial Policy affects grant and contract applications submitted to the NCI by the imaging community. Investigators can access information on DCTD's R01 FOA for Clinical Trials, PAR 18-560, and other resources to aid in the grant and contract application process.

The Cancer Imaging Archive Expands to Provide Imaging Data Linked to Proteogenomics and Clinical Trials

CIP supports the Cancer Imaging Archive (TCIA), which is a publicly accessible database of medical images.

TCIA is expanding its efforts to host imaging data directly linked to proteomic, genomic, and clinical data.

- In collaboration with the Department of Defense and Department of Veterans Affairs,

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TCIA is part of the Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network and provides radiological and pathological image collection, curation, and hosting support.

- TCIA provides researchers access to Clinical Proteomic Tumor Analysis Consortium (CPTAC) imaging through its data portal.
- Starting in 2019, TCIA will collect and host imaging data for the NCI National Clinical Trials Network (NCTN), which coordinates and supports cancer clinical trials across more than 3,000 sites throughout the United States and Canada.

CIP Program Director Receives SAASCR Outstanding Achievement Award

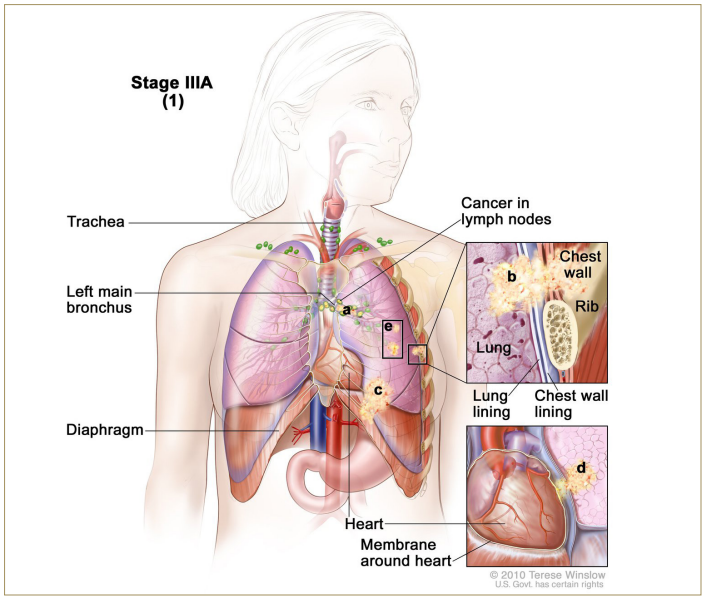
Pushpa Tandon, PhD, a Program Director in CIP's Image Guided Intervention Branch, will receive the "Outstanding Achievement Award" from the Society of American Asian Scientists in Cancer Research (SAASCR). The award will be presented to her on March 30, 2019 at the Annual American Association of Cancer Research (AACR) meeting in Atlanta, GA. Dr. Tandon is being recognized for her extensive work in cancer research support and international outreach. She works with international investigators within the Quantitative Imaging Network and facilitates collaboration between U.S. and foreign scientists to support other NCI efforts. She was the recipient of the Embassy Science Fellowship in 2018 to develop an Indo-U.S. joint program on cancer care and Indian traditional medicine. The SAASCR award recognizes Dr. Tandon's work to cultivate and build the global cancer research community.

News about DCTD Programs and Activities

Program Updates

Lung-MAP Trial Eligibility Expanded to Include Patients with All Non-small Cell Lung Cancers

The Lung-MAP ("Lung Cancer Master Protocol") trial is a precision medicine clinical trial that opened in June 2014 to patients with advanced squamous cell lung cancer, a type of non-small cell lung cancer (NSCLC), whose disease has progressed after treatment with chemotherapy. The trial uses genomic profiling to match patients to one of several investigational treatments that are designed to target specific genomic alterations in their tumor. Originally open to patients with squamous cell lung cancer, the trial's eligibility has recently expanded to include patients who have progressed on immunotherapy with all types of NSCLC. NSCLC represents approximately 85% of all lung cancer diagnoses in the US.



