New Gift Fuels Precision Medicine Approaches to Diabetes

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UCSF has a bold vision to create a first-of-its-kind clinical diagnostic center that will advance precision diabetes research. The goal is to provide a central resource for families with type 1 diabetes and other heritable immunological conditions to receive personalized care and genetic counseling. This crucial multi-disciplinary effort will work to unravel the mysteries behind complex immunological disorders and exemplifies the translational research, from bench lab to bedside, being conducted by UCSF's clinician-scientists across the campuses.

Type 1 diabetes is a chronic condition in which the body produces little or no insulin, a hormone that controls blood sugar levels. Different factors, including genetics and some viruses, may contribute to the onset of type 1 diabetes, which can develop in adults even though it usually appears during childhood or adolescence.

The idea that type 1 diabetes can be a hereditary disease is not new; about 10 percent of patients have a family member with the condition. But only recently have scientists had access to genome-sequencing tools that can rapidly determine which errant gene might be driving the disease and whether multiple gene variants or only one are involved.

A generous gift of $1 million from an anonymous donor recently created the Breakthrough Initiative in Type 1 Diabetes Precision Medicine and Discovery. The initiative will provide clinician-scientists and their collaborators with additional resources to help find candidate genes for different forms of type 1 diabetes, evaluate them, create animal models in the laboratories, and then start thinking about targeted therapies.

"We're calling it a breakthrough initiative because it's really an engine that can fuel a lot of different early-stage research projects," says immunologist Mark Anderson.

Leading the way in this field, Anderson and his colleagues have already seen some tremendous successes. With support over the past several years from the Helmsley Charitable Trust, the researchers have begun identifying several novel genes that by themselves can put someone at a very high risk of developing type 1 diabetes.

Anderson is also encouraged by a recently reported case of an adolescent patient with type 1 diabetes at Texas Children's Hospital in Houston, which is affiliated with the Baylor College of Medicine. Because of a genetic finding and subsequent precision therapy, the patient no longer needs insulin to maintain blood sugar levels. Could this be the first-ever reversal of type 1 diabetes? A letter describing the patient's experience is published in the *New England Journal of Medicine*.

“Reversing diabetes is tough,” says endocrinologist Mike German, clinical director at Diabetes Center. “But in the Baylor case, it worked—possibly because the child had only had type 1 diabetes for a few years. If we can identify the particular pathways involved with type 1 diabetes and catch the disease at the right point, we may be able to prevent or reverse it.”

German says that for patients, knowing that they or their family members might have a higher than normal risk for the disease is important because opportunities may exist to target the biological pathways with precision therapies before diabetes takes hold and the body’s beta cells, which make insulin, are destroyed. “The sooner you have that information, the quicker you can do something about it,” he says.

Zoe Quandt MD, a clinical fellow in Anderson lab, captures patients’ clinical histories and ensures access to a robust database that accurately records family information. She says finding culprit genes can be challenging.

“One of the ways we whittle down the pool is by looking through databases of the genes and seeing where they are expressed. If we find something that is expressed in the pancreas, that might be interesting to us,” she says.

Quandt sees this work as personalized medicine in the sense that they are trying to figure out precisely why a family has this disease. The hope is answering that question will lead to a new type of intervention that might be applicable to larger groups.

“This is precision or personalized medicine for diabetes,” says Steve Gitelman. “Once the mutation of a pathway is discovered, targeted therapies might be possible that either prevent or halt the disease.”

Gitelman maintains that we are at a perfect moment in time to bring new understanding to type 1 diabetes. He studies the genetics of different family groupings in which, for example, one family member has type 1 diabetes while other family members do not but have other autoimmune conditions; or patients have all the classic markers of type 1 diabetes but not the antibodies typically seen with that disease; or patients have a protective gene against diabetes but have the disease anyway.

“Resources provided by the new UCSF Precision Medicine and Discovery Fund will result in more patient stories like the one at Baylor College of Medicine,” Anderson says. “Ultimately, our research at UCSF will lead to greater opportunities for prevention, targeted treatments, and better outcomes for patients and their families. I am so grateful for the support we receive from donors that allows us to continue this exciting journey of discovery.”

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