Dr. Darren Yuen (L) and Dr. Lisa Robinson (R)

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TURNING DOWN INFLAMMATION IN

VASCULAR INJURY

Vascular injury is a common and complicating factor in renal disease. During injury, inflammation signals the recruitment of leukocytes (white blood cells) to the affected site to help. However, since leukocytes also release pro-inflammatory chemicals, excessive migration can compound the damage.

For nearly a decade, HSRLCE member Dr. Lisa Robinson, Canada Research Chair in Leukocyte Migration in Inflammation and Injury and head of Nephrology at the Hospital for Sick Children, has been examining the problem of massive white blood cell traffic, and searching for an "anti-migration" signal in the body. Specifically, she has been shedding new light on the role of a protein known as Slit2 (and its receptor, Robo) and demonstrating that it can reduce white blood cell migration, thus stemming progressive injury.

Known for its involvement in neurodevelopment, Slit2's role in regulating vascular inflammation has only emerged recently. Dr. Robinson's research has also shown that Slit2 boasts anti-platelet activity (prevents clots) and inhibits vascular smooth muscle cell migration (which causes progressive narrowing of blood vessels). "People have looked at individually targeting these different events that occur in cardiovascular disease. But we found that Slit2 can address all those things at once, which makes it a potential therapy for preventing progressive disease," says Dr. Robinson.

Dr. Robinson has also been investigating the role of Slit2 in renal ischemia-reperfusion injury (IRI). Dr. Darren Yuen, a nephrologist and scientist in the Keenan Research Centre of the Li Ka Shing Knowledge Institute of St. Michael's Hospital, has been collaborating with Dr. Robinson on this research. They co-authored two papers published in 2013 in *Current Opinion in Nephrology and Hypertension* and the *Journal of the American Society of Nephrology*, reporting on Slit2's signalling function in vascular injury and its specific role in IRI, respectively. More recently, they have been examining the progressive scarring that follows acute vascular injury. "Slit2 is the only agent to date that can slow that scarring process and injury progression," suggests Dr. Robinson.

Their next goal is to address vascular injury in diabetes kidney disease by targeting the overgrowth of blood vessels that occurs early in the disease process. "Possessing both pro- and anti-angiogenic effects, Slit2 may be able to block this early diabetes-induced blood vessel growth that leads to kidney damage later," explains Dr. Yuen.

> "Helping to illuminate the pathophysiology of vascular injury in renal disease, and proposing a new therapeutic target"

Their work to date has helped to illuminate the pathophysiology of vascular injury in renal disease, and propose new therapeutic targets, including Slit 2 or a Slit2-based therapy, which may help to attenuate organ damage in kidney, heart and other forms of vascular disease.