



DCTD Staff Highlight: Lisa McShane, PhD



Lisa McShane, PhD, is Chief of the Biostatistics Branch, Biometric Research Program, Division of Cancer Treatment and Diagnosis, NCI, NIH

Lisa McShane, PhD has earned a reputation over her 20 years in DCTD as an expert in development and use of tumor markers for prognosis, therapy selection, and disease monitoring. She holds a PhD in Statistics from Cornell University and is a Fellow of the American Statistical Association. She began her career in the National Institute for Neurological Disorders and Stroke where she stayed for a few years before moving on to NCI. Currently, she is Chief, Biostatistics Branch, Biometric Research Program.

Dr. McShane's early research interests focused mainly on biomarker or laboratory-based research and eventually transitioned into precision medicine, representing a convergence of laboratory and clinical research. Dr. McShane is a study statistician for the NCI-MATCH precision medicine clinical trial, which is simultaneously evaluating efficacy of dozens of molecularly targeted therapies. She is also the lead statistician on DCTD's Exceptional Responders

Initiative, which uses tumor genomic sequencing to search for clues about why some patients' tumors have dramatic responses to certain cancer therapies while others do not. Her other major activities in service to DCTD include statistical review and advisory responsibilities with the Cancer Diagnosis Program and the Cancer Therapy Evaluation Program.

Dr. McShane's statistical research interests include biomarker-driven clinical trial design, analysis methods for high-dimensional omics data, multiple comparisons methods, surrogate endpoints, measurement error adjustment methods, and biomarker assay analytical performance assessment. A recent example is her collaboration with colleagues to develop and apply statistical methodology to assess the reliability of pathologic complete response (pCR) as a surrogate (replacement) clinical endpoint for event-free survival in neoadjuvant trials in order to complete those

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trials much more rapidly. Despite the prevailing opinion favoring use of pCR as a trial-level surrogate endpoint, Dr. McShane and her colleagues demonstrated, through rigorous analysis of available data, that the evidence does not support use of pCR as a surrogate in the neoadjuvant setting (Korn, 2016).

Dr. McShane co-lead efforts to develop "Reporting recommendations for tumor marker prognostic studies (REMARK)" and "Criteria for the use of omics-based predictors in clinical trials." She is a coauthor of more than 100

peer-reviewed statistical and biomedical publications and the book [Statistical Design and Analysis of DNA Microarray Investigations](#). Dr. McShane serves on the Scientific Advisory Board for [Science Translational Medicine](#) and on the Editorial Board for [BMC Medicine](#). She has served on several American Society of Clinical Oncology panels and committees, including those developing guidelines for HER2 and hormone receptor testing in breast cancer, EGFR mutation testing in lung cancer, and use of tumor biomarkers in early stage breast cancer. She has also served on Institute of Medicine Committees, most recently the

Committee on the State of the Science in Ovarian Cancer Research.

Dr. McShane is a firm believer in the importance of biostatisticians becoming conversant in the biomedical field in which they collaborate. She says that's what makes the work most fun for her, referring to a quote from the famous statistician John Tukey, "The best thing about being a statistician is that you get to play in everyone else's backyard."

DCTD is grateful for Dr. McShane's commitment to cancer research and two decades of service in the division.

Spotlight: The NCI Formulary

The [NCI Formulary](#) is a public-private partnership whose purpose is to provide academic investigators at NCI-designated Cancer Centers with rapid access to agents for cancer clinical trial use, including for combination trials involving agents from multiple collaborating pharmaceutical companies. As genomic sequencing data become mainstream in cancer therapy, requests for and access to multiple targeted agents for the conduct of clinical research are becoming more common. The NCI Formulary supports an efficient mechanism to provide pharmaceutical collaborators' agents to academic clinical researchers at NCI-designated Cancer Centers, with

the goal of improving the clinical trial implementation process for investigator-initiated and sponsored trials.

To develop the NCI Formulary, the [Cancer Therapy Evaluation Program \(CTEP\)](#) negotiated specific NCI Formulary Clinical Cooperative Research and Development Agreements (CRADAs) with pharmaceutical collaborators. The NCI Formulary CRADAs provide academic investigators at NCI-designated Cancer Centers with access to the



collaborators' proprietary agents, thus eliminating the often lengthy agreement negotiation process that occurs between individual investigators and pharmaceutical collaborators. Following collaborator approval of a proposal,

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the agents within the NCI Formulary are available to investigators at NCI-designated Cancer Centers for the conduct of pre-clinical research, as well as for clinical trials performed under investigator-held INDs. The NCI clinical trial infrastructure will facilitate conduct of the trials, from proposal submission and timely review by the collaborating pharmaceutical companies, to agent distribution, serious adverse event submission, and clinical data reporting, while providing a coordination

mechanism between the clinical investigators and the pharmaceutical collaborators. A clinical Material Transfer Agreement between NCI and the NCI-designated Cancer Center will formalize the expectations of each party.

