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Locally acting antiplatelet and anticoagulant APAC, a mimic of heparin proteoglycan, inhibits acute ischemic kidney injury

APACs are unique dual antiplatelet and anticoagulant molecules, which mimic the vascular tissue residing mast cell heparin proteoglycans. Platelet activation and interaction with vascular wall with ensuing coagulation are important pathogenic mechanisms underlying various diseases, including kidney disease. We have shown that in ANCA-vasculitis kidney function is associated with strong coagulation activity during the acute phase, and that vascular access problems are prevalent in dialysis patients with coagulation abnormalities or thrombophilias. We have studied our potent, naturally occurring, locally acting antithrombotic in prevention of ischemic short- and long-term reversible or irreversible kidney injuries. APACs show strong inhibition of collagen induced platelet aggregation and procoagulant activity in association with vascular damage. In various animal models we have shown that APAC is able to target vascular injury site from the circulation and upon local application, having a long vascular retention time. Being highly negatively charged large molecules (MW 200-400 kDa) APACs interact avidly with vascular von Willebrand factor, laminin and collagen, whereas PECAM and podocalyxin positive vascular sites fail to colocalize with APAC. When infused intravenously 10 min prior to arterial clamping APAC protected kidneys from ischemic reperfusion injury, assessed both by clinical and laboratory or pathology findings. Intriguingly, in severe irreversible injury of 60 min ischemia time, APAC provided renoprotection. We are currently working with a diabetic nephropathy mouse model to study the possible role of APAC in the development of streptozotocin-induced diabetes and kidney damage.

Biography

Riitta Lassila has completed her MD in 1983 from Helsinki University, PhD in 1989, and Postdoctoral studies at Mount Sinai University School of Medicine in NY. She is an Internist and the Head of Coagulation Disorders Unit in Helsinki University Hospital since 2000 and Professor of Coagulation Medicine in Helsinki University since 2013. She has published more than 220 papers in peer-reviewed journals and has served as Editor in *Thrombosis Research* and Editorial Board Member of *Haemophilia* journal. She is the Secretary of European Association of Haemophilia and Allied Disorders and Steering Committee Member of EUHANET and EUHASS. She is CSO in Aplagon Oy developing APACs as pharmaceutical entities.

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