



Worldwide study looks to find causes of type 1 diabetes

Toni Baker - 2006 February 13

Scientists are casting a wide, tightly woven net with the goal of catching the causes of type 1 diabetes.

Study sites around the world are screening 220,800 healthy babies for genes that put them at risk for type 1 diabetes.

They expect to identify the genes in about 13,000 babies in this four-year screening. About half those babies will embark with their families on a 15-year journey that may help cure the disease.

“Our hope is to identify environmental factors that determine the risks for type 1 diabetes,” says Dr. Jin-Xiong She, director of the Center for Biotechnology and Genomic Medicine at the Medical College of Georgia and Georgia Research Alliance Eminent Scholar in Genomic Medicine. “Once you know the risk factors, you can modulate the risk factors to prevent diabetes,” says Dr. She, who five years ago sat around

a table with other diabetes researchers to discuss such research opportunities. Those conversations led to a request for applications from the National Institutes of Health to investigate environmental triggers of the disease that turn the body's immune system on the insulin-producing cells of the pancreas.

A few dozen centers applied and six were chosen by NIH to meet again and devise a comprehensive plan for studying this expansive topic that includes nearly everything in child's life, from the water he drinks to when he eats his first cookie.

Dr. Jin-Xiong She, director of the Center for Biotechnology and Genomic Medicine. (Phil Jones photo)

“Risk factors for type 1 diabetes include two major components. One is the genetic factors and the other is the environmental factors. They are about equally important,” says Dr. She. “We have quite a few of the genes identified.” In fact, Dr. She and his colleague Dr. Cong-Yi Wang, molecular geneticist, reported in the August 2004 issue of Nature Genetics the discovery of the fourth gene, dubbed SUMO-4. Having these genes increases a child's risk of developing type 1 diabetes tenfold.

But the environmental factors, which researchers such as Dr. She believe are responsible for the increasing incidence of the disease, are still elusive. “There are many suspects like cow's milk, like coxsackie viral infection (cause of the common, painful and blistering hand, foot and mouth disease) that have been suggested as triggers for type 1 diabetes. But the literature is very controversial: some studies are for it, some are against it,” says Dr. She.

That's why TEDDY – The Environmental Determinants of Diabetes in the Young – was born.

The study includes newborns in four states and three countries. MCG is the lead site for seven hospitals, including MCG Medical Center, University Hospital and St. Joseph Hospital in Augusta; Northside Hospital in Atlanta; and three hospitals in Gainesville, Fla. Additional lead sites include Barbara Davis Center at the University of Colorado;

Pacific Northwest Research Institute in Seattle; the University of Turku in Finland; Lund University in Sweden; and the Diabetes Research Institute in Munich, Germany. Moffitt Cancer Center and Research Institute at the University of South Florida is analyzing the extensive data collected by study sites as they enroll participants over the next four years.

Image: Map of centers where TEDDY study is being performed.

TEDDY is similar to another screening study driven by Dr. She called PANDA – Prospective Assessment in Newborns for Diabetes Autoimmunity – which also uses a drop of blood taken from the umbilical cord or the traditional heel prick to screen newborns for high-risk genes. PANDA will follow those with the genes for five years.

While that study continues, the more expansive study that is following so many aspects of these children’s lives is now getting priority when it comes to enrolling newborns, says Diane Hopkins, study coordinator for the Center for Biotechnology and Genomic Medicine and multi-site research manager for TEDDY in Georgia and Florida.

“The families make a real commitment to this research,” she says. “We are asking them to record every time the child is sick, every time the child receives medication, whether it’s over-the-counter or prescription. Every time the child goes to a health care provider, even if it’s a well-baby visit, we want to know about it. When they go to the emergency after-hours clinic at 4 o’clock in the morning, we want to know. We are very much involved in what is going on with this child’s health whether or not we suspect it has anything to do with type 1 diabetes. We are just throwing this giant net of what is happening with these babies and reeling in as many answers as we can before we know they are answers.”

“One school of thinking is the triggering of the disease actually starts in utero and whether it’s true or not, no one really knows,” echoes Dr. She. “We need to have more evidence and we need to know what really triggers the disease.”

They definitely will have plenty of evidence.

Project managers such as Mrs. Hopkins will see study children every three months for the first four years of life and every six months after that to age 15. During that first visit, they will extensively revisit the pregnancy with the mother.

Those earliest years are important because they are formative years for the immune system as well, says Dr. She. “What your infant comes in contact with determines how the immune system develops. If you encounter infectious agents, bacteria, viruses, that will influence how the immune system will work for a long, long time to come. Most people believe that the early years are more important but that does not mean the later years are not important.”

So TEDDY will follow children through puberty and the two age peaks for type 1 diabetes: ages 2-4 and 12-15.

They’ll even analyze the water children drink. Every city’s water is different, says Mrs. Hopkins, and some children drink well water or run their water through the refrigerator or filter.

The researchers also are collecting any hard evidence they can, including nail clippings and stool samples and blood, regularly throughout the first 15 years of life.

They are looking extensively because, just as the water is different, the triggers may be different for different people and in different cities, states and countries. The extensive data will be examined collectively and by individual center to tease out regional differences.

Clearly there are regional differences in incidence. Finland and Sweden, for example, which have largely homogenous populations, have the highest rates of type 1 diabetes in the world, says Dr. She.

No doubt the TEDDY study is a tremendous undertaking for the researchers, as well as the children and parents willing to open up their lives to such scrutiny. But, says Dr. She, the problem with past studies is that they took isolated looks at a very complex disease.

“The bottom line is that it’s not going to be a simple answer,” Mrs. Hopkins says.

Key members of the TEDDY team include Dr. Andrew B. Muir, MCG pediatric endocrinologist; Dr. Desmond Schatz, University of Florida endocrinologist; Katherine Silvis, MCG nutritionist; Leigh Steed, study coordinator in Atlanta; and Angie Choate, study coordinator in Gainesville, Fla.

To find out more about type 1 diabetes research at MCG, call 706-721-4161 or 1-888-225-7785 in Augusta or in the Atlanta area 1-866-938-3339.

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