NIH NATIONAL CANCER INSTITUTE

pipeline news

August 2020

DCTD Division of Cancer Treatment and Diagnosis

STAFF HIGHLIGHT – C. Norman Coleman, MD

C. Norman Coleman, MD
Associate Director,
Radiation Research
Program, DCTD

C. Norman Coleman, MD, arrived at NCI in 1999 as chief of the Radiation Oncology Branch (ROB) in NCI's Center for Cancer Research (CCR) and as the associate director of the Radiation Research Program (RRP) in DCTD to create the virtual Radiation Oncology Sciences Program that also included the Radiation Biology Branch. Now an adjunct member in ROB, his lab focuses on radiation-induced molecular and immunotherapy targets. Dr. Coleman discusses how his scientific and personal interests have guided him through a career in global cancer care and research.

How did you become interested in science and medicine?

In college, I majored in math and minored in chemistry and biology. My interest in understanding biological mechanisms and solving complex problems prompted me to study medicine. I graduated from Yale Medical School in 1970, and at that time, while no exams were given, a thesis of original research was required for graduation. The thesis was critical for original discovery and showed me that I could solve unsolved problems, which is a crucial concept for scientists. During medical school in New Haven during the riots of the late 1960's, I also became interested in societal inequality and had a desire for a broader understanding of global issues and society.

What did you focus on after medical school?

When I finished medical school, it was the early 1970s and still the Vietnam War era. I was fortunate to be accepted by the US Public Health Service for the NCI. I first completed my internship and residency in internal medicine at the University of California, San Francisco, then a fellowship in medical oncology at NCI, and subsequently a fellowship in radiation oncology at Stanford University being board certified in all three specialties. While at NCI, I did cancer drug development research in Dr. Bruce Chabner's lab, and at Stanford, I studied radiosensitizers building on pharmacologic principles

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learned at NCI. A critical event in 1974-5 that shaped my life's perspective was that in order to educate ourselves more broadly, my wife and I sold everything we had and traveled around the world for a year. This trip greatly impacted my life and career and showed me how much we can learn from each other's cultures, many being millennia older than ours in the US.

By the early 1980's, I became a tenured faculty member in radiation and medical oncology at Stanford, having started a lab there, and I've had a lab ever since. I moved to Harvard in 1985 as Professor and Chair of Radiation Oncology, then back to NCI in 1999. My goals in the lab have focused on understanding things at the basic level, specifically radiation modifiers. The facilities at NCI have enabled us to study the molecular effects of radiotherapy fractionation, which people hadn't done before. We now know that there are persistent effects of radiation and cancer treatment over time that are targetable, and this is a new approach to radiation therapy. The kinds of programs our terrific team in RRP is working on include understanding the biological consequences and basic mechanisms of radiation therapy and working with the extramural community through the formation of extensive Working Groups that support the development of clinical trials that incorporate novel radiation approaches.

What other projects interest you?

I've focused a lot of my career on global health and assisting underserved communities. While at Harvard, I was aware that some communities had limited cancer care, so my department (Joint Center for Radiation Therapy) developed an outreach network to cities around Boston. Our network successfully demonstrated how one can deliver university-level care within the community, and a lot of healthcare systems are trying to do that now. We have also done that through the RRP Cancer Disparities Resources Partnership, where NIH grants were given to community centers, who in turn, partnered with universities. The goal is to empower people on the ground who know the issues, and we are trying to do that globally. I also work with an NGO, the International Cancer Expert Corps, which is trying to establish a global cancer network that promotes mentor-mentee relationships in low-income countries or geographically isolated areas in the US. This is an interesting model for the future because of the resurgence in social consciousness and a potential career-path for those interested in healthcare inequality.

