Humanin peptide linked to neuronal cell survival and regulation of glucose metabolism

April 22 2009

Recent studies have shown that the mitochondrial peptide Humanin (HN) protects against neuronal cell death such as happens in Alzheimer's disease. Now, in a study presented April 22 at Experimental Biology 2009 in New Orleans, Dr. Nir Barzilai reports that a small infusion of HN is the most potent regulator of insulin metabolism that his research team has ever seen, significantly improving overall insulin sensitivity and sharply decreasing the glucose levels of diabetic rats.

The finding is the first evidence of a role for HN in glucose metabolism and provides new insight into how this metabolism may be involved in the development of seemingly diverse age-related diseases such as Type 2 Diabetes Mellitus and Alzheimer's. The finding also provides support for the growing understanding that the brain (not just the pancreas, liver and other peripheral organs) is heavily involved in glucose metabolism.

Furthermore, says Dr. Barzilai, the Ingeborg and Ira Leon Rennert Chair of Aging Research and Director of the Institute for Aging Research at the Albert Einstein College of Medicine, the power of HN on insulin action suggests a new therapeutic approach to diabetes. Further understanding of how HN interactions with the growth hormone/insulin-like growth factor system may also lead to strategies to protect against age-related diseases including Alzheimer's.

Dr. Barzilai's presentation at Experimental Biology 2009 is part of the

scientific program of the American Society for Biochemistry and Molecular Biology.

Dr. Barzilai is internationally known as a leading discoverer of longevity genes, especially those he has identified in a well-established group of almost 500 Ashkenazi Jews, aged 95 to 112, and their families. Last year, he reported that some of the oldest in this group have mutations in the gene for insulin-like growth factor 1 (IGF-1) receptor, genetic alterations that have been shown to prolong life span in worms and some mammals. In this Experimental Biology presentation, he reports that, while the production of HN generally decreases as people age, it decreases less in the centenarians and is the highest in their offspring. Studies are now underway at the Institute for Aging Research to determine if the centenarians have a mutation in the HN gene in the mitochondria.

How do these genes fit together? Although there is still much to learn, says Dr. Barzilai, his team increasingly understands how HN interacts with the GH/IGF system. In earlier studies, the team found that insulin-like growth factor binding protein-3 (IGFBP-3) binds Humanin and tempers its effects on promotion of cell survival.

In this new study, the effects of HN on insulin action also were found to be tempered by IGFBP-3. Inhibiting IGFBP-3 allowed the peptide to exert a more potent effect. That suggests a drug target, says Dr. Barzilai.

He says that in this preclinical testing period, it is still too soon to know how HN would perform in humans, but he believes the naturally occurring peptide's ability to preserve cells is promising. One concern of anti-diabetic drugs is increased risk for cardiovascular disease. When Dr. Barzilai's team administered Humanin to rats before or after they were induced to have heart attacks, however, the area of infarction (area of dead cells caused by lack of blood) actually decreased by almost 50

percent, compared to that in rats not given the peptide.

Source: Federation of American Societies for Experimental Biology (news : web)