



DCTD Staff Highlight: Roy S. Wu, PhD



Roy Wu, PhD, was Branch Chief, Clinical Grants and Contracts Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, NCI, NIH.

Roy Wu, PhD began his career at NCI in the intramural program in 1979. Seven years later, Dr. Wu joined the Division of Cancer Treatment and Diagnosis (DCTD) in the Cancer Therapy Evaluation Program (CTEP) as the sole Program Director for the clinical grants program. In 2000, after 14 years of success in which Dr. Wu was responsible for the 12-fold increase in the CTEP grants portfolio, he became Branch Chief of the newly formed Clinical Grants and Contracts Branch (CGCB). This accomplishment has led to CGCB's oversight of grants, contracts, and cooperative agreements that average \$300 million per year during the period of the doubling of the NIH budget. The CGCB focuses on clinical and surgical oncology and pharmacogenomics, with emphasis on the development of investigative clinical agents, related correlative studies, novel treatment regimens and trial designs, and clinical surgical methods development.

Dr. Wu is particularly proud of his efforts in supporting two areas of cancer treatment research: (1) sentinel node biopsy research and (2) blood and marrow transplantation research. Both areas of research produced practice-changing findings. Sentinel node biopsy is now widely practiced in breast cancer and melanoma treatment and has eliminated the morbidity associated with complete lymphadenotomy. Improvements

in blood and marrow transplantation have allowed an increase in cancer patient access to this life-saving modality. Reduced intensity transplants, cord blood transplants, and haplo-identical transplants have allowed those patients in frail health or without matched donors to be safely transplanted. African Americans and the elderly have greatly benefitted from these types of transplants. Dr. Wu played an instrumental role in the establishment of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) in 2001. He received the 2001 Public Service Award from the American Society for Blood and Marrow Transplantation. The BMT CTN has accrued over 8,600 patients since 2003.

Dr. Wu has published nearly 40 peer-reviewed publications over his career, starting with his first publication in 1971. Topics of his publications have included histone gene expression and activity, DNA repair, the cell cycle, and several NIH consensus documents. Dr. Wu has received many NIH and external awards, including the 2008 NIH Award of Merit for Effective Team Work, the 2009 NIH Award of Merit, and the 2008 DHHS Hubert H. Humphrey Award for Science to America. Dr. Wu retired from the federal government in April 2016 and was an asset to DCTD, NCI, and NIH.

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Spotlight: A Joint Clinical Trial between the Comparative Oncology Program and DCTD

The [Comparative Oncology Program](#) and DCTD recently completed a clinical trial, [COTC007b](#), in pet dogs with lymphoma, evaluating three new anticancer drugs that target topoisomerase I, an enzyme involved in DNA replication. These drugs, belonging to the indenoisoquinoline class, were developed within DCTD. This clinical trial was conducted through the [NCI Comparative Oncology Trials Consortium \(COTC\)](#), a network of 22 veterinary teaching hospitals in North America. This was the third joint clinical trial between the Comparative Oncology Program and DCTD.



Patient at University of Pennsylvania

The goals of the study were to define the safety and biological response of a common canine cancer to these three related drugs. Eighty-four dogs with lymphoma were enrolled on study over a 3-year period. The study was designed to collect critical data to enable and guide the design and execution of Phase I human studies of these same drugs.

Nine COTC sites, Colorado State University, Ohio State University, Purdue University, University of California, Davis, University of Missouri, University of Pennsylvania, University of

Tennessee, Tufts University, and the University of Wisconsin-Madison, participated in this study, and all dogs were evaluated following a defined protocol and standard operating procedures. The study protocol was reviewed and approved by each participating site's Institutional Animal Care and Use Committee and, where applicable, Clinical Trials Review Board. All study data were managed by the Comparative Oncology Program utilizing the Cancer Central Clinical Database (C3D).

Privately-owned pet dogs with a confirmed diagnosis of lymphoma were eligible for inclusion in the study. All dogs received routine veterinary care during the course of the study, which lasted up to 28 days. Dogs were randomized to receive one of the three agents on a fixed schedule of five daily infusions within a 28-day observation cycle. Biological samples were standardized across all three drugs, with each dog on study undergoing over 40 biological collections. Four tumor biopsies were collected in the first week along with two 24-hour blood collection curves to determine drug pharmacokinetics following the first and last doses. Plasma, serum, and tumor and bone marrow aspirates were also collected over the 28-day cycle in order to correlate drug exposure with downstream molecular events within tumor cells and sensitive normal tissues such as bone marrow.

COTC007b highlighted the efforts of a multi-investigator clinical trial and the collection of high-quality biologic samples and clinical data that directly enable and inform follow-on assay development and human clinical trial activities. Publications are planned for later this year.

News about DCTD Programs and Activities

Publications

- Results from an NCI-sponsored, Phase 2 clinical trial showing durable responses in Merkel cell carcinoma patients treated with pembrolizumab were released at AACR on April 19, 2016 and published in the [New England Journal of Medicine](#).
- On March 21, 2016, several members of DCTD's staff published a paper in [Clinical Cancer Research](#) describing a new assay to detect MET phosphorylation in tumor biopsies.
- A [Cancer Current blog post](#) authored by Jo Anne Zujewski entitled, "Keeping Pace: How New Data Can Affect Ongoing Clinical Trials" was published online on March 16, 2016.

