Correction of the genetic defect in Alport syndrome using the TALEN approach
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Alport syndrome is the second commonest monogenic cause of inherited end-stage renal failure after polycystic kidney disease, and, overall, accounts for 3% of all patients on dialysis or with a transplant. Most patients have X-linked disease with mutations in the *COL4A5* gene. In these families, disease is worse in males than females. Fifty % of these patients have either a nonsense mutation (10%), or a change that results in a downstream nonsense mutation (40%). These families usually have severe disease with early onset renal failure (in males at less than 30 years), hearing loss, and sometimes lenticonus and retinopathy. Forty % of patients have missense mutations where an amino acid (often glycine) is replaced by another, which disrupts the regular collagen triple helix sequence. In the past decade, much has been learned on how these mutations cause disease and how injury may be modified.

Specific aims of the project are:

1. To use the TALEN strategy to repair the genetic mutations in cell lines from patients with Alport syndrome due to missense or nonsense mutations, and to confirm that these mutations are corrected *in vitro*. And to determine any increase in cell stress or apoptosis.

2. To use the TALEN strategy in autologous iPS (induced pluripotential stem cell/podocyte) from affected individuals with Alport syndrome, and to confirm that the mutation is repaired. And, to determine any increase in cell stress or apoptosis