

Eight Innovative Early Career Cancer Scientists Receive \$3.2M in Grants From Damon Runyon

The Damon Runyon Cancer Research Foundation's innovation grants support high-risk, high reward ideas in cancer research.

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The Damon Runyon Cancer Research Foundation has announced eight recipients of the 2025 Damon Runyon-Rachleff Innovation Award, established to support high-risk, high-reward ideas with the potential to significantly impact the prevention, diagnosis, or treatment of cancer. Five extraordinary early-career researchers will receive initial grants of \$400,000 over two years, and each will have the opportunity to receive two additional years of funding (for a potential total of \$800,000). This year, this "Stage 2" continuation support was granted to three current Innovators who demonstrated significant progress on their proposed research during the first two years of the award.

The Innovation Award is designed to provide funding to exceptionally creative thinkers with a revolutionary idea who lack sufficient preliminary data to obtain traditional funding. The awardees are selected through a highly competitive and rigorous process by a scientific committee comprised of leading cancer researchers with their own history of innovative work.

"It's important that Damon Runyon continues to have awards like this one, which funds projects that can potentially positively impact cancer patients' lives, even when it's just a really good idea," says David G. Kirsch, MD, PhD, a former Innovator who developed the first handheld device capable of detecting residual cancer during surgery. "We need to have this kind of funding within the portfolio of investments we make in cancer research, and Damon Runyon is the ideal organization to make these investments because it attracts high-caliber scientists."

This program was established thanks to the generosity of Andy and Debbie Rachleff.

New 2025 Damon Runyon-Rachleff Innovators

Yiyin Erin Chen, MD, PhD, Broad Institute of MIT and Harvard

"Skin commensal bacteria as a novel source of systemic antitumor immunity"

Dr. Chen's research aims to harness a common skin-colonizing bacterium, present on all our skin, to train the immune system to attack cancer without causing infection or inflammation. This process is known to occur—notably, across an intact skin barrier—but its mechanism is not well understood. Dr. Chen is investigating which skin cells sense these bacteria and transmit the signal to immune cells, and why the immune cells that respond are so effective at killing cancer. Ultimately, she intends to develop a new type of cancer vaccine using engineered skin bacteria to activate immune cells to effectively target and destroy tumors. While the project's current focus is melanoma, the goal is to apply this therapeutic approach across cancer types.

Meghan A. Morrissey, PhD, University of California, Santa Barbara

"Nibbled to death: improving macrophage's ability to kill solid tumors by trogocytosis"

Certain immunotherapies work by instructing macrophages, a type of innate immune cell, to attack the tumor by phagocytosing, or eating cancer cells. However, macrophages rarely eat an entire cancer cell within a solid tumor. Instead, they nibble pieces off the cancer cell, a process called trogocytosis. While phagocytosis kills the cancer cell, trogocytosis usually doesn't – and worse, nibbling removes the markers on the cancer cell that allow the immune system to recognize it as a threat. Dr. Morrissey is studying why some cancer cells die after being nibbled while others survive, with the goal of making macrophage-activating immunotherapies more effective. Specifically, she is studying HER2-positive breast and ovarian cancers, as it has been shown that HER2 immunotherapies cause trogocytosis instead of phagocytosis. This research could enhance any immunotherapy that is designed to activate macrophage phagocytosis, improving treatment of diverse cancers like lung cancer, lymphoma and glioblastoma.

Natasha O'Brown, PhD, Rutgers, The State University of New Jersey

"Leveraging zebrafish models to overcome the blood-brain barrier in glioblastoma treatment"

Glioblastoma is the most lethal primary brain tumor in adults, largely due to the blood-brain barrier (BBB), which blocks potentially effective chemotherapeutic drugs from entering the brain. Using zebrafish, Dr. O'Brown aims to identify small molecules that can temporarily increase BBB permeability, enhancing drug delivery to brain tumors like glioblastoma and potentially improving patient outcomes. To achieve this, she will screen for small molecules that enhance BBB permeability and then validate promising candidates in mammalian systems to confirm their relevance for human use. Additionally, she will engineer "humanized" zebrafish to test advanced drug delivery methods in clinical trials. This innovative approach provides a new platform for discovering BBB-modulating therapies and paves the way for tailored treatments, offering hope for improved outcomes in aggressive brain cancers.