Since 2004, I've served in the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR). I am the Co-Chair of the Radiological/Nuclear Working Group of the Global Health Security Initiative under ASPR and Office of Global Affairs. In response to 9/11, we put together a multi-dimensional response for nuclear and radiological terrorism, including working with NIAID and BARDA on biomarkers of and mitigators for normal tissue radiation injury. I was deployed to the US embassy in Japan in 2011 during the Fukushima nuclear power plant crisis. This work was recognized by the Homeland Security Service to America Award. I am still involved with ASPR related to scarce resources/mass casualty issues and have been working to help solve the scarcity of personal protective equipment occurring now during the SARS-CoV-2 pandemic. This relates to my interest in solving complex multi-dimensional problems from my undergraduate background and the challenge of developing the necessary complex systems solutions. Cancer care certainly fits this description!

In what other ways did your early global travel experiences affect your life?

The round-the-world trip in the 1970s completely shaped my outlook on life. My wife and I visited so many unique places, and because we traveled for a year, we were able to acquire a broad first-hand cultural understanding. We have affinity for mountains and local cultures having been to Tibet, Bhutan, Nepal, Sikkim, and other places in the Himalayas, including three Mount Everest treks

(from Nepal and Tibet). Recently, we've explored Patagonia and the Andes. We learned along the way that if you find a passion and a hard problem that needs solving, don't ever give up on it, despite apparent roadblocks. Our family's interest in being healthy, active, and learning has fostered a love of traveling, trekking, backpacking, and running, including competing in marathons and triathlons, which I still do. I think that motivation is important, and that's why mentorship is so crucial to help others develop and sustain their interests. Whatever we each accomplish is important, but in perspective, it is a step along the way that will surely be replaced with something better. Conveying the idea that life is about the joy of discovery and service, we in NCI/NIH are fortunate to be a part of discovery to address human disease and societal issues for the benefit of many others.

Dr. Norm Coleman with his wife, Karolynn, in Bhutan near Mt. Chomolhari.

SPOTLIGHT – NCI Spearheads First Integrative Medicine Course

The practice of integrative medicine reaffirms the importance of the relationship between physician and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches and disciplines to achieve optimal health and healing. Only those complementary interventions and lifestyle modifications with solid scientific and/or clinical evidence of *safety* and *efficacy* are integrated into the care of the patient. Achievement of well-being through *safe, effective*, and *evidence-based*, multi-modality approaches is the goal.

Recommendations from a 2016 DCTD Strategic Workshop and extensive needs assessment discussions with patients at the NIH Clinical Center, as well as physicians, fellows-in-training, students, and post-doctoral researchers at NIH, led to the development of an integrative medicine educational tool. The NCI spearheaded and now leads the Trans-NIH Integrative Medicine Course that introduces the concept, research, and evidence-based practice of integrative medicine to NIH researchers. This first-of-its kind NIH course that utilizes a holistic perspective of medicine is the newest addition to an ongoing training curriculum for NIH clinical and post-doctoral fellows, which includes the flagship course *Translational Research in Clinical Oncology (TRACO)*.

Facts about the Trans-NIH Integrative Medicine Course

- Launched in the fall of 2019 with more than 300 registrants, spanning students through senior staff
- Implemented by the NCI Center for Cancer Training (CCT) within the NCI Office of the Director (OD) and coordinated by the Trans-NIH Integrative Medicine Training Course Committee:
  - Ann Berger, MD, Clinical Center, NIH
  - Terry Moody, PhD, NCI
  - David Shurtleff, PhD, NCCIH, NIH
  - Dan Xi, PhD, NCI
  - Farah Zia, MD, NCI
- Offered each fall/spring with the following curriculum:
  - Expert speakers from academia, government, and the community
  - Material with research evidence, followed by clinical examples

  - Prioritization of newsworthy and timely subjects each semester, adding distinction to the design
  - Unique observational experience provided to students by the NIH Clinical Center Pain and Palliative Care Clinic, and Sleep Lab

- Broader objectives include:
  - Reporting the state-of-the science
  - Dispelling myths
  - Identifying research gaps
  - Developing white paper summaries where appropriate

