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DIABETES

RAGE links genes and environmental factors in type 1 diabetes mellitus

Excess consumption of dietary advanced glycation end products (AGEs)—pro-oxidant metabolic derivatives of nonenzymatic reactions—may be a risk factor for type 1 diabetes mellitus (T1DM), suggest authors of a recent study in *Diabetologia*.

Lifestyle changes and new technologies employed in mass production over the past 50 years have increased chemical and thermal processing of foods to improve safety, transportability or flavor. However, these changes amplify the formation and ingestion of AGEs.

AGEs induce oxidative stress and inflammation, two major pathways implicated in pancreatic β-cell dysfunction and destruction, predominantly via binding to RAGE, a multiligand receptor with a critical role in the amplification of immune and inflammatory responses.

Forbes *et al.* noted that changes in *AGER*, the gene that encodes RAGE, seemed to affect the incidence of T1DM. "We therefore examined if mutations in *AGER* could explain the currently rising incidence of T1DM, independent of genes already known to contribute," explains lead investigator Josephine Forbes (Baker IDI Heart and Diabetes Institute). The researchers also tested for changes in RAGE protein levels in an animal model of T1DM, the nonobese diabetic mouse.

Two polymorphisms in *AGER* predicted an increased risk of T1DM, and circulating soluble RAGE levels declined at seroconversion to positivity for T1DM-associated autoantibodies. Also, both changes in RAGE expression and the onset of T1DM could be prevented by medicines that lower AGE accumulation.

Linda Koch

Original article Forbes, J. M. *et al.* Receptor for advanced glycation end-products (RAGE) provides a link between genetic susceptibility and environmental factors in type 1 diabetes. *Diabetologia* doi:10.1007/s00125-011-2058-z