CRI Cancer Research Institute™

2025 CRI LLOYD J. OLD

STARs

The CRI Lloyd J. Old STAR Program

The Cancer Research Institute (CRI) Lloyd J. Old STAR Program (**S**cientists **TA**king **R**isks) empowers bold and visionary science that has potential to fundamentally transform the field of cancer immunology and result in more lives saved. With grants of $1.25 million over five years, CRI enables STARs to pursue high-risk, high-reward research that otherwise would go unfunded, providing a significant degree of freedom and flexibility to exceptional tenure-track scientists who are working at the forefront of discovery and innovation in cancer immunotherapy.

Launched in 2019, the CRI Lloyd J. Old STAR Program is named in memory of CRI's founding scientific and medical director, whose vision and expertise guided CRI's programs for forty years. Old is recognized as the "Father of Modern Tumor Immunology", and his lifelong passion for scientific excellence created a legacy that is reflected in the outstanding quality of the STARs who have been selected for this prestigious program.

To date, 37 scientists hailing from 25 academic research institutions in 10 U.S. states, Australia, China, Israel, Italy, and Switzerland have been named CRI STARs. New awards are made annually, with a total of $46+ million invested so far. The enclosed profiles provide a glimpse into the STAR Class of 2025 and their innovative research and remarkable approaches to exploring today's most important questions in cancer immunology.

A Letter from the CEO

Each year, CRI has the privilege of identifying and empowering scientists whose ideas have the potential to reshape what we know about cancer – and how we cure it. The researchers we honor as Lloyd J. Old STARs don't just follow established paths; they forge new ones. They are bold thinkers with the creativity, the insight, and the tenacity to challenge the status quo and ask the biggest questions.

It is my great pleasure to introduce the STAR Class of 2025 – five extraordinary rising scientific leaders whose work is pushing the boundaries of what's possible in cancer immunotherapy. From decoding ancient viral remnants in our DNA to engineering smarter cellular therapies and investigating how tumors evolve to outwit the immune system, these researchers are charting entirely new territory.

Each STAR will receive $1.25 million in unrestricted funding over the next five years. The STAR program is a direct investment in people, not projects. We fund scientists with a track record of insight and originality, who are entering a pivotal stage in their careers – a moment when unrestricted support can unlock their most transformative ideas. It is a commitment not only to their science, but also to the future of cancer treatment.

We are honored to support these scientists, and I believe their work will spark discoveries that transform patient care and, ultimately, bring us closer to cures.

With admiration,

Alicia Zhou, PhD
Chief Executive Officer
Cancer Research Institute

> Through the STAR program, we're able to identify and invest in exceptionally talented scientists who are early in their independent paths. These researchers are pushing boundaries with bold, innovative ideas – true barrier breakers. Their work has the potential to redefine how we understand and treat patients with cancer. The STAR program is an investment in hope that has a high rate of return.

Carl F. Nathan, MD
Professor and Chairman, Microbiology and Immunology, Weill Cornell Medicine
Associate Director, CRI Scientific Advisory Council

> What excites me most is that these rising STARs aren't just keeping pace with the field – they're charting its course. Their projects represent the next pivotal steps in cancer immunotherapy, and in some cases, leaps beyond where we are today. By supporting them now, we're picking people who are really our next leaders in the field of immunotherapy.

Elizabeth M. Jaffee, MD
Professor and Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine
Associate Director, CRI Scientific Advisory Council

Judith Agudo, PhD

Principal Investigator, **Dana-Farber Cancer Institute**; Associate Professor of Immunology, **Harvard Medical School**

Decoding Cancer Cell Plasticity as a Driver of Immune Evasion During Tumor Evolution

Research focus:
Cancer metastasis, cancer stem cells, immune surveillance

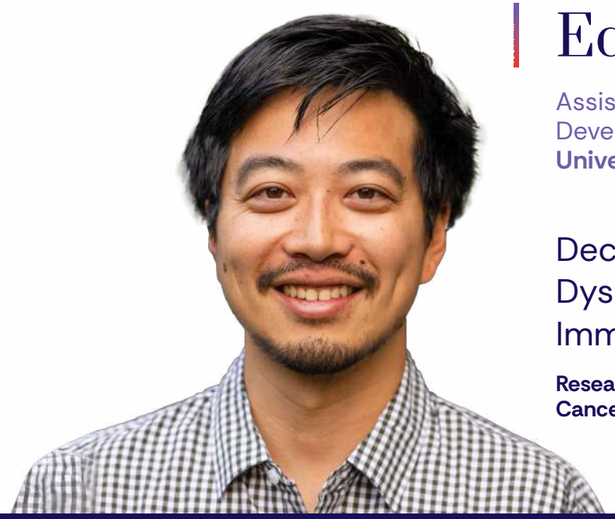
Dr. Judith Agudo is focused on understanding why some cancer cells escape the immune system, even in patients receiving immunotherapy. While these treatments can be highly effective, many patients don't respond, and the reason often lies in the diversity of cancer cells within a single tumor. Not all cancer cells are the same, and Dr. Agudo's research has shown that a specialized, stem-like subset of cancer cells is particularly resistant to immune attack.