- Timely and newsworthy topics are open to registered students, as well as to staff and the public, including the following presented thus far:
  - Pain and Opioids
  - Chronomedicine
  - Cannabis and Cancer (first-ever topic offered at NCI)
  - Integrative Modalities and COVID-19

- Mainstay topics include acupuncture, chronomedicine, sleep, mind-body techniques, exercise, botanicals and traditional medicine, dietary supplements, and regulatory policy

Through this unique initiative undertaken in collaboration with the NCI/OD/CCT, and implemented through a Trans-NIH Committee, the hope is to not only educate, but to inform collaborative, future research across NIH intramural, academia, and industry.

SPOTLIGHT – NCI Launches Integrated Canine Data Commons

NCI support for canine cancer research is meant to further human cancer research via comparative analysis across the two species. NCI's Division of Cancer Treatment and Diagnosis, in collaboration with the Center for Biomedical Informatics and Information Technology, recently launched a repository–the Integrated Canine Data Commons (ICDC)–for the storage of large amounts of various data types essential to this endeavor. The ICDC, which is one repository in the larger NCI Cancer Research Data Commons (CRDC), was developed to incorporate genomic, proteomic, imaging, clinical trial, and immuno-oncology data from spontaneously arising canine cancer studies.

The ICDC provides open access to clinical trial and correlative data derived from NCI-funded canine immunotherapy clinical trials, such as the PRECINCT Network and the Center for Cancer Research's Comparative Oncology Trials Consortium (COTC), as well as sequencing data from studies supported by P30 grant supplements and other NCI-supported grants. Researchers can explore data directly from the data portal's study viewer or connect the data to the NCI Cloud Resources for robust analysis with more than 1,000 tools, workflows, and pipelines. The ICDC serves as a resource for canine researchers to submit and access data related to cancer and empowers the cancer research community to generate new hypotheses that can be tested by comparative analysis in dogs and humans.

Get started accessing data in the ICDC, and learn more about the CRDC by watching a short video on how repositories like the ICDC harmonize within the NCI Data Ecosystem.

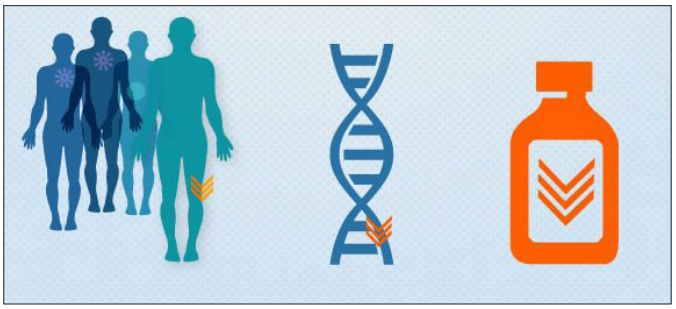
NEWS ABOUT DCTD PROGRAMS AND ACTIVITIES

Program Updates

DCTD Seeking Project Proposals for Viral Vector and Cell Therapy Production at NCI

Building upon its initial efforts to support the production of CAR-T cells for clinical studies, the NCI Biopharmaceutical Development Program (BDP) at Frederick National Laboratory for Cancer Research (FNLCR) is expanding its capabilities to also offer viral vector production. DCTD is currently seeking project proposals from intramural and extramural investigators in need of clinical grade vector and/or cell therapy product manufacturing. Beginning in early 2021, the BDP will have the capability to manufacture lentiviral and retroviral vectors for the genetic modification step in cell therapy production. Learn more about viral vector and cell therapy production at NCI and how to apply for manufacturing support.

