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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Invention; Availability for Licensing

AGENCY: National Institutes of Health

ACTION: Notice

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing in the U.S. to achieve expeditious commercialization of results of federally-funded research and development.

FOR FURTHER INFORMATION CONTACT: Licensing information may be obtained by emailing the indicated licensing contact at the National Heart, Lung, and Blood, Office of Technology Transfer and Development Office of Technology Transfer, 31 Center Drive Room 4A29, MSC 2479, Bethesda, MD 20892-2479; telephone: 301-402-5579. A signed Confidential Disclosure Agreement may be required to receive any unpublished information.

SUPPLEMENTARY INFORMATION: Notice of Licensing of Government-Owned Inventions in accordance with 35 U.S.C. 209 and 37 CFR Part 404. Technology description follows.

ApoA-1 Mimetic Peptides Promoting Lipid Efflux from Cells for Treatment of Vascular Disorders

Description of Technology: This invention involves ApoA-1 mimetic peptides with multiple amphipathic alpha-helical domains that promote lipid efflux from cells and are useful in the treatment and prevention of dyslipidemic, inflammatory and vascular disorders. IND-enabling studies for one of the peptides, named Fx-5A, are completed in preparation for an IND filing at the FDA, to be followed by a Phase I clinical trial planned for 2017. Disorders amenable to treatment with the peptides include hyperlipidemia, hyperlipoproteinemia, hypercholesterolemia, HDL deficiency, hypertriglyceridemia, apoA-I deficiency, acute coronary syndrome, angina pectoris, aortic valve stenosis, atherosclerosis, carotid atherosclerosis, congestive heart failure, cerebral stroke, coronary artery disease, inflammation of the cardiovascular system, intermittent claudication, myocardial infarction, peripheral vascular disease, post-ischemic reperfusion, renal artery stenosis, reperfusion myocardial injury, restenosis, and thrombotic stroke.

Potential Commercial Applications:

- Treatment and prevention of many hereditary, chronic and acute dyslipidemic and vascular disorders, where other treatments are not effective or too invasive, such as statins, partial ileal bypass surgery, portacaval shunt, liver transplantation, and removal of atherogenic lipoproteins by one of several apheresis procedures.

- Also applicable to the treatment of inflammation, asthma, colitis, inflammatory bowel disease (IBD), chronic kidney disease (CKD).

Development Stage: Early-stage; In vitro data available; In vivo data available (animal)

Inventors: Alan T. Remaley, Stephen J. Demosky, John A. Stonik, Marcelo J.A. Amar, Edward B. Neufeld, Fairwell Thomas, H. Bryan Brewer (all of NHLBI)

Publications:

1. Jin X, et al. ABCA1 (ATP-Binding Cassette Transporter A1) Mediates ApoA-I (Apolipoprotein A-I) and ApoA-I Mimetic Peptide Mobilization of Extracellular Cholesterol Microdomains Deposited by Macrophages. *Arterioscler Thromb Vasc Biol.* 2016 Dec;36(12):2283-2291. [PMID 27758769]
2. Nowacki TM, et al. The 5A apolipoprotein A-I (apoA-I) mimetic peptide ameliorates experimental colitis by regulating monocyte infiltration. *Br J Pharmacol.* 2016 Sep;173(18):2780-92. [PMID 27425846]
3. Yao X, et al. The A's Have It: Developing Apolipoprotein A-I Mimetic Peptides Into a Novel Treatment for Asthma. *Chest.* 2016 Aug;150(2):283-8. [PMID 27327118]
4. Souza AC, et al. Antagonism of scavenger receptor CD36 by 5A peptide prevents chronic kidney disease progression in mice independent of blood pressure regulation. *Kidney Int.* 2016 Apr;89(4):809-22. [PMID 26994575]

5. Schwendeman A, et al. The effect of phospholipid composition of reconstituted HDL on its cholesterol efflux and anti-inflammatory properties. *J Lipid Res.* 2015 Sep;56(9):1727-37. [PMID 26117661]
6. Sviridov DO, et al. Hydrophobic amino acids in the hinge region of the 5A apolipoprotein mimetic peptide are essential for promoting cholesterol efflux by the ABCA1 transporter. *J Pharmacol Exp Ther.* 2013 Jan;344(1):50-8. [PMID 23042953]
7. Dai C, et al. Apolipoprotein A-I attenuates ovalbumin-induced neutrophilic airway inflammation via a granulocyte colony-stimulating factor-dependent mechanism. *Am J Respir Cell Mol Biol.* 2012 Aug;47(2):186-95. [PMID 22427535]
8. Yao X, et al. 5A, an apolipoprotein A-I mimetic peptide, attenuates the induction of house dust mite-induced asthma. *J Immunol.* 2011 Jan 1;186(1):576-83. [PMID 21115733]
9. Osei-Hwedieh DO, et al. Apolipoprotein mimetic peptides: Mechanisms of action as anti-atherogenic agents. *Pharmacol Ther.* 2011 Apr;130(1):83-91. [PMID 21172387]
10. D'Souza W, et al. Structure/function relationships of apolipoprotein a-I mimetic peptides: implications for antiatherogenic activities of high-density lipoprotein. *Circ Res.* 2010 Jul 23;107(2):217-27. [PMID 20508181]
11. Amar MJ, et al. 5A apolipoprotein mimetic peptide promotes cholesterol efflux and reduces atherosclerosis in mice. *J Pharmacol Exp Ther.* 2010 Aug;334(2):634-41. [PMID 20484557]
12. Tabet F, et al. The 5A apolipoprotein A-I mimetic peptide displays antiinflammatory and antioxidant properties in vivo and in vitro. *Arterioscler Thromb Vasc Biol.* 2010 Feb;30(2):246-52. [PMID 19965776]

13. Sethi AA, et al. Asymmetry in the lipid affinity of bihelical amphipathic peptides. A structural determinant for the specificity of ABCA1-dependent cholesterol efflux by peptides. *J Biol Chem.* 2008 Nov 21;283(47):32273-82. [PMID 18805791]

Intellectual Property: NIH Reference No. E-114-2004/0 - Issued Patents:

- US 7,572,771 issued 2009-11-08;
- US 8,071,746 issued 2011-12-06;
- US 8,148,323 issued 2012-04-03;
- US 8,835,378 issued 2014-09-16;
- AU 2005295640 issued 2011-11-10;
- CA 2584048 issued 2016-08-09;
- EP 1812474 issued 2010-05-26, validated in CH, DE, ES, FR, GB and IT; and
- JP 5,091,679 issued 2012-09-21.

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Collaborative Research Opportunity: The National Heart, Lung, and Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize ApoA-1 mimetic peptides. For collaboration opportunities, please contact Denise Crooks, Ph.D. at 301-435-0103 or crooksd@nhlbi.nih.gov.

Dated: November 30, 2016

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