

Type 1 Diabetes and Celiac Disease Share Several Common Susceptibility Alleles

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By Karla Gale

NEW YORK (Reuters Health) Dec 10 - Certain gene variants confer susceptibility to both type 1 diabetes and celiac disease, according to research published online today by The New England Journal of Medicine ahead of the scheduled December 25 printed issue.

"It has been known for a long time that there is clinical overlap of about 3 per cent between the two diseases," senior author Dr. John A Todd told Reuters Health. "Because of this, we knew there might be shared genes."

"The big surprise is that almost every celiac disease gene is involved in type 1 diabetes, and that the causes of these diseases overlap considerably," he added. "Even though the clinical overlap is small, the basic causal overlap was much larger than we expected."

Dr. Todd, at the University of Cambridge, UK, and co-investigators evaluated the relationships between non-HLA loci associated with type 1 diabetes and celiac disease. Their analysis was based on genotyping of DNA from 8064 patients with type 1 diabetes, 3064 parent-diabetic child trios, 2560 patients with celiac disease, and 9339 controls.

Their research confirmed the existence of 11 loci associated with celiac disease, three of which are associated with type 1 diabetes - regulator of G-protein signaling 1 (RGS1), interleukin 18 receptor accessory protein (IL18RAP), and T-cell activation RhoGTPase activating protein (TAGAP).

Of 21 loci associated with type 1 diabetes, two -- chemokine receptor 5 (CCR5) and protein tyrosine phosphatase, non-receptor type 2 (PTPN2) -- have an association with celiac disease.

Also, seven loci in the cytotoxic T-lymphocyte-associated protein 4 (CTLA4) region on chromosome 2q33 are shared between the two diseases.

The authors note that four alleles "show the same direction of association in the two diseases, constituting evidence for shared causal variants."

A possible explanation for these findings is "a common genetic background with respect to autoimmunity and inflammation and that further combinations of more disease-specific variation at HLA and non-HLA genes, in interaction with epigenetic and environmental factors, determine the final clinical outcome."

"Our results spotlight that much more research needs to go into investigating the environmental factors involved and why autoimmune diseases are increasing," Dr. Todd said.

Also, he added, "More research should be directed to identifying common genetic factors and investigating whether there are benefits for type 1 diabetics knowing they are positive for celiac."

N Engl J Med 2008;359:2767-2777.