Methods of Inhibiting Platelet Activation and Recruitment

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Technology description

Upon vascular injury, platelets attach to the injured spot and release ADP which triggers further platelet activation, recruitment and aggregation. When too many platelets accumulate at this site, the vessel can be blocked, possibly restricting blood flow and oxygen transport, such as occur in ischemic stroke and coronary artery disease.

Because adenosine diphosphate (ADP) can trigger platelet activation, recruitment & aggregation, a substance which degrades ADP would be useful in treating or preventing these diseases that involve inappropriate platelet aggregation. CD39 is an enzyme with ADPase (apyrase,) and ATPase activity that is found on the surface of vascular endothelial cells and controls blood fluidity and inhibits platelet formation. Dr. Aaron Marcus, a pioneering biomedical researcher in hematology and vascular biology at Weill Cornell Medical College, has determined that adding a soluble form of CD39 (solCD39), could play an important therapeutic role in inhibiting clot formation in the vasculature.

Current therapies for such conditions include leukocyte adhesion receptors and recruited neutrophils which contribute to halting postischemic hypoperfusion, are not completely effective since progressive microvascular thrombosis persists after stroke. Thrombolytic agents, including rtPA and pro-urokinase, have limited utility due to their risk of intracranial hemorrhage. Contrary to other platelet inhibitors currently in use for patients, solCD39 does not damage platelets in order to exert its therapeutic effects.

Administering solCD39 to rodents subjected to occlusion of a middle cerebral artery (MCAO stroke model) reduced both infarct volume and neurological deficit by half, even when administered 3 hours after the stroke. Further, in pigs, solCD39 has a half life of 5-7 days, thereby able to provide prolonged protection after a single administration. solCD39 represents a promising antithrombotic therapy with the ability to disaggregate platelets under recruitment by ADP signaling, reduce intravascular thrombosis, without increasing intracranial hemorrhage risk, that does not effect primary hemostasis. Hence, solCD39 may prove useful in treating and preventing vascular diseases such as atherosclerosis, embolism, coronary and cerebral ischemia, injury from myocardial infarction, and in combination with procedures such as angioplasty.

Institution

Cornell University

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com