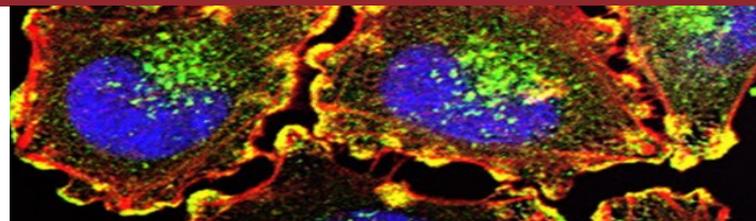




NATIONAL CANCER INSTITUTE

DCTD Division of Cancer Treatment & Diagnosis



DCTD PIPELINE NEWSLETTER

February 2016

The DCTD Pipeline Newsletter highlights recent initiatives, activities, staff, and events across the division. For more information on DCTD visit DCTD's website: <http://dctd.cancer.gov/>

IN THIS ISSUE

[DCTD Staff Highlight: Dr. Barry O'Keefe](#) _____ page 2

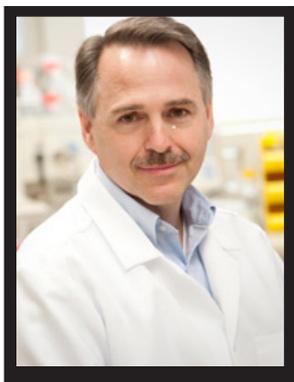
[In the Spotlight: The Quantitative Imaging Network](#) _____ page 3

[News about DCTD Programs and Activities](#) _____ page 4

[DCTD Staff News](#) _____ page 5



DCTD Staff Highlight: Dr. Barry O'Keefe



[Dr. Barry O'Keefe](#) has been a researcher at NCI for 22 years, until recently exclusively in the [Molecular Targets Laboratory \(MTL\) of the Center for Cancer Research \(CCR\)](#). His most recent work focuses on screening natural products and identifying novel bioactive molecules, including those housed in NCI's repository at the [Frederick National Laboratory for Cancer Research \(FNLCR\)](#).

Recently, Dr. O'Keefe's has taken over direction of FNLCR laboratories in the [Natural Products Branch \(NPB\) of the Developmental Therapeutics Program](#), including the [NCI's Natural Products Open Repository Program](#) and the [Active Repository Program](#). These programs involve acquisition and sharing of a large repository (~230,000) of crude natural product materials from terrestrial and marine environments for extraction and screening in the NCI-60 human tumor cell lines screen.

The NPB is engaged in a joint effort with CCR, the NCI Program for Natural Product Discovery (NPNPD), to add value to the NCI Extract Repository by producing a library of 1,000,000 partially purified or "prefractionated" extracts. In addition, the NPB is adding more microbial diversity to the NCI collection with a recent agreement to add U.S. soil fungi through a "citizen science" program in collaboration with the University of Oklahoma. These new programs are part of the effort to increase the chemical diversity readily available for screening programs such as those performed in the [Chemical Biology Consortium](#). With concurrent efforts at improving the efficiency of natural products chemistry and enhancing the bio-informatics support for screening and compound isolation, the NPNPD is designed to increase the identification of targeted chemotherapies from natural sources.

Dr. O'Keefe's current research focuses on: 1.) cell-free assay

development and identification of active compounds from chemical and natural product libraries; 2.) isolation and characterization of bioactive proteins from natural product extracts. This research requires a multi-



disciplinary approach among CCR, NCI, and extramural collaborators. Advances in biological agent utility for therapy have improved our understanding of how exogenous proteins and peptides interact with human physiology, which enables increasing utility of non-human proteins in therapy. Several non-human proteins are used in the clinic for diseases ranging from osteoporosis to diabetes. Efforts that have combined the unparalleled chemical diversity in the NCI Extract Repository and isolation of understudied proteins and peptides have led to discoveries, such as the protein griffithsin. Griffithsin was isolated in the MTL from an extract of the red algae *Griffithsia* sp. found in the NCI Extract Repository. Two separate groups have been funded to bring this novel antiviral protein into human clinical trials as an anti-HIV microbicide.