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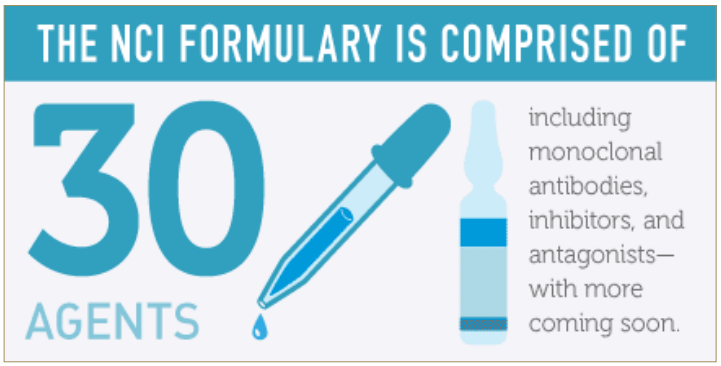
Lung-MAP Facts

- The trial will screen up to 1,000 patients per year and is offered at more than 650 U.S. medical centers and community hospitals under the NCI's National Clinical Trials Network (NCTN) and the NCI Community Oncology Research Program (NCORP).
- Patients whose tumor does not match any of the genetic alterations that are being tested in the trial may join a sub-study to receive immunotherapy combinations.
- Two new sub-studies are in development and will open in 2019.
- Lung-MAP is being funded and implemented through a unique public-private partnership among NCI, Friends of Cancer Research, SWOG, which is a member of NCI's NCTN, the Foundation for the National Institutes of Health, and five pharmaceutical companies.
- A January 2019 press release from SWOG and Friends of Cancer Research provides further details on the trial's eligibility expansion.

The NCI Formulary Expands to Offer 30 Agents from 10 Companies

The NCI Formulary is a public-private partnership between NCI and pharmaceutical and biotechnology companies that offers investigators at NCI-audited clinical research centers who are main member sites of NCTN and ETCTN with rapid access to agents or combinations of agents for clinical or preclinical research.



NCI Formulary Facts

- The availability of agents through the NCI Formulary will expedite the start of clinical trials by alleviating the lengthy negotiation process—sometimes up to 18 months—that has been required for investigators to access such agents on their own.
- Following company approval, investigators will be able to obtain NCI Formulary agents and test them in new preclinical or clinical studies, including combination studies of Formulary agents from different companies.
- The NCI Formulary was launched on January 11, 2017 (NCI press release) with six participating companies - Bristol-Myers Squibb, Eli Lilly and Company, Genentech, Kyowa Hakko Kirin Co, Ltd., Loxo Oncology, and Xcovery Holding Company LLC - offering 15 targeted agents. Since that time, AstraZeneca, Amgen, Syntrix Biosystems, Inc., and now, EMD Serono, Inc., have agreed to provide agents to the NCI Formulary. See the list of the thirty agents that are now available.

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A New Treatment Standard for AYA patients with ALL

A prospective study (CALGB 10403) found that older adolescent and young adult (AYA) patients with acute lymphoblastic leukemia (ALL) experienced better outcomes when treated with a pediatric treatment regimen (overall survival at 3 years was 73% vs 55% for earlier studies). Results of this trial support the use of an intensive pediatric approach as a standard of care for young adults up to age 40 with ALL and as the platform for future therapeutic development to improve survival in AYAs.

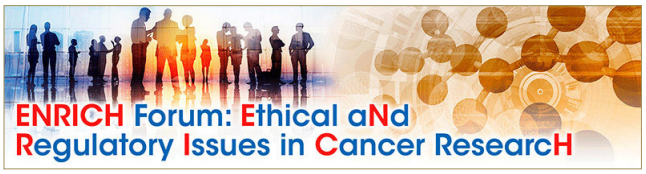
Accelerated FDA Approval for Treatment of Merkel Cell Carcinoma

PD-1 blockade with pembrolizumab in patients with advanced Merkel cell carcinoma (MCC) showed an objective response rate of 56% and a 67% rate of progression-free survival at 6 months in this Phase 2 study, which is part of the NCI-supported Cancer Immunotherapy Trials Network (CITN). In December 2018, the drug received accelerated approval from the FDA for this cancer. Read NCI's Cancer Currents blog about MCC and the FDA approval.