- A [Cancer Currents blog post](#) authored by Irina Lubensky, Rodrigo Chuaqui, and Joanne Demchok entitled, "Fueling Basic Discovery: NCI's Cooperative Human Tissue Network" was published online on March 7, 2016.
- Alice Chen and Robert Meehan co-authored a paper on PARP inhibitors as treatment for ovarian cancer. The paper was published in [BioMed Central](#) on February 26, 2016.
- p97 is a protein that plays a role in maintaining protein quality and is an attractive target for cancer therapy. A paper published online in [Science](#) on January 28, 2016 reported the high-resolution cryo-EM structures for the full-length, hexameric p97 in the presence and absence of a novel allosteric inhibitor developed by a collaborative team of academic scientists participating in the [NCI Chemical Biology Consortium](#).

Meeting Participation

- Several DCTD staff will participate in the [Innovation and Biomarkers in Cancer Drug Development \(IBCD\)](#) meeting from September 8-9, 2016 in Brussels. The goal of the collaborative meeting is to promote multi-stakeholder strategies for cancer drug development.
- Mansoor Ahmed will co-chair a joint session at the [Radiosurgery Society meeting](#) from June 16-18, 2016 in Orlando, FL. The session is entitled, "Hypo-fractionated Radiation Therapy, Immune-modulation and Immunotherapy," and is being jointly organized by the Radiosurgery Society, Society for Immunotherapy of Cancer, Radiation Research Society, and NCI. This symposium will bring together clinicians and researchers with an interest in radiotherapy and/or immunology to open a dialogue on the potential for exploiting radiation-induced immune responses in the context of cancer therapy.
- Several DCTD staff will present at the 2016 Annual Meeting of the American Society of Clinical Oncology (ASCO; June 3-7, 2016; Chicago, IL). [View](#) the complete list of oral, poster, and meet-the-expert sessions.
- The [Accelerating Anticancer Agent Development and Validation \(AAADV\) workshop](#) was held on May 4-6, 2016 in Bethesda, MD. Helen Chen was a member of the Planning Committee, and Alice Chen, Barbara Conley, and Lisa McShane were speakers.
- Members of the translational ovarian and gynecologic cancer research communities participated in a [workshop](#) at NCI on May 3, 2016. The workshop was planned by NCI staff with input from SPORE investigators.
- Several DCTD staff participated as faculty in the [Markers in Cancer Diagnostic Development Tutorial](#), which was held on May 2-3, 2016 in Bethesda, MD. The workshop objective was to train young investigators on how to construct clinical trials that report valid biomarker results. As part of the goal of developing precision medicine for cancer patients, biomarker results could be applied to patient selection for specific therapies. Areas covered included: selecting and stating the hypothesis being tested and proposed biomarker utility, identification of the appropriate patient population to be enrolled and tested, assay selection and validation, required statistical considerations for protocol design, and presentation of the protocols by teams of participating students.
- Carol Weil discussed NCI's [tissue donation video](#) at the [2016 Annual Conference of the Association for the Accreditation of Human Research Protection Programs](#) (April 19-21, 2016; Long Beach, CA) and the [2016 Annual Meeting of the International Society for Biological and Environmental Repositories](#) (April 5-8, 2016; Berlin).
- Many DCTD staff presented at the 2016 Annual Meeting of the American Association for Cancer Research (AACR; April 16-20, 2016; New Orleans, LA). [View](#) the complete list of oral, poster, and meet-the-expert sessions.
- Members of the prostate cancer translational research community participated in a [workshop](#) at NCI from April 4-5, 2016. The workshop was planned collaboratively by NCI staff from the Translational Research Program and prostate cancer SPORE investigators.
- Magdalena Thurin co-chaired a session ("Immunologic Monitoring Assay Standardization and Validation")

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Meeting Participation ... *continued*

at the [Immunotherapy Biomarkers 2016: Overcoming the Barriers](#) meeting on April 1, 2016. The meeting was a co-sponsorship between the Society for Immunotherapy of Cancer and NCI.

- DCTD staff participated in the March 31, 2016 [Radiation and Immunotherapy Leadership Summit](#), which was a co-

sponsorship between the Society for Immunotherapy of Cancer and NCI. DCTD staff included: Norman Coleman, Mansoor Ahmed, Howard Streicher, Elad Sharon, Bhadrasain Vikram, Pat Prasanna, and Eric Bernhard.

- On January 14-15, 2016, DCTD convened a cancer immunotherapy workshop with extramural and intramural thought leaders. The goals

were for attendees to provide insight into gaps that limit clinical success with cancer immunotherapy and to advise NCI on new directions and initiatives in basic, translational, and clinical studies to address unmet needs critical to immunotherapy development. A report from the meeting is under development.

