Low level of neuronal receptor linked to mild cognitive impairment and Alzheimer's disease

September 4 2007

Results of a new study indicate a strong link between the loss of the neuronal receptor LR11and onset of mild cognitive impairment (MCI), often a harbinger of Alzheimer's disease.

LR11, like all receptors, selectively receives and binds specific substances. Researchers found reduced levels of LR11, also known as sorLA or SORL1, in the brain tissue of people diagnosed with MCI. In addition, the findings show that levels of LR11 in the brain tissue reflect the severity of cognitive impairment and may predict which individuals will progress to Alzheimer's disease.

Results of the study by scientists at Emory University School of Medicine, along with scientists at Rush University Medical Center in Chicago, are published online in the *Annals of Neurology* and will be published in a future print edition.

The research was conducted by James Lah, MD, PhD, Emory associate professor of neurology, and graduate student Kristen Sager,in the Center for Neurodegenerative Disease. The research team also included Howard Rees, PhD, research specialist, Marla Gearing, PhD, assistant professor of pathology and laboratory medicine and Allan Levey, MD, PhD, professor and chair of neurology. The team at Rush University Medical Center included Joanne Wu, biostatistician, Susan Leurgans, PhD, professor of biostatistics, and Elliot Mufson, PhD, Alla V. and Solomon

Jesmer Chair in Aging and professor of neurological sciences.

Mild cognitive impairment is an abnormal condition in which memory or cognitive ability is mildly impaired, yet individuals can perform everyday activities. However, they may have difficulty remembering recent events or following a conversation. It is estimated that 10 to 15 percent of those diagnosed with MCI go on to develop Alzheimer's disease each year and over 5 million Americans have been diagnosed with Alzheimer's.

"We donÕt yet know what causes LR11 levels to drop," Dr. Lah says. "But we do know that LR11 binds apolipoprotein E (ApoE), a protein that carries cholesterol and other fats throughout the bloodstream. LR11 also interacts with another molecule, the amyloid precursor protein, and regulates the production and deposition of the toxic amyloid-beta peptide in the brain. Both ApoE and amyloid-beta are strongly linked to degeneration of nerve cells in Alzheimer's disease. Thus, the implication is that there may be genetics, environmental, dietary or lifestyle factors that directly influence the expression of LR11."

The researchers collected data from participants in Rush University's Religious Orders study, which includes more than 1,000 religious clergy who have agreed to annual medical and psychological evaluations and brain donation after death. The clergy were diagnosed before death with either no cognitive impairment, MCI or Alzheimer's disease.

"After death, we looked at protein levels in the brain cells and found the level of LR11 expression correlated directly with cognitive ability, implying a direct and highly relevant link to the human condition," Dr. Lah says.

"We think this study is particularly important because of the groups we are studying, in particular those with MCI. In many cases, these

individuals will go on to develop Alzheimer's disease," Dr. Lah says. "So, we are getting to look at people in very early clinical stages of illness. The fact that at autopsy we see that the LR11 is lost in the group with MCI is compelling evidence that the loss occurs early in the disease and therefore may be a biomarker that can predict Alzheimer's or an important new therapeutic target. If we can restore the level of the receptor, then the implication is that we may be able to protect against the development of the disease."

Source: Emory University