

CKD treatment strategy: Self-assembling beta-peptide hydrogels for therapeutic delivery of mesenchymal stem cells

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Introduction. Kidney fibrosis is a hallmark of chronic kidney disease (CKD), and currently no therapies exist which halt the progression of fibrosis and restore renal function. Mesenchymal stem cells (MSCs) have been demonstrated to modulate inflammation underlying fibrosis and potentially reverse existing fibrosis, however their reparative effect is transient when delivered systemically. Local delivery and longer-term retention of MSCs has the potential to improve their efficacy in reversing established fibrosis. We aim to develop an injectable, non-degrading, self-assembling hydrogel to promote long term MSC retention following *in vivo* transplantation. *N*-acetylated β -tripeptides self-assemble into 14-helical ropes which form hydrogels at sufficient concentrations. We can introduce functionality into the peptide monomer by the incorporation of a specially designed β -amino acid with an orthoganol protecting group. Using this strategy, we can tailor the hydrogel properties to improve MSC anti-inflammatory efficacy in the kidney by optimising the biological signals within the gel. **Methods.** β -tripeptides functionalised with cell adhesive epitopes, RDG and SIKVAV, and fluorophores, will be synthesised using solid-phase peptide synthesis. Human bone-marrow derived MSCs that have a GFP+ luciferase reporter will be encapsulated in the hydrogel, and delivered to the kidney subcapsular space of mice with fibrotic kidney damage. Hydrogels and cells will be tracked for 7 days using *in vivo* fluorescence and bioluminescence imaging, respectively, before kidneys are harvested for assessment of fibrosis and inflammation. **Significance.** Development of an injectable hydrogel to deliver MSCs directly to the kidney could provide a novel treatment option for CKD patients who require dialysis or transplant, greatly improving their quality of life and easing the mounting pressure on our healthcare systems.

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