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A personalized approach to halting