Breakthrough Genetic Discovery in Insulin Resistance and Type 2 Diabetes

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Twenty-six million Americans now have type 2 diabetes and nearly 79 million more have prediabetes. Genetic defects play a role in causing type 2 diabetes, but for almost all patients these defects have been unknown. Now, researcher Ira Goldfine, MD, of the UCSF Diabetes Center, and his colleagues, Clive Pullinger, PhD, and John Kane, MD, PhD, of the UCSF Cardiovascular Research Institute, participated in an international collaboration that discovered a flaw in a gene that causes type 2 diabetes.

Their collaborators were Antonio Brunetti, MD, PhD, of the University of Catanzaro, Italy, a former UCSF post-doc with Dr. Goldfine, and Vincent Durlach, MD, of the University of Reims, France, a former visiting professor with Dr. Kane.

In 10% of diabetic patients, but in less than 0.5% of controls, the team discovered defects in the gene for the nuclear protein HMGA1 which regulates the insulin receptor. When this gene isn’t functioning, there is markedly reduced insulin receptor expression causing insulin resistance, and a very high risk for type 2 diabetes. In isolated cells from these patients, replacement of the defective HMGA1 gene with a normal one restored the cells to normal.

Recently these data were published in the prestigious *Journal of the American Medical Association* (JAMA). This research should lead to predictive markers for insulin resistance and type 2 diabetes, and could lead to the identification of new drugs and treatments to prevent these conditions.