Researcher finds genetic link between obesity and Alzheimer's disease

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(PhysOrg.com) -- An Auburn University researcher has discovered a genetic link between obesity and Alzheimer's disease, which could be the first step in curing the memory-debilitating illness that affects millions of individuals, especially the elderly.

Marie Wooten, associate dean for research and professor of biological sciences in the College of Sciences and Mathematics, found that if a certain protein molecule, called p62, is absent from the brain in mice, they are much more susceptible to Alzheimer's disease.

"When we deleted the p62 gene from mice, unexpectedly they became obese and memory-impaired, leading to insulin-resistance and Alzheimer's-like symptoms," said Wooten, who has been conducting the research for 10 years through support from the National Institutes of Health's National Institute of Neurological Disorders and Stroke.

"Our work revealed that p62 plays a critical role in receptor trafficking, which supports survival of neurons in the brain," Wooten said. Receptor trafficking is a process in the brain that allows neurons, or nerve cells, to communicate information to each other. Alzheimer's disease occurs when neurons deteriorate and die, causing memory loss.

Results from the ongoing research have been published in journals such as Free Radical Biology & Medicine, Feb. 15, 2009, and the *Journal of Neurochemistry*, March 13, 2008.

Based on Wooten's findings, the National Institute of Neurological Disorders and Stroke has awarded Wooten continued funding for a new four-year, $1.3 million grant, "Mechanisms of Ubiquitin Trafficking in Neurons," to genetically engineer mice to have high levels of the p62 protein in the brain and to further understand the basic function of p62.

The mice will be fed a high-fat diet to induce obesity and to increase the odds of developing diabetes, allowing Wooten to see if the increased level of p62 protects the mice against Alzheimer's disease. She said the mice also will be mated to mice that have human genes implicated in Alzheimer's disease.

Wooten will observe the mice as they age and compare the occurrences of Alzheimer's disease to the percentage among normal mice or the Alzheimer mice with reduced p62.

"If the increased p62 protein keeps the mice from getting the disease or delays the onset, then we can start looking into ways to apply the findings in combating the disease in humans," Wooten said. "We also hypothesize the mice with extra p62 may be smart mice possessing an ability to learn quicker and retain information longer, given p62's role as a trafficking molecule for receptors."

The major risk factor for Alzheimer's is age. According to the NIH's National Institute on Aging, as many as 4.5 million people in the United States have Alzheimer's, which is a slow disease that starts with mild memory problems and ends with severe brain damage. There is a growing incidence of the disease which has placed a tremendous burden on the health care system, Wooten said. Obesity puts one at risk for insulin-resistance and Type 2 Diabetes, which affects 23.6 million people in the U.S., according to the American Diabetes Association.

"We have known for a long time that individuals who are obese are at

risk for Type 2 diabetes and that older individuals are at risk for cognitive impairment," Wooten said. "It is now apparent that elderly people who are obese have higher incidence of Alzheimer's earlier in life. In the past few years, clinicians have begun calling Alzheimer's as Type 3 diabetes."

Wooten, who is collaborating with Alzheimer's disease research centers at the University of Alabama at Birmingham and Emory University and faculty in Auburn's Scott-Ritchey Research Center, said her next research proposal would be to examine levels of p62 in the human population, looking at individuals with mild cognitive impairment and moderate to severe Alzheimer's as a function of age.

"We would like to pinpoint a biomarker or early indicator, so we could determine the likelihood of Alzheimer's when examining living persons," she said. "Currently, Alzheimer's only can be accurately confirmed in humans by examining the brain after death. The brain will have protein-fragment tangles and deposits that are believed to have blocked communication between the neurons."

Results from that study would indicate whether or not it would be feasible to develop drug compounds to enhance the amount of p62 in the brain.

"Research and development of treatments is not a short-term process, often taking many years and an interdisciplinary approach," Wooten said. "A major goal for the National Institutes of Health is to accelerate the impact that research in basic science has upon treating human diseases."

Provided by Auburn University