



DCTD Staff Highlight: Alice Chen, MD



Alice Chen, MD, is Head, Early Clinical Trials Development Program, Office of the Director, Division of Cancer Treatment and Diagnosis, NCI, NIH.

In 1991 Alice Chen, MD began her career at NCI in a combined FDA/NCI drug development fellowship and then as Attending in the Navy Medical Oncology Branch. Following a departure in 1998 to work in private practice, Dr. Chen returned to NCI in 2005 to join DCTD as a Medical Officer in the Investigational Drug Branch of the Cancer Therapy Evaluation Program (CTEP). In 2014, after nine years in CTEP during which Dr. Chen served as Program Manager for a portfolio of investigational agents, including PARP inhibitors, HSP 90 inhibitors, and DNA repair inhibitors with a combined budget of more than \$10 million, she became Head, Early Clinical Trials Development program in DCTD's Developmental Therapeutics Clinic (DTC). In the DTC, Dr. Chen oversees approximately 15 active early-phase clinical trials and the coordinating center for several phase 1 and phase 2 trials. Dr. Chen is a liaison between the intramural and extramural communities on all aspects of early phase clinical trials.

In addition to her responsibilities in the DTC, Dr. Chen consults with oncologists around the world

regarding cancer therapeutics decision-making. She led the revision of the Common Terminology Criteria Adverse Events (CTCAE) v4 and is responsible for the maintenance and revision of this document. Dr. Chen has a particular interest in patient-reported outcomes and is a member of the Strategic Leadership Group for the NCI PRO-CTCAE, which is the Patient-Reported Outcomes version of the CTCAE. Dr. Chen is particularly proud of her efforts as principal investigator of two NCI-sponsored precision medicine trials, Molecular Profiling-Based Assignment of Cancer Therapy (NCI-MPACT) and Molecular Analysis of Therapy Choice (NCI-MATCH).

Dr. Chen has published more than 50 peer-reviewed publications over her career. Topics of her publications have included PARP inhibitors, phase 0 trials, and CTCAE. Dr. Chen has received eight NIH Merit Awards for her work in adverse event evaluation and international relations. The Division of Cancer Treatment and Diagnosis is honored to have Dr. Chen as a member of its staff for more than ten years.

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Spotlight: An Interview with Jason Cristofaro, JD, PhD on Intellectual Property Management in DCTD



*Jason Cristofaro, JD, PhD,
is Intellectual Property
Program Manager, Office
of the Director, Division
of Cancer Treatment and
Diagnosis, NCI, NIH.*

“Why don’t you ask the lawyer…”
The response to this is usually, “We have a lawyer?” DCTD does have a team to coordinate external agreements and agreement policy for the division. Legal issues related to the division’s programs usually lead to **Jason Cristofaro, JD, PhD** who serves as the Intellectual Property (IP) Program Manager for DCTD. Dr. Cristofaro has worked for DCTD for the past decade and has built a group and infrastructure to manage agreements and agreement issues related to DCTD programs.

Dr. Cristofaro answered some questions related to the management of IP in DCTD, a unique topic at the intersection of science and policy.

What is the history of IP management in DCTD?

JC: Ten years ago, Dr. Doroshow was looking for someone with a legal background to come to DCTD and review agreements. At the time, there was no coherent agreement policy in the division, and almost all agreements were negotiated de novo. As a result, it often took a long time to negotiate agreements between Industry and the division, and Cooperative Research and Development Agreements (CRADA) in particular were very troublesome, often taking in excess of 2 years to successfully negotiate. With the implementation of the [NCI Experimental Therapeutics Program \(NExT\)](#), we developed a more formalized and rapid process to negotiate agreements. Now there is a clear delineation of what agreements we use for what projects and how long we expect those negotiations to take.

What staff within DCTD collaborate to provide IP services?

