Molecular Signatures in Post-Mortem Brain Tissue of Younger Individuals at High Risk for Alzheimer's Disease

While the majority of Alzheimer’s researchers focus their attention on the classic pathological signs of the mind-robbing disease – the plaques and tangles --- scientists at The Feinstein Institute for Medical Research have new evidence that there are molecular hints of trouble in the brains of people decades before these signs lay claim in the brain.

Manhasset, NY (Vocus) June 3, 2010 -- While the majority of Alzheimer’s researchers focus their attention on the classic pathological signs of the mind-robbing disease – the plaques and tangles --- scientists at The Feinstein Institute for Medical Research have new evidence that there are molecular hints of trouble in the brains of people decades before these signs lay claim in the brain.

Concepcion Conejero-Goldberg, MD, PhD, and her colleagues have an interest in prevention and thus headed back in time to younger adults who carry a risk gene for Alzheimer’s disease called APOE4. They were hoping to find molecular differences in the brains of people with one or two copies of the APOE4 gene and those who do not carry a copy of the risk gene. Having one copy increases the odds of developing Alzheimer’s three to four times more than people without the genetic variant. They were able to obtain brain tissue from young to middle age adults who died from a variety of causes. They choose tissue from two different brain areas, one that is hard hit by Alzheimer’s (middle temporal gyrus) and one that is not (primary somatosensory cortex). Then they sampled brain tissue from the cerebellum to find out whether the person had been born with an APOE4 gene or not. They had tissue from 41 people who had died on average around 42 years old and no one in the bunch had any pathological signs of Alzheimer’s – at least no plaques and tangles.

“We wanted to know whether young people can give us a lead on the development of the disease,” said Dr. Conejero-Goldberg. Once they had the human brain tissue and the genotype of the people whose lives were cut short for a variety of reasons they set out to conduct microarray gene expression studies of the tissue itself. Did having an apoE4 genotype have an impact on the genetic expression of the specific tissue and was the tissue that gets destroyed by the illness molecularly different than the tissue that remains healthy until the very end of the illness?

The findings of the study were published in Molecular Psychiatry.

They found 70 gene transcripts that differed significantly between the two groups, those with APOE4 and those without. And there were regional differences in the expression of APOE4 itself. Some of the genes are known to be involved with pathways that regulate mitochondrial function, calcium regulation and cell-cycle reentry. The differences in the regulation of the genes between the APOE4 carriers and non-APOE4 carriers and the fact that the changes were observed in the tissue hard hit by Alzheimer’s suggests to these scientists that these molecular hits could be working for a lifetime to set in motion a disease in old age that wipes away memories and so much more. On the contrary, changes in the spared brain area may be neuroprotective.
“Our findings tell us that something is going on in the brains of at-risk people very early on, decades before the plaques and tangles begin to appear,” said Dr. Conejero-Goldberg, part of the Litwin-Zucker Research Center for the Study of Alzheimer's Disease. Her collaborators outside of the Feinstein include researchers from the National Institute of Mental Health and Albert Einstein College of Medicine.

None of the genes that they identified were involved with the classical Alzheimer’s pathway that leads to amyloid plaques and tau tangles. “These findings may give us clues why some brains are more susceptible to Alzheimer’s than others,” the Feinstein scientist said. Also, the identification of genes that damage pathways also opened the door to genes that may protect the brain against Alzheimer’s.

Contact: Jamie Talan, science writer-in-residence
516-562-1232

###
Contact Information
Jamie Talan
516-562-1232

Online Web 2.0 Version
You can read the online version of this press release here.