

Meet the Six Damon Runyon Cancer Researchers Awarded \$3.6M

And learn about the cutting-edge work of these early-career physician-scientists named the 2023 Damon Runyon Clinical Investigators.

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The Damon Runyon Cancer Research Foundation has named six new Damon Runyon Clinical Investigators. The recipients of this prestigious award are outstanding, early-career physician-scientists conducting patient-oriented cancer research at major research centers under the mentorship of the nation's leading scientists and clinicians.

The Clinical Investigator Award program was designed to increase the number of physicians capable of moving seamlessly between the laboratory and the patient's bedside in search of breakthrough treatments. Each awardee will receive \$600,000 over three years. Because the need to repay medical school loans is often cited as a disincentive for physicians otherwise interested in pursuing research alongside their clinical practice, Damon Runyon will also retire up to \$100,000 of medical school loan debt owed by the awardee. This program is possible through the generous support of the William K. Bowes, Jr. Foundation.

"The quality of research proposed by our Clinical Investigators is exceptionally strong. We are thrilled to be funding brave and bold physician-scientists who are taking risks to experimentally address the most important questions in cancer research and then translate them into improving patients' lives," says Yung S. Lie, PhD, Damon Runyon's President and Chief Executive Officer. "We are helping to launch the careers of tomorrow's brightest cancer researchers."

Through partnerships with generous donors, industry sponsors, and its Accelerating Cancer Cures initiative, the Damon Runyon Cancer Research Foundation has committed over \$84 million to support the careers of 125 physician-scientists across the United States since 2000.

2023 Clinical Investigators

Sylvan C. Baca, MD, PhD, with mentor Toni K. Choueiri, MD, at Dana-Farber Cancer Institute, Boston

Promising new treatments for cancers of the bladder and kidney have been developed, but, as with many cancer therapies, tumors eventually develop resistance. Research has shown that

cancer cells resist treatment in part via epigenetic changes—those that do not affect the DNA sequence itself but turn important genes on or off, allowing cancers to survive under therapeutic stress. Dr. Baca is using novel techniques to study the epigenomes of cancer cells from blood samples. His goal is to understand how changes in the epigenomes of bladder and kidney cancers lead to treatment resistance. This knowledge will enable the design of better treatments and drug combinations that will benefit patients with metastatic bladder or kidney cancers.

Pavan Bachireddy, MD, with mentor Jeffrey J. Molldrem, MD, at University of Texas MD Anderson Cancer Center, Houston

A major cause of relapse after therapy is the persistence of measurable residual disease (MRD) cells—cancer cells that remain after treatment and eventually spread. Due to technical and logistical challenges in accessing and analyzing MRD cells, the molecular and cellular pathways that enable MRD progression remain poorly understood. Dr. Bachireddy will use innovative molecular tools to analyze tissue samples from blood cancer patients at a single-cell level to unlock insights into MRD progression. Using cutting-edge machine learning approaches, he will identify immunosuppressive mechanisms that may be targeted to halt MRD progression. Beyond these blood cancers, he aims to reveal organizing principles of MRD progression that are relevant across human cancers.

Andrew L. Ji, MD, with mentor Miriam Merad, MD, PhD, at Icahn School of Medicine at Mount Sinai, New York

Cutaneous squamous cell carcinoma (cSCC) is the second most common cancer in the U.S. While most cases are caught early and cured with excision, this cancer is more aggressive in the organ transplant recipient (OTR) population, with higher rates of recurrence and metastasis. Treatment options are severely limited in these cases. OTRs require immunosuppression, which is linked to cSCC aggression, but the underlying molecular and cellular mechanisms are poorly understood. Dr. Ji has discovered an invasive cSCC subpopulation that communicates with non-malignant cell types in the tumor's environment. By profiling OTR tumors using cutting-edge single-cell and spatial technologies, he aims to better understand how this harmful subpopulation emerges in the immunosuppressed setting, aided by crosstalk with these neighboring cells. His goal is to develop strategies for disabling invasion and improving treatment of cSCC in both OTRs and advanced cases in the general population.

Benjamin A. Nacev, MD, PhD, with mentor Jeremy N. Rich, MD, at University of Pittsburgh, Pittsburgh

Sarcomas are a family of tumors for which there are few targeted treatments and outcomes are poor once the cancer has metastasized. Many sarcomas harbor recurrent mutations in proteins, known as epigenetic regulators, that control which genes are expressed and when. Among the regulators most frequently impacted is ATRX, which condenses regions of DNA into tightly packaged chromatin that cannot be accessed for transcription, effectively “silencing” these genes. The effect of ATRX loss in sarcomas is poorly understood, however, and treatments that leverage ATRX deficiency are lacking. Using patient-derived sarcoma cell lines and tumor samples, Dr. Nacev aims to understand epigenetic dysregulation in ATRX-deficient sarcomas, to determine how

this affects antitumor immunity, and to identify new therapeutic vulnerabilities.

Fyza Y. Shaikh, MD, PhD, with mentors Cynthia L. Sears, MD, and Drew M. Pardoll, MD, PhD, at Johns Hopkins University School of Medicine, Baltimore

Immunotherapy has significantly changed how lung cancer and melanoma are treated. Unfortunately, only a small percentage of patients experience long-lasting responses. Gut bacteria have emerged as a potential predictor of how patients will respond to immunotherapy and may even be adjusted to enhance the effect of immunotherapy. Dr. Shaikh aims to identify features of the gut microbiome that correlate with immunotherapy responses. She will focus on both individual bacteria as they change over the course of treatment and the metabolites made by the entire bacterial community in the colon. The goal of this project, since gut bacteria can be modified, is to develop microbiome-based treatments to be used in combination with immunotherapy to improve response rates or overcome immunotherapy resistance for patients.

Santosha A. Vardhana, MD, PhD [Gordon Family Clinical Investigator], with mentor Charles L. Sawyers, MD, at Memorial Sloan Kettering Cancer Center, New York

Dr. Vardhana is exploring the hypothesis that gastric cancers create an inhospitable environment for immune T-cells by limiting the availability of essential nutrients needed by T-cells to produce the cytotoxic proteins that, when released, kill cancer cells. There is evidence that T-cells lose the ability to produce cytotoxic proteins within gastric tumors, while gastric tumors take up and sequester amino acids—the building blocks of all proteins, including cytotoxic proteins—such that they cannot be accessed by T-cells within tumors. Understanding and reversing this metabolic sequestration within gastric tumors may be a novel strategy to enhance T-cell immunity within gastric tumors.

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