



TECHNOLOGY

Monoclonal antibodies inhibiting fibrin-VLDL receptor-dependent inflammation

OVERVIEW

Fibrin is a fibrous, non-globular protein involved in blood clotting and promotes leukocyte transmigration through its interaction with the endothelial cell receptor, the very low density lipoprotein (VLDL) receptor. The VLDL receptor is predominantly expressed in the heart, skeletal muscle, fat, brain and macrophages and involved in neural development, plasticity, angiogenesis, fibrin-dependent inflammation, and wound healing. Increased levels of serum fibrins are associated with the increased risk ischemic heart disease which can lead to a heart attack, arrhythmia, and heart failure.

Anti-VLDLR monoclonal antibodies, 1H5 and 1H1O, have been generated that interacted with the VLDLR fragment containing the fibrin binding region (?15–66)². Studies with the anti-VLDLR antibodies demonstrated the ability to inhibit fibrin interactions with the fibrin-binding region of the VLDL receptor. This in turn significantly reduced the transendothelial migration of leukocytes in in vitro and in vivo experiments. Mouse model studies of peritonitis confirmed the reduction of leukocyte infiltration into the peritoneum with the treatment of the 1H5 and 1H1O antibodies. Additionally, the cardioprotective effect of both mAbs have been shown in a mouse model of myocardial ischemia-reperfusion injury (see figure). This technology can be developed into novel anti-inflammatory agents for treatment of inflammation-related cardiovascular diseases including myocardial ischemia-reperfusion injury.

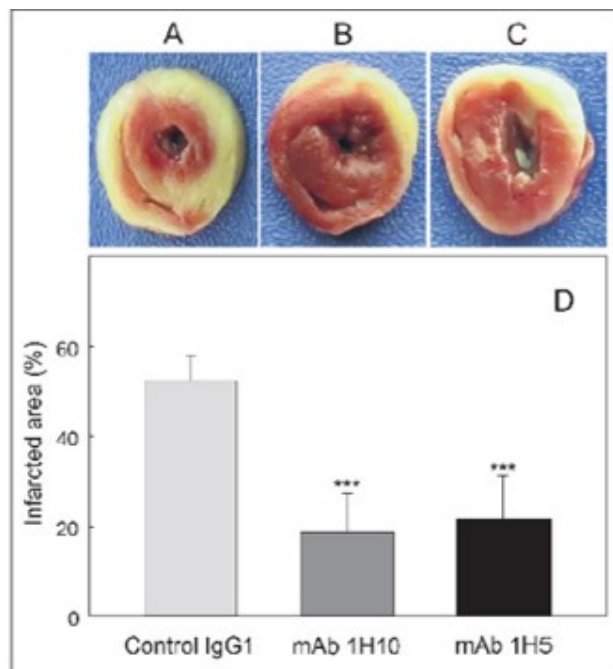


Figure 7: Cardioprotective effect of mAb 1H10 and 1H5 during myocardial ischaemia-reperfusion injury. Representative mouse heart slices after myocardial ischaemia-reperfusion in mice treated with control IgG1 (A), mAb 1H10 (B), or mAb 1H5 (C). The size of infarcted areas, which appear pale in colour in (A-C), was determined with ImageJ (NIH), and the results are presented in (D) as a percentage of total area of the slices. The results are means \pm SD (n = 5). ***P < 0.001.

APPLICATIONS

Myocardial ischemia is an insufficient flow of blood to the myocardium due to an obstruction or constriction in the coronary arteries leading to inflammation and endothelial dysfunction. The global myocardial ischemia market is anticipated to reach \$50 billion by 2023 largely due to the high prevalence of coronary heart disorders, diabetes, and contributing lifestyle factors such as smoking, obesity, high blood pressure, and a sedentary lifestyle. Current methods of treatment for myocardial ischemia involves improving blood flow to the heart muscle via medications (aspirin, nitroglycerine, calcium channel blockers, angiotensin converting enzyme inhibitors, ranolazine) or a procedure to open blocked arteries (angioplasty, stenting, coronary artery bypass surgery, enhanced external counter pulsation).

In the early 1990s, Fibrex Medical, Inc. developed a peptide called FX06 as an anti-inflammatory drug for the treatment of myocardial ischemia-reperfusion injury. Phase I and II showed relative safety but efficacy studies failed to show significant differences in the sizes of the infarctions. The FX06 peptide targeted the inhibition of the fibrin-VEcadherin dependent pathway. The 1H5 and 1H10, anti-VLDLR technology specifically inhibits the fibrin VLDLR-dependent pathway of leukocyte transmigration and was found to be two-fold more efficient than the FX06.

RB- 1/22/19

STAGE OF DEVELOPMENT

Initial in vivo and in vitro studies completed

LICENSING POTENTIAL

Available for licensing

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PATENT STATUS

US Patent Pending, PCT/US2017/035654

LICENSE STATUS

Available for licensing

CATEGORIES

- Therapeutics
- Biologics

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ATTACHMENTS

-  [Download LM-2016-049 marketing summary.pdf](#)

EXTERNAL RESOURCES

- [Anti-VLDL receptor monoclonal antibodies inhibit fibrin-VLDL receptor intx and reduce fibrin-dependent leukocyte transmigration](#)

LM-2016-049