Submission Deadline Extended to September 30, 2020 for Letters of Intent for Laboratories to Participate in the NCI-ComboMATCH Clinical Trial



NCI recently began requesting letters of intent for laboratories to participate in the NCI-ComboMATCH clinical trial, the first successor trial of NCI-MATCH. Approved designated labs will test tumor specimens to identify patients for specific gene abnormalities needed for trial eligibility. These laboratories will join a network of 30 designated laboratories already put in place last year to identify cases for NCI-MATCH. NCI-ComboMATCH will evaluate targeted drug combinations in part based on preclinical *in vivo* evidence of activity.

NCI has published two solicitations for the recruitment of CLIA-accredited laboratories to support NCI-ComboMATCH:

- Laboratory sites identifying cases from the general population
- Laboratory sites identifying exclusively pediatric cases

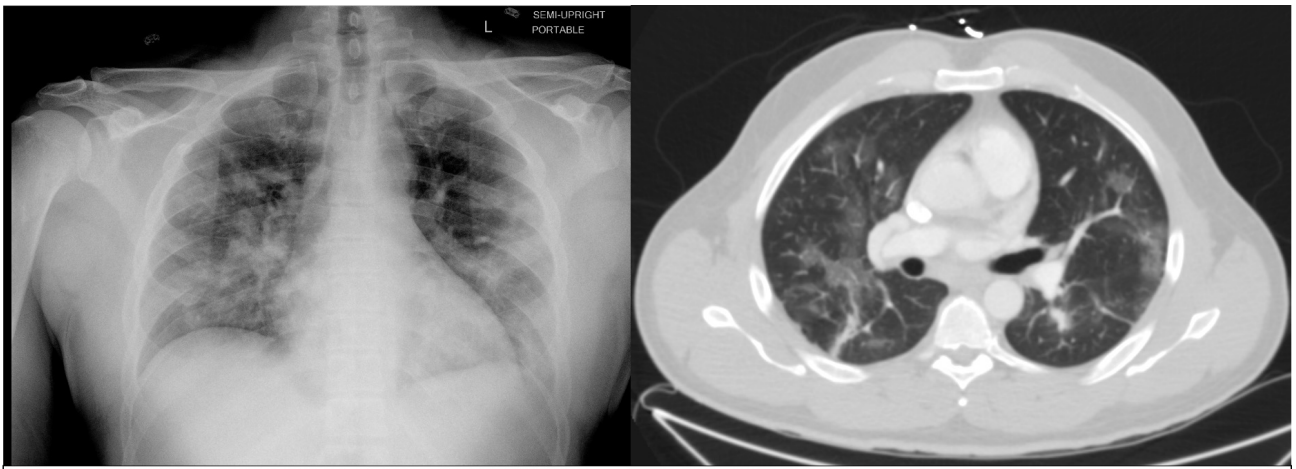
FDA Approves Commercially Available F-18 Fluoroestradiol (Cerianna) for PET Imaging Tissue Estrogen Receptor Status

The Cancer Imaging Program's Molecular Imaging Branch and Clinical Trials Branch would like to share news of the recent FDA approval announcement for commercially available F-18 Fluoroestradiol (FES) (Cerianna) for PET imaging tissue estrogen receptor status. Approval is for PET imaging detection of estrogen receptor positive lesions throughout the body and as an adjunct to biopsy in patients with recurrent or metastatic breast cancer. This is the first F-18 radiolabeled PET imaging agent approved specifically for use in patients with breast cancer. The commercial sponsor, Zionexa USA, announced the approval on May 27, 2020.

Several NCI CIP-funded projects supported FES development, including early clinical trials, toxicology studies, and evaluation of target engagement of the investigational drug, endoxifen. This PET imaging agent was also one of the first imaging agent IND exemptions held by CIP to facilitate local production for clinical evaluations by the cancer imaging research community. ECOG-ACRIN is currently completing a multicenter trial evaluating the predictive ability of FES to assess response to hormone therapy in women with breast cancer - FES PET / CT in Predicting Response in Patients with Newly Diagnosed Metastatic Breast Cancer Receiving Endocrine Therapy (EAI142) NCT02398773.

