DCTD Staff Highlight: Jeff Abrams, MD

After 25 years with the Cancer Therapy Evaluation Program (CTEP), **Jeff Abrams, MD**, will retire from the federal government in November 2018. Jeff describes his career in oncology and some highlights in cancer research during his time at NCI.

How did you decide to become a clinical researcher, and how did you eventually come to NCI?

I was a history major in college, and while I took pre-medical school courses, I didn’t think about pursuing a career in medicine early on. I was most fascinated by literature and history courses, and for a while, I thought about becoming a lawyer. I had two uncles who were doctors, and by my senior year, I started considering medicine as a career. I attended medical school in Belgium, and during my seven years there, I became fluent in French, an avid skier, and met my wife, who is also a physician. Following medical school, we left Belgium, and both did residency training at St. Agnes Hospital in Baltimore, MD. I then went to the University of Maryland for a fellowship in oncology. I intended to be a practicing oncologist in the community; however, a unique opportunity arose to do a clinical research fellowship in oncology at the Jules Bordet Institute in Brussels, which allowed us to spend a very nice year back in Belgium where our first son was born. This experience pushed me to consider pursuing clinical research, and I returned to the University of Maryland as a faculty member in 1985. In 1988, I became the Director of the Breast Cancer Evaluation Program and an Associate Professor of Medicine and Oncology at Maryland. One of my mentors during my oncology fellowship, Rick Kaplan, MD, had left Maryland to work at the NCI in the Clinical Investigations Branch (CIB), and he told me about a CTEP opportunity to oversee the breast cancer treatment trials portfolio and participate in clinical trials at the NIH Clinical Center. That’s how I arrived...
at NCI in 1993. In CIB, I worked on breast cancer treatment trials, but I also later became involved in melanoma, kidney cancer, brain cancer, and hematologic malignancies. In 2003, I was appointed CIB’s Branch Chief, and in July 2008, I became CTEP’s Associate Director.

**What were some noteworthy changes in cancer clinical trials over the years?**

In the early 2000s, there was great interest to modernize the clinical trials process to adapt to the improved understanding of cancer, in part due to the human genome project and other basic science advances. This began with the institution of the Central Institutional Review Board (CIRB) and the Cancer Trials Support Unit (CTSU). I worked closely with former CTEP staff, including Michaele Christian, MD, CTEP’s Associate Director, Richard Ungerleider, MD, CIB Branch Chief, Richard Kaplan, MD, and many others to form these centralized NCI resources. In the late 2000s, an Institute of Medicine report called for further modification of the Cooperative Group program. With Jim Doroshow, MD’s appointment as DCTD Director, he emphasized improving operational efficiency and developing disease-specific Steering Committees. In concert with the earlier changes, we also decided to consolidate the Cooperative Groups from 10 to 5 to form a more tightly integrated trials system. This ultimately led to NCI’s National Clinical Trials Network (NCTN), which was finalized in 2014 under Meg Mooney, MD, CIB Branch Chief.

In 2012, we undertook a multi-year initiative to re-engineer CTEP’s information technology processes because the software and hardware hadn’t been updated since the late 1990’s. Mike Montello, PharmD, Chief, Clinical Trials Operations and Informatics Branch and Meg Mooney, MD, led this effort, and now we have a modernized, agile platform capable of supporting new types of precision medicine trials like NCI-MATCH, Pediatric-MATCH, ALCHEMIST, and Lung MAP. We also modified how we conduct early phase clinical trials by creating the Experimental Therapeutics Clinical Trials Network (ETCTN) in 2014. I was fortunate to have very able leaders in CTEP’s Investigational Drug Branch - James Zwiebel, MD, Branch Chief until January 2018, Percy Ivy, MD, Associate Branch Chief, and Jeff Moscow, MD, current Branch Chief - who were instrumental in the creation of national project teams to assist with developing clinical trials for CTEP IND agents.