MutSpliceDB – A Database of Splice Site Variants Effects on Splicing

DCTD's Biometric Research Program (BRP) is providing a resource for the scientific community: MutSpliceDB. Splice site mutations are one of the well-known classes of genetic alterations playing an important role in biology. Splice site mutations in cancer are most frequently observed as inactivating alterations in tumor suppressor genes (e.g., TP53 or RB1) and to a lesser degree as activating alterations in oncogenes (e.g., MET). Interpreting the consequences of a specific splice site mutation is not straightforward, especially if the mutation is located outside of the canonical splice sites. Accurate interpretation of a splice site mutation's impact can further our understanding of biology, influence patient treatment, and, in case of germline splice site mutations, may have relevance to familial disease predisposition. To facilitate the interpretation of splice site mutation effects, BRP's Computational and Systems Biology Branch developed MutSpliceDB: a database of splice sites variants, documenting mutation effect(s) on splicing based on RNA-seq BAM files from sample(s) with splice site mutations.

NCI's ENRICH Forum Archived Presentations Now Available



NCI's ENRICH Forum is designed to stimulate dialogue on ethical and regulatory issues in cancer research and promote awareness of developing policies and best practices. The Forum, sponsored by the Division of Cancer Control and Population Sciences (DCCPS) and DCTD, presents educational programs and occasional deliberative sessions focused on specific ethical, legal, and social issues involving cancer research.

ENRICH Forum speakers present both in-person at Shady Grove and via WebEx. The January 2019 presentation by **Yvonne Lau, MBBS, MBHL, PhD,** of the Office for Human Research Protections in the U.S. Department of Health and Human Services was recorded and can be viewed by visiting the ENRICH Forum website. ENRICH Forum sessions will be recorded and posted on the series website if permitted by the speakers.

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Publications and Outreach

Peer-reviewed Publications

Yang SX and Polley EC. Systemic Treatment and Radiotherapy, Breast Cancer Subtypes, and Survival after Long-term Clinical Follow-up. *Breast Cancer Res Treat*. 2019 Feb 12. Epub ahead of print.

Nghiem P, Bhatia S, Lipson EJ, et al. Durable Tumor Regression and Overall Survival in Patients with Advanced Merkel Cell Carcinoma Receiving Pembrolizumab as First-line Therapy. *J Clin Oncol*. 2019 Feb 6. Epub ahead of print.

Sharpless NE and Doroshow JH. Modernizing Clinical Trials for Patients with Cancer. *JAMA*. 2019 Jan 23. Epub ahead of print.

Mehralivand S, Shih JH, Harmon S, et al. A Grading System for the Assessment of Risk of Extraprostatic Extension of Prostate Cancer at Multiparametic MRI. *Radiology*. 2019 Jan 22. Epub ahead of print.

Ramsey SD, Unger JM, Baker LH, et al. Prevalence of Hepatitis B Virus, Hepatitis C Virus, and HIV Infection among Patients with Newly Diagnosed Cancer from Academic and Community Oncology Practices. *JAMA Oncol*. 2019 Jan 17. Epub ahead of print.

Barber DL, Sakai S, Kudchadkar RR, et al. Tuberculosis following PD-1 Blockade for Cancer Immunotherapy. *Sci Transl Med*. 2019 Jan 16;11(475).

Rao A, Vaught J, Tulskie B, et al. Critical Financial Challenges for Biobanking: Report of a National Cancer Institute Study. *Biopreserv Biobank*. 2019 Jan 14. Epub ahead of print.

