

Taking on Multiple Myeloma Together

In the past decade, new therapies have transformed treatment for people facing an initial diagnosis of multiple myeloma and those experiencing a relapse. People are living longer with the disease. Yet, for all the progress that's been made, the heartbreaking fact remains that multiple myeloma is not yet curable. It inevitably comes back.

Together, Fred Hutch Cancer Center and Defeat Multiple Myeloma are changing that. With your support, our scientists are making landmark discoveries about how to engineer and modulate T-cell function to better target multiple myeloma. We are helping more patients achieve lasting remission by developing new antibody-based myeloma drugs, cell therapies, and radioimmunotherapy, in which antibodies ferry powerful radioactive isotopes straight to myeloma cells. And we're unlocking the secrets of relapse on the way to finding cures.

Patients are partners in research

Participants in and donors to the 2023 Defeat Multiple Myeloma 5K raised nearly \$200,000, which will sustain our multiple myeloma biobank — a one-of-a-kind collection of precious, patient-donated specimens — for three years.

Since Damian Green, MD, established the biobank in 2011, more than 600 patients have donated blood and bone marrow samples. The biobank includes samples from people at every stage of disease and who have undergone many types of treatments. The physical specimens — along with clinical data about the donor's disease, treatments, outcomes, and more — give scientists the power to evaluate emerging therapies and delve deeply into the biology of the disease to improve clinical practice. **The biobank will facilitate discoveries for decades, as future scientists scrutinize samples using tools and technologies that don't yet exist.**

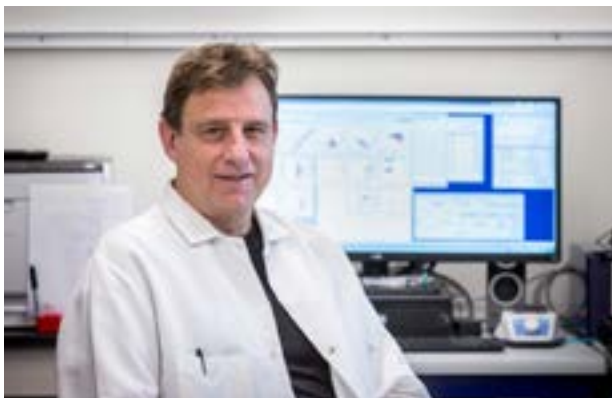
Fred Hutch Cancer Center is an independent, nonprofit organization that also serves as UW Medicine's cancer program.

Fred Hutch is proud to raise funds that fuel the adult oncology program on behalf of both Fred Hutch and UW Medicine.

UW Medicine

A bridge from the lab to the bedside

For researchers like Geoffrey Hill, MD, senior vice president and director of stem cell transplantation, the biobank is indispensable for translating laboratory discoveries into clinical advances. Dr. Hill, who also leads the Immunotherapy



Dr. Geoffrey Hill relies on the multiple myeloma biobank for his research. "Our ultimate focus," he says, "is to bring approaches with truly curative potential to this disease."

Integrated Research Center and the Translational Science and Therapeutics Division, is world-renowned as both a blood stem cell transplant physician and a translational scientist whose research has led to the development of drugs that improve outcomes for patients. His team partners with colleagues across Fred Hutch to develop methods to integrate transplantation with other forms of cancer immunotherapy, like T-cell therapy, for patients with multiple myeloma and other blood cancers.

Dr. Hill and his team rely on cells from the biobank to confirm that the biological mechanisms they discover in preclinical models of multiple myeloma hold true in humans. Here are some recent examples:

- The team discovered that as multiple myeloma progresses, patients' immune cells express more of a protein called TIGIT, a type of "stop" signal for the immune system — a finding they confirmed in patient samples from the biobank. Counteracting this effect with an antibody that blocks TIGIT helped control the tumor's growth, especially when combined with another immunotherapy drug used in multiple myeloma — a strategy that is currently in clinical testing.¹
- Dr. Hill's lab also used biobank samples to demonstrate that regulatory T cells mute the immune system's response to multiple myeloma when they're mobilized during autologous stem cell transplant — in which a patient's own stem cells are collected before high-dose chemotherapy and returned after. Importantly, the team showed that reducing the number of these regulatory T cells, or administering a synthetic protein designed to have the same effect, could dramatically improve anti-myeloma immune responses after stem cell transplantation. The clinical translation of this approach is now drawing significant interest.²
- Most recently, Dr. Hill's group showed for the first time that T cells thought to be nonfunctional after responding to multiple myeloma in the bone marrow (due to a process known as exhaustion) do, in fact, expand after transplantation to help control myeloma. Samples from the biobank made it possible to confirm this effect in patients, and clinical trials using these T cells as the target for a new immunotherapy are about to begin.³

Goodbye and hello

From 2017 to 2022, funds raised by Defeat Multiple Myeloma's incredible 5K participants fueled the work of Damian Green, MD, a blood cancer specialist and immunotherapy researcher. Earlier this year, Dr. Green became the chief of the Division of Transplantation and Cellular Therapy and assistant director of translational research at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine.

A search is now underway to recruit an international leader in multiple myeloma, and we expect a prominent researcher to join Fred Hutch soon. Proceeds from the 2024 Defeat Multiple Myeloma 5k will support the work of this faculty member and others who undertake cutting-edge multiple myeloma research at Fred Hutch.

Dr. Hill's team is just one of a half dozen research groups at Fred Hutch using samples from the biobank, which have also been shared externally with scientists at the Allen Institute. Teams are using the samples to study the effects of different treatments, pinpoint differences between newly diagnosed and relapsed disease, and more. For translational scientists studying multiple myeloma, the biobank is a bridge from the lab to the clinic, making possible a wide range of research — from work to improve blood stem cell transplants and immunotherapies to the science of tailoring treatments to individuals.

Thank you

We are proud of our partnership and the work we're doing together to defeat multiple myeloma. The biobank is critically important to this effort, and we are immensely grateful for your generous and visionary support. We look forward to sharing more stories about the progress you are making possible.

Andrea Larson, Director, Peer-to-Peer Programs, Philanthropy

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1. Minnie et. al., TIGIT inhibition and lenalidomide synergistically promote antimyeloma immune responses after stem cell transplantation in mice. *J Clin Invest.* 2023 Feb 15;133(4):e157907.

2. Takahashi et. al, Regulatory T cells suppress myeloma-specific immunity during autologous stem cell mobilization and transplantation. *Blood.* 2024 Apr 18;143(16):1656-1669.

3. Minnie et. al., TIM-3⁺ CD8 T cells with a terminally exhausted phenotype retain functional capacity in hematological malignancies. *Sci Immunol.* 2024 Apr 19;9(94):eadg1094.