**What are some advances in cancer treatment that you’ve seen over the last few decades?**

When I arrived at NCI, adjuvant therapy for breast cancer was just taking hold. NCI put out Clinical Alerts to physicians that adjuvant chemotherapy could prolong survival for most women who were at risk for metastases. We then spent several years doing chemotherapy-based studies. We were heavily involved in taxane trials to treat breast cancer, which is still a mainstay of treatment today. NCI also supported multiple hormonal therapy studies to determine the best treatment for women with estrogen receptor positive (ER+) breast cancer. One of the first breakthrough therapies in solid tumors that changed the paradigm in the late 1990s was Herceptin for HER2-positive breast cancer. NCI supported two major adjuvant trials, and suddenly women who previously had the worst prognosis were doing much better. We began to think of breast cancer as more than just hormone positive or negative, but rather a series of distinct, genetically defined diseases. This led to a seminal study, TAILORx, in which
a genetic signature was tested for its ability to select women who would or would not benefit from adjuvant chemotherapy. The trial began in 2009, and the results came out at ASCO 2018. The trial proved that most women with ER+ breast cancer on a hormonal agent do not need chemotherapy, while a small subset at high risk of recurrence do indeed benefit. We are in a new era where more studies are genetically classifying patients to determine who may be more likely to benefit from a targeted agent, and some new examples are CDK4-6 inhibitors for hormone receptor positive tumors and checkpoint inhibitors for PDL-1 positive, triple negative breast cancer.

**What are some fond memories you have of working in CTEP?**

Working in CTEP was a great career choice because of the uniformly excellent and dedicated colleagues there and across DCTD. I learned a lot working alongside creative, resourceful physicians like Malcolm Smith, MD, PhD, Helen Chen, MD, John Wright, MD, PhD, and multiple others. I had excellent Branch Chiefs, Jan Casadei, PhD in Regulatory Affairs, Gary Smith in the Clinical Trials Monitoring Branch, and Charles Hall in the Pharmaceutical Management Branch who saw to it that our trials were compliant with all federal rules, safe, and agile enough to deliver investigational drugs nationwide. During my tenure, the Division offered many opportunities for different projects, challenges, and innovative research areas. As much as I enjoyed designing clinical trials and making sure they were scientifically sound, I also enjoyed the work to improve the infrastructure, which presented a different sort of challenge.

I will retain fond memories of CTEP’s Protocol Review Committee (PRC) meetings. While often lasting three to five hours, staff have done a fantastic job educating each other there. It shows DCTD’s ability to bring together diverse expertise, and it’s rare to find this. At this single meeting, we assemble high quality statistical, disease, early drug development, basic science, radiology, and radiation oncology expertise. PRC has met on Thursday mornings since before I joined CTEP, and it’s still the same. It has improved over the years - staff now use technology and prepare slides so that we all become educated. It’s a better meeting and more interesting for me and staff as well. The PRC is a place where NCI can do its best job at adding value to the national system by focusing expertise to make clinical trials as meaningful as possible. That’s why I see this meeting as symbolic as the best of what NCI can do.

**What plans do you have for your retirement?**

I’ve always been an avid winter sports enthusiast - downhill and cross-country skiing, especially, and fortunately my wife shares this with me. So, we are going to spend our first winter in Steamboat Springs, CO. My longer-term plans include spending more time in Belgium, visiting with my grandkids, and volunteering in politics and perhaps in medically deprived areas as well.
**Spotlight – The Cancer Diagnosis Program: Shaping the Future of Biomarkers in the Post-Genomic Era**

**Introduction from Lyndsay Harris, MD, Associate Director, CDP**

The mission of the Cancer Diagnosis Program (CDP) is to support the development of diagnostic and therapeutic biomarkers, biospecimen resources and best practices, and novel technologies. But CDP’s role in the cancer community is much more than this! In this ‘Precision Medicine’ era, where our understanding of biomarkers informs therapy choices, as well as resistance to treatment, CDP has led the way in the development of:

- novel therapeutic frameworks around immune-oncology and genomic biomarkers
- innovative approaches for the community to access much needed specimens for research
- unique assay-driven networks that support enrollment onto clinical trials for patients and providers

In the future, CDP will continue to develop innovative and far-reaching programs that will connect our growing understanding of the biology of cancer with novel assays that predict this biology in a consistent and reproducible fashion for patient-specific therapy. Only in this way can we hope to make the greatest inroads and someday win the fight against this devastating disease.