Justin Perry, PhD, Memorial Sloan Kettering Cancer Center

"Tumor-macrophage metabolic symbiosis as a driver of disease progression and therapeutic resistance"

Dr. Perry is investigating how a key immune cell in the tumor microenvironment, the macrophage, contributes to cancer's development and progression. His work focuses on triple-negative breast

cancer, as it remains one of the deadliest cancers, especially to young women and Black women, with decades of treatment efforts failing to improve patient outcomes. Specifically, Dr. Perry aims to combine novel methods of manipulating and imaging the cellular metabolism to better understand how macrophages contribute nutrients to help cancer cells meet their nutrient demand and escape treatment. This work will not only provide a method for diagnostic biomarker identification but also establish a novel platform for developing individualized treatments. Importantly, his work has the potential of being broadly applicable to all difficult-to-treat metastatic adenocarcinomas.

Mark Yarmarkovich, PhD, New York University Grossman School of Medicine

“Unveiling the tumor antigenome through immune intelligence”

CAR T cells, or genetically engineered immune cells, have transformed the treatment of cancer in recent years, achieving cures for many patients who previously faced terminal diagnoses. Despite the remarkable impact that CARs have had on patients and families, however, fewer than 5% of cancer patients currently benefit from these therapies. A major barrier to broader CAR applications lies in the identification of tumor-specific targets: only ~0.00000001% of the cell surface distinguishes tumor cells from healthy cells. To date, CARs have targeted molecules on the surface of tumor cells, but the majority of tumor-specific molecules reside within the cell, where they are inaccessible to conventional CARs. Dr. Yarmarkovich’s team has pioneered a new class of CAR T cells that are able to target key drivers of cancer. These CARs completely eradicate aggressive tumors in preclinical testing and are entering the clinic in 2025. Encouraged by this success, he has proposed three new strategies to comprehensively map the landscape of subtle molecular differences that distinguish tumor cells from healthy cells. He will map the “known unknowns” using cutting-edge technologies for characterizing the surface of tumor cells, as well as the “unknown unknowns” by harnessing the immune system’s intrinsic capacity for identifying foreign targets. The goal of this study is to significantly expand the landscape of actionable immunotherapy targets, paving the way for curative therapies that benefit a much larger population of cancer patients.

2025 Stage 2 Damon Runyon-Rachleff Innovators

Lucas Farnung, PhD, Harvard Medical School

“Understanding the mechanistic basis of gene expression regulation by MLL complexes in cancers”

About 70% of pediatric leukemias and 10% of adult leukemias are caused by a genetic disruption in which the mixed lineage leukemia (MLL) 1 gene breaks off and attaches to a different chromosome. This event, known as a chromosomal translocation, gives rise to a distinct subset of leukemias called MLL-rearranged acute myeloid and lymphoblastic leukemias (AML or ALL). Novel treatments for these cancers represent a major unmet medical need. However, the development of therapeutics is hampered by a lack of basic understanding of how the MLL translocations disrupt the function of affected cancer cells. Dr. Farnung will use biophysical and structural biology approaches to visualize how MLL translocations function at the atomic level and influence the

important process of gene transcription. His work will elucidate the precise molecular mechanisms that drive acute leukemias and provide a platform for the development of novel therapeutic strategies against these cancers.

Ryan A. Flynn, MD, PhD, Boston Children's Hospital

"Tools to target novel cell surface ligands in cancer"

Many cancer diagnostic and treatment strategies use markers on the cell surface to find and kill cancer cells in a sea of healthy tissue. Dr. Flynn's research aims to expand our knowledge of what molecules are found on the surface of cancer cells. He will focus on acute myeloid leukemia (AML), as there is a major unmet clinical need for new curative treatments. Specifically, he aims to define RNA as a new cell surface molecule that could have unique structures on AML cells. With this knowledge he will develop antibodies to selectively detect cancer cells and enable tumor killing. Because tumors from other parts the body also express RNA on their surface, this strategy is expected to be broadly applicable to other cancer types.

(Kathy) Fange Liu, PhD, University of Pennsylvania

"Y chromosome proteins in sex bias of cancers in non-reproductive organs"

Sex differences are markedly evident in many types of cancer, and one of the major contributors to sex-biased differences lies in the sex chromosomes. In contrast to the traditional view that Y chromosome-encoded proteins only function in male reproductive organs, recent evidence suggests that select Y chromosome-encoded proteins are also expressed in male non-reproductive tissues. Furthermore, dysregulation of the Y chromosome-encoded proteins has been implicated in cancers in non-reproductive organs. Upon closer examination, this subgroup of Y chromosome proteins each has corresponding proteins on the X chromosome. Dr. Liu will study the function of the Y chromosome-encoded proteins and whether and how protein sequence differences from their X chromosome-encoded counterparts lead to functional distinctions in cancer development.

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