The NCI Formulary was publicly launched on January 11, 2017 (view [NCI's press release](#)). There are now 16 targeted agents from six pharmaceutical companies available. Prior to initiation, NCI solicited participation from pharmaceutical collaborators willing to commit to maintaining a

supply of their targeted agents in the NCI Formulary. Additional pharmaceutical collaborators and agents will be accepted to the NCI Formulary at any time, and it is expected that the number of partnerships and available drugs will double by the end of 2017. Use of agents from the NCI Formulary, the number of trials implemented and completed, the timeliness of completion of these trials, and the overall benefit of these trials on the agent development process will be monitored and evaluated.

News about DCTD Programs and Activities

Publications and Outreach

Peer-reviewed Publications

- Lih C-J, Harrington RD, Sims DJ, Harper KN, Bouk CH, Datta V, Yau J, Singh RR, Routbort MJ, Luthra R, Patel KP, Mantha GS, Krishnamurthy S, Ronski K, Walther Z, Finberg KE, Canosa S, Robinson H, Raymond A, Le LP, McShane LM, Polley EC, Conley BA, Doroshow JH, Iafrate AJ, Sklar JL, Hamilton SR, Williams PM. [Analytical validation of the Next Generation Sequencing assay for a nationwide signal-finding clinical trial: Molecular Analysis for Therapy Choice Clinical Trial \(NCI-MATCH, EAY131\)](#). *J Mol Diagn*. 2017;19:313-327.

Read a summary of the paper on the DCTD website: ["Validation of a Next Generation Sequencing Assay for NCI-MATCH: Implications for Precision Medicine Clinical Trials."](#)

- O'Sullivan Coyne G, Chen AP, Meehan R, Doroshow, JH. [PARP inhibitors in reproductive system cancers: Current use and developments](#). *Drugs*. 2017 Feb;77(2):113-130.
- Ji J, Zhang Y, Redon CE, Reinhold WC, Chen AP, Fogli LK, Holbeck SL, Parchment RE, Hollingshead M, Tomaszewski JE, Dudon Q, Pommier Y,

Doroshow JH, Bonner WM. [Phosphorylated fraction of H2AX as a measurement for DNA damage in cancer cells and potential applications of a novel assay](#). *PLoS One*. 2017 Feb 3;12(2):e0171582.

- Allen MA, Laetsch TW, Mody R, Irwin MS, Lim MS, Adamson PC, Seibel NL, Parsons W, Cho YJ, Janeway K, on behalf of the Pediatric MATCH Target and Agent Prioritization Committee. [Target and agent prioritization for the Children's Oncology Group – National Cancer Institute Pediatric MATCH Trial](#). *J Natl Cancer Inst*. 2017;109(5):djw274.

