Vascular Restoration Therapy with Cell-Penetrating CRADD Protein

Addressed Need

Vascular inflammation caused by metabolic, autoimmune, and microbial insults mediates cardiovascular diseases that include hypertension and atherosclerosis (heart attacks, strokes), systemic lupus, and giant cell arteritis. An estimated 35 million Americans have hypercholesterolemia, contributing to 500,000 deaths underlying heart attacks and strokes. In these diseases, metabolic, autoimmune, and microbial insults continually challenge blood and vascular cells by triggering signaling to the nucleus mediated by BCL10. Genetic ablation of BCL10 rescues animals from atherosclerosis, aortic aneurysms, and fatty liver and insulin resistance due to overnutrition. Intracellular therapy with CP-CRADD is designed to extinguish BCL10-mediated noxious signals to avert vascular inflammation and its life-threatening complications including ruptured aneurysms in aorta and brain.

Technology Description

Scientists at Vanderbilt have engineered a cell penetrating (CP) recombinant protein termed CP-CRADD that mimics physiologic protein Caspase and Receptor interacting protein Adaptor with Death Domain (CRADD). Intracellular delivery of CP-CRADD restored endothelial barrier function and suppressed production of inflammatory mediators Interleukin 6 and Monocyte Chemoattractant Protein-1. CP-CRADD counteracts its intracellular target BCL10, the key mediator of proinflammatory signaling responsible for atherosclerosis and aortic aneurysm formation. Intracellular therapy with injectable or slowly released CP-CRADD is designed to counteract BCL10 action and stop the progression of atherosclerosis and the growth of aortic aneurysms that might pop, or rupture, a life-threatening complication with 50% mortality. By counteracting vascular dysfunction due to atherosclerosis and hypertension, CP-CRADD may restore physiologic signaling not only in diseased aorta but also in brain circulation prone to aneurysm development and rupture. Moreover, CP-CRADD may counteract metabolic inflammation and insulin resistance due to high fat diet.

Commercial Applications

This recombinant cell-penetrating protein can potentially be applied to treatment of vascular diseases mediated by inflammation, including:

Atherosclerosis,

Hypertension,

Aortic and Brain Aneurysms

Giant Cell Arteritis complicated by vision loss and stroke

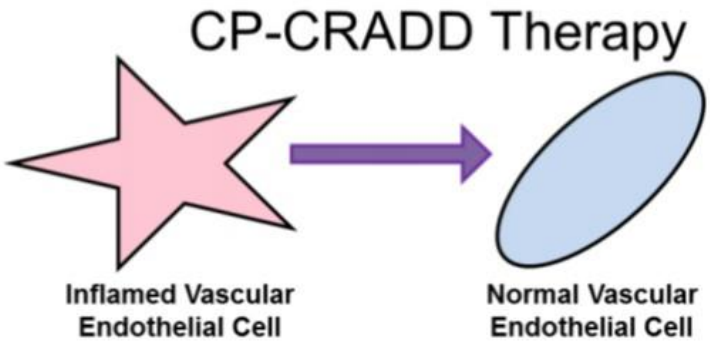
Fatty Liver and Insulin Resistance

Technology Development Status

This therapy has been fully developed and validated.

Intellectual Property Status

Patent Pending



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