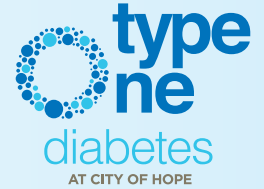




THE WANEEK FAMILY PROJECT NEWSLETTER

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THE WANEEK FAMILY
PROJECT TO CURE



A Legacy to Build On

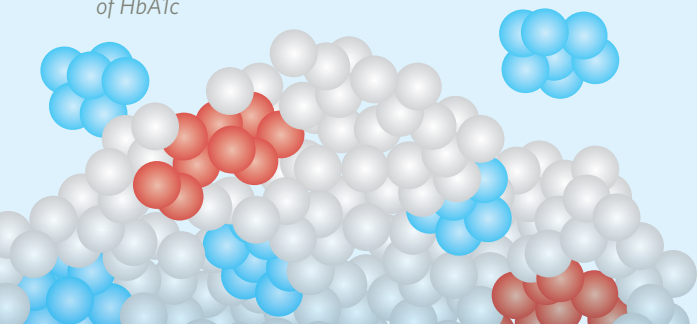
For nearly 50 years, researchers who made pivotal discoveries about diabetes have called City of Hope home. Their breakthroughs helped to transform the understanding and treatment of the disease.

That history goes all the way back to the founder of City of Hope's Division of Diabetes, who had uncovered how insulin regulates sugar in the body. Our faculty later welcomed the physician-scientist who first identified HbA1c, a protein in the blood of diabetes patients. It is now a widely used marker for measuring glucose control. Scientists working at City of Hope also broke new ground: the technology to produce synthetic human insulin and the isolation of the insulin receptor — a leap forward in understanding how insulin interacts with cells on a molecular level.



Gonda Center complex
at City of Hope

Visual model
of HbA1c



The spirit of innovation continues today. City of Hope has assembled experts in every major area of investigation into diabetes at the Diabetes & Metabolism Research Institute. There, ingenious scientists who are part of the Waneek Family Project for Type 1 Diabetes dig into the secrets of genetics and the immune system, metabolism and diabetic complications, united in pursuit of a singular ambition: finding a cure for type 1 diabetes.



A Unique Approach

With the goal of curing type 1 diabetes firmly at the center of research activities supported by The Wanek Project, City of Hope is pioneering a new way of looking at the disease.

Type 1 diabetes involves the immune system attacking insulin-producing beta cells in the islets of the pancreas as if they were enemies. To date, the standard approach has been looking for ways to tamp down the body's natural defenses. We believe that the cure will come not from curbing the immune system, but rather from educating it so that it recognizes beta cells as the friends that they are.

We combine this trailblazing strategy with connections to the expertise in immunotherapy that comes from City of Hope's world-renowned cancer research and treatment programs. This synergy holds the potential to yield new,

extraordinarily precise treatments — ones that go beyond controlling blood sugar to instead stop type 1 diabetes in its tracks.

We are able to push forward our work toward a cure thanks to the generosity of partners who share our vision. This is where the Wanek family's leadership gift has been crucially important. Their philanthropy, bolstered by funding from other donors, government grants and institutional investments, supplies the resources to cultivate a unique approach with great promise for making type 1 diabetes a thing of the past.

The Pace of Progress

In just a few years, research supported by The Wanek Project has produced new advances on the path to a cure.

For instance, recent research led by City of Hope has boosted the drive toward personalized therapies. The scientists characterized differences in the immune responses of children with type 1 diabetes, finding three distinct categories of cases that will likely call for different treatment approaches.

The leader of that study was part of a consortium of type 1 diabetes experts who explored the implications of these findings in more depth. That team laid out a detailed plan of action for bringing the concept of disease subtypes into research and treatment.



Meanwhile, a "reverse vaccine" developed by a scientist now at City of Hope underwent first-in-human clinical trials, showing the therapy to be safe and feasible.

Thanks to additional grants and philanthropic support, we essentially tripled the value of the Wanek family's giving. Twenty-four discoveries have been made that are already being developed for clinical use. We are actively securing patent protection for new drugs based on some of these discoveries. Findings from our leading-

edge research have already been shared with the clinical and research community in 155 publications in medical and scientific journals.