These "cancer stem cells" have the unique ability to survive treatment, regrow tumors, and spread to other parts of the body. Dr. Agudo is investigating how these cells manage to stay hidden from the immune system and how they actively suppress immune responses at different stages of cancer progression.

Her research spans three key questions: 1) how do cancer stem cells evade early immune surveillance, 2) how do they resist immune attacks in established tumors, and 3) how do they spread and colonize new tissues while avoiding detection.

By uncovering the tactics these cells use to escape the immune system, Dr. Agudo hopes to develop strategies that make immunotherapy more comprehensive, ensuring that it targets and eliminates even the most elusive cancer cells and ultimately reducing relapse and metastasis.

> For immunotherapies to succeed, we must understand how some cancer cells escape or resist immune attack. This award allows us to develop systems that truly reflect patient biology and uncover how certain tumor cells survive and drive resistance to treatment.



Edward Chuong, PhD

Assistant Professor of Molecular, Cellular and Developmental Biology, **BioFrontiers Institute at University of Colorado Boulder**

Decrypting Transposon-Driven Dysregulation of Cancer Immune Function

Research focus:
Cancer biology, transposons, immune regulation

Dr. Edward Chuong is investigating the unexpected role of transposons in shaping immune responses and potentially influencing cancer immunotherapy outcomes. Long considered genomic "junk" or inert fossils, transposons – mobile genetic elements that make up over 50% of the human genome – are now emerging as important regulators of host gene expression. Dr. Chuong's research has revealed that transposon-derived regulatory elements have been co-opted as enhancers and transcriptional switches, playing essential roles in innate immune signaling across multiple mammalian lineages, including primates, rodents, and bats.

Building on these findings, Dr. Chuong now aims to uncover how transposons may drive dysregulated immune signaling in cancer, where immune evasion is a hallmark. His lab hypothesizes that transposon-derived regulatory networks contribute to altered cytokine and interferon responses in the tumor microenvironment, potentially influencing the success or failure of immunotherapies.

To explore these questions, Dr. Chuong's team uses cutting-edge genomic profiling, CRISPR-based perturbations, and cross-species comparative analyses to identify functionally relevant transposon elements. By decoding the hidden regulatory impact of these genomic elements, this work promises to reveal novel mechanisms of immune dysregulation in cancer and highlight new targets for therapeutic intervention.

> "We're diving into the most ambitious and high-impact parts of our research plan right away: large-scale mouse studies and single-cell sequencing. This support lets us finally explore those ideas at full scale and bring new perspectives to the field.

Ryan Flynn, MD, PhD

Principal Investigator, Stem Cell Program, **Boston Children's Hospital**; Assistant Professor of Stem Cell and Regenerative Biology, **Harvard University**

Defining Mechanistic Features of Cell Surface RNA-Binding Proteins

Research focus:
Acute myeloid leukemia, solid tumors, cancer cell markers

> "One of the biggest challenges in cancer research is the need to make bold ideas appear polished and low-risk to secure funding. But real innovation is rarely linear. The STAR award offers the freedom to pursue transformative ideas as they develop and evolve.

Dr. Ryan Flynn is tackling a major hurdle in cancer treatment: finding unique markers on the surface of cancer cells that aren't present on healthy tissues. These markers are essential for designing safe and effective immunotherapies. Surprisingly, his lab discovered that molecules traditionally thought to exist only inside cells – specifically, RNAs and RNA-binding proteins (RBPs) – also appear on the surface of many cancer cells.

These cell-surface RBPs are found across both blood cancers like acute myeloid leukemia (AML) and various solid tumors. They have even been linked to immune responses in patients who went into remission after immunotherapy, suggesting that cell-surface RBPs may play an active role in immune recognition. Unlike typical cancer targets, cell-surface RBPs aren't mutated or presented as fragments – they appear as full-length proteins in distinct clusters.

Dr. Flynn's work now focuses on understanding the function of cell-surface RBPs in tumors and uncovering how they are selectively displayed by cancer cells. This may not only reveal new biology about the cancer cell surface, but also unlock powerful new strategies for targeted treatment that spare healthy tissues.

Anusha Kalbasi, MD

Associate Professor of Radiation Oncology,
Stanford University School of Medicine

Decoding the Cell-Intrinsic Language of Cytokines for Cancer Immunotherapy

Research focus:
Sarcoma and other solid tumors, cytokines, T-cell therapy

Dr. Anusha Kalbasi is creating a detailed map of how cytokines influence cancer-fighting T cells – information that is essential for designing next-generation immunotherapies that are both more effective and predictable. Cytokines are small protein messengers that help immune cells communicate and function, and Dr. Kalbasi has uncovered a promising new role for IL-9, a lesser-known cytokine with unique signaling properties that can supercharge T-cell function.