Publications and Outreach... continued

- Srivastava AK, Navas T, Herrick WG, Hollingshead MG, Bottaro DP, Doroshow JH, Parchment RE. [Effective implementation of novel MET pharmacodynamic assays in translational studies.](#) *Ann Transl Med.* 2017 Jan;5(1):3.
 - Buchsbaum, JC. [Are treatment toxicity issues in particle therapy a clarion call for biologic treatment planning overall?](#) *International Journal of Radiation Oncology·Biology·Physics.* Available online December 19, 2016.
 - Cristofaro JV, Ansher SS, Zwiebel JA, Ivy P, Conley B, Abrams JS, Doroshow JH. [The NCI Formulary: A public-private partnership providing investigators access to investigational anticancer agents.](#) *Clin Pharmacol Ther.* 2016 Dec 16. doi: 10.1002/cpt.585. [Epub ahead of print].
 - Masucci GV, Cesano A, Hawtin R, Janetzki S, Zhang J, Kirsch I, Dobbin KK, Alvarez J, Robbins PB, Selvan SR, Streicher HZ, Butterfield LH, Thurin M. [Validation of biomarkers to predict response to immunotherapy in cancer: Volume I – pre-analytical and analytical validation.](#) *J Immunother Cancer.* 2016 Nov 15;4:76.
 - Meehan RS, Chen AP, Doroshow JH. [Role of adaptive randomization in developing novel therapies for patients with breast cancer.](#) *Translational Cancer Research.* 2016 Oct 27;5:Supplement 6.
- ### Cancer Currents Blog Posts
- [NCTN/NCORP Data Archive: Expanding Access to Clinical Trial Data;](#) **Jeff Abrams, MD,** Cancer Therapy Evaluation Program and **Warren Kibbe, PhD,** Center for Bioinformatics and Information Technology; February 6, 2017.
 - [More Immunotherapy Options Approved for Lung Cancer;](#) **Shakun Malik, MD,** Cancer Therapy Evaluation Program; November 7, 2016.
- ### Interviews, Press, and Social Media
- #### NCI Formulary
- [“NCI Launches Drug Formulary,”](#) **James Doroshow, MD** for *Cancer Discovery*; January 26, 2017.
 - [“NCI develops a “Formulary” to make it easier for cancer centers to test drug combinations,”](#) **James Doroshow, MD** for *The Cancer Letter*; January 13, 2017.
 - [“National Cancer Institute unveils new effort to speed drugs to researchers,”](#) *STAT News*; January 11, 2017.
- [“National Cancer Institute and drug companies aim to speed up clinical trials,”](#) **James Doroshow, MD** for the *Washington Post*; January 11, 2017.
 - [New Drug Formulary Will Help Expedite Use of Agents for Clinical Trials,](#) NCI Press Release; January 11, 2017.
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- [“How a ‘cool’ trial in rare cancers was born,”](#) **Elad Sharon, MD, MPH,** Cancer Therapy Evaluation Program for *The Cancer Letter*; January 27, 2017. A discussion of the [DART trial](#).
 - [“3 Questions on...The Best Way to Help Patients Understand Genetic Test Results,”](#) **Carol Weil, JD,** Cancer Diagnosis Program for *Oncology Times*; January 10, 2017. A discussion of the [COMET study](#).
 - [“The Cancer Lottery,”](#) **Barbara Conley, MD,** Cancer Diagnosis Program, for *MIT Technology Review*; December 12, 2016. A discussion of precision oncology.
 - [“Lung Cancer Clinical Trials: Advances in Immunotherapy.”](#) **Shakun Malik, MD,** Cancer Therapy Evaluation Program for a Facebook Live event; November 23, 2016. Moderated by Janet Freeman-Daily, lung cancer patient and founding member of Twitter’s #LCSM chat.

Meeting Participation

- **Keyvan Farahani, PhD** and **John Freymann**, Cancer Imaging Program and the Frederick National Laboratory for Cancer Research, collaborated with members of the extramural research community to host [Computational Precision Medicine - Workshop and Challenges on Radio-Pathomics, Digital Pathology & Radiomics](#) at the [MICCAI 2016 Annual Meeting](#) (October 17-21, 2016; Athens, Greece). The workshop was composed of sessions on advances in radio-pathomics and radiomics, innovative challenges of computed tomography radiomics, classification and nuclei segmentation in digital pathology, and mammographic computer-aided detection.
- **James Zwiebel, MD**, Cancer Therapy Evaluation Program, participated in the President's Cancer Panel's meeting, "[Emerging Opportunities to Streamline Cancer Drug Development](#)" (December 9, 2016; Arlington, VA). Dr. Zwiebel contributed to the session, "Accelerating Throughput and Learning from Clinical Trials – the NCI Experience."
- Several DCTD staff presented at the [EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics](#) (November 29-December 2, 2016; Munich, Germany). Posters on a variety of topics and an oral presentation on assays in early-stage clinical trials were highlighted, and **James Doroshow, MD** co-chaired a proffered paper session.
- Formalin-fixed, paraffin-embedded tissue (FFPE) is increasingly utilized in cancer research and molecular diagnostic assays, and it is important to better understand how pre-analytical variation in FFPE may affect the reproducibility of research and patient tests. Staff from the [Biorepositories and Biospecimen Research Branch \(BBRB\)](#), Cancer Diagnosis Program, organized a workshop on "Biospecimen Evidence-based Practices for Collecting and Utilizing FFPE Tissues" (November 9, 2016; Rockville, MD) that focused on the development of biospecimen evidence-based best practices (BEPBs) for optimal handling of FFPE biospecimens for DNA, RNA, and protein analysis platforms. Participants included pathologists and genomics and proteomics scientists, as well as representatives from the Food and Drug Administration, the National Institute of Standards and Technology, the College of American Pathologists, and patient advocacy groups. Data to support improved processes for biospecimen collection, processing, and storage, as well as strategies to mitigate pre-analytical effects, were presented and discussed. The following BBRB staff were involved in the planning and implementation of this meeting: **Helen Moore, PhD, Ping Guan, PhD, Merlyn Rodrigues, MD, PhD, Kelly Engel, PhD, Sarah Greytak, PhD, and Emi Casas-Silva, PhD.**
- Additional data from BBRB-sponsored investigations were presented at the symposium, "[Research Findings on FFPE Tissue from the Biospecimen Preanalytical Variables \(BPV\) Program](#)," as part of the International Society for Biological and Environmental Repositories (ISBER) regional meeting (November 8, 2016; Rockville, MD). **Helen Moore, PhD, Ping Guan, PhD, and Rachana Agrawal, PhD (Leidos)** presented at the meeting along with several BPV investigators.
- Staff from the Cancer Imaging Program (CIP) and its Frederick National Laboratory component (**John Freymann, Justin**

