Local research gives doctors early jump on Type 1 diagnosis, treatment

By Tom Fuszard

JDRF-funded research on autoimmunity undertaken at the Max McGee National Research Center in Milwaukee will soon help doctors pinpoint those most likely to develop Type 1, allowing for early intervention and treatment.

Marty Hessner, Ph.D., discussed his team's research during the Summer Garden Party for JDRF on Aug. 5, and elaborated on it in a phone interview. About 60 people attended the Garden Party, which was hosted by Don and Kate Wilson at their beautiful home in Brookfield, Wis. While sampling fine hors d'oeuvres and beverages, guests learned about the breakthrough research performed by Hessner's team.

Type 1 is an autoimmune disease, Hessner said, in which the body's immune system attacks insulin-producing beta cells in the pancreas. Scientists aren't exactly sure of the cause, but contributing factors include genetics and environmental factors (which can include viruses).

Approximately 1.4 million Americans have Type 1, and it affects 10 million to 20 million people worldwide. Roughly 30,000 new cases are diagnosed in the United States each year, Hessner said. The rate of diagnosis is growing 2-3% each year, and the average age of diagnosis is decreasing.

Founded in 1999, the mission of the McGee Center is to establish an internationally recognized center for diabetes research. The late Max McGee, a star wide receiver for the Green Bay Packers during the Lombardi era, had firsthand experience with Type 1. A brother had Type 1, as does his son, Dallas. The Center aims to determine how and why Type 1 occurs with the goal of developing strategies to prevent and cure juvenile diabetes.

Hessner, Director of the McGee Center, explained that immune cells enter the pancreas and release substances known as cytokines. The actions of these immune cells and their cytokines impair beta cell function, and eventually kill the beta cells. Blood tests currently are not sensitive enough to directly detect these cytokines related to T1D pathogenesis in the blood, so his team took an indirect approach that uses healthy cells as biosensors.

Blood cells from a healthy donor are mixed with plasma from a patient they are testing. That plasma may contain the cytokines. Researchers are looking for a reaction in the healthy blood cells. The cells don't die, Hessner said, but any cytokines cause genes in the cells to turn on.

Using a gene chip manufactured by Affymetrix, researchers can tell if there is any inflammation and what kind it is. “We can differentiate the type of inflammation of Type 1 from MS, Crohn’s [disease], flu or rabies,” he said.

Reviewing a host of studies funded in part by JDRF, Hessner’s team wondered how this technology could change and possibly improve treatment of Type 1. Researchers can now study Type 1 in the context of other diseases. “We may not need to make a new drug for Type 1 diabetes,” he said. “There may be a drug that has never been thought about being used with Type 1diabetes that would be potentially beneficial here.” And because each person’s diabetes may be slightly different, what’s learned by this research could help develop individualized medicines and therapies, he said.

Hessner likens this process to the canary in the coalmine of years ago. “We’re taking cells [from a healthy donor] and using the cells as a canary,” he said. This research allows them to see Type 1 coming years before it’s diagnosed in the patient. That can lead to early intervention and, one day, a cure.

McGee Center research important for understanding diabetes

Over the past decade, the McGee Center has been building a bio repository that possesses samples on more than 400 families and more than 2000 people. Their goal is 700 families. There are several other biobanking efforts like it around the world, including the large TrialNet Natural History Study. By sharing their research, these organizations help the scientific world better understand how and when diabetes develops, Hessner said.

Type 1 diabetes patients are diagnosed after years of ongoing autoimmunity towards the insulin-producing beta cells. Understanding how the disease is triggered and progresses is vital to prevention and cure. To gain this understanding, samples collected prior to onset are needed. To obtain preonset samples from the general population would be prohibitively expensive, since fewer than 1 in 250 subjects would be expected to develop Type 1.

The sample collection efforts at the McGee Center focus on families of children treated at Children’s Hospital in Milwaukee, where the likelihood of capturing this progression is greater (approximately 1 in 20 for siblings). This gives Hessner and his staff much more useful blood samples to test. He said they focus on the healthy siblings only, because they’re looking for any preonset issues in those children. That data forms the foundation for their research. Some children are drawn only once a year, while others visit more often.

Because this autoimmunity is going on for years before diagnosis, it’s difficult for doctors to pinpoint a cause. Was it that bout of flu five years ago? Hessner’s team has upwards of 10 years’

worth of data on some of the children in their study. It might be possible one day, he said, to look back at a patient's clinical records and pinpoint an event that may have caused the person's autoimmunity to kick in.

Hessner said this research has been a "major investment" on the part of the McGee Center. But it can pay big dividends. They have a longitudinal series of data for each participant. "Our studies have followed healthy kids that went on to develop Type 1 diabetes," he said. They have proven that this type of research works and offers valuable information for the medical community.

JDRF has been a major source of funding for this research, supplying three grants. Additional funding has come from the National Institutes of Health and the American Diabetes Association.

Immune issues aren't the only possible causes, Hessner said. The environment – and in particular, our food – may play a big part in the onset of Type 1. "What we eat today is vastly different from what we ate 100 years ago," he said. That, along with the antibiotics that are taken so readily today, affect the bacteria in our gastrointestinal tracts, which in turn influence the functioning of the immune system. But how, and what does that mean for the onset of Type 1? The technology and methodology used in the McGee Center study may someday answer those questions.

Hessner, who is also Professor of Pediatrics at the Medical College of Wisconsin, said these longitudinal studies are the best way to determine what triggers the autoimmune system and see how it progresses into Type 1. This can lead to early prediction and intervention.

His dream is that one day his team will be able to say, "We know with high confidence who is going to get diabetes and we know how this is happening. We would be able to successfully intervene and prevent diabetes from happening in our subjects."

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