While IL-2 has been the mainstay cytokine in cancer immunotherapy since 1992, IL-9 appears to drive T cells in a fundamentally different and potentially more effective way. Dr. Kalbasi's team will use techniques from protein and cell engineering, genomics, structural biology, and advanced T-cell biology to understand how IL-9 and other cytokines like it influence T-cell behavior at the molecular and cellular level, providing a blueprint for designing smarter cell- and protein-based therapies.

Dr. Kalbasi is also working to bring these findings into the clinic by integrating IL-9 signaling into new T-cell therapies. This includes optimizing both conventional T-cell therapy and emerging approaches like *in vivo* T-cell engineering, which may especially benefit from cytokine-based control. His research aims to deliver more effective, durable treatments for patients, guided directly by the insights gained from clinical application.

> We now have the tools to engineer almost any immune cell phenotype, but we still don't understand the rules that determine which cells will be most effective in patients. This support gives us the freedom to define those rules and translate them into smarter therapies.

Tuoqi Wu, PhD

Assistant Professor of Immunology,
The University of Texas Southwestern Medical Center

Engineering CAR T Cells with Tunable Chemical Switches to Counter Exhaustion and Senescence

Research focus:
Blood cancers, aging, CAR T-cell therapy

> Too often we prioritize the safe, incremental questions – that approach limits progress towards eradicating cancer. The STAR program gives us the opportunity to ask paradigm-shifting questions, and that's exactly what's needed to move the field forward.

Dr. Tuoqi Wu is working to improve CAR T-cell therapy, a treatment that has shown promise for some patients with some blood cancers but remains less effective for older patients. This is partly because older individuals often have T cells that are more prone to exhaustion and less fit for the demands of therapy. Since CAR T-cell therapy depends on a patient's own T cells, age-related declines can limit both the manufacturing process and the therapy's effectiveness.

To address this, Dr. Wu's team is developing innovative strategies to combat CAR T-cell exhaustion and aging. Their approach centers on a special subset of T cells that act like stem cells – cells that stay "younger" and more active in fighting cancer. By identifying key proteins that control this stem-like state, they've created CAR T cells with chemical switches that allow precise control over when and how these rejuvenating programs are turned on.

These programmable CAR T cells offer a flexible and safer alternative to conventional methods, aiming to improve therapeutic outcomes, especially in older patients. With this research, Dr. Wu hopes to expand the benefits of CAR T-cell therapy to a broader and more vulnerable group of patients with cancer.

Reflections from Current CRI STARs

CRI has supported me throughout my career. First as a trainee – with a postdoctoral fellowship – and then as a faculty member and a principal investigator. Thank you for believing in me, thank you for supporting me, and thank you for inspiring me and my lab to do the best science we can do.

Andrea Schietinger, PhD
Associate Member, Memorial Sloan Kettering Cancer Center
CRI STAR Class of 2019, CRI Irvington Postdoctoral Fellowship Class of 2011

CRI motivated us to accelerate our research and take risks and also provided the concrete means to do so. There is no substitute for discretionary funding to translate new ideas into results and there are too few opportunities for mid-career scientists to secure these funds.

Alexander Marson, MD, PhD
Professor, UCSF School of Medicine and Director, Gladstone-UCSF Institute of Genomic Immunology
CRI STAR Class of 2019

About CRI

The Cancer Research Institute (CRI) is a nonprofit organization dedicated to advancing the field of cancer immunotherapy through rigorous scientific research and global collaboration. Since 1953, CRI has been instrumental in uncovering the fundamental biology of the immune system and its application to cancer treatment, laying the groundwork for breakthroughs such as checkpoint blockade, cancer vaccines, and engineered cell therapies.

CRI's mission is to create a world immune to cancer by driving scientific discovery, accelerating collaboration, and turning breakthroughs into life-saving treatments. Our work bridges the gap between discovery and patient impact, ensuring that scientific innovation translates into real-world treatments.

To date, CRI has committed over $560 million to research impacting more than 30 cancer types. Our funding strategy is built on the framework of People × Biology × Data: supporting world-class scientists, deepening understanding of tumor-immune system interactions, and harnessing data to guide discovery and translation. By uniting these elements, CRI catalyzes innovation through our global research ecosystem to drive the next generation of discoveries forward.

Contact Us
Cancer Research Institute
29 Broadway, Floor 4
New York, NY 10006-3111
800-992-2623 | 212-688-7515

info@cancerresearch.org

Learn more at **cancerresearch.org**