The Cancer Imaging Archive (TCIA) Announces Its First COVID-19 Data Set Available to the Scientific Community

Established in 2011, the Cancer Imaging Archive (TCIA) is a service to the cancer imaging research community that de-identifies and hosts a large archive of medical images of cancer accessible for public download. Data are published as "collections" where patients' imaging data are typically arranged by a common disease, image modality or type (e.g., MRI, CT, digital histopathology), or research focus. TCIA is dedicating a portion of its resources to provide free and open access to imaging data from patients with COVID-19. Learn more about the first publicly available TCIA COVID-19 data set.

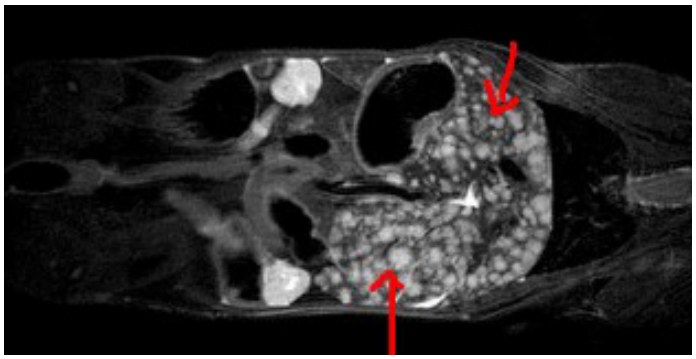


Chest Radiograph (left) and Computed Tomography (CT) image (right) of the same patient taken one day apart. Patchy bilateral ground-glass/consolidative opacities are seen in both lungs.

NCI's Patient-Derived Models Repository and The Cancer Imaging Archive Announce Identification and Imaging Characterization of Metastatic Patient-Derived Models

The NCI Patient-Derived Models Repository (PDMR) is a publicly accessible, national repository for early-passage, molecularly characterized patient-derived models developed from patients with solid tumors.

In collaboration with the NCI's Cancer Imaging Program and the Frederick National Laboratory for Cancer Research's Small Animal Imaging Program, four spontaneous metastatic PDX models were identified and released to the public with the accompanying imaging characterization through The Cancer Imaging Archive (TCIA), a public repository of medical images of cancer. These four PDX models include the histologies colon adenocarcinoma, pancreatic adenocarcinoma, melanoma, and bladder cancer, with metastases observed in MRI images in an appropriate time frame to be useful in evaluating therapies to reduce metastatic spread. A total of 17 metastatic PDX models have been identified in the NCI PDMR with ongoing imaging studies for future inclusion in TCIA. Learn more about the PDMR's spontaneous metastatic PDX models.



MRI image of the bladder cancer model BL0293-F563 that reliably metastasizes to the liver before or after removal of the primary subcutaneous tumor in NSG host mice; arrows indicate liver metastases

Meetings of Interest

- The Co-Clinical Imaging Research Resources Program (CIRP) Network is a trans-NCI initiative designed to:
  - provide the broader cancer community with web-accessible research resources for quantitative imaging of co-clinical trials (simultaneous investigations in patients and in animal models)
  - encourage consensus on how quantitative imaging methods are optimized to improve the quality of imaging results for co-clinical therapeutic or prevention trials of adult and pediatric cancer

  The Cancer Imaging Program convened the CIRP Annual Meeting virtually on June 22-23, 2020. The goals of the meeting were:
  - review the progress of the CIRP program
  - identify challenges in all four essential areas of CIRP
  - seek solutions for harmonization and standardization
  - explore integrative strategies for co-clinical imaging research and multi-scale information integration
- On July 23, 2020, Ned Sharpless, MD, Mickey Williams, PhD, and Lisa McShane, PhD presented at the Friends of Cancer Research Virtual Meeting – TMB Results: Future Use of Complex Biomarkers.
- DCTD-supported research was presented in oral and poster presentations at ASCO 2020. See the list of presentations.