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(L to R) Erich Huang, PhD, BRP, DCTD, NCI, Maryellen Giger, PhD, University of Chicago, Evis Sala, MD, PhD, Memorial Sloan Kettering, Sandy Napel, PhD, Stanford University, Juan Ibarra, MD, Baylor College of Medicine, John Freymann, Leidos Biomedical Research, CIP, DCTD, NCI at the Radiological Society of North American Meeting.

Kirby, Brenda Fevrier-Sullivan, and Carl Jaffe) created and presented two refresher courses at the Radiological Society of North America's 2016 Annual Meeting (November 27-December 2, 2016; Chicago, IL). "[The Cancer Imaging Archive: Using 'Big Data' for the study of Cancer Radiomics, Proteomics, Genetics and Pathology \(Hands-on\)](#)"

provided a live demo of the site's functionality and content. Participants learned how to browse, query, and download the ~70 collections of imaging, clinical, and 'omic data found in The Cancer Imagine Archive (TCIA). "[Imaging Integration with Cancer Genomics/ Proteomics: Methodologies Leveraging the Cancer Imaging Archive](#)" focused

on the precision medicine research enabled by TCIA data. Six CIP-supported, multi-institutional volunteer research groups presented data from the Cancer Genome Atlas (TCGA)-related image sets that enable imaging-genomics and imaging-proteomics correlations. Invited speakers discussed radiologist-generated image feature extraction by the TCGA-Bladder group, computer-automated quantitative imaging pipelines, statistical methodologies for correlating imaging-omic data (presented by **Erich Huang, PhD**, Biometric Research Program), imaging-proteomic correlations in ovarian cancer, and deep learning approaches using TCIA breast cancer data. In addition to these CIP-led classes, there were [nine scientific sessions](#) with new discoveries based on TCIA data.

Program Updates



- The [NCTN/NCORP Data Archive](#) was launched on February 6, 2017 and is a resource for the research community. The new centralized database is a repository of patient-level data from Phase 3 clinical trials conducted by the five trials groups in the NCTN, NCI's Community Oncology Research Program, and the National Cancer Institute of Canada-Clinical Trials Group. Read the Cancer Currents blog post authored by **Jeff Abrams, MD** and **Warren Kibbe, PhD**: "[NCTN/NCORP Data Archive: Expanding Access to Clinical Trial Data.](#)"
- The Computational & Systems Biology Branch (CSB) of the [Biometric Research Program \(BRP\)](#) has recently released a new bioinformatics system called [BRB-SeqTools](#). It was designed to help cancer scientists efficiently and easily preprocess and analyze Next Generation Sequencing (NGS) data. CSB

and BRP are led by Dr. Richard Simon and develop analytic tools that empower cancer scientists to utilize genome-wide tumor characterization data in translational research.

BRB-SeqTools runs in the Linux environment on local physical or virtual machines or on remote servers such as Amazon Cloud. A detailed web-based user guide is available to walk the user through installing a Linux virtual machine on their local computer and installing and using the software. Bioinformatics or Linux expertise is not required for effective use of the software. BRB-SeqTools processes include alignment, gene counting, variant calling, and variant annotation. A graphical user interface (GUI) lets the user select options, such as the data and analysis types and the input and output directories, as well as the reference genome profile. For RNA-Seq data, gene-level counts are generated and can be read into [BRB-ArrayTools](#) for gene expression analysis.

