



STAFF HIGHLIGHT - Meg Mooney, MD, MS



Meg Mooney, MD, MS Associate Director, Cancer Therapy Evaluation Program, DCTD, NCI

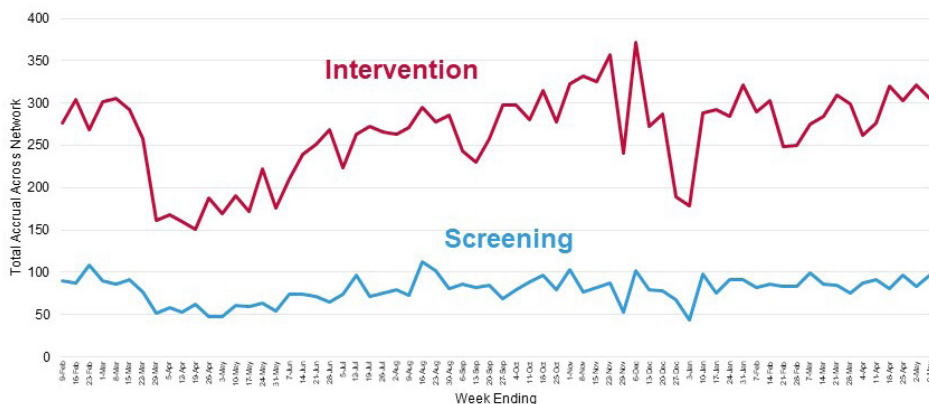
Meg Mooney, MD, MS, is the Associate Director of the Cancer Therapy Evaluation Program (CTEP), DCTD, NCI, and she is also the Chief of CTEP's Clinical Investigations Branch (CIB). Dr. Mooney describes NCI's responses to the impact of the COVID-19 pandemic on cancer clinical trials as well as NCI's continued support of cancer research during this difficult time.

NCI's Response to the Effects of COVID-19 on Cancer Clinical Trials

As patient accrual to NCI's National Clinical Trials Network (NCTN) treatment (intervention) clinical trials began to decrease dramatically in mid-March 2020 due to the emerging pandemic, CTEP quickly worked with NCI's Division of Cancer

Prevention (DCP) to address how investigators at sites in the NCTN, the NCI Community Oncology Research Program (NCORP), the NCI Experimental Therapeutics Clinical Trials Network (ETCTN), and other CTEP-supported clinical trials consortia could help physicians and patients participating in clinical trials adjust to this new environment.

NCTN Accrual for "Screening" and "Intervention" Steps by Week February 3, 2020 to May 9, 2021



Source: National Cancer Institute

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By late March 2020, NCI provided special guidance on [clinical trial management](#) to address constraints imposed by the pandemic. It became apparent that local physicians could help perform some clinical trial activities, such as periodic physical exams, performance assessments, research blood collection, and imaging, with appropriate oversight from the physicians who had initially enrolled the patients on trials. This minimized the need for patient travel to clinical centers located remotely from them. In addition, the U.S. Food and Drug Administration and the NCI CTEP Pharmaceutical Management Branch made it easier to have a trial site's dispensing pharmacy ship oral investigational agents used in CTEP IND studies directly to people participating in those studies. We believe that many of the adjustments that were made to manage the constraints encountered due to the pandemic may become permanent operational options in our clinical trial processes. Fortunately, we saw NCTN accrual as well as accrual across all CTEP and DCP trial networks return to near pre-pandemic levels in the early Fall of 2020, followed by the usual fluctuations seen in accrual around major holidays.

NCI's Response to the Effects of COVID-19 on People with Cancer

People with cancer are at high risk for the deleterious effects of COVID-19. In May 2020, NCI staff in CTEP and DCP collaborated with extramural investigators from Vanderbilt University Medical Center to quickly develop and launch the [NCI COVID-19 in Cancer Patients Study \(NCCAPS\)](#). This is a national, longitudinal, natural history study designed to understand the unique interaction that COVID-19 and cancer may have on the course of both diseases as well as identify factors associated with short- and long-term outcomes of COVID-19. NCCAPS is open to adults and children who have tested positive for COVID-19 and are undergoing active cancer treatment and also includes a special sub-study of other pediatric cancer patients who have a positive SARS-CoV-2 viral test but are not eligible for the main NCCAPS study (e.g.,

they are no longer on active cancer therapy). As of May 2021, more than 1,000 people have enrolled onto this study at NCTN, NCORP, and ETCTN sites.