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**NCI-MATCH Designated Lab Network**

NCI-MATCH is a precision medicine clinical trial run by CDP and the ECOG-ACRIN Cancer Research Group. It was designed to ‘match’ patients to novel therapies based on their tumor’s molecular profile. The initial phase of the trial screened more than 6,000 patients in fewer than 2 years, with more than 1,000 clinical sites involved. The initial group of screened patients allowed the study to fill 40% of the planned treatment arms; however, many of the trial arms involve genetic mutations that are not commonly found in tumors, and it was necessary to identify more patients with the rare alterations to fill those arms. This led to the development of the ‘NCI-MATCH Designated Laboratory Network,’ led by Jim Tricoli, PhD, Chief, Diagnostic Biomarkers and Technology Branch, CDP, which contains nearly 30 academic and commercial laboratories that use next-generation sequencing to identify actionable mutations of interest for patients to help guide their treatment. The NCI-MATCH study now uses this network to identify cases for the rare variant arms of NCI-MATCH and to eliminate the need for expensive biopsies. The network will also be utilized for future arms of the trial and is now the only way for new patients to enroll in NCI-MATCH. Read a recent NCI Cancer Currents blog on NCI-MATCH.

next page ...
The National Clinical Laboratory Network

The National Clinical Laboratory Network (NCLN), led by Tracy Lively, PhD, Chief, Diagnostics Evaluation Branch, Deputy Associate Director, CDP, is a DCTD-supported laboratory network capable of providing centralized robust assays and biorepository support for clinical trials conducted by the NCI Experimental Therapeutics Clinical Trials Network (ETCTN). These assays will yield data that are comparable across supported studies and are performed at the NCI’s expense. This resource should prove a boon to ETCTN researchers.

Cancer Moonshot Biobank and BBRB

CDP’s Biorepositories and Biospecimen Research Branch (BBRB), led by Branch Chief, Helen Moore, PhD, will be coordinating the Cancer Moonshot Biobank, which will ask patients to donate biospecimens throughout the patient’s entire course of cancer treatment. The recently released Biospecimen Evidence-Based Practices (BEBP) document provides step-by-step procedural guidelines on biospecimen collection and processing that are based upon literature evidence and expert recommendations. The most recent BEBP is the first to be vetted by a panel of internationally recognized experts in the field.

Cancer Immune Monitoring and Analysis Centers

CDP supports a multidisciplinary network that encompasses four Cancer Immune Monitoring and Analysis Centers (CIMACs) and a single Cancer Immunologic Data Commons (CIDC). The Network, led by Magdalena Thurin, PhD, Program Director, Diagnostics Evaluation Branch, CDP, was established to address the critical importance of biomarkers in the management of cancer patients receiving immunotherapy. CIMACs are expected to provide a wide range of state-of-the-art analyses for genomic, phenotypic, and functional characterization of responses of patients in NCI-sponsored early phase clinical trials using analytically-validated and standardized platforms and to harmonize these across laboratories. The CIDC will facilitate network activities in the following areas:

- optimization of data collection methodologies suitable for immune-related biomarkers
- data integration
- building a biomarker database for secondary use by the large immuno-oncology community

The long-term goal of the CIMACs-CIDC Network is to define a set of molecular features that characterizes immune response categories to correlate with the clinical outcomes of immunotherapy in cancer. Collectively, the outcome of the Network research should lead to the identification of biomarkers with potential for optimizing the therapeutic strategies for patients.
**Spotlight: NCI’s Patient-Derived Models Repository Offers Its First Patient-Derived Cell Cultures and Cancer Associated Fibroblasts to the Scientific Community**

The NCI Patient-Derived Models Repository (PDMR) is a publicly accessible, national repository for early-passage, molecularly characterized patient-derived models developed from patients with solid tumors.

The first patient-derived xenograft (PDX) models were publicly released in May 2017, and the first patient-derived cell cultures (PDCs) and cancer-associated fibroblasts (CAF) were distributed in September 2018. Currently, 193 PDX models, 52 PDCs, and 108 CAF cultures from a variety of cancer types are available for investigators to request for their research.

**PDMR Facts**

- Models are generated from tumor tissues collected from patients at NCI-designated Cancer Centers, NCI’s Developmental Therapeutics Clinic (DTC), participating sites within NCI’s Experimental Therapeutics Clinical Trials Network (ETCTN), NCI’s Community Oncology Research Program (NCORP), and other participating centers.

- Researchers not interested in performing wet lab studies can mine the metadata associated with the models using the PDMR database.

- The numbers of PDX, PDC, and CAF models continue to expand, and patient-derived organoid cultures will be available for distribution in early 2019.

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News about DCTD Programs and Activities

Program Updates

NCI Expands Access to Clinical Trials for Patients with Pre-existing Conditions

The Cancer Therapy Evaluation Program (CTEP) brought together NCI Divisions, Offices, and Centers that sponsor NCI clinical trials to review the October 2017 published recommendations of the American Society of Clinical Oncology (ASCO) and Friends of Cancer Research (Friends). The goal of the ASCO/Friends report was to expand clinical trial access and remove barriers for patients with pre-existing conditions.

