

Doctors map out diabetes in genes

In the past few months, they narrowed down a cause of inherited diabetes to a single genetic defect, like finding a typo in a word 3 billion letters long. Now, researchers at the Medical College of Georgia are looking to translate the entire book on autoimmune disease.

Using \$5 million in recent grants, Jin-Xiong She and colleagues at the Center for Biotechnology and Genomic Medicine at MCG are running samples from those with type 1 diabetes against a broad array of genetic tests and protein identifiers in hopes of understanding the entire pathway of the disease.

"We can pretty much look at every single gene we have in our cells," Dr. She said, running a couple of hundred samples at a time against gene chips that contain 55,000 sets of probes.

The problem is that variation or change can happen at many levels, from what the DNA is encoded for to how it is translated to how the proteins are formed to how they interact after they're formed. Thinking of the body as a restaurant - disease might happen if the recipe is wrong, if the cook makes a mistake, if the waiter drops the order, or if the diner pours too much salt on the dish.

"So what we're doing is looking as close as we can to gene sequence all the way to, as close as we can, actual function," said Robert Podolsky, a statistical geneticist who recently joined the center.

"Mistakes happen. Variations can happen," Dr. She said. "Pretty much you have to look at everything to understand what is going on."

Over the past 12 years, Dr. She and his team have recruited more than 3,000 patients from around the world to provide samples for comparison, and that paid off in July when the team published a paper identifying a single defect in a gene called SUMO4 that could distinguish between diabetics and those without the disease.

Now Dr. She is turning his attention to a master gene called autoimmune regulator, or AIRE. Type 1 diabetes is a form of autoimmune disease in which the body's immune system mistakenly attacks insulin-producing beta cells. But blocking AIRE in mice can produce a dozen different autoimmune diseases, such as diabetes and lupus, Dr. She said. Blocking the expression of AIRE in mice affects about 4,000 genes, Dr. She said.

"It controls so many things, it's unbelievable," Dr. She said. "We're using AIRE to find out what about the other genes that are important for autoimmunity. We now have many, many candidates."

That's part of what makes Dr. She's research so powerful; he is taking the "nonbiased" approach first, to do an objective search for candidates, and then refine what they do, said MCG School of Medicine Dean David Stern. The level of technology he is using is also top-rate, Dr. Stern said.

"To me, the reason he is such a terrific investigator, and for me very valuable, is that the technology that he uses lifts up the whole campus," Dr. Stern said. It could be used to try and tease out almost any disease process and likely will be applied to others. "Here's a case where the biotechnology platform is something that is so easily applied to multiple different areas," he said.

Having that technology available should make the area more attractive for biotechnology development, along with providing a new work force with highly-sought-after skills, Dr. Stern said.

"What he has to teach is particularly valuable because that's the kind of technology that the companies use," Dr. Stern said. "If industry were to come here, his people would be swept up because of their ability with the technology."

To do all that requires some heavy investment, such as the \$500,000 twin banks of computers, which are actually 26 linked processors stacked 6 feet high that require their own air-conditioning unit to keep from overheating.

The Impact: Dr. Jin-Xiong She has hired 36 people to do research for the Center for Biotechnology and Genomic Medicine. The center also has brought in more than \$18 million in grants.

Reach Tom Corwin at (706) 823-3213 or tom.corwin@augustachronicle.com.

Click here to return to story:

http://chronicle.augusta.com/stories/111404/met_2527702.shtml