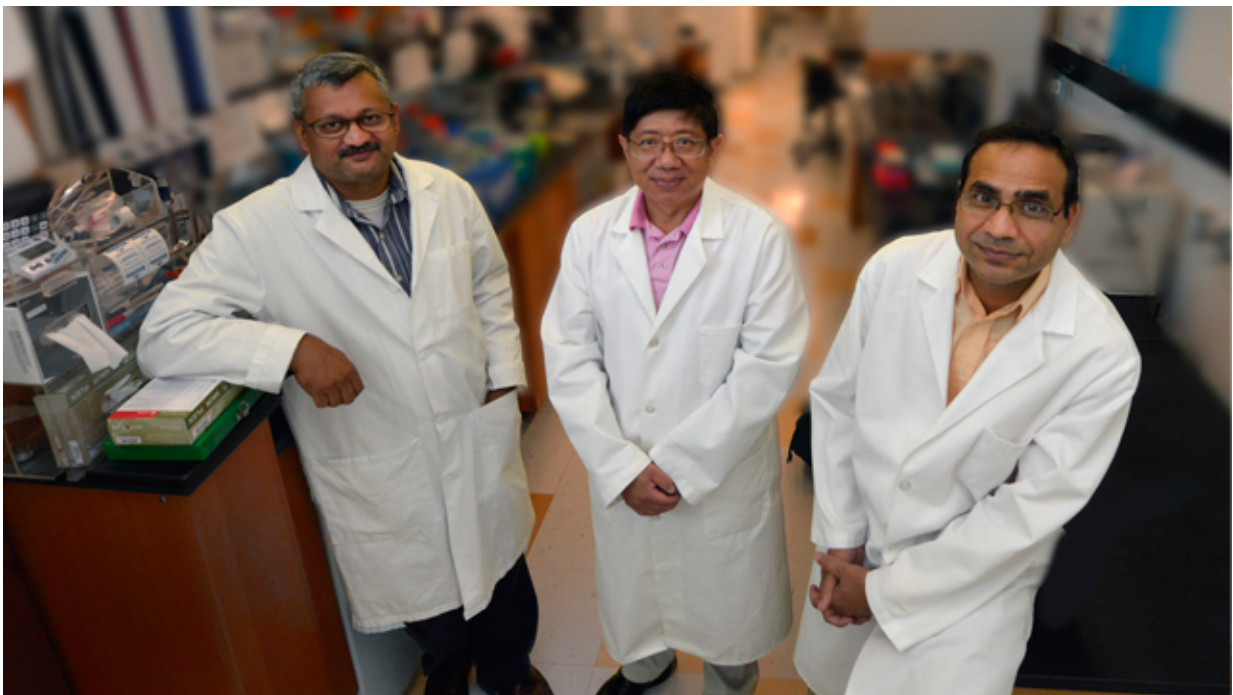


Type 1 diabetes patients have lower blood levels of four proteins that protect against immune attack

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Dr. Sharad Purohit, MCG biochemist and the study's first author; Dr. Ashok Sharma, an MCG bioinformatics expert and study co-first author; Dr. Jin-Xiong She, director of the Center for Biotechnology and Genomic Medicine at the Medical College of Georgia at Georgia Regents University. Credit: Phil Jones

Patients with type 1 diabetes have significantly lower blood levels of

four proteins that help protect their tissue from attack by their immune system, scientists report.

Conversely, their first-degree relatives, who share some of the high-risk genes but do not have the disease, have high levels of these proteins circulating in their blood, said Dr. Jin-Xiong She, director of the Center for Biotechnology and Genomic Medicine at the Medical College of Georgia at Georgia Regents University.

Healthy individuals without the risky genes also have higher levels of the four proteins, IL8, IL-1Ra, MCP-1 and MIP-1 β , according to the study in the *Journal of Clinical Endocrinology & Metabolism*.

The findings point toward a sort of [protein](#) cocktail that could help at-risk children avoid disease development as well as new biomarkers in the blood that could aid disease diagnosis, prognosis and management, said She, Georgia Research Alliance Eminent Scholar in Genomic Medicine and the study's corresponding author.

The scientists looked at a total of 13 cytokines and chemokines, which are cell signaling molecules involved in regulating the immune response. They first looked at blood samples from 697 children with [type 1 diabetes](#) and from 681 individuals without antibodies to insulin-producing cells, a hallmark of this autoimmune disease. They then analyzed the blood of a second and larger set of individuals, which included 1,553 children with type 1 diabetes and 1,493 individuals without any sign of antibodies.

In this largest study of its kind, they consistently found a higher percentage of type 1 diabetes patients had significantly lower levels of the same four proteins.

"Their pancreatic cells are not secreting enough of these proteins," said

Dr. Sharad Purohit, MCG biochemist and the study's first author.
"Normally you are secreting enough of these cytokines so you prevent attack by the immune system."

Individuals who have three of the known high-risk genes for type 1 diabetes but high serum levels of these four proteins are less likely to have disease, suggesting that these proteins may provide dominant levels of protection against type 1 diabetes even in a genetically high-risk group, Purohit said.

"If the individuals with high-risk genes weren't making more of the proteins, they likely would have diabetes, said Dr. Ashok Sharma, an MCG bioinformatics expert and study co-first author.

One of the proteins found at low levels in patients, MIP-1 β , has been shown in animal models to protect against type 1 diabetes development. A recombinant version of IL-1Ra, already used to combat rheumatoid arthritis, is also under study for both type 1 and 2 diabetes. And, human studies have shown that newly diagnosed patients with type 1 diabetes who go into remission have [higher levels](#) of IL-1Ra than those who don't.

Cytokines and chemokines can promote or inhibit inflammation - cytokines such as MIP-1 β can do both - and the proper mix helps keep inflammation in check. As an example, IL-1Ra, a cytokine secreted by several cell types, including immune cells, is a natural antagonist of the inflammation promoting cytokine IL-1 β .

"We are providing evidence that clinical trials with any of these four molecules may work, and if we use them in combination, they may work even better," She said. "One of the major research foci in our group is to identify biomarkers for various diseases, diabetes, cancer and others. We also want to identify new therapeutic strategies or targets through the discovery of biomarkers."

Type 1 diabetes is an autoimmune disease, which primarily surfaces in childhood, where the immune system attacks the insulin-producing cells of the pancreas, leaving children facing a lifetime of daily insulin therapy to try to keep blood sugar levels under control.

Some of the 13 cytokines and chemokines originally screened for the study were known factors in type 1 [diabetes](#), and the scientists were curious about the role of others.

Provided by Medical College of Georgia

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