

Singapore designs preclinical model to strategise treatment for a genetic kidney disease

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Tests using a preclinical model of Alport syndrome suggest that turning off a cell-signaling protein may significantly prolong life by preventing kidney scarring



Scientists from Duke-NUS Medical School, Singapore have designed a treatment strategy for genetic kidney disease 'Alport syndrome' using antibody inhibitor against interleukin-11 (IL-11), a cell-signaling protein. The findings can lead to new hope for people with a debilitating condition. The study findings are reported in the *Journal of the American Society of Nephrology*.

Alport syndrome is an inherited genetic condition that affects approximately one in every 50,000 newborns globally. The gene mutations linked to this syndrome can eventually lead to chronic kidney failure. Currently, there are no curative treatments for the condition. Though drugs like angiotensin-converting enzyme inhibitors (ACEi) can reduce the rate of kidney damage, they lower blood pressure and reduce leakage of protein into the urine.

Lead author of the study, Dr Anissa Widjaja (Duke-NUS' Cardiovascular & Metabolic Disorders Programme) and Professor Stuart Cook, (senior author of the study) said, "Together with our collaborators in Singapore and Germany, we wanted to find out if IL-11 played a role in Alport syndrome disease development. This cell signalling protein had recently been implicated by other research in kidney scarring and dysfunction. We also found that administration of anti-IL11 therapies, in the form of an antibody drug, has beneficial effects in reducing the severity of Alport syndrome in the preclinical model. This happened by reducing kidney injury, inflammation and scarring. Importantly, combining ACEi and anti-IL11 therapies increased the lifespan of the experimental group by more than 400 per cent relative to those that were treated with an ACEi drug alone."

Professor Thomas Coffman, dean of Duke-NUS Medical School and a senior co-author of the study, commented, "This discovery spells new hope for treatment in Alport syndrome—not just to arrest the progress of the disease, but even to restore lost kidney function. Also, the study suggests that anti-IL11 therapeutics can have additive effects with ACEi treatment, enhancing its potential utility in the clinical arena."

Asst Prof Widjaja and her colleagues are continuing their research by investigating whether anti-IL11 therapies can reverse kidney failure by promoting tissue regeneration.