Mishkin G, Arnaldez F, and Ivy SP. Drivers of Clinical Trial Participation-demographics, Disparities, and Eligibility Criteria. *JAMA Oncol*. 2019 Jan 10. Epub ahead of print.

Fang J. Tightly Integrated Genomic and Epigenomic Data Mining Using Tensor Decomposition. *Bioinformatics*. 2019 Jan 1;35(1):112-118.

Rimm DL, Leung SCY, McShane LM, et al. An International Multicenter Study to Evaluate Reproducibility of Automated Scoring for Assessment of Ki67 in Breast Cancer. *Mod Pathol*. 2019 Jan;32(1):59-69.

Seibel NL, Chi YY, Perlman EJ, et al. Impact of Cyclophosphamide and Etoposide on Outcome of Clear Cell Sarcoma of the Kidney Treated on the National Wilms Tumor Study-5 (NWTS-5). *Pediatr Blood Cancer*. 2019 Jan;66(1):e27450.

Harmon SA, Mena E, Shih JH, et al. A Comparison of Prostate Cancer Bone Metastases on ^{18}F-Sodium Fluoride and Prostate Specific Membrane Antigen (^{18}F-PSMA) PET/CT: Discordant Uptake in the Same Lesion. *Oncotarget*. 2018 Dec 28;9(102):37676-37688.

Xia F, Shukla M, Brettin T, et al. Predicting Tumor Cell Line Response to Drug Pairs with Deep Learning. *BMC Bioinformatics*. 2018 Dec 21;19(Suppl 18):486.

Tray N, Taff J, Singh B, et al. Metaplastic Breast Cancers: Genomic Profiling, Mutational Burden and Tumor-infiltrating Lymphocytes. *Breast*. 2018 Dec 20;44:29-32.

Mathieson W, Mommaerts K, Trouet JM, et al. Cold Ischemia Score: An mRNA Assay for the Detection of Extended Cold Ischemia in Formalin-fixed, Paraffin-embedded Tissue. *J Histochem Cytochem*. 2018 Dec 18. Epub ahead of print.

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Hobbs BP, Barata PC, Kanjanapan Y, et al. Seamless Designs: Current Practice and Considerations for Early-phase Drug Development in Oncology. *J Natl Cancer Inst*. 2018 Dec 17. Epub ahead of print.

Yock AD, Mohan R, Flampouri S, et al. Robustness Analysis of External Beam Radiation Therapy Treatment Plans: Describing Uncertainty Scenarios and Reporting Their Dosimetric Consequences. *Pract Radiat Oncol*. 2018 Dec 15. Epub ahead of print.

Dunleavy K, Fanale MA, Abramson JS, et al. Dose-adjusted EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) in Untreated Aggressive Diffuse Large B-cell Lymphoma with MYC Rearrangement: a Prospective, Multicentre, Single-arm Phase 2 Study. *Lancet Haematol*. 2018 Dec;5(12):e609-e617.

Liu JF, Lee JM, Strock E, et al. Technology Applications: Use of Digital Health Technology to Enable Drug Development. *JCO Clin Cancer Inform*. 2018 Dec;2:1-12.

Mottok A, Wright G, Rosenwald A, et al. Molecular Classification of Primary Mediastinal Large B-cell Lymphoma Using Routinely Available Tissue Specimens. *Blood*. 2018 Nov 29;132(22):2401-2405.

Young CR, Adler S, Eary JF, et al. Biodistribution, Tumor Detection and Radiation Dosimetry of F-18 5-Fluoro-2'-Deoxyctidine (^{18}F-FdCyd) with Tetrahydrouridine in Solid Tumors. *J Nucl Med*. 2018 Nov 2. Epub ahead of print.