The combination of pre-fractionating the NCI Natural Products Extract Repository, enhancing the speed and efficiency of compound identification, and looking at new microbial sources of chemical diversity and understudied compound classes within these extracts should provide short- and long-term benefits for the discovery of new compounds targeted against cancer and other human disease.

Dr. Barry O'Keefe is Branch Chief, Natural Products Branch, Developmental Therapeutics Program, DCTD, Deputy Chief, Molecular Targets Laboratory, Associate Scientist and Head, Protein Chemistry and Molecular Biology Section, CCR.

In the Spotlight: The Quantitative Imaging Network

The [Quantitative Imaging Network \(QIN\)](#) within DCTD's [Cancer Imaging Program \(CIP\)](#) is designed to create, optimize, and validate software tools for use in clinical trials to support decision-making in response to therapy. Imaging is a front-line method for noninvasive analysis of tumor status and response to therapies, but often the information obtained through clinical images is qualitative and requires expert interpretation. QIN's mission is to create and distribute data acquisition tools and image analysis methods that will create the condition where all clinical imaging devices perform as measuring devices. Results will be scanner agnostic and quantitative, providing accurate single timeframe and longitudinal information on tumor parameter measurements and prediction of outcomes.

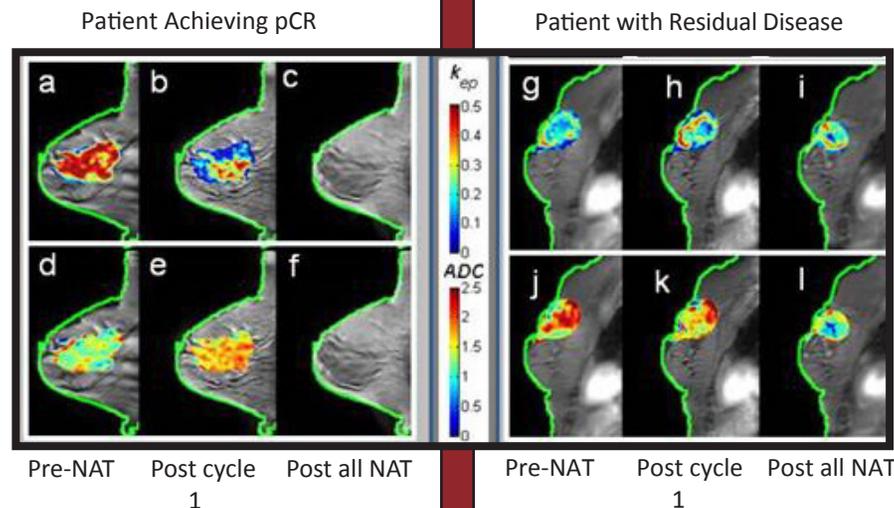
To accomplish the task of eventually introducing quantitative measurements into clinical trials, CIP has chosen to create a network of research teams. Currently, 27 teams are participating in the activities of consensus building and dissemination of information through numerous publications as they each work to develop and optimize software tools and methods for applying quantitative methods to therapy response. Teams enter the network through application to the current program announcement and are reviewed by a NCI DEA panel. Research applications with exceptional scores are presented first to DCTD senior staff and then to the NCI Senior Program Leadership for discussion and evaluation.

The network has extended internationally, adding two research teams from the Canadian Institutes of Health Research (CIHR) that are funded by the Canadian Government. Cont. page 4

**Images a – f: Patient showing pathological complete response to neoadjuvant therapy.
Images g – l: Patient showing residual disease after therapy.
The quantitative visualization parameters are computed from magnetic resonance images called dynamic contrast enhanced MRI. Image from Vanderbilt University (U01CA142565).**

Parameter 1: k_{ep} computed from DCE-MRI images

Parameter 2: ADC computed from DCE-MRI images



In the Spotlight: The Quantitative Imaging Network (cont.)