BRB-ArrayTools is a bioinformatics system previously developed by the Biometric Research Program that has over 15,000

registered users worldwide and has been cited in over 3,000 publications. BRB-ArrayTools is used for the analysis of microarray-based gene expression, gene copy number, and methylation data. It combines state-of-the-art statistical methods with large scale computational efficiency and extensive biological annotation. It has extensive features for the development of predictive and prognostic classifiers using complete cross-validation for proper analysis.

- [SWOG launched a clinical trial for rare cancers](#) in January 2017. [DART](#) (Dual Anti-CTLA-4 & Anti-PD-1 blockade in Rare Tumors) is being offered to patients if they are registered to NCI-MATCH, their rare cancer is eligible, and they either had no treatment option available on NCI-MATCH or enrolled on NCI-MATCH but later progressed on therapy. DART investigators plan to enroll 300 patients who will be treated with a combination of two immunotherapy drugs, nivolumab and ipilimumab. **Elad Sharon, MD, MPH**, Cancer Therapy Evaluation Program, was interviewed about the trial for [The Cancer Letter](#).
- Over the past six years, the Cancer Imaging Program (CIP) has developed and managed [The Cancer Imaging Archive \(TCIA\)](#). The archive has been used

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Program Updates... continued

heavily since inception, with over 420 scientific papers published using its ~70 data sets, furthering NIH's mission to enhance research reproducibility. TCIA continues to support the image data sharing component of numerous NCI activities including the Cancer MoonshotSM/APOLLO, The Cancer Genome Atlas, Clinical Proteomic Tumor Analysis Consortium, and Exceptional Responders. TCIA also serves NCI's



extramural investigators as the official repository for CIP's Quantitative Imaging Network (QIN), providing a safe and effective way to share data among QIN investigators for collaborative projects and analysis competitions. Several clinical trial data sets from the [National Clinical Trials](#)

[Network](#) are also stored in TCIA from ECOG-ACRIN and RTOG. TCIA also partners with academic societies and other entities to provide data to image analysis competitions. Most notably, computed tomography images from TCIA are being used in the [Data Science Bowl](#), which was launched on January 12, 2017. This competition will award \$1 million in prizes for efforts to develop better algorithms to reduce false positive rates in diagnosing lung cancer.

New Funding Opportunities

In September 2016, DCTD announced [approval of five concepts](#) in precision medicine oncology. The following [funding opportunities](#) were announced in December 2016.

- [RFA-CA-17-004 \(U24\)](#) PDX Data Commons and Coordinating Center (PDCCC) for the PDX Development and Trial Centers Research Network (PDXNet)

[RFA-CA-17-003 \(U54\)](#) PDX Development and Trial Centers (PDTCs)

- [RFA-CA-17-009 \(U54\)](#) Mechanisms of Cancer Drug Resistance and Sensitivity

- [RFA-CA-17-016 \(U24\)](#) Resource Center for the Consortium for Pancreatic Ductal Adenocarcinoma (PDAC) Translational Studies

[RFA-CA-17-015 \(UO1\)](#) Consortium for Pancreatic Ductal Adenocarcinoma (PDAC) Translational Studies on the Tumor Microenvironment

- [RFA-CA-17-002 \(U24\)](#) Coordinating Center for Canine Immunotherapy Trials and Correlative Studies

[RFA-CA-17-001 \(UO1\)](#) Canine Immunotherapy Trials and Correlative Studies

- [RFA-CA-17-005 \(U24\)](#) Cancer Immune Monitoring and Analysis Centers (CIMACs)

[RFA-CA-17-006 \(U24\)](#) Cancer Immunologic Data Commons (CIDC)

The Cancer Imaging Program has announced two [funding opportunities](#):

- [PAR-17-128 \(UG3/UH3\)](#) Quantitative Imaging Tools and Methods for Cancer Therapy Response Assessment
- [PAR-17-129 \(UO1\)](#) Quantitative Imaging Tools and Methods for Cancer Assessment

Honors and Awards

Roy Wu, PhD, former chief of the Clinical Grants and Contracts Branch, Cancer Therapy Evaluation Program,

received the [2016 American Society of Hematology's Outstanding Service Award](#). Dr. Wu received the award at

the 58th ASH Annual Meeting (December 2-6, 2016; San Diego, CA).