Making Friends With the Immune System

Our vision to engage the immune system, rather than suppress it, could not have been more timely: Our bodies rely on the immune response to fight off cancer and infections, including the coronavirus behind the current pandemic. Of course, the standard way of addressing type 1 diabetes — quashing the immune response — could be disastrous in the era of COVID-19.

The Wanek Project's game plan comes out of a City of Hope discovery. It seems that the genesis of type 1 diabetes is not in the immune system itself. Instead, the disease originates with an error within the beta cell. This glitch causes the body's natural defenses to identify it as an invader. The next step, the destruction of the beta cell, is simply the immune system doing its job.

This vital knowledge is informing numerous avenues for developing immunotherapies. We believe that we can convince the immune system to make friends with beta cells, despite the aberrations that seem to be at the root of type 1 diabetes.

One way is the "reverse vaccine," which involves treating a patient's immune cells with vitamin D. Initial studies showed that this potential treatment helps immune cells to tolerate beta cells instead of attack them. Following the success of first-stage tests in patients, the next round of clinical trials for the vaccine are expected to begin later this year.

Meanwhile, another cell therapy, adapted from an effective cancer treatment, will soon be presented to the Food and Drug Administration for clinical assessment.



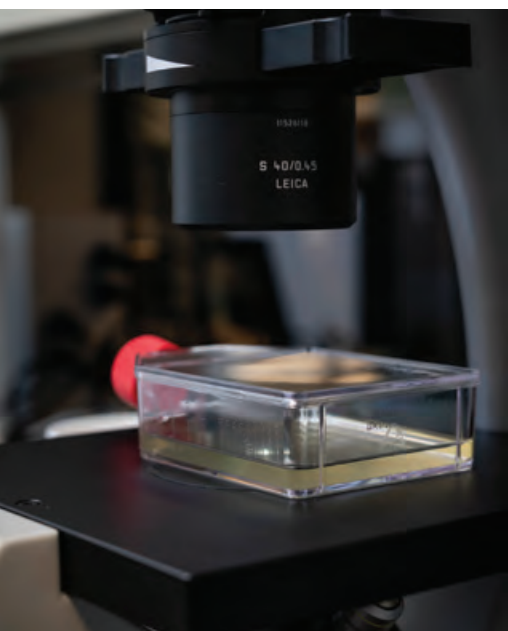
Repopulating the Pancreas

Convincing the immune system not to attack beta cells will not necessarily bring back the ones that have already become dormant or been destroyed. As a result, we're also looking at another side of the equation with type 1 diabetes: How can we revive a patient's beta cells?

Researchers supported by The Wanek Project are developing a new drug meant to do just that. We repurposed and altered a therapeutic antibody already

in use to treat psoriasis and arthritis — conditions in which the immune system attacks the body, as in type 1 diabetes. The antibody is also currently being deployed to save the lives of COVID-19 patients suffering from out-of-control inflammation as a result of the "cytokine storm."

City of Hope's version of this therapy has dual action: It may selectively block immune cells in the inflamed pancreatic islets, while also delivering a therapeutic "cargo" that revives damaged beta cells, so they can once again produce insulin.





To Sideline Side Effects

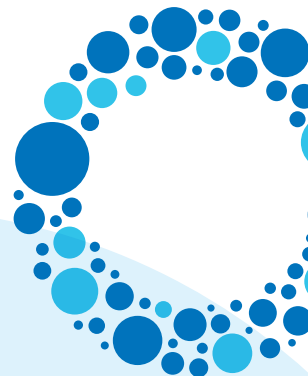
Anyone who has suffered from type 1 diabetes, or watched as a loved one struggled with it, knows that the most dangerous consequences are the complications brought on by the disease.

In the short term, extreme spikes or dips in blood sugar can result in headaches, fatigue or even seizures. Over the course of years, type 1 diabetes can cause heart disease, blindness, nerve damage and kidney disease.

We want to free patients from fear of these complications. Our researchers are exploring changes to genes that happen during a person's lifetime, among other scientific areas, in search of clues revealing how and why side effects occur. At the same time, a City of Hope-developed medicine targeting the complications of type 1 diabetes is moving toward testing in patients.



Every day, Wanek Project researchers are working hard, focused on the drive for a cure. We are grateful for the support of our donors and all the individuals and families living with type 1 diabetes.



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For more information, please visit CityofHope.org/WanekProject and stay tuned for opportunities to join our studies.