News Release

The Hebrew University of Jerusalem האוניברסיטה העברית בירושלים

Points Way to Development of More Efficient Treatment

ANTI-INFLAMMATORY FUNCTION OF ALZHEIMER'S DISEASE DRUGS REVEALED BY HEBREW UNIVERSITY RESEARCHERS

Jerusalem, July 10, 2005 – The mechanism in anti-Alzheimer's disease drugs that inhibits the production of a destructive, inflammation-causing protein in the brain has been revealed by researchers at the Hebrew university of Jerusalem.

Their work, described in a recent issue of the American journal, *Annals of Neurology.*
is likely to lead to the development of more efficient drugs than are currently in use for treating Alzheimer's Disease as well as other neurological conditions resulting from infections, autoimmune diseases such as multiple sclerosis, or brain inflammation resulting from trauma or stroke.

The research team working on this project was headed by Prof. Raz Yirmiya of the Psychology Department at the Hebrew University, Dr. Yehuda Pollak, a post-doctoral fellow in Prof. Yirmiya's laboratory; and in cooperation with Hermona Soreq, the Charlotte Slesinger Professor of Cancer Studies at the Silberman Institute of Life Sciences at the Hebrew University, and Prof. Tamir Ben-Hur of the Hebrew University Faculty of Medicine.

Alzheimer's Disease is a degenerative disease of the brain, characterized by a deterioration of both cognitive and physical abilities. It first affects memory and the ability to carry out complex, coordinated tasks. It also can bring on depression, inattention and outbursts of anger. In a more progressive stage, the disease can cause difficulties in the ability to perform even simple tasks such as speaking and comprehending, eating and sleeping. The affected person can even forget his name and identity.

The medicines administered today to Alzheimer's Disease patients focus on preventing the breakdown of acetylcholine, a chemical produced by brain cells which transmits information within the brain and is vitally involved in cognitive processes that include memory, attention and thought. Because acetylcholine-producing cells are among the first to die in Alzheimer's Disease patients, drug-induced elevation of acetylcholine levels partially attenuates the cognitive deterioration.

In recent years it has been shown that another pathological process that occurs in the brain of Alzheimer's Disease patients is excessive immune activation and inflammation, which are induced by overproduction of an inflammation-producing protein called interleukin-1, as well as a few other related compounds. This process can impair the functioning of nerve cells and can even lead to their death.

Furthermore, genetic alterations in the interleukin-1 gene have been associated with increased risk for the appearance and severity of Alzheimer's Disease symptoms.

The Hebrew University researchers found that anti-Alzheimer's Disease drugs currently in use not only block the activity of the enzyme responsible for breaking down acetylcholine but also cause a marked reduction in the production of interleukin-1. Furthermore, they describe the use of a novel drug (EN101), developed by Prof. Soreq's team, which produces these effects in a more efficient way than known heretofore by destroying the molecular antecedent (messenger RNA) of the enzyme, rather than simply blocking the enzyme's activity.

In a series of experiments, conventional anti-Alzheimer's Disease drugs, as well as the novel drug EN101, were injected into mice with brain inflammation. It was found that these injections reduced significantly the activity of the enzyme that breaks down acetylcholine and blocked almost entirely the production of interleukin-1.

"These findings suggest a new role for acetylcholine in the brain," said Prof. Yirmiya. "When the anti-Alzheimer's Disease drugs block the enzyme which breaks down acetylcholine, the level of this chemical in the brain goes up, and there is a reduction of the production of the inflammatory material, interleukin-1, and its destructive influence in the brain."

"The discovery of this mechanism in the anti-Alzheimer's Disease medicines points the way towards development of new forms of these medicines which will block even more efficiently and specifically the inflammatory and destructive activity of inteleukin-1," Prof. Yirmiya stressed. "Beyond that, it is likely that the drugs that are currently used for treatment of Alzheimer's Disease, and particularly the new drug EN101, will also be effective in dealing with other inflammatory illnesses."

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