Engineered sphingosine 1-phosphate (S1P) chaperone protein compositions and methods for treating vascular and non-vascular diseases and conditions

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Technology description

The inventors have disclosed the engineering and purification of a recombinant S1P chaperone, called ApoM (Apolipoprotein M) fusion product. It contains the ApoM domain covalently linked to the N-terminus of IgG1-Fc, and serves as an excellent means of delivering S1P, which can be used to reduce hypertension.

Technology Overview

Endothelial cells play a key role in vascular diseases. Plasma high-density lipoprotein (HDL) strongly supports endothelial cell function. However, only certain species of HDL are useful in this regard. Specifically, Apolipoprotein M-containing HDL (ApoM $^{+}$ HDL) that carries the bioactive lipid S1P, can activate G-protein coupled S1P receptors, thereby suppressing inflammatory responses. Therefore, ApoM is thought to function as an S1P chaperone. S1P is vital for health since decreased plasma S1P levels were observed in coronary artery disease, diabetes, and myocardial infarctions among others. The inventors have described a method to engineer and purify a fusion protein called ApoM-Fc that contains the ApoM moiety covalently linked to the IgG1-Fc. This fusion product serves as a safe and effective means of delivering S1P to endothelial cells. The inventors found thatin vivo, the fusion protein could raise plasma levels of S1P and deliver S1P to various organs. The fusion product could also reduce experimental hypertension in animals for at least 7 days.In vitro, the fusion product could activate S1P receptors.

Additional Information

Publications

· Swendenman SLet. al. , An engineered S1P chaperone attenuates hypertension and ischemic injury.Sci Signal.2017.

Application area

Safe and effective method for raising S1P plasma levels, and hence can be used to treat chronic hypertension, target reperfusion injury or strokes. This fusion product can be used for furtherin vivoanalyses or therapies. Can be used as a tool for pre-clinical studies.
· PCT Application : Apom-fc fusion proteins, complexes thereof with sphingosine l-phosphate (sip), and methods for treating vascular and non-vascular diseases (WO2018052615A1)

Advantages

The fusion product has an extended life span of at least 96 hours, vs. other agents with much shorter half lives.
It is the first product shown to raise S1P plasma levelsin vivo.
The fusion product is also highly and easily purifiable.

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