These teams (University Health Network, Toronto and the University of British Columbia), along with several other institutes, applied for admission into the QIN through the normal review channel and were scored by study section. These two applications had exceptional scores, and through NCI and CIHR agreement were added to the QIN under Canadian support. The director of the QIN, Dr. Robert Nordstrom, is looking to export this model for international collaboration and data sharing to other countries including the United Kingdom, India, and China.

The Annual Meeting of the QIN members will take place on April 11 – 12, 2016. Over 150 participants are expected, providing presentations, posters, and software demonstrations.

News about DCTD Programs and Activities

- In late January, DCTD launched its Twitter feed: [@NCItreatment](https://twitter.com/NCItreatment). News about NCI-supported treatment and diagnosis research will be posted regularly. Follow DCTD on Twitter:

<https://twitter.com/NCItreatment>

- The [NCI Experimental Therapeutics \(NExT\) Program's](#) next application cycle opens on May 15, 2016. The NExT Program accepts applications focusing on anticancer therapies. Accepted applications will gain access to NCI's discovery or development resources to advance their agent.

- On January 5, 2016 NCI hosted a Google Hangout on NCTN and precision medicine in cancer clinical trials with Dr. Jeff Abrams, Dr. Nita Seibel, and Andrea Denicoff. View the archived video on [NCI's YouTube page](#).
- Several [DCTD staff presented data](#) at the International Conference on Molecular Targets & Cancer Therapeutics (Nov 5-9, 2015; Boston, MA).
- In October, DCTD researchers [published a paper](#) in *Clinical Cancer Research* describing a new assay that detects drug-induced cell death in tumor biopsies.
- The Genotype-Tissue Expression (GTEx) Project team of the Cancer Diagnosis Program's Biorepositories and Biospecimen Research Branch and the GTEx Consortium published a [guest editorial](#) and a [paper](#) in the October issue of *Biopreservation and Biobanking*.
- Researchers in the Molecular Pharmacology Branch of the Developmental Therapeutics Program recently published two papers on:
 - Screening with 445 FDA approved and investigational agents in 63 sarcoma cell lines along with gene and microRNA expression ([Molecular Cancer Therapeutics](#)) and
 - Sensitivity of 23 small cell lung cancer cell lines to etoposide, topotecan, a bromodomain inhibitor, and Smo and Gli antagonists ([Cancer Letters](#)).

Cont. page 5

News about DCTD Programs and Activities (cont.)

- For a third year, Cancer Imaging Program staff conducted a workshop on “[Computational Imaging in Precision Medicine](#)” at the annual meeting of the Society for Medical Image Computing and Computer Assisted Interventions (October 9, 2015). This was followed by three challenge sessions on gliomas, which included: Segmentation of Nuclei in Digital Pathology Images, Combining Imaging and Digital Pathology Tumor Classification, and Guess the Primary.
- The Cancer Imaging Program, in collaboration with the Foundation for the NIH (FNIH), is planning a [Coding 4 Cancer - Lung Cancer Screening Challenge](#) in 2016. The competition’s goal is to develop computer algorithms to identify lung cancer in low-dose screening CT images. Up to \$1.8 million in prizes will be awarded. The project was made possible through a generous grant from the Laura and John Arnold Foundation (non-profit) to the FNIH.
- The Developmental Therapeutics Clinic (DTC) conducts early-phase clinical trials of novel cancer treatment agents. View the new [DTC website](#) to learn about DTC’s activities.

DCTD Staff News

Honors and Awards



Larry Clark, Ph.D., Chief of the Imaging Technology Development Branch in the Cancer Imaging Program, has been elected as a Fellow of the Society of Photo-optical Instrumentation Engineers (SPIE), the international society for optics and photonics. He will be presented the Fellowship award at the SPIE Medical Imaging conference in San Diego, CA in February 2016. Dr. Clark is honored with this award based on a long record as an active member of the Society since the late 1980’s as well as his work in promoting CAD methods for cancer detection/classification and the use of multi-spectral MRI to measure therapy response.