

Key action of a gene linked to both Alzheimer's disease and type 2 diabetes identified

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A research team led by Mount Sinai School of Medicine has identified the mechanism behind a single gene linked to the causes of both Alzheimer's disease and Type 2 diabetes. The data show that a gene for a protein called SorCS1, which can cause Type 2 diabetes, impacts the accumulation of amyloid-beta (Abeta) in the brain. Abeta plays a key role in the development of Alzheimer's disease. The study is published in the September 29th issue of the *Journal of Neuroscience*.

Sam Gandy, MD, PhD, the Mount Sinai Professor in Alzheimer's Disease Research, Professor of Neurology and Psychiatry, and Associate Director of the Alzheimer's Disease Research Center at Mount Sinai School of Medicine, led the study, together with first author Rachel Lane, PhD, a postdoctoral researcher in Gandy's Lab. Lane and Gandy analyzed both the brains of mice genetically engineered to be deficient in SorCS1 as well as cells engineered to express high levels of SorCS1. They found an increased level of Abeta in SorCS1-deficient mice, and low levels of Abeta in the cells overexpressing SorCS1.

"We knew that Type 2 diabetes could increase the risk for [Alzheimer's disease](#), but we were not sure how that risk was caused or whether that diabetes risk would impact Abeta levels in the brain," said Dr. Gandy. "These results elucidate a common mechanism between diabetes and Alzheimer's and will bring us a step closer to identifying effective treatments for both diseases."

The researchers were also interested to find that the SorCS1-deficient mice had decreased levels of the protein Vps35, which was linked to Alzheimer's by Scott Small, MD, Associate Professor of Neurology, Columbia University College of Physicians and Surgeons, who co-authored the new study with Gandy. They propose that depleted SorCS1 may cause Vps35 levels to also decrease, leading to further accumulation of Abeta in mice. Further studies are required to better understand the impact of SorCS1 on Vps35 levels.

SorCS1 deficiency has been linked to Type 2 [diabetes](#) by geneticist Alan Attie, PhD, Professor of Biochemistry, University of Wisconsin, who also co-authored the new study. Rudolph E. Tanzi, PhD, Joseph P. and Rose F. Kennedy Professor of Neurology and Director of Genetics and Aging Research Unit at Harvard Medical School also contributed genetic data to the new study. Now that Dr. Gandy and his team have connected the same protein to increased Abeta levels, they can evaluate this protein and the family of proteins of which it is a member as drug targets for the treatment of both diseases.

"Alzheimer's and [Type 2 diabetes](#) are reaching epidemic levels, afflicting millions of Americans," said Dr. Gandy. "Their risk factors overlap and include high cholesterol, obesity, vascular disease, and inflammation. Now that we have a better understanding of where the connection between these two diseases originates on a molecular level, the next step is to develop drugs that will help reduce their devastating impact. Such drugs will require much more research, but having this new target helps put us on the right track."

Provided by The Mount Sinai Hospital

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