Featured Clinical Trial

A Precision Medicine Clinical Trial for Patients with ALK-positive Non-small Cell Lung Cancer

This phase II trial studies how well an ALK inhibitor works in treating patients with stage IV ALK positive non-squamous non-small cell lung cancer after developing resistance to first line ALK inhibitor. Patients are treated based on the genetic resistant alterations of their tumors. The trial is also evaluating the effectiveness of liquid biopsies to detect ALK alterations in circulating cfDNA to corroborate the results with the tumor biopsies.

Publications and Outreach

Publications

Connolly RM, Laille E, Vaishampayan U, et al. Phase I and Pharmacokinetic Study of Romidepsin in Patients with Cancer and Hepatic Dysfunction: A National Cancer Institute Organ Dysfunction Working Group Study. *Clin Cancer Res*. 2020 Aug 14; Online ahead of print.

St. James S, Bednarz B, Benedict S, et al. Current Status of Radiopharmaceutical Therapy. *Int J Radiat Oncol Biol Phys*. 2020 Aug 14;S0360-3016(20)34125-0.

Salama AKS, Li S, Macrae ER, et al. Dabrafenib and Trametinib in Patients with Tumors with $BRAF^{V600E}$ Mutations: Results of the NCI-MATCH Trial Subprotocol H. *J Clin Oncol*. 2020 Aug 6; Online ahead of print.

Freidlin B, Allegra CJ, and Korn EL. Moving Molecular Profiling to Routine Clinical Practice: A Way Forward? *J Natl Cancer Inst*. 2020 Aug 1;112(8):773-778.

Eary JF. Cancer Imaging Program Update: 2020. *Radiol Imaging Cancer. 2020* Jul 31;2(4):e204021.

Chae YK, Hong F, and Vaklavas C. Phase II Study of AZD4547 in Patients with Tumors Harboring Aberrations in the EGFR Pathway: Results from the NCI-MATCH Trial (EAY131) Subprotocol W. *J Clin Oncol*. 2020 Jul 20;38(21):2407-2417.

Nguyen D, Yu J, Reinhold WC, and Yang SX. Association of Independent Prognostic Factors and Treatment Modality with Survival and Recurrence Outcomes in Breast Cancer. *JAMA Netw Open*. 2020 Jul 1;3(7):e207213.

ENCODE Project Consortium. Expanded Encyclopaedias of DNA Elements in the Human and Mouse Genomes. *Nature*. 2020 Jul;583(7818):699-710.

Hadjiiski LM and Nordstrom RJ. Quantitative Imaging Network: 12 Years of Accomplishments. *Tomography*. 2020 Jun;6(2):55.

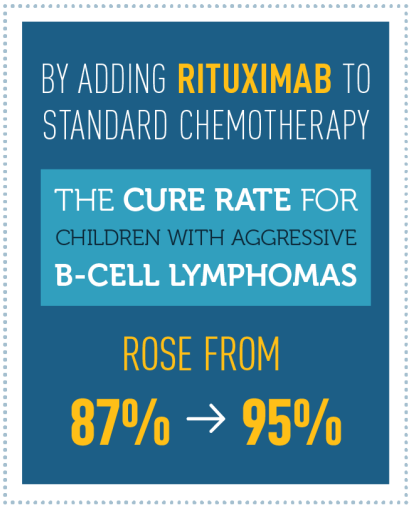
Nordstrom, RJ. Quantitative Imaging Enters the Clinical Arena: Personal Viewpoint. *Tomography* 2020 Jun;6(2):56–59.

