Promising new treatment for Alzheimer's suggested

July 20 2009

Research carried out at the Hebrew University of Jerusalem has resulted in a promising approach to help treat Alzheimer's disease in a significant proportion of the population that suffers from a particularly rapid development of this disease.

In the research at the Silberman Institute of Life Sciences of the Hebrew University, scientists solved a mystery as to why people who carried a mutated gene known as BChE-K were prone to more rapid development of Alzheimer's than those who had a normal version of the gene. This mutation appears in about 20 percent of the American and Israeli populations.

In theory, the carriers of the mutated gene should actually be more protected from the devastating effects of the disease, since the mutated protein (the enzyme that is the product of the gene) breaks down the neurotransmitter acetylcholine at a slower rate than in those who have the normal gene. The result is that the carriers maintain higher levels of this neurotransmitter, so they should in principle be protected from Alzheimer's disease, in which acetylcholine levels decrease.

Indeed, these carriers tend to develop the disease later than others, but when that happens, it progresses more rapidly and does not respond to medication. Therefore, the bottom line is that carriers of the mutated gene have a greater risk than others for disease progression.
The reason for this anomalous situation has been a puzzle for a long time, but the studies by the Hebrew University scientists solved it by

finding the explanation for this increased risk, thereby offering as well a possible new therapeutic solution.

At the Wolfson Center for Structural Biology at the Hebrew University, the researchers found that the mutation in the BChE-K gene damages the very end, or tail, of the resultant mutant enzyme protein. This tail is the part of BChE which is important for protection from the Alzheimer's disease plaques. It does this by interacting with the Alzheimer's disease β-amyloid protein and preventing it from precipitating and forming those brain plaques which are the neuropathological hallmark of this disease.

To compare the normal protein to the K mutant, the researchers used synthetic tails of the normal and the K proteins, as well as engineered human BChE produced in the milk of transgenic goats at a U.S. company, Pharmathene. The goat- produced protein is prepared at Pharmathene for the U.S. military as protection from nerve gas poisoning (a result of earlier research at the Hebrew University). It was much more stable and efficient than the mutant protein, which suggests that the BChE-K carriers' susceptibility to Alzheimer's could be substantially improved by treating them with the engineered normal protein that is produced in the milk of the transgenic goats.

An article by the researchers on this work was recently selected as a *Journal of Biological Chemistry (JBC)* Paper of the Week and featured on the cover of the publication.

Source: The Hebrew University of Jerusalem