Program Updates

- The NCI Experimental Therapeutics (NExT) Program's next [application cycle](#) opened on May 15, 2016. The NExT Program accepts applications focusing on anticancer therapies. Accepted applicants will gain access to NCI's discovery or development resources to advance their agent.
- On May 2, 2016, the NExT program launched the [Experimental Therapeutics Consultation](#) as a means to streamline access to this service to the scientific community. After completing a simple online form, investigators can request a consultation on nonclinical safety, good manufacturing processes for small molecules and biologics, and the development of imaging products that are intended for cancer patients. Investigators who request the consult will be contacted by members of DCTD staff with the appropriate expertise to obtain the needed assistance. Ultimately, investigators will be encouraged to also consider application to the NExT program to request resources if

they are needed to enable the projects discussed.

- Established in 2009, [NCI's Chemical Biology Consortium \(CBC\)](#) is a flexible network of scientists working to discover drug candidates for novel and challenging targets for cancer treatment. In April 2016, the CBC network was expanded from 12 to 22 centers, including seven Dedicated Centers and 15 Specialized Centers, with world-class expertise in high-throughput screening, structural biology, medicinal chemistry, compound profiling, cancer cell biology, and animal models for oncology.
- In April 2016, the NCI's Biorepositories and Biospecimen Research Branch, CDP announced the release of the 2016 version of the [NCI Best Practices for Biospecimen Resources](#). This foundational document for biobanking has been updated and revised to provide more current and detailed recommendations related to biospecimen and data quality for addressing ethical, legal, and social issues (ELSI) and technical aspects of biobanking.

- Posters about the Ethical, Legal and Social Issues (ELSI) sub-study of the [GTEx \(Genotype-Tissue Expression\)](#) project were on display in Spanish and English at NCI in March. The posters described the process and rationale for biospecimen donation for the GTEx project. The ELSI sub-study is being performed to better understand and improve the factors affecting informed consent for tissue donation. The posters were used for communicating what the Community Advisory Board of Hispanic community members had learned about the process and rationale for biospecimen donation for the GTEx project with their community. The GTEx project is a Common Fund Program that is being conducted to correlate genetic variation with gene expression in multiple tissues collected from over 900 reference/non-diseased postmortem donors.
- DCTD is part of the NCI-Department of Energy collaboration in advanced computing solutions in cancer research. The DCTD-specific effort, "[Patient Level Pilot: Modeling for Pre-Clinical](#)

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Program Updates ... continued

Screening," involves developing large-scale data and predictive models based on experimental data collected from patient-derived xenographs.

- DCTD has supported the development and validation of [multiplex immunoassays](#) for 15 cytosolic and membrane-

associated proteins that are indicative of the induction, onset, and commitment to apoptosis in human tumors. These immunoassay kits, constructed on the Luminex multiplex technology platform, are now commercially available. [The Tumor Biopsy Lysate Fractionation for the Apoptosis Multiplex Immunoassay Panels SOP](#), a validated procedure

for preparing tumor biopsies prior to multiplex analysis, is being transferred to the cancer research community. Training and certification are provided for interested investigators at the Frederick National Laboratory for Cancer Research (FNLCR) campus.

New Funding Opportunities

- [PAR-16-176: NCI Clinical and Translational Exploratory/Development Studies \(R21\)](#)
The scope of the work in this PAR focuses on early/pilot clinical trials, correlative studies and biomarker development, target and agent discovery and development, and model development and analysis.

- [PAR-16-166: Integrating Biospecimen Science Approaches into Clinical Assay Development \(UO1\)](#)
This FOA will support extramural research to investigate and mitigate challenges facing clinical assay development due to biopsy biospecimen preanalytical

variability. The program will tie in with current efforts to optimize clinical biomarker assays utilized in NCI-sponsored clinical trials.

DCTD Staff News



In Memoriam

Larry Clarke, Branch Chief, Imaging Technology Branch, Cancer Imaging Program, passed away on April 16th after a short illness. We will miss him, both personally and scientifically. Dr. Clarke's [obituary](#) is available on the Cancer Imaging Program's website.

Honors and Awards

- The Radiation Research Society has awarded its prestigious 2016 [Failla Award to Norman Coleman, MD](#), Associate Director, Radiation Research Program. This annual award is given to an outstanding member of the

radiation research community in recognition of their history of significant contributions to radiation research and their ongoing efforts. Please join us in congratulating Dr. Coleman on this truly outstanding recognition.

- Geraldine O'Sullivan Coyne and Robert Meehan, both clinical fellows in the Developmental Therapeutics Clinic, received 2016 Conquer Cancer Foundation of ASCO Merit

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Honors and Awards ... *continued*

Awards for their [abstracts submitted to ASCO 2016](#).

- NCI received an Excellence in Technology Transfer Award for the project, "[From Discovery to Commercialization, Monoclonal](#)

[Antibody Ch14.18, Unituxin™ \(dinutuximab\)](#)." The award was formally given at the Federal Laboratory Consortium's annual meeting April 26-28, 2016.

- Keyvan Farahani was elected to the [American Institute for Medicine & Biological](#)

[Engineering's](#) College of Fellows in April 2016 for pioneering work in the creation of the new field of image-guided drug delivery.



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