NCI Cancer Currents Blog Posts

Trastuzumab May Improve Survival in Women with Rare Endometrial Cancer; Elise Kohn, MD, Cancer Therapy Evaluation Program; August 13, 2020

Rediscovered Drugs Hit Leukemia from Two Different Angles; Joel Morris, PhD, Developmental Therapeutics Program; July 21, 2020

New Drug Regimen Cures More Children with Aggressive B-Cell Lymphoma; Malcolm Smith, MD, PhD, Cancer Therapy Evaluation Program; July 1, 2020



Responding to Coronavirus, Cancer Researchers Reimagine Clinical Trials; Meg Mooney, MD, MS, Cancer Therapy Evaluation Program; June 29, 2020

Interviews and Press

The Nuclear Option: Radiation Drugs in Cancer Care; Cure; Charles Kunos, MD, PhD, Cancer Therapy Evaluation Program; July 17, 2020.

Listen: Dr. Meg Mooney, Associate Director of CTEP, NCI; Healthcast, Government CIO Media & Research; Meg Mooney, MD, MS, Cancer Therapy Evaluation Program; June 29, 2020

'We have a job to do': Cancer patients and their doctors carry on with clinical trials during Covid-19; STAT; Meg Mooney, MD, MS, Cancer Therapy Evaluation Program; June 16, 2020.

New DCTD Funding Opportunity and Funding Information

Title	Announcement Number	Open Date	Expiration Date	Activity Code
Glioblastoma Therapeutics Network (Clinical Trial Required)	RFA-CA-20-047	October 19, 2020	November 20, 2020	U19

A Solicitation of the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) for Small Business Innovation Research (SBIR) Contract Proposals (General Announcement) *Response Date: October 26, 2020*		
DCTD-related Topic Title	**Topic Goals**	**Topic Number/Link**
Next Generation 3D Tissue Culture Systems with Tertiary Lymphoid Organs	Advance the development of next generation 3D tissue/tumor cell culture systems that develop and maintain self-assembled TLOs for months	NIH/NCI 413
Applicator-Compatible Electronic Brachytherapy Sources for Cancer Radiotherapy	Stimulate research, development, and commercialization of innovative devices to replace and enhance the radiation space currently occupied by radioactive sources in brachytherapy	NIH/NCI 415
Quantitative Imaging Software Tools for Cancer Diagnosis and Treatment Planning	Produce robust, well documented and well supported software tools after iterative optimization and validation through quality management controls	NIH/NCI 417
Understanding Cancer Tumor Genomic Results: Technology Applications for Providers	Design and develop tools, technologies, or products to: - inform oncologists and other health care providers treating cancer patients in settings with low access to genetic counselors about NGS testing and current NCCN guidelines - help such providers evaluate the need for NGS somatic testing for their cancer patients - assist providers with interpretation of NGS results - help providers communicate NGS results to their patients	NIH/NCI 419
Single-Cell "Unbiased Discovery" Proteomic Technologies	- stimulate the development of unbiased discovery proteomic technologies with the capacity to identify proteins in a single cell with a typical size (~10 µm in diameter) - provide efficient research tools with the ability to generate more complete and accurate human cancer proteome information without relying on antibodies or inferring proteomes from mRNA sequencing - provide efficient clinical tools for precision medicine, earlier cancer detection, and better assessment of treatment response and monitoring	NIH/NCI 420

Quantitative Biomimetic Phantoms for Cancer Imaging and Radiation Dosimetry	- stimulate growth in development of scalable quantitative tissue-equivalent technologies that would benefit patients who rely on cancer imaging modalities for diagnosis, dosimetry, and treatment	NIH/NCI 421
Spatial Sequencing Technologies with Single Cell Resolution for Cancer Research and Precision Medicine	- stimulate the development of technologies that generate sequence information from slides without losing the histological context of the targets. - provide research and/or clinical tools to improve cancer early detection, diagnosis, prognosis for precision medicine	NIH/NCI 422
Advanced Manufacturing to Speed Availability of Emerging Autologous Cell-Based Therapies	- stimulate the development of advanced manufacturing technologies that substantially improve the speed and cost of producing autologous cell-based therapies	NIH/NCI 429