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seeks partner to license

PXR agonism to upregulate apoA1

The University of Toledo is currently seeking companies interested in licensing new chemical entities and a strategy for the prevention and treatment of atherosclerosis and coronary heart disease. The Framingham heart studies have established a clear inverse correlation between HDL-cholesterol and coronary artery disease. This relationship has led to the recent discovery that apo A1 milano may itself constitute a therapy for atherosclerosis and coronary artery disease. Other drug-related approaches to increasing HDL-cholesterol and/or apo A1 include the development of agonists at the LXR receptor in the liver and CETP inhibitors. In addition DP1 receptor antagonists are being developed in order to reduce the flushing effect of niacin, a drug that is currently available and that increases HDL-cholesterol.

Researchers at the University of Toledo have targeted the PXR in the liver as a strategy for increasing both HDL-cholesterol and apo A1. Studies in rodents (both rats and mice) have produced substantial increases in both when animals were treated with PXR agonists. These increases failed to materialize in PXR knockout mice. Moreover, it has recently been shown that only a very small percentage (~5%) of PXR agonists have the potential to cause clinically significant drug-drug interactions. In wild-type mice, some of these PXR agonists increased HDL-cholesterol by more than 50% and apo A1 by more than 300%.

Advantages: In rodent models PXR agonists have been shown to dramatically increase HDL-cholesterol and apoA1 levels in blood. Targeting the PXR could represent a novel strategy for protecting against atherosclerosis and heart disease. Drugs developed as PXR agonists for this purpose could also be combined with existing medications that have been designed to lower LDL-cholesterol levels which are only marginally effective at raising HDL-cholesterol or apoA1 levels.

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