



THE UNIVERSITY of TEXAS

HEALTH SCIENCE CENTER AT HOUSTON

Office of Technology Management

ATHEROSCLEROSIS-PRONE MOUSE MODELS

Market: The American Heart Association reports that Coronary heart disease, caused by atherosclerosis, or the narrowing of the coronary arteries due to fatty build ups of plaque, caused 452,300 deaths in the U.S. in 2004. Coronary Heart Disease was the cause of 1 out of every 5 deaths in America in 2004, with direct and indirect costs in the U.S. totaling near \$151.6 billion.

Current Problems: It is well recognized that plasma apolipoprotein B (apoB) levels are a strong predictor of atherosclerosis. Therefore, extensive clinical and molecular investigations have been carried out to understand the association of apoB with heart disease. The most common cause of increased plasma apoB is over-secretion of apoB-containing low density lipoprotein particles (LDL) by the liver. Humans express apoB mRNA editing enzyme (ApoBec1) only in the gut, while mice produce this enzyme in both the liver and small intestine. ApoBec1 activity results in a smaller apoB (apoB48), and apoB48-containing lipoproteins catabolize efficiently by a different receptor. Hence, mice have minute amount of LDL. This difference is recognized as one of the main reasons that wild-type mice are resistant to atherosclerosis. Wild-type mice have high density lipoprotein (HDL) as the major lipoprotein, not LDL, and therefore do not mimic the human condition as closely as an animal model could.

The Technology: Researchers at the University of Texas Health Science Center at Houston (UTHSC-H) have developed two mouse models to study the pathogenesis of atherosclerosis. Both mouse lines lack the LDL receptor and the ability to edit apoB mRNA (designated LDb: LDLR^{-/-}ApoBec1^{-/-}). One mouse line additionally over-expresses human apoB100 gene (designated LTp: LDLR^{-/-}ApoBec1^{-/-}ERhB^{+/+}). Both mouse lines have elevated LDL levels with decreased HDL cholesterol, with a lipoprotein distribution profile similar to that seen in human patients with hyperlipidemia. The mice readily develop diet-independent atherosclerosis as early as 3 months, with diet-dependent acceleration possible. The phenotypes developed are similar to that of human atherosclerosis, making them an ideal model for atherosclerosis in humans. For more information about the mouse lines as well as availability and Materials Transfer License Agreement terms, please contact the Office of Technology Management at UTHSC-H.

NON-CONFIDENTIAL TECHNOLOGY DESCRIPTION

The preceding is intended to be a non-confidential summary of a novel technology created at the University of Texas Health Science center at Houston.

UTHSC-H Ref. No.: 2006-0021

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Publications: *Clinical Science* (2004) 106, 421–432; *Atherosclerosis* 169 (2003) 51-62.

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