The report recommended expansion of clinical trial eligibility criteria for the following:

- brain metastases
- minimum age at enrollment
- HIV infection
- organ dysfunction
- prior and concurrent malignancies

After internal reviews at NCI that included staff from DCTD, the Division of Cancer Prevention, the Office of Cancer Centers, the Center for Cancer Research, and the Coordinating Center for Clinical Trials and additional consultation from NCI’s Investigational Drug Steering Committee pharmacology task force, NCI broadened the eligibility criteria in the above instances to make clinical trials more representative. For investigators who submit protocols to CTEP, the CTEP Protocol Review Committee now requires protocols to use these criteria, which have been incorporated into an updated protocol template. NCI is appreciative of the ASCO-Friends initiative and all those who participated in this important effort to expand access to clinical trials. Read the ASCO-Friends press release.

A New Publication Outlines Best Practices for Improving the Quality of Biopsy Specimens Collected in Clinical Trials

As part of a continuing effort to improve how researchers measure the effect of new targeted anti-cancer drugs on early-phase clinical trials, a multidisciplinary team of DCTD and NIH Clinical Center researchers collaborated with investigators from the extramural research community to better understand the challenges of obtaining “fit-for-purpose” research tumor biopsies. The results of this work were recently published in the Journal of Oncology Practice and suggest best practices for improving the quality of biopsy specimens collected on clinical trials. Biopsies are needed on both molecular targeted clinical trials to measure whether the investigational drug exhibits anti-tumor activity and precision medicine clinical trials for genomic assessment, yet data collected by DCTD indicate that too often, the biopsies had insufficient tumor content, were not processed under conditions necessary to measure the drug target, or were not collected at all because the patient was not a suitable candidate for the biopsy. Any of these issues can compromise the objectives of the trial and the patient’s contribution to
clinical research. Despite its seeming simplicity, the authors found that including interventional radiologists, who perform the biopsy procedure, on the clinical trial research team and improving communication among all members of this team notably improved biopsy quality outcomes at the NCI Developmental Therapeutics Clinic, likely because optimal procedures for biopsy collection could be more fully discussed and planned. Read more details about these recommendations in a recent NCI Cancer Currents blog.

**DCTD Releases a New Resource for Exploring Cell Line Transcriptional Responses to Anti-cancer Agents: The NCI Transcriptional Pharmacodynamics Workbench**

Assessing changes in cancer cell gene expression following treatment with oncology drugs enables better understanding of drug mechanisms of action and the molecular basis of drug sensitivity and resistance. A recent publication in *Cancer Research* outlines the extensive development and application of a resource for such analyses of gene expression changes: the NCI Transcriptional Pharmacodynamics Workbench (NCI TPW).

The NCI TPW complements existing platforms such as the Genomics of Drug Sensitivity in Cancer (GDSC), Cancer Cell Line Encyclopedia (CCLE), and the NIH Library of Integrated Network-based Cellular Signatures (LINCS) project by offering a centralized compilation of both drug sensitivity and directly measured longitudinal transcriptional response data for a large, common set of cancer cell lines.

The NCI TPW is a publicly available resource that offers:

- Gene expression data for more than 12,000 genes in the NCI-60 panel of human tumor cell lines at multiple time points following exposure to 15 different anticancer agents

- Heatmaps of genes affected by anti-cancer agents, organized by signaling pathway, interactions with a specific transcription factor, or receptor type

- Corresponding drug sensitivity data

- Analysis tools to assess these data in the context of signaling pathways and mutations of interest

- Mechanistic insights from gene expression data that can identify agent combinations that may be appropriate for further preclinical or eventual clinical studies

The NCI TPW is a valuable resource for the scientific community that could provide information for drug development decisions. [Access the NCI TPW.](#)
The Translational Research Program Announces Fiscal Year 2018 SPORE Grantees

TRP announced its successfully competed FY2018 Specialized Program of Research Excellence (SPORE) grantees, which included four new and seven renewed grants. The cancer types being studied in these grants are: brain, prostate, skin, lymphoma, leukemia, breast, ovarian, and hepatobiliary. See more information on the FY2018 SPORE grantees.

Publications and Outreach

Peer-reviewed Publications


**NCI Cancer Currents Blog Posts**

Olaparib after Initial Treatment Delays Ovarian Cancer Progression; Elise Kohn, MD, Cancer Therapy Evaluation Program; November 20, 2018.