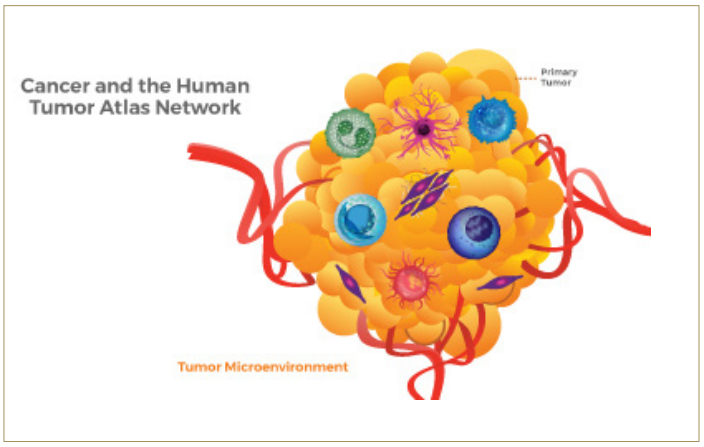
Danos AM, Ritter DI, Wagner AH, et al. Adapting Crowdsourced Clinical Cancer Curation in CIViC to the ClinGen Minimum Variant Level Data Community-driven Standards. *Hum Mutat*. 2018 Nov;39(11):1721-1732.

Tsao AS, Lindwasser OW, Adjei AA, et al. Current and Future Management of Malignant Mesothelioma: A Consensus Report from the National Cancer Institute Thoracic Malignancy Steering Committee, International Association for the Study of Lung Cancer, and Mesothelioma Applied Research Foundation. *J Thorac Oncol*. 2018 Nov;13(11):1655-1667.

Walsh MF, Ritter DI, Kesserwan C, et al. Integrating Somatic Variant Data and Biomarkers for Germline Variant Classification in Cancer. *Hum Mutat*. 2018 Nov;39(11):1542-1552.

Riscuta G, Xi D, Pierre-Victor D, et al. Diet, Microbiome, and Epigenetics in the Era of Precision Medicine. *Methods Mol Biol*. 2018;1856:141-156.

NCI Cancer Currents Blog Posts



HTAN: Mapping Tumors across Space and Time Using Cutting-Edge Technologies; **Tracy Lively, PhD,** Cancer Diagnosis Program; February 12, 2019.

Immunotherapy Effective in Alveolar Soft Part Sarcoma; **Alice Chen, MD,** and **Geraldine O'Sullivan Coyne, MD, PhD,** Developmental Therapeutics Clinic; January 9, 2019.

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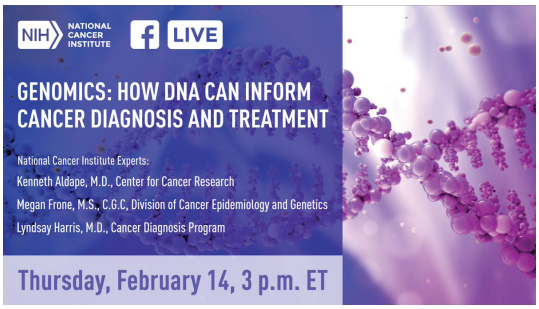
Interviews, Press, and Social Media



L to R: Megan Frone, Kenneth Aldape, and Lyndsay Harris speaking at NCI's Facebook Live on Genomics

Lyndsay Harris, MD, Cancer Diagnosis Program, participated in a trans-NCI Facebook Live event on Genomics on February 14, 2019. The archived event can be viewed on NCI's Facebook page.

NCI-MATCH Results Offer Clues for the Use of Agents across Tumor Types; **Lyndsay Harris, MD,** Cancer Diagnosis Program; OncLive; February 1, 2019.

Comorbidity Exclusion Criteria Impair Participation in Cancer Trials; **Percy Ivy, MD,** Cancer Therapy Evaluation Program; Journal of Clinical Pathways; February 1, 2019.

Ibrutinib Plus Rituximab Superior to Standard Treatment for Some Patients with Chronic Leukemia; NCI Press Release; December 4, 2018.

FDA Approves Second Drug for a Site-agnostic Indication; Larotrectinib Was Tested across 17 Cancer Types; **Nita Seibel, MD**, Cancer Therapy Evaluation Program; The Cancer Letter; November 30, 2018.