JC: Most of the staff I work with resides in the [Regulatory Affairs Branch \(RAB\)](#) in DCTD’s [Cancer Therapy Evaluation Program](#). I have a particularly close working relationship with Sherry Ansher, PhD who is the divisional guru for regulatory issues related to agreements. Over the past decade we have built out the RAB group that is responsible for agreements by adding both negotiators and support staff as the number and complexity of agreements have increased. The NExT Program required a mechanism to allow us to both bring in funding and offer licensing rights to government inventions to our industry and academic partners. Thus, we have moved from use of clinical trial agreements to CRADAs, and that has necessitated greater efficiency in all areas of agreement management and negotiation. In addition, our group works closely with the [NCI Technology Transfer Center](#) for our preclinical agreements.

Were there opportunities to improve any processes within DCTD related to IP services?

JC: There were two big early changes that have had far-reaching impacts. First, the revision of the CTEP IP Option to Collaborators (the standard set of rights we offer to industry partners conducting clinical trials with CTEP) was necessary because the prior version did not account for the disposition of biomarker inventions; prior to 2005 most of industry and academia did not understand the

importance that biomarker inventions would have in therapeutic development. By the time we were doing the revision in 2011, biomarker inventions were an issue in every negotiation because of the concern that assays developed by biomarkers would have regulatory and commercial impacts, as well as play an enormous role in drug development as the field moved toward personalized medicine. The revision resulted in an influx of new collaborators and helped revive declining participation with pharmaceutical companies. Second, the establishment of a Technology Development

Coordinator (TDC) position within CTEP allowed us to have greater control over agreement negotiation metrics. We were able to establish a hard stop date for negotiations that reduced the time to complete an agreement from more than 2 years to fewer than 6 months.

What future projects are on the horizon for the IP Group?

JC: We have had a lot of success over the past few years getting our standard agreements in place expeditiously. That success allowed us to move forward with a series of special projects that would not have been possible

otherwise. Master protocols, [NCI-MATCH](#), the [Exceptional Responders Study](#), and the new NCI Drug Formulary initiative would not have been possible if not for the foundational work we did with the IP Option and the TDC. The ability to cut down the time and activation energy of these agreements has resulted in an influx of special projects. We anticipate that our productivity will continue, as precision medicine-based treatments are going to require the cooperation of many parties, and that means a lot more agreements coming our way.

News about DCTD Programs and Activities

Publications

- A paper published in *Cell Chemical Biology* on July 14, 2016 describes the "[Structural Basis for KDM5A Histone Lysine Demethylase Inhibition by Diverse Compounds](#)". The study was funded in part by [NCI's Chemical Biology Consortium](#) to Emory University. [View Emory's press release](#).
- Results of two high-impact, DCTD-sponsored clinical trials with checkpoint inhibitors were published in the *New England Journal of Medicine*. The papers were published within two weeks of each other in June and July 2016 and include Cancer Therapy Evaluation Program's **Elad Sharon, MD, MPH** and **Howard Streicher, MD** as authors on the papers, respectively: [PD-1 Blockade with Pembrolizumab in Advanced Merkel-Cell Carcinoma](#) and [Ipilimumab for Patients with Relapse after Allogeneic Transplantation](#).
- On May 24, 2016, the *Annals of Internal Medicine* published a review by **Richard Simon, DSc**, Biometric Research Program, entitled, "[Genomic Alteration-driven Clinical Trial Designs in Oncology](#)."

Meeting Participation

- DCTD's Translational Research Program (TRP) convened a Lung Cancer SPORE Workshop on June 23-24, 2016. **Scott Antonia, MD, PhD**, H. Lee Moffitt Cancer Center and **Matthew Meyerson, MD, PhD**, Dana-Farber Cancer Institute were the co-chairs. Nine panel sessions included 53 presentations on the following topics: Molecular Profiling and Biomarkers; EGFR and Other Signaling Pathways; KRAS, LKB1 and Related Pathways; Patient Screening and Advocacy; Immunotherapy & Immune-based Resistance and Immunotherapy Clinical Trials; Novel Targets; Therapeutic Resistance; Small Cell Lung Cancer; and Premalignancy, Risk Stratification, and Chemoprevention. Contact **Peter Ujhazy, MD, PhD, TRP**, with questions about the meeting.

