Slit2: A Novel Method of Preventing

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Technology description

Dr. Lisa Robinson, scientist and Division Head of Nephrology at
The Hospital for Sick Children and her team have shown that:
i) recombinant Slit2 protein inhibits neutrophil and monocyte chemotaxis, as well as platelet spreading and function, both in vitro and in vivo. (figure 1) and references- JLB 2009 and Circulation 2012
ii) that Slit2 can limit vascular injury by impairing recruitment and attachment of monocytes, and platelets within the injured blood vessel. Slit2’ s properties render it an ideal agent to target the vascular inflammation, neointimal proliferation, and thrombosis that cause occlusion of native and stented vessels. (figure 2)
iii) that Slit2 protects kidney function in IRI by inhibiting neutrophil adhesion to the endothelium in ischemia reperfusion injury. (figure 3) and reference J Am Soc Nephrol July 2013

Additional

i) Slit2 is a very promising anti-platelet technology given its unique properties: prevents recruitment of inflammatory cells and VSMC, as well as inhibiting platelet activation and thrombus formation.
ii) Slit2’ s has potential uses in preventing chronic kidney disease fafter acute or repeated injury

Background

The interaction of Slit proteins, together with their transmembrane receptor, Roundabout (Robo) plays a role in the mammalian inflammatory process by recruitment of various cell types in response to
vascular injury. There are three known mammalian Slit family members. Slit1 is predominantly expressed in
the CNS and was shown to repel axons and neuronal migration during CNS development; while Slit2 and, to a
lesser degree, Slit3 are expressed in other tissues, especially kidney, heart, and lung. Robo-1 is expressed in
megakaryocytes, platelets,neutrophils, and lymphocytes and is present on the cell surface in humans. In the kidney, Ischemia-reperfusion-injury (IRI) is a leading cause of Acute Kidney Injury and may

progress to
Chronic Kidney Disease (also known as chronic renal injury) as a result of progressive renal fibrosis. The population prevalence of CKD exceeds 10% in the US, (Bonventre and Yang, 2011; Quaggin and Kapus, 2011; Venkatachalam et al., 2010). A central feature of AKI is recruitment of inflammatory leukocytes into the
injured kidney, as well as microthrombosis.

Institution

The Hospital For Sick Children