Conferences and Meetings

NCI Workshop on Lineage Plasticity and Androgen Receptor–Independent Prostate Cancer

The National Cancer Institute organized a Workshop on Lineage Plasticity and Androgen Receptor-Independent Prostate Cancer in a joint effort by the NCI's DCTD, Division of Cancer Biology, Center for Cancer Research, Coordinating Center for Clinical Trials, together with investigators of the NCI SPOREs in Prostate Cancer and the Prostate Cancer Task Force of the NCI Genitourinary Steering Committee. This workshop occurred on December 6-7, 2018 at the NIH Main Campus in Bethesda, MD and was chaired by Drs. Himisha Beltran, Bill Dahut, and Peter Nelson. The meeting assembled leaders in the field to share scientific insights and identify emerging opportunities in basic, translational, and clinical research.

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Workshop Goals

Advance the state-of-the-science to address the following crucial needs:

- Fundamental understanding of how lineage plasticity occurs
- Determination of the temporal contribution and cooperation of emerging drivers
- Development of preclinical models that recapitulate the biology of the disease and the recognized phenotypes
- Identification of therapeutic targets and novel trial designs dedicated to the entity as it is defined

Workshop Highlights

- Scientists and clinicians focused on enhancing knowledge of the fundamental role of lineage plasticity in driving the progression of multiple cancer subtypes and in impacting treatment response.
- Four working groups tackled molecular, preclinical, and clinical aspects of this continuum.
- Experts who are investigating the role of lineage plasticity in other cancer types provided their knowledge and experience.
- Scientific sessions covered the scope of the problem and the cellular and molecular biology of androgen receptor-independent prostate cancer, and attendees discussed translational strategies to advance basic discoveries into the clinic.

Workshop Outcomes and Potential Deliverables

- Identification of major gaps of knowledge in the field
- Generation of novel ideas on how to address the scientific and clinical challenges
- The following two focus groups will organize the next steps of this endeavor:

  1. The basic biology of Rb loss in small cell/neuroendocrine prostate cancer (NEPC), small cell lung cancer, and other small cell carcinomas
     - Attempt to better define the method of loss (e.g., deletion, phosphorylation) and the impact of co-occurring alterations (e.g., TP53)
     - Explore collaborative ideas to improve knowledge of the clinical, pathologic, and molecular features underlying Rb-deficient tumors
     - Discuss strategies for model development and drug discovery (e.g., CRISPR)
  2. Imaging capabilities to accelerate clinical translation of emerging data in this field
     - Discuss strategies for using prostate-specific membrane antigen or dihydrotestosterone positron emission tomography (PET) combined with fluorodeoxyglucose PET imaging as a non-invasive means to detect androgen receptor signaling heterogeneity and lineage plasticity
     - Utilize these data, in combination with clinical and molecular features, to develop a working definition of lineage plasticity for future therapeutic trials

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The scientific expertise, dedication, and genuine passion of the late **Andrew Hruszkewycz, MD, PhD** were instrumental in the success of this workshop.

Meeting attendees (L to R): Tim Thompson, University of TX/MD Anderson Cancer Center, Jeff Hildesheim, Division of Cancer Biology, NCI, Abdul Tawab-Amiri, Coordinating Center for Clinical Trials, NCI, Peter Nelson, Fred Hutchinson Cancer Center, Himisha Beltran, Dana-Farber Cancer Institute, Bill Dahut, Center for Cancer Research, NCI, Andrew Hruszkewycz, DCTD, NCI, Tamara Walton, DCTD, NCI

DCTD Workshop on Cell-based Immunotherapy for Solid Tumors

On December 10-11, 2018, DCTD sponsored a Workshop on Cell-based Immunotherapy for Solid Tumors. The workshop addressed scientific, clinical, and manufacturing issues related to adoptive cell therapies, including transfer of tumor infiltrating lymphocytes (TILs), T cells that have been modified with chimeric antigen receptors (CAR), T cells with engineered T-cell receptors (TCR), and other immune cells.