Meeting Participation... *continued*

- **Farah Zia, MD** (Chair) and **Oluwadamilola Olaku, MD** (Co-Chair), Office of Cancer Complementary and Alternative Medicine (OCCAM) conceptualized, organized, and convened a conference entitled, "*Acupuncture for Cancer Symptom Management*," on June 16-17, 2016. The objectives of the meeting were to:

- Assess the current state-of-the-science of acupuncture for cancer symptom management, including understanding of local and central mechanisms
- Identify cancer symptom(s) with the best evidence of response to acupuncture
- Identify gaps in basic and clinical research
- Stimulate further research in areas identified as gaps, in the forms of intramural collaborations and increased grant applications

Invited speakers included 19 scholars from the United States, Europe, and China, with expertise in acupuncture and cancer research. The following topics were covered:

- NCI's portfolio on acupuncture
- The needs of cancer patients, safety issues, and the application of acupuncture in oncology care
- Acupuncture clinical trials, including their methodology and statistical aspects
- The characteristics and status of acupuncture in clinical care in the US, Europe, and China

- Current understanding of cost-effectiveness and reimbursement issues, providing strategies for improvement
- Current state-of-the-science of the local and central mechanisms of action of acupuncture
- Gaps in basic and clinical research, as well as those in acupuncture's clinical applications

The conference affirmed the potential for use of acupuncture in the management of cancer symptoms, in which the experts urged further integration into oncology care, and called for establishing a dedicated field for "oncology acupuncture." The responsibilities of this subspecialty would include training qualified acupuncturists in the care of cancer patients and establishing inpatient oncology acupuncture centers for high risk patients, as well as

NIH NATIONAL CANCER INSTITUTE

DIVISION OF CANCER TREATMENT AND DIAGNOSIS

Office of Cancer Complementary and Alternative Medicine

**ACUPUNCTURE FOR
CANCER SYMPTOM
MANAGEMENT CONFERENCE**

June 16-17, 2016
8:30 am - 5:00 pm

Natcher Auditorium, Balcony B
National Institutes of Health
Main Campus
Bethesda, Maryland

Conference Co-Chairs

Farah Zia, MD
Medical Officer
OCCAM, DCTD
National Cancer Institute

Oluwadamilola Olaku, MD, MPH, MRCOG
OCCAM, DCTD
National Cancer Institute

U.S. Department of Health & Human Services | National Institutes of Health

OCCAM Acupuncture Conference

outpatient services for those with less critical needs. A white paper summary of this seminal event will be published in an upcoming special monograph of the *Journal of the National Cancer Institute (JNCI)*.

- The [2016 Precision Medicine Workshop](#) was held June 16-17, 2016 and was co-sponsored with NCI, the American Society for Therapeutic Radiology and Oncology, and the American Association of Physicists in Medicine. DCTD's **Paula Jacobs, PhD**, Cancer Imaging Program (CIP), **Bhadrasain Vikram, PhD**, Radiation Research Program (RRP), and **Charles Kunos, MD** (Keynote), Cancer Therapy Evaluation Program (CTEP), were speakers at the event.
- DCTD's OCCAM convened the workshop, "[The State-of-the-Science: Cancer Complementary and Alternative Therapeutics Research](#)," on May 25-26, 2016. Planned by OCCAM's **Dan Xi, PhD**, the meeting included more than 40 speakers and about 70 attendees from the federal government, academia, cancer centers, and integrative medicine programs.
- The FDA, the International Society of Image Guided Surgery, the World Molecular Imaging Society, and DCTD's CIP, collaborated to convene the workshop, "Regulatory Pathways for Clinical Use of Optical Methods and

Exogenous Targets for Cancer Detection" on May 4, 2016. The goal of the meeting was to promote the understanding of regulatory pathways related to clinical evaluation of optical imaging and detection of surface malignancies and tumor margins during surgical resections. [View the participant list, workshop agenda, PowerPoint slides, and full videocast.](#)

- The Society of Nuclear Medicine and Molecular Imaging partnered with DCTD's CIP to convene the workshop, "Immune Modulation Therapy and Imaging: What can we do in clinical trials now?" on May 2, 2016. The meeting focused on alternative methods of tumor response assessment in patients receiving immunotherapy because current assessment with anatomic imaging and with the standard Response Evaluation Criteria in Solid Tumors (RECIST) criteria has not been very helpful in these patients. [View the participant list, workshop agenda, PowerPoint slides, and full videocast.](#)
- **Avi Rasooly, PhD**, OCCAM and **Min He, PhD**, Developmental Therapeutics Program (DTP), organized and co-chaired a program on complementary and alternative medicine (CAM) at the [12th International Conference of Asian Clinical Oncology Society](#) on April 8-10, 2016 in New Delhi, India. This activity was sponsored by NCI's

Center for Global Health and was done in collaboration with **Dr. G. K. Rath**, head of India's National Cancer Institute.