NCI Continues Its Mission

Although the past year has been challenging in many ways due to COVID-19, NCI and the cancer research community have continued to work towards improving the lives of people with cancer. We have witnessed some exciting results from NCI-supported research. For example, the first genomic results from the [Exceptional Responder's Initiative](#), which was launched in 2014, were published in the journal [Cancer Cell](#). This groundbreaking paper described the possible molecular mechanisms for unexpected responses to cancer treatment seen in some patients. In addition, results of a [phase 3 clinical trial](#) demonstrated that postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer and a 21-gene recurrence score (RS) of ≤ 25 (Oncotype Dx) with limited spread to the lymph nodes do not benefit from the addition of chemotherapy to hormone therapy. In contrast, benefits for the combination were found in premenopausal women.

Another effort of great importance to NCI is fostering the continued evolution of NCI-supported clinical trials. One crucial component of this effort is to expand patient eligibility and ensure that clinical trials are available to people in different populations across the country. We are looking ahead to 2030 with a vision to improve the clinical trials process further, as detailed in the November 2020 [Working Group Report](#) from the NCI Clinical Trials and Translational Research Advisory Committee. Our goals include decreasing regulatory hurdles and implementing clinical trials that are faster and less expensive. I consider myself fortunate to be working at NCI at a time of great potential positive impact on the future of cancer research and patient care.

Dr. Mooney arrived at NCI in 2002 as Head of Gastrointestinal and Neuroendocrine Cancer Therapeutics in CTEP's Clinical Investigations Branch. She was appointed Chief of the Branch in May 2009, Deputy Associate Director of CTEP in 2014, and CTEP Associate Director in 2020. Dr. Mooney oversees and coordinates the responsibilities for the programmatic, financial, and administrative functions for the entire CTEP program, which covers a broad, multidisciplinary, clinical research effort to coordinate nationwide phase 1-3 clinical trials programs testing new treatment approaches for cancer. DCTD would like to express our gratitude for Dr. Mooney's tireless efforts, patience, and leadership throughout her time at NCI and especially during the past year.

SPOTLIGHT - Updates from the Developmental Therapeutics Clinic (DTC)

Congratulations to Rafeh Naqash, MD, Advanced Investigational Cancer Therapeutics Fellow



Rafeh Naqash, MD, joined the Early Clinical Trials Development Program and the DTC in July 2019 as an advanced fellow. During his time here, Dr. Naqash has focused on incorporating a genomically driven approach to early

phase clinical trials and identifying biomarkers in immunotherapy trials. After several notable accomplishments and finishing his fellowship in June 2021 at the DTC, Dr. Naqash will be joining the phase 1 group at the University of Oklahoma Stephenson Cancer Center.

Dr. Naqash received the [Allen S. Lichter, MD, Endowed Merit Award](#) from the Conquer Cancer Foundation for his first-authored abstract to be presented at the 2021 ASCO Annual Meeting on research resulting from DTC's phase 2 trial of atezolizumab in alveolar soft part sarcoma (ASPS). This Merit Award is given to the second highest ranking abstract in the Merit Award

category. Dr. Naqash also received a 2020 ASCO Young Investigator Award from the Conquer Cancer Foundation for his planned biomarker work on the ASPS clinical trial with mentors Alice Chen, MD and Naoko Takebe, MD, PhD. The Pharmacodynamics Assay Development and Implementation Section and the Molecular Characterization Laboratory at the Frederick National Laboratory for Cancer Research collaborated with DTC on this work. Dr. Naqash has been an ASCO editorial fellow and serves on early-career committees for ASCO and SITC.