Meeting Goals

- Review successes and challenges of adoptive cell therapies for hematological malignancies
- Examine current use of cell therapies in solid tumor patients
- Understand scientific, technological, and regulatory challenges to advancing cell-based treatments for solid tumors
- Develop consensus around bottlenecks preventing the timely implementation of clinical and research studies of cell-based therapies for solid tumors, which might be addressed by NCI action

Read the full meeting summary on the DCTD website.

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Helen Moore, PhD, Branch Chief, Biorepositories and Biospecimen Research Branch, Cancer Diagnosis Program, and Janet Freeman Daily, a patient advocate, together conducted an interactive workshop at the November 2018 PRIM&R (Public Responsibility in Medicine and Research) meeting in San Diego. The workshop, entitled "Building a Better Biobank: Promise and Challenges of the National Cancer Institute Cancer Moonshot Biobank," gave an overview of the Cancer Moonshot Biobank project and a patient's perspective on biobanking. The leaders also conducted breakout sessions where audience members were assigned roles of patient, medical provider, or family member, and deliberated over project-specific questions related to longitudinal engagement of research participants, research biopsies, patient and provider understanding of tumor molecular testing, and postmortem biospecimen donation.

New DCTD Funding Opportunities and Funding Information

TITLE	ANNOUNCEMENT NUMBER	OPENING DATE	EXPIRATION DATE	ACTIVITY CODE
The Experimental Therapeutics Clinical Trials Network (Clinical Trial Required)	RFA-CA-19-007	April 22, 2019	May 23, 2019	UM1
The Experimental Therapeutics Clinical Trials Network (ETCTN) Pharmacokinetic Resource Laboratories (Clinical Trial Not Allowed)	RFA-CA-19-008	April 22, 2019	May 23, 2019	U24

Administrative Supplements to Support Research on Bioethical Issues

The NIH OD Office of Science Policy intends to publish an FOA for administrative supplements to support research on bioethical issues to inform future policy directions, or to incorporate bioethics questions within NIH-supported research. Applicants may propose to supplement parent awards focused on bioethics, or to add a component related to bioethics to a parent award in which bioethics was not the focus.

Ethical considerations are intrinsic to the protection of human research participants and the responsible conduct of clinical research involving cancer therapies and diagnostics. Ethical challenges include (but are not limited to):

- consent for the collection and future uses of research tissue
- the return of research results and incidental findings
- data sharing, genetic privacy, and concerns about re-identification of research participants
- therapeutic misconception and "hope vs. hype" in precision medicine clinical trials
- equal access to innovative therapies
- the acceptability of research biopsies in pediatric research

View the NIH published notice of intent.

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Staff Retirements

Jan Casadei, PhD, will retire from the federal government in February 2019 after 28 years working with CTEP. Dr. Casadei's areas of expertise cover FDA regulations, policies, and guidelines for the conduct of clinical studies with investigational agents. She became Chief of the Regulatory Affairs Branch (RAB) in 2008 and has been responsible for facilitating the development of promising investigational anti-cancer agents by providing regulatory/IND support. She has supervised RAB staff, a team focused on solving regulatory issues and fostering pharmaceutical collaborations to accelerate drug development. Find out more about Dr. Casadei's career at NCI in the May 2019 DCTD newsletter.

Sherry Ansher, PhD, retired February 1, 2019 after 24 years at CTEP and 36 years in the federal government at NIH and FDA. Over the last two decades, Dr. Ansher has been central to CTEP's achievements and collaborative operations. She was the Associate Chief of the Regulatory Affairs Branch and the head of the Agreement Coordination Group. She was responsible for the collaborative agreements for the clinical and nonclinical development of potential anticancer agents by CTEP and the interactions between the investigators, CTEP, and the collaborating pharmaceutical companies. Learn more about Dr. Ansher's career at NCI and her plans to continue part-time work with CTEP in the May 2019 DCTD newsletter.