ApoM Complex Inhibits Endothelial Cell Injuries

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Technology description

This invention discloses a way to therapeutically deliver the endothelial protective ability of sphingosine-1-phosphate (S1P) in high density lipoprotein, HDL, to inhibit diseases caused by endothelial cell injuries, such as inflammatory diseases, sepsis, atherosclerosis, acute lung injuries and other infectious diseases that cause tissue edema induced by vascular permeability.
The physiologic function of apolipoprotein M (apoM), a component of high density lipoprotein, HDL（“good cholesterol”）is not fully understood. X-ray crystallography studies indicate that apoM forms a tight complex with sphingosine-1-phosphate (S1P). The inventors demonstrated from in vivo investigations with apoM knockout mice and mice that overexpress apoM, that the apoM complex with S1P (apoM/S1P) is the physiological carrier of S1P in HDL. Their additional research shows that the apoM/S1P complex can activate the S1P receptors on endothelial cells, thereby inducing survival and migratory/reparative signaling, and inhibiting vascular inflammation and vascular permeability by causing adherens junction assembly.
The apoM/S1P complex can be delivered therapeutically in various forms, either alone, or in an artificial HDL preparation, or as nanoparticles or nanodiscs. It provides a new treatment option for various diseases, such as inflammatory diseases, sepsis, atherosclerosis and acute lung injury, ventilator induced pneumonia, dengue hemorrhagic fever, SARs, influenza, swine flu, and other infectious diseases that cause tissue edema, by preserving endothelium, allowing endothelial regeneration and maintaining vascular integrity. It can also be administered, following ischemia, reperfusion injury of the heart (heart attack), brain (stroke) and vital organs (kidney, liver or intestines), to preserve the viable tissues by promoting endothelial integrity.

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