The program included the following sessions:

- Analytical Approaches and Challenges for CAM Material Analysis; speakers from the U.S. and China
- Comparative Cancer CAM Modalities, Interventions and Analysis in Asia; speakers from Japan, Korea, and India
- Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) and Indian Integrated Therapies for Cancer; speakers from India

Dr. He also delivered a podium speech on DCTD/DTP's support for global cancer research entitled, "NCI Developmental Therapeutics Program: Providing Resources to Promote Cancer Research Worldwide," and Dr. Rasooly moderated a panel discussion entitled, "Incorporation of CAM in Modern Medicine."



2016 Summer Interns in the Developmental Therapeutics Clinic

- NIH Summer Interns in DCTD's Developmental Therapeutics Clinic discussed their research projects at the NIH Summer Research Program Poster Day on July 29, 2016. The interns and their projects were:
 - **Amul Choudhary:** Quality of Life Assessment using MDASI in Patients with Desmoid Tumors Treated with PF03084014
 - **Caroline Moore:** Patient Demographics Trends over 5 Years in the Developmental Therapeutics Clinic at the NCI
 - **Nomi Gordon:** Comparing Response Rates of Two Cediranib Trials in ASPS Tumors
 - **Ann Lih:** Volumetric Assessment, and its Relation to RECIST 1.1 Response, in Desmoid Tumors
- [Research from DCTD's CIP](#) was instrumental to the May 27, 2016 FDA approval of a PET imaging diagnostic agent for recurrent prostate cancer. The strength of this targeted, radiolabeled agent is its specific uptake into prostate cancer cells, thus allowing diagnostic imaging of the tumor.
- In May 2016, NCI's precision medicine clinical trial, [NCI-Molecular Profiling-based Assignment of Cancer Therapy \(NCI-MPACT\)](#) opened at sites across the country. This expansion is expected to increase patient accrual and confirm the feasibility of multi-site, real-time molecular profiling to guide cancer treatment.
- Staff from DTP conducted a five-session PRESTO (Program and Review Extramural Staff Training Office) training program, which was offered to NCI extramural grant program directors and review staff. This training covered DTP's broad research resources for supporting the discovery and pre-clinical development of small molecules, natural products, and biological anti-cancer therapeutic agents. The ultimate goal of this training program is to encourage NCI grantees to utilize these government resources to facilitate their research. Collectively, these five sessions have attracted more than 200 attendees from five NCI divisions and the Office of the Director.

Honors and Awards

Myrtle Davis, DVM, PhD, Developmental Therapeutics Program, was invited to serve on the [National Toxicology Program](#) Board of Scientific Counselors for the term beginning July 1, 2016 and ending June 30, 2020.

2016 NIH Director's Awards

GTEX Implementation Team

Ping Guan, PhD, Cancer Diagnosis Program
Helen Moore, PhD, Cancer Diagnosis Program
Abhi Rao, PhD, Cancer Diagnosis Program

Team to Assure Sterile Products for Human Administration at NIH

Jerry Collins, PhD, Developmental Therapeutics Program

NCI-NHLBI Cancer Treatment-related Cardiotoxicity Team

Myrtle Davis, DVM, PhD, Developmental Therapeutics Program

NIH-Wide Strategic Plan Working Group

Pamela Harris, MD, Cancer Therapy Evaluation Program

Gabriella Miller Kids First Pediatric Research Program Coordination Team

Malcolm Smith, MD, PhD, Cancer Therapy Evaluation Program

Public Access Support Center Pilot Team

Tamara Walton, MHA, MPA, Translational Research Program

Stimulating Peripheral Activity to Relieve Conditions (SPARC) Working Group

Yantian Zhang, PhD, Cancer Imaging Program



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