AACR 2021 Presentations Involving DTC Research Studies

Among the [DCTD-supported research](#) presentations at this year's AACR annual meeting, the following were DTC research studies:

- Phase I trial of the triplet berzosertib (M6620, VX-970), veliparib and cisplatin (BVP) in patients with advanced solid tumors
- Phase I trial of the combination of bortezomib and clofarabine in adults with refractory solid tumors, lymphomas, or myelodysplastic syndromes

ASCO 2021 Presentations Involving DTC Research Studies

- A phase 2 study of Defactinib (VS-6063) in patients with NF2 altered tumors: Results from NCI-MATCH (EAY131) subprotocol U
- Phase I trial of 5-aza-4'-thio-2'-deoxycytidine (Aza-TdC) in patients with advanced solid tumors
- Phase II study of Atezolizumab in advanced alveolar soft part sarcoma (ASPS)

Clinical Trial Highlight

Testing the Biological Effects of DS-8201a on Patients with Advanced Cancer

DTC leads this phase 1 trial, which is treating people with advanced HER2+ cancer with DS-8201. This study is looking at how DS-8201a may affect the levels of certain proteins and immune cells in tumors.

SPOTLIGHT - The NCI Patient-Derived Models Repository (PDMR) Reaches Milestone

The PDMR is a national repository for early-passage, molecularly characterized patient-derived models developed from solid tumors. Since 2017, the PDMR has been developing models as a resource for public-private partnerships and for academic drug discovery efforts.

Staff from DCTD and the Frederick National Laboratory for Cancer Research presented PDMR research at the 2021 AACR Annual Meeting. The abstracts – studies ranging from rare cancers to imaging characterization – are included in the [full list of DCTD's AACR 2021 presentations](#).

The PDMR recently surpassed development of its **500th patient-derived xenograft (PDX) model**.

Numbers of Available PDMR Models (May 2021)	
Cryopreserved PDX material	514
Patient/PDX-derived cell cultures	171
Cancer-associated fibroblasts	243
Patient-derived organoid cultures	140

NEWS ABOUT DCTD PROGRAMS AND ACTIVITIES

Program Updates

NCI Drug Development Workshop: How to Advance a Therapeutic Candidate from Bench to Bedside



NCI Drug Development Workshop:
How to Advance A Therapeutic Candidate from Bench to Bedside

Ten Discrete Webinars
Fridays, 12:00 pm – 2:30 pm ET · July 23, 2021 – December 10, 2021

The Developmental Therapeutics Program will convene a 10-part webinar series on Fridays from 12:00 pm – 2:30 pm ET starting July 23, 2021 through December 10, 2021.

See the [workshop agenda](#), and [register](#) for individual sessions.

This workshop is intended for researchers who are interested in learning about key activities that are needed to take their discoveries from the lab to the clinic. Junior faculty and trainees

are encouraged to attend. Recordings will be available on the [meeting website](#) following each webinar (registration not required to view recordings).

Annual NIH Integrative Medicine and Women’s Health Webinar

National Women’s Health Week (NWHW) begins on Mother’s Day each year. It reminds women to prioritize their health and prompts biomedical researchers to include sex and gender as variables in their research. With these considerations in mind, the Trans-NIH Integrative Medicine Course Committee launched the “[Annual NIH Integrative Medicine and Women’s Health Webinar](#)” on May 13, 2021 in conjunction with its [Integrative Medicine Course](#).

In partnership with the NIH Office of Research on Women’s Health (ORWH) and the NIH Pain & Palliative Care Service, the Trans-NIH Integrative Medicine Course Committee developed this webinar to increase women’s health awareness at the NIH.

2021 Webinar Details

- Provided time-sensitive and evidence-based scientific information from leading experts in government, academia, and the scientific community
- Assessed the current state-of-the science
- Identified research gaps
- Theme: Supportive care research for women with breast and gynecologic cancers across the lifespan
- Keynote: Janine Clayton, MD, Director, ORWH: “Studying Sex Differences within Integrative Medicine: Opportunities and Challenges.”