**NCI-MATCH Update:** More Labs, New Arms, and Initial Findings; Lyndsay Harris, MD, Cancer Diagnosis Program; November 15, 2018.

Study Improves the Quality of Biopsy Specimens for Cancer Research; Kate Ferry-Galow, PhD, Frederick National Laboratory for Cancer Research; October 23, 2018.
Immunotherapy Drug Cemiplimab Approved for Advanced Squamous Cell Skin Cancer; Larissa Korde, MD, Cancer Therapy Evaluation Program; October 19, 2018.

Using Artificial Intelligence to Classify Lung Cancer Types, Predict Mutations; Paula Jacobs, PhD, Cancer Imaging Program; October 10, 2018.

Nivolumab and Ipilimumab Effective against Melanoma That Has Spread to the Brain; Elad Sharon, MD, MPH, Cancer Therapy Evaluation Program; September 20, 2018.

Appendix Cancers Are Genetically Distinct from Other Gastrointestinal Cancers, Study Shows; Carmen Allegra, MD, Cancer Therapy Evaluation Program; September 12, 2018.

Interviews, Press, and Social Media

The Role of the NCI Investigational Drug Branch; Jeff Moscow, MD, Cancer Therapy Evaluation Program; Clinical Advances in Hematology & Oncology; November 2018.

ESMO 2018: HIV-Positive Cancer Patients Might Benefit from Immunotherapy; Elad Sharon, MD, MPH, Cancer Therapy Evaluation Program; Practice Update; October 30, 2018. Free login required.

Conversation with The Cancer Letter. NCI’s Korde: Follow-Up Needed to Validate PFS with Mature OS Results for Tecentriq; Larissa Korde, MD, Cancer Therapy Evaluation Program; The Cancer Letter; October 26, 2018.

A Look Inside NIH Clinical Center: The Largest Clinical Research Hospital in the Country; Larissa Korde, MD, Cancer Therapy Evaluation Program; Scripps News; October 12, 2018.

Advancing Academic Successes to the Clinic with Barbara Mroczkowski & Andrew Flint; Barbara Mroczkowski, PhD and Andrew Flint, PhD, Office of the Director; RxNet; October 4, 2018. Free login required.

Conferences and Meetings

The Chemical Biology Consortium (CBC) in the NCI Experimental Therapeutics (NExT) Program brought together chemical biologists and molecular oncologists from government, industry, and academia to address unmet therapeutic needs in oncology. The CBC operates as a collaborative network of 7 Dedicated and 15 Specialized Centers across the U.S. that support the advancement of NExT discovery projects, provide scientific leadership, and provide technologies to projects. The CBC Fall Symposium, sponsored by NCI, convened on November 16, 2018 at the University of California, San Francisco's Mission

L to R: Michelle Arkin, PhD, UCSF, Pamela Munster, MD, UCSF Helen Diller Family Comprehensive Cancer Center, Barbara Mroczkowski, PhD, NCI NExT Program
Bay Campus in San Francisco, CA. Members of the CBC and the Bay Area scientific community met to discuss emerging concepts, novel technologies, and therapeutic strategies in drug discovery and development, with a particular emphasis on bridging the gaps between discoveries in academic settings and translation or advancement of those hypotheses into novel therapeutics.
CTEP held its second annual Symposium on Mechanisms of Cancer Drug Resistance and Sensitivity on October 4-5, 2018. The goal of the meeting was to feature preclinical research focused on innovative strategies to understand and combat mechanisms of tumor resistance and to exploit tumor sensitivity to anti-cancer therapies. Read the meeting summary.

[Image: Poster presenters at the Symposium on Mechanisms of Cancer Drug Resistance and Sensitivity]

On October 1-2, 2018, CTEP convened its annual Early Drug Development Meeting. The EDD meeting is an educational event focused on enhancing communications between the NCI and the network of CTEP-supported Experimental Therapeutics Clinical Trials Network (ETCTN)-funded early clinical trial investigators. Read the meeting summary.

[Image: Wells A. Messersmith, MD, University of Colorado, receives the Michaele C. Christian Oncology Drug Development Award. L to R: Wells A. Messersmith, MD, Michaele C. Christian, MD, John Wright, MD, PhD, Jeff Abrams, MD]
New DCTD Funding Opportunities

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Awards and Recognition

Geraldine O’Sullivan Coyne, MD, PhD, Developmental Therapeutics Clinic, received a CTOS Young Investigator Award for her presentation on November 16, 2018 at the Connective Tissue Oncology Society 2018 Annual Meeting.