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Researchers identify how a gene linked to both Alzheimer's disease and type 2 diabetes works

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Researchers at Mount Sinai School of Medicine have identified how a gene for a protein that can cause Type 2 diabetes, also possibly kills nerve cells in the brain, thereby contributing to Alzheimer's disease.

The gene, called SorCS1, controls the generation of amyloid-beta (Abeta) in the brain. Abeta plays a key role in the development of Alzheimer's disease. The researchers previously linked SorCS1 to Alzheimer's disease and identified where the molecules lived in the cell, but not how they control Abeta. The new data were presented today at the Alzheimer's Association's Annual International Conference in Paris.

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 research team with Rachel Lane, PhD, a postdoctoral researcher in Dr. Gandy's lab.

The researchers determined various "traffic patterns" in the cell for the amyloid precursor protein (APP) that makes Abeta and uncovered how much APP is converted into the toxic, and ultimately nerve-killing, Abeta. In some experiments Drs. Lane and Gandy altered the dose of the diabetes gene, SorCS1, and evaluated how that changed the "traffic pattern" that APP used to move around the cell and generate Abeta. In other experiments, Dr. Lane made small changes in the SorCS1 gene's

and again saw dramatic changes in the "traffic pattern" of APP around the cell.

These data suggest that SorCS1 controls the movement of APP within the cell between areas where Abeta is readily made to areas where Abeta is not so easily made. In turn, the "traffic pattern" of influences the amount of Abeta being made by cells. The implication is that people with deficiencies in SorCS1 are at higher risk of developing Alzheimer's disease because their APP spends too much time in the region of the cell where APP is broken down to make the toxic Abeta.

"The great thing about studying SorCS1," said Dr. Gandy, "is that we already have entirely new ideas about how to treat both Alzheimer's disease and type 2 diabetes. Our hunch is that SorCS1 also controls how the insulin receptor moves around the cell, but we have not yet proven that," he said. "With both diseases reaching epidemic proportions, this discovery is encouraging news that brings us one step closer to developing treatments."

Provided by The Mount Sinai Hospital