NEWS ABOUT DCTD PROGRAMS AND ACTIVITIES ... continued

The hope is that this annual event will be a small piece of the larger effort to bridge gaps for women's representation in medical research.

Trans-NIH Integrative Medicine Course Organizing Committee

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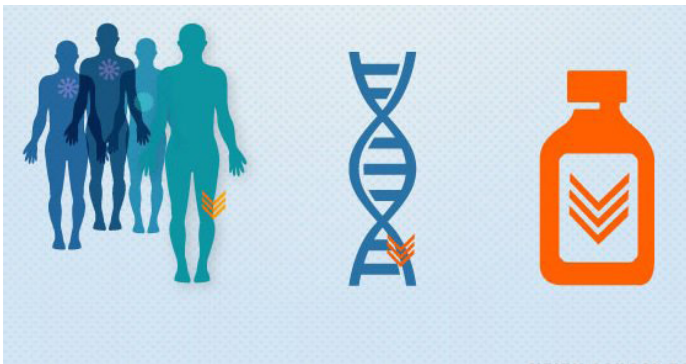
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NCI-MATCH Opens Final Arm, Continues to Enroll Patients



The final arm of the NCI-MATCH Trial (Molecular Analysis for Therapy Choice) opened in April – Arm Z1D targets tumors that have DNA mismatch repair deficiency and LAG3 protein expression with relatlimab and nivolumab. The opening of this final arm brings the total number of MATCH arms over the course of the trial to 39, with 12 currently open for new patients. Details on the status of all arms are found on [ECOG-ACRIN's website](#).

NCI's Revision of the Common Terminology Criteria for Adverse Events (CTCAE) Is Underway

The **CTCAE** is the international standard for reporting adverse events (AE) in oncology clinical trials. It provides the following essential functions:

- facilitates the evaluation of new cancer therapies and treatment modalities
- facilitates the comparison of safety profiles between interventions
- allows for standardization and reproducibility of results
- defines protocol parameters (e.g., maximum tolerated dose, dose-limiting toxicity)
- provides eligibility assessment and guidelines for dose modification

- allows for direct comparison of patient experience across trials from around the world

The Cancer Therapy Evaluation Program (CTEP) developed the precursor to CTCAE - the CTC (Common Toxicity Criteria) - in 1983 to aid in the documentation and analysis of AEs of chemotherapy. CTEP maintained and updated the CTC through its third version when it was rebranded as CTCAE v3.0, published in 2003. The updated CTCAE v3.0 comprised a list of AE terms commonly encountered in oncology therapeutic trials, accompanied by a severity grading scale for each AE. NCI has subsequently released two more versions, v4.0 and v5.0 and is now embarking on the eagerly awaited v6.0 update. The CTCAE Core Committee, which comprises staff from DCTD, the Division of

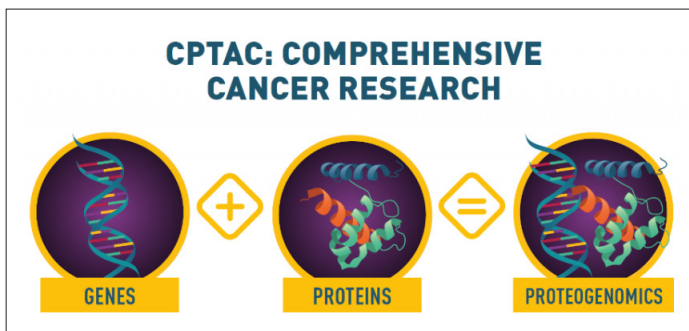
Cancer Prevention, and the Food and Drug Administration, is developing this update, which will be available in the fall of 2022.

