

Fundamental research is paving the way for development of first vaccine for heart disease

July 16 2014

Researchers at Wayne State University have made a fundamental discovery and, in subsequent collaboration with scientists at La Jolla Institute for Allergy and Immunology (LIAI), are one step closer to the goal of developing the world's first T-cell peptide-based vaccine for heart disease—the number one killer in the nation.

Atherosclerosis is a [chronic inflammatory disease](#) of the arterial walls, which thicken due to accumulation of fatty materials such as cholesterol and triglycerides. Blocking of arteries supplying blood to the heart is the underlying cause of many heart diseases. Nearly 600,000 Americans die of [heart disease](#) every year. Although cholesterol is believed to be a major factor in creating the plaque that leads to heart disease, immune inflammation is another important contributor in arterial [plaque buildup](#). The goal of the vaccine is to reduce immune-based inflammation in the arteries, leading to decreased plaque buildup.

The scientists published their findings in the December 2013 issue of *Frontiers in Immunology*, entitled "Atheroprotective vaccination with MHC-II restricted peptides from ApoB-100." These experiments show proof of concept for the development of an autoantigen-specific vaccine for reducing the amount of atherosclerotic plaques in mice. If successful, the vaccine could aid in preventing heart disease and stop or reduce disease progression. In addition to heart disease, the vaccine could target strokes, which are also a product of plaque buildup in arteries.

The published work, performed in the laboratory of Klaus Ley, M.D., a

prominent vascular biologist of LIAI, was based on the fundamental discovery made by Harley Tse, Ph.D., professor of immunology and microbiology in Wayne State's School of Medicine, and professor in Wayne State's Cardiovascular Research Institute, and Michael Shaw, Ph.D., adjunct assistant professor of immunology and microbiology at Wayne State. Shaw and Tse are the first to demonstrate that two T cell epitopes of the autoantigen apoB100 are deeply involved in the development of the disease. Their novel discovery is reported in the article, "Identification of two Immunogenic T cell Epitopes of ApoB-100 and their Autoimmune Implications," published in the April – June 2014 issue (volume 2) of *Journal of Immunology and Clinical Research*.

"ApoB100 is an apolipoprotein of the LDL (low-density lipoprotein) particle which is the notorious 'bad cholesterol' that contributes to the formation of plaques in the vessel wall," said Tse. "Although T [cells](#) of the immune system are known to participate in the development of heart disease, by what and how these T cells are directed to act have not been elucidated. The lack of this knowledge has greatly hampered the development of immune peptide-based therapeutics to control the disease. With the discovery of the disease-causing T cell epitopes, we can now manipulate the activities of the T cells responding to these epitopes to control the disease."

Since immune T cells are normally activated by a short sequence (called an epitope), and not by the whole molecule of an antigen, Shaw and Tse conceptualized that finding the apoB100 epitopes capable of stimulating the disease causing (atherogenic) T cells is a prerequisite for understanding how these T cells are involved in heart disease development and for finding ways to control their adverse effects.

Based on this idea, they identified two short sequences (3501–3515 and 978–992) of ApoB100 (ApoB3501-3515 and ApoB978-992, also

designated peptides P3 and P6, respectively) that were able to direct specific T cells to proliferate as well as to cause worsening atherosclerosis. This discovery is significant because it identifies the target T cells and makes it possible to manipulate this population of pathologic T cells away from their harmful activities.

The subsequent collaboration with Ley's laboratory bears the first fruits of this effort.

Provided by Wayne State University

Citation: Fundamental research is paving the way for development of first vaccine for heart disease (2014, July 16) retrieved 2 May 2024 from <https://medicalxpress.com/news/2014-07-fundamental-paving-vaccine-heart-disease.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--