Medical Xpress

Progress towards Alzheimer's vaccine: Israeli researcher

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An Israeli researcher working on a vaccine to combat Alzheimer's disease said on Monday he had made important progress following tests on gene-altered laboratory mice.

A researcher who is working on a vaccine for Alzheimer's disease (AD) has demonstrated that it is possible to test and measure specific immune responses in mice carrying human genes and to anticipate the immune response in Alzheimer's patients. This continuing research at Ben-Gurion University of the Negev could one day lead to specific Alzheimer's vaccines that reduce plaque, neuronal damage and inflammation associated with the disease.

Amyloid beta-peptide accumulates in the brain of AD patients where it appears to promote neuronal damage. In the new article published in the *Journal of Immunology*, BGU researcher Dr. Alon Monsonego determined that introducing A-beta into the brain triggers a natural immune response which can be detected in humans.

Importantly, the research team showed that the specificity and magnitude of this body response to A-beta depends on certain key genes of the immune system, which are highly polymorphic in the population (this means that except for identical twins, almost each of us has a different combination of genes termed "HLA alleles").

Furthermore, this research took an unusual approach combining humans and humanized mouse models. "We began with characterizing the genes

in humans in a collaboration with the laboratories of Dr. Weiner and Dr. Selkoe at Harvard, then did the same study in mice using a mouse model of multiple sclerosis witht the laboratory of Dr. Altmann- Imperial College School of Medicine, UK," Monsonego explains. "We then generated a humanized mouse model of AD, with a specific gene that was present in approximately 30 percent of our study group (HLA DR15 allele). Conceivably, those people that have this gene could receive the same vaccine which will teach a person's immune system to better fight the disease."

Monsonego continues, "As in other mouse models of the disease, we show that with aging A-beta aggregates accumulate in brain areas of cognitive functions and stimulate an inflammatory reaction in the brain. However, stimulating an immune response to A-beta in these humanized mice not only resulted in a highly efficient clearance of A-beta (plaque) from the brain, but also in a markedly reduced inflammatory reaction. Furthermore, we were able to predict that the characteristics of immune response in mice were the same as in the humans.

"This study thus provides the basis for developing an individual-based (personalized medicine) immunotherapeutic approach to Alzheimer's disease since different populations will respond differently to a vaccine based on their genetic background," Monsonego explains. "Now that we've proven we can anticipate the specific responses for several abundant genes in the population, further study is needed to ensure safety and efficacy in our humanized mouse model of AD."

Dr. Monsonego, who holds the Zehava and Chezy Vered Career Development Chair for the Study of Alzheimer's and Neurodegenerative Diseases, is a member of BGU's Shraga Segal Department of Microbiology and Immunology and the National Institute for Biotechnology in the Negev.

The research is funded in part by the Israel Science Foundation, the Alzheimer Association and by the New York real estate developer Leonard Litwin and the Aaron Gural family.

"It is so rewarding to see how donors of American Associates, Ben-Gurion University of the Negev are contributing to the groundbreaking progress on discovering a viable Alzheimer's vaccine," states Executive Vice President Doron Krakow. "It's another example of how BGU's research helps people around the world."

Provided by Ben-Gurion University of the Negev