The inter-agency effort to develop the CTCAE depends on international feedback from the public and our pharma partners. NCI staff read and consider all comments that suggest changes for versions in preparation. During the current revision, the Core Committee is reviewing several important issues, including:

1. How best to grade AEs in patients with abnormal lab values at the beginning of a study (i.e., how do you recognize and quantify abnormal on top of abnormal?)
2. Grading AEs related to immunotherapeutics (the newest major class of anticancer agents)
3. Categorizing cardiac-related AEs (an important topic since the previous version)

Updates from the Office of Cancer Clinical Proteomics Research

- Henry Rodriguez, PhD, MS, MBA, Director, Office of Cancer Clinical Proteomics Research, Jean Claude Zenklusen, PhD, Director, Cancer Genome Atlas Program, Louis Staudt, MD, PhD, Director, NCI Center for Cancer Genomics, James Doroshow, MD, Director, DCTD, and Douglas Lowy, MD, Principal Deputy Director, NCI, published a forward looking perspective article recommending the full integration of proteogenomics into clinical trials and patient care. The article was **published on April 1 in the journal *Cell***, and outlines the journey, accomplishments, and future direction of proteogenomics and the **Clinical Proteomic Tumor Analysis Consortium (CPTAC)** program.
- CPTAC gave several **presentations** at this year's annual AACR meeting. Sessions included a symposium titled "The Clinical Proteomic Tumor Analysis Consortium: Building a Proteogenomic Atlas of Cancer," a session titled "NCI Proteomic Initiatives and Resources," and several posters.
- OCCPR's **International Cancer Proteogenome Consortium (ICPC)** added two new teams to its program via new memorandums of understanding:
 - Spain - Josep Carreras Leukaemia Research Institute
 - South Korea - Daegu Gyeongbuk Institute of Science and Technology with Kyung Hee University



- Cell Press released a **dedicated webpage to CPTAC studies**, which will collate current and future CPTAC studies published by the journal, including PanCancer studies.

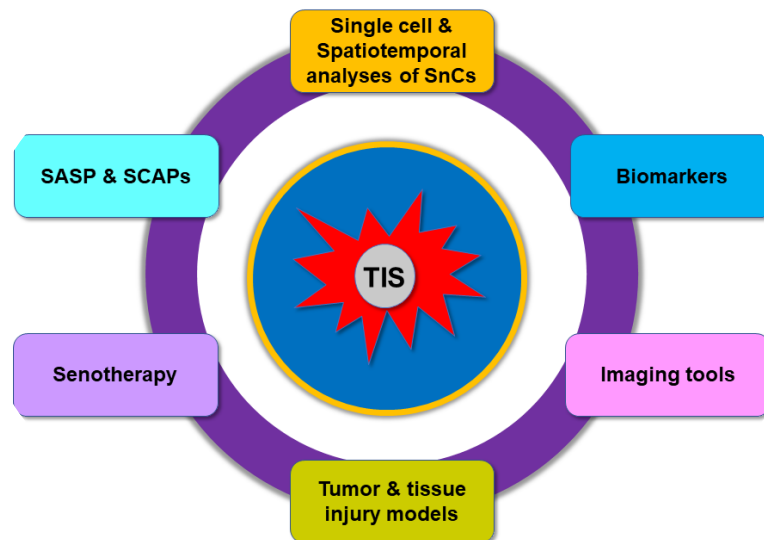
The ICPC, which now includes 14 countries, has published 5 comprehensive tumor characterization studies since its formation in late 2016. A new study on intrahepatic cholangiocarcinoma (Shanghai ICPC Team) is under revision in *Cancer Cell*.

Therapy-Induced Senescence: Opportunities to Improve Anti-Cancer Therapy

DCTD, in collaboration with the NCI Center for Cancer Research, Division of Cancer Biology, Division of Cancer Prevention, and the Office of the Director, conducted a virtual workshop on “Radiation, Senescence, and Cancer” on August 10-11, 2020. The workshop reviewed:

- the status of senescence research
- heterogeneity of therapy-induced senescence (TIS)
- senotherapeutics and molecular biomarkers
- integration of personalized adaptive tumor therapy with "one-two punch" cancer therapy, which is an emerging concept consisting of therapeutics to induce tumor cell senescence followed by selective clearance of senescent cells

The workshop identified knowledge gaps and outlined future directions in this cross-disciplinary field to improve treatment outcomes for people with cancer. The summary of this workshop was recently published as a commentary in *JNCI*. This effort is expected to stimulate and synergize research across NCI on therapy-induced senescence and its application to improve anticancer therapy.



Senescent cell as a target of “one-two punch” cancer therapy (SASP – senescence-associated secretory phenotype; SCAPs – senescent cell anti-apoptotic pathway; SnCs – senescent cells; TIS – therapy-induced senescence)

Publications and Outreach

Publications

[DCTD staff presentations at AACR 2021](#)

[Geisler PB, Zahabi L, Lang AE, et al.](#) Repurposing existing medications for coronavirus disease 2019: Protocol for a rapid and living systematic review. *Syst Rev.* 2021 May 7;10(1):143.

[Ouwkerk R, Hamimi A, Matta J, et al.](#) Proton MR spectroscopy measurements of white

and brown adipose tissue in healthy humans: Relaxation parameters and unsaturated fatty acids. *Radiology.* 2021 May;299(2):396-406.

[Bagchi A, Madaj Z, Engel KB, et al.](#) Impact of preanalytical factors on the measurement of tumor tissue biomarkers using immunohistochemistry. *J Histochem Cytochem.* 2021 May;69(5):297-320.

Moore HM. NCI launches the Cancer MoonshotSM Biobank to accelerate research in cancer treatment. *IASLC News*. 2021 Apr 21.

Patel SP, Mayerson E, Chae YK, et al. A phase II basket trial of Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors (DART) SWOG S1609: High-grade neuroendocrine neoplasm cohort. *Cancer*. 2021 Apr 21. Online ahead of print.

Welch A, Ernstoff M, and Yovandich J. Future-proofing cell therapy manufacturing capability: lessons from the NCI. *Immuno-Oncology Insights*. 2021 Apr 21;2(2):51-55.

Takebe N, Naqash AR, O'Sullivan Coyne G, et al. Safety, anti-tumor activity, and biomarker analysis in a phase 1 trial of the once-daily Wee1 inhibitor adavosertib (AZD1775) in patients with advanced solid tumors. *Clin Cancer Res*. 2021 Apr 16. Online ahead of print.

Wang L-B, Karpova A, Gritsenko MA, et al. Proteogenomic and metabolomic characterization of human glioblastoma. *Cancer Cell*. 2021 Apr 12;39(4):509-528.

Albain KS, Gray RJ, Makower DF, et al. Race, ethnicity, and clinical outcomes in hormone receptor-positive, HERs-negative, node-negative breast cancer in the randomized TAILORx trial. *J Natl Cancer Inst*. 2021 Apr 6;113(4):390-399.

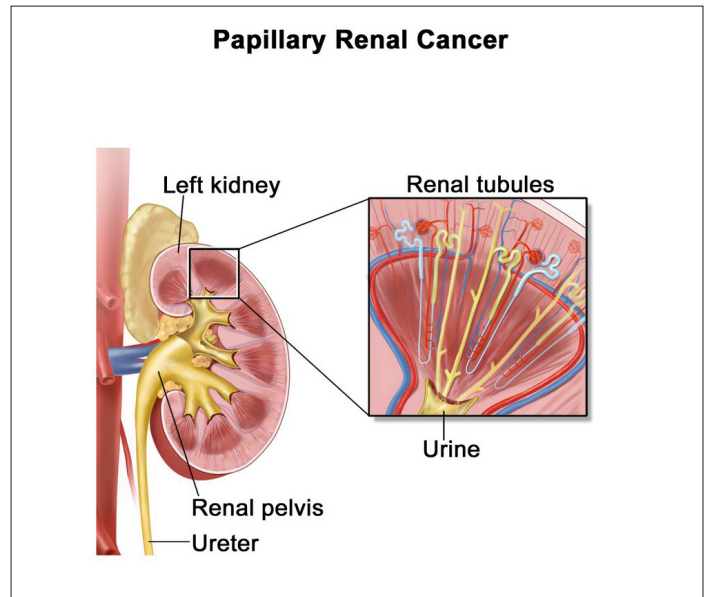
Rodriguez H, Zenklusen JC, Staudt LM, et al. The next horizon in precision oncology: Proteogenomics to inform cancer diagnosis and treatment. *Cell*. 2021 Apr 1;184(7):1661-1670.

Kalen JD, Clunie DA, Liu Y, et al. Design and implementation of the pre-clinical DICOM standard in multi-cohort murine studies. *Tomography*. 2021 Feb 5;7(1):1-9.

NCI Cancer Currents Blog Posts

Blinatumomab Improves Survival in Children with Relapsed Leukemia; Malcolm Smith, MD, PhD; April 1, 2021

Targeted Therapy Cabozantinib Slows Progression of Rare Kidney Cancer; John Wright, MD, PhD; March 24, 2021



Imaging Test Could Help Guide Breast Cancer Treatment Decisions; Janet Eary, MD; March 11, 2021

Interviews and Press

[Dr. Doroshow on the Importance of Modernizing Clinical Trials after COVID-19.](#) OncLive; May 18, 2021.



[50 Years of Cancer: The Road to Better Treatment and Diagnostics.](#) Meg Mooney, MD, MS and James Doroshow, MD. GovernmentCIO Podcast; April 29, 2021.



[ACR Data Science Institute Links Use Cases to NCI Archive to Speed AI Development.](#) Janet Eary, MD; ACR; April 26, 2021.

[Vaccines Won't Protect Millions of Patients with Weakened Immune Systems;](#) Elad Sharon, MD, MPH; New York Times; April 15, 2021.

[Most Cancer Drug Trials Still Exclude People with HIV. That's Both Unfounded and Dangerous.](#) Rich Little, MD; TheBodyPro; April 12, 2021.

[NCI-MATCH Trial Reveals Actionable Mutations and Matches Cancer Patients to Targeted Therapies.](#) Alice Chen, MD; MD Edge Podcast; February 11, 2021.

New DCTD Funding Opportunity and Funding Information

Funding Opportunity Announcements

Title	Announcement Number	Open Date	Expiration Date	Activity Code
Proteome Characterization Centers (PCCs) for Clinical Proteomic Tumor Analysis Consortium (Clinical Trial Not Allowed)	RFA-CA-21-023	May 30, 2021	July 1, 2021	U24
Proteogenomic Data Analysis Centers (PGDACs) for Clinical Proteomic Tumor Analysis Consortium (Clinical Trial Not Allowed)	RFA-CA-21-024	May 30, 2021	July 1, 2021	U24
Proteogenomic Translational Research Centers (PTRCs) for Clinical Proteomic Tumor Analysis Consortium (Clinical Trial Not Allowed)	RFA-CA-21-025	June 30, 2021	July 31, 2021	U01
3D Technologies to Accelerate HTAN Atlas Building Efforts (Clinical Trial Not Allowed)	RFA-CA-21-037	May 30, 2021	November 23, 2021	UH2
Academic-Industrial Partnerships for Translation of Technologies for Diagnosis and Treatment (Clinical Trial Not Allowed)	PAR-21-166	May 5, 2021	January 8, 2024	R01

Notices of Intent to Publish

Title	Announcement Number	Estimated Publication Date of FOA	First Estimated Application Due Date	Activity Code
Pancreatic Ductal Adenocarcinoma Stromal Reprogramming Consortium Coordinating and Data Monitoring Center (PSRC CDMC)	NOT-CA-21-076	July 1, 2021	November 1, 2021	U24
Coordinating and Data Management Center for Acquired Resistance to Therapy Network (ARTNet)	NOT-CA-21-064	July 1, 2021	November 1, 2021	U24
Acquired Resistance to Therapy Network (ARTNet)	NOT-CA-21-063	July 1, 2021	November 1, 2021	U54
Coordinating Center for Canine Cancer Immunotherapy Network (K9CIN)	NOT-CA-21-069	July 1, 2021	October 5, 2021	U24
Canine Cancer Immunotherapy Network (K9CIN)	NOT-CA-21-068	July 5, 2021	October 5, 2021	U01