Richard Simon, PhD recently retired from NIH after nearly five decades of service and a prolific career. He provides a personal narrative of his years at NIH below.

After earning a doctoral degree in Applied Mathematics and Computer Science from Washington University in St. Louis in 1969, I joined NIH’s Computer Systems Laboratory of the Division of Computer Research and Technology. During this time, I met Vince DeVita, and after two years, I joined NCI’s Clinical Oncology Program (COP) to work on cell kinetic modeling of tumors. Once in COP, my office was filled with clinical investigators needing statistical collaboration, and I met many talented physicians who were interested in curing cancer, like Paul Carbone, Steve Rosenberg, Ed Henderson, Brigid Leventhal, Art Levine, Bob Young, Bruce Chabner, George...

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I was not trained as a statistician but had a strong theoretical foundation in probability theory, so I turned myself into a statistician, learning from the perspective of clinical medicine. After a few years, I got my own office and my own research fellow, Larry Norton, and we worked on new strategies based on modeling the effect of chemotherapy on tumor dynamics. I took courses in biology from Lee Hood, Mike Potter, and others, and I researched the use of intensive therapy schedules to achieve cures for solid tumors. Over the next 15 years, I built a small Biometric Research Branch (BRB), and in 1984 I transferred to the Cancer Therapy Evaluation Program (CTEP). Under Bob Wittes and the successive leaders of CTEP, BRB grew and thrived. We combined review and oversight of clinical trials with development of new statistical designs and methods of analysis, and top biostatisticians were attracted to and retained in this environment. I required that the statisticians learn about the kinds of cancer for which they were responsible so that they could collaborate in a knowledgeable way and make fundamental contributions rather than serve as purely super-technicians calculating p values and sample sizes. Marvin Zelen’s Statistical Science group, Tom Fleming at the Mayo Clinic, and SWOG served as important models. During this time, I published important new designs and methods of analysis, but the objective was to cure cancer, not do statistics.

By the mid-1990’s the Human Genome Project was underway, and DNA micro-arrays were available to better understand gene expression in tumors. I took courses in biotechnology at NIH and spent hours in the laboratory educating myself in the methods of DNA analysis and cancer genomics. I established a section in BRB on Molecular Statistics, provided opportunities to post-docs, and collaborated on the use of microarray technology. One collaboration involved Jeff Trent, head of the Laboratory of Tumor Genetics, National Human Genome Research Institute, who had the only DNA microarray on the NIH campus at the time.

I started to develop a software program called BRB-ArrayTools, designed to aid scientists in the use of microarray technology. The goal was to provide access to state-of-the-art statistical methods for analyzing high dimensional assay results and to a system to become educated on proper analysis of expression data. I developed it with my own initiative and resources, using a contractor for programming assistance, and it has been a great success with more than 15,000 registered users in 65+ countries. Many statisticians believe that only they know enough to analyze complex data, and they don’t support efforts like BRB-ArrayTools; however, I have received emails from scientists around the world who have thanked and told me how the system was indispensable to their research. Systems such as this provide an important new approach to use of high-dimensional genomic data by the biologists and pharmacologists who best understand the problems to be solved. I believe that BRB-ArrayTools has been NCI’s most important and successful bioinformatic resource (cited in more than 3,000 publications), and I hope that this system and the follow-on BRB-SeqTools continue to be available to the international community. They represent an important new way that statisticians can contribute to helping to cure cancer.

In the early 2000’s, I focused on using genomic technology in clinical trial design. I gave talks to most of the large pharmaceutical and biotech companies and learned that their focus was restricted to pharmacodynamic biomarkers, not on predictive biomarkers. I gave similar talks to the FDA to discuss the strengths of using the targeted enrichment design, as there was strong biological evidence that biomarker negative patients were extremely unlikely to benefit from a molecularly targeted drug. I found that publishing papers that made cogent points based on quantitative analysis was an effective way to bring about change; I believe these publications on the advantages of the enrichment phase III trial design were influential in...
she received the American Cancer Society Career Development Award for research on the pharmacology of differentiating agents in cancer. She was a co-investigator on the Phase I Clinical Trials of Anticancer Agents cooperative agreement, as well as a principal investigator on the master agreement Phase II Clinical Trials of New Chemopreventive Agents, both funded by NCI.

Following 10 years in academia, Dr. Conley joined NIH in 1997 as a senior investigator in the Clinical Investigations Branch, Cancer Therapy Evaluation Program (CTEP), DCTD where her portfolio included cancers of the head and neck, lung, and gastrointestinal tract. In 1999, her interest in biomarkers led her to become Chief, Diagnostics Research Branch, Cancer Diagnosis Program (CDP), DCTD where she was responsible for the initial Director’s Challenge initiative with Dr. James Jacobson, as well as leading the head and neck cancer intergroup. After several years, she was drawn back to clinical medicine in the Clinical Center and became Head, Aerodigestive Cancer Clinical Research Section, Co-chair, Early Drug Development Coordinating Committee, and Head, Internal Phase I Consult Service for the Center for Cancer Research. From 2005-2010, Dr. Conley briefly left NCI to become Chief, Division of Hematology and Oncology and Scientific Director of the MSU Clinical Translational Science Institute and MSU’s Hematology/Oncology Fellowship Director, where she was active in cooperative group trials and was PI of a planning grant for a Clinical and Translational Science Award.

Dr. Conley returned to NCI in 2010 as Associate Director of CDP. During her tenure as Associate Director, Dr. Conley steered CDP into precision medicine initiatives, especially in concert with CTEP. She had a personal interest in the clinical validity and clinical use of diagnostics for clinical trials, with a focus in early drug development and in aerodigestive cancers. She led two NCI novel precision medicine initiatives – the Exceptional Responders initiative, which uses nucleic acid sequencing on tissues from patients who had remarkable responses to systemic treatments to which few patients respond, and the NCI-MATCH (Molecular Analysis for Therapy Choice) trial, a basket trial in patients with refractory solid tumors, lymphomas, and myelomas that assigns patients to appropriate targeted treatment based on the genetic changes found in their tumors through genomic sequencing and other tests.

The pace of advances in targeted agents and multiple analyte diagnostics has placed CDP at the forefront of precision medicine trial development, including new trials using immune checkpoint inhibitors. “These trials require some serious team work, which has been one of the best parts of the job,” said Dr. Conley. “The adoption of this design for so many new drug approvals starting around 2010.

I’m proud to have built an effective group of senior investigators in what is now the Biometric Research Program (BRP). The post-docs in BRP have come from many different fields, and working with them on projects designed to elucidate the changes in cancer cells and to reconstruct the early stages of tumor development has been stimulating. Many BRP alumni have gone off to leadership positions elsewhere, both in academia and industry. I stayed on at NCI for about 8 years past my eligible retirement age because I enjoyed my work. Recently, I have wanted more time for other things and an opportunity to work on some projects outside of NIH. I still believe that major successes are possible, and I hope to stay involved in cancer therapeutics, to work with some companies that are developing breakthrough products, and to help bring about changes in scientific focus that expedite progress. I am grateful for the opportunities I have had at NCI to work with and learn from great people.
Spotlight:

New to DCTD’s Developmental Therapeutics Program: The Immuno-Oncology Branch

Enhancing the efforts of the Office of the Associate Director and its existing branches, DCTD’s Developmental Therapeutics Program (DTP) established the Immuno-Oncology Branch (IOB) in December 2016 to leverage DTP’s role in providing expertise to this important and rapidly advancing field. IOB staff includes Connie Sommers, PhD, Health Science Administrator, with additional staff to be added in the future.

The branch will manage a grants portfolio of immunotherapy product development, propose and establish new initiatives such as Cooperative Agreements with academia and industry to advance immunotherapy, and provide support/resources for preclinical development of immunotherapy products for use in clinical studies. Specifically, IOB will provide the biomedical community (academia and pharma) with the guidance and resources required to develop new immunotherapeutic agents, including efficacy evaluation, preclinical toxicology and pharmacology support, product manufacturing and testing, and IND-directed activities to meet regulatory requirements.

Efforts will be taken to identify new immunotherapeutic agent candidates to recommend for development through the NCI Experimental Therapeutics (NExT) Program. The branch will also collaborate with DCTD’s Cancer Therapy Evaluation Program (CTEP) to evaluate new immunotherapeutic agents and to provide investigators with guidance on optimum combination drug strategies, clinical trial design, and biomarker identification/assays. IOB will facilitate access to combination drugs both from within CTEP’s portfolio, from other pharmaceutical partners, and from investigators supported by NCI research grants. View details of a new DTP Funding Opportunity Announcement related to IOB’s work:

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Barbara Conley, MD ... continued

professionals in CDP and all of DCTD have been critical to this effort and a pleasure to work with! NCI is a terrific place to be to make a real difference for patients with cancer, and I will really miss that."

Dr. Conley’s additional accomplishments include working to advance diagnostics by leading the Clinical Assay Development Program, which was an American Recovery and Reinvestment Act program that provided resources to develop assays for prediction and prognosis. As a member of DCTD’s Developmental Therapeutics Clinic, she was involved in NCI’s MPACT precision medicine trial. She has also published extensively in many journals, including the Journal of Clinical Oncology and Nature Medicine, and has been on the editorial board of several professional publications. Dr. Conley participated in several taskforces and groups aimed at providing better diagnostics for cancer patients.
News about DCTD Programs and Activities

Peer-reviewed Publications


- Chen CE, Laetsch TW, Mody R, Irwin MS, Lim MS, Adamson PC, Seibel NL, Parsons DW, Cho YJ,
Publications and Outreach... continued


Cancer Currents Blog Posts

- Cancer Researchers Report Progress in Studying Exceptional Responders; Barbara Conley, MD, and Lyndsay Harris, MD. Cancer Diagnosis Program; July 6, 2017.


- Midostaurin Approved by FDA for Acute Myeloid Leukemia; Richard Little, MD. Cancer Therapy Evaluation Program; June 1, 2017.

Interviews and Press

NCI-COG Pediatric MATCH, Nita Seibel, MD, Cancer Therapy Evaluation Program


CAR T Therapy, Malcolm Smith, MD, Cancer Therapy Evaluation Program


“Barbara Conley: Learning from the First Broad Foray into Precision Medicine,” Barbara Conley, MD, Cancer Diagnosis Program; The Cancer Letter; July 7, 2017. Read the full article on NCI-MATCH from the July 7, 2017 issue of The Cancer Letter.


“Imaging at the Forefront of Precision Medicine,” Janet Eary, MD, Cancer Imaging Program, and Elad Sharon, MD, MPH, Cancer Therapy Evaluation Program; RSNA News; June 1, 2017.

Meeting Participation

The Office of Cancer Complementary and Alternative Medicine, DCTD, initiated the first NIH-sponsored, comprehensive meeting on microbial-based cancer therapy, which convened on July 11–12, 2017. A trans-NCI working group consisting of staff from DCTD, the Division of Cancer Biology, the Division of Cancer Prevention, and the NCI Small Business Innovation Research program planned and supported this important meeting.

While microbial-based cancer therapy dates from the late 19th century, this potentially promising research area remains understudied. Recent scientific advances in tumor biology, microbial pathogenesis, cancer immunity, and new molecular tools have made it possible to revisit this old concept from new perspectives. The goals of NCI’s multidisciplinary conference were to provide a forum for the nearly 300 participants from academia, industry, and the federal government to learn about these recent advances in the field and to develop new scientific collaborations, interactions, and research programs.

The conference’s agenda included 19 speakers in sessions on the biology of microbe-tumor interactions, virus- and bacteria-based therapies, translational aspects of microbial-based therapies, and a poster session. Opportunities for microbial-based therapy where conventional therapy is inadequate were highlighted, such as tumor cell dormancy, tumor cells that are not well affected by drugs, hypoxia, or poorly vascularized tumors. In addition, speakers described the complex nature of the microbe-tumor interaction and discussed recent advances in the field.

Future research could involve studying the unique potential of viruses and bacteria to invade, damage, or destroy human cells and induce immune responses to create new, safe, and effective therapeutic approaches. Post-meeting activities include preparation of a white paper by a Working Group, and a possible journal special issue aimed to highlight the clinical potential of microbial-based cancer therapy.

Robert Hoffman, PhD, University of California, San Diego and AntiCancer, Inc, Keynote Speaker presents: "Microbial-Based Cancer Therapy"

Neil S. Forbes, PhD, University of Massachusetts, Amherst presents: "Engineered Salmonella for Drug Delivery to Solid Tumor"
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) is a phase 2 clinical trial that is enrolling children and adolescents with advanced solid tumors - including non-Hodgkin lymphomas, brain tumors, and histiocytoses - that have not responded to treatment or have progressed on standard therapy. The trial opened to accrual on July 24, 2017 (NCI’s press release) with six treatment arms, has since expanded to seven arms, and plans to expand further to eight or more. Tumors from 200 to 300 children and adolescents are expected to be screened each year (1,000 patients total) for targeted mutations that match a study drug aimed at the specific molecular abnormality in the tumor; therefore, patients are assigned to an experimental treatment based on the genetic changes found in their tumors rather than on their type of cancer or cancer site. Current research suggests that 1 out of 10 (10%) patients screened for this study will match one of the targeted drugs being tested. A unique aspect of Pediatric MATCH (in contrast to the adult NCI-MATCH trial) is that germline testing will be performed on DNA from the patient's peripheral blood, collected at the time of study enrollment. The germline testing results will be used to determine if the genetic variants identified in the tumor were inherited or not, which is information that can help oncologists counsel families about.
genetic testing, genetic counseling, and follow-up care. The study was developed and is jointly led by NCI and the Children’s Oncology Group (COG), part of the NCI-sponsored National Clinical Trials Network (NCTN).

- The NCI Formulary is a public-private partnership between NCI and pharmaceutical and biotechnology companies that provides Cancer Center investigators with rapid access to agents or combinations of agents for clinical or preclinical research. The NCI Formulary was launched on January 11, 2017 (NCI press release) with six participating companies (Bristol-Myers Squibb, Eli Lilly and Company, Genentech, Kyowa Hakko Kirin Co, Ltd., Loxo Oncology, and Xcovery Holding Company LLC) offering 15 targeted agents. In July 2017, AstraZeneca agreed to provide 11 agents to the Formulary bringing the total number of available agents to 27. Review the list of available agents.

- On June 27, 2017, the Office of Cancer Clinical Proteomics announced new Proteomic Translational Research Centers (PTRCs), Proteome Characterization Centers, and Proteogenomic Data Analysis Centers. The PTRCs will collaborate with NCI-sponsored clinical trials in coordination with CTEP. The goal of these centers is to promote proteogenomics to understand the molecular basis of cancer.

- NCI has published a Request for Information (RFI) (NOT-CA-17-079) in the NIH Guide for Grants and Contracts seeking input from all stakeholders with interests in bioethics and cancer research, clinical care, and/or public health by October 6, 2017. In 2016, a Cancer and Bioethics Working Group comprised of NCI staff members was formed; its goals are to foster bioethics/ELSI (Ethical, Legal, and Social Implications) research, and to coordinate outreach activities to educate members of the cancer community on bioethics/ELSI issues. To better realize these goals, the members are seeking input from community members, patients, cancer researchers, physicians and other health practitioners, bioethicists, advocates, and others to help identify bioethics areas clearly relevant to cancer but in need of further development, as well as bioethics areas that are ready for translation in a cancer context. They are also seeking input on approaches for enhancing bioethics and cancer collaborations, and timely issues for bioethics and cancer outreach.

Comments can be submitted by E-mail (cancerandbioethics@nih.gov) or U.S. Postal Service (Charlisse Caga-anan, National Cancer Institute, DCCPS/EGRP/Genomic Epidemiology Branch, 9609 Medical Center Drive, Room 4E236, Bethesda, MD 20892-9763 [or Rockville, MD 20850 for express delivery]). Please include the RFI Notice number (NOT-CA-17-079) in the subject line of your email or letter.
Retirements

Dana Heckman, Deputy ARC Director, DCTD, is retiring in September after 36 years working in the federal government. Dana joined NCI in 1991 after ten years working for the Department of the Navy in Norfolk and Arlington, Virginia; and Bath, Maine; and the Department of the Army in Fort Ritchie, Maryland. Her first position in NCI was as an Administrative Officer supporting labs in the Biological Response Modifiers Program in the Division of Cancer Treatment, (now DCTD), located at Fort Detrick.

She subsequently transitioned to supporting the Developmental Therapeutics Program as an Administrative Officer in 1993, becoming the Program Administrative Officer for DTP in 1995. In 2004, she accepted her current position as Deputy ARC Director for DCTD, and has served in that capacity ever since. Look for more about Dana’s career and accomplishments at NIH in the November 2017 newsletter.

Summer Interns

DCTD welcomed four summer interns to assist with research projects in the Developmental Therapeutics Clinic. While taking a break from their work, the interns toured the Frederick National Laboratory for Cancer Research (FNLCR) with DCTD staff earlier this summer.

From left: Min He, PhD, Developmental Therapeutics Program, Seroh Chang, Sean Alexander, Jon Alexander, Chana Levine, and Kay Gray, PhD, Applied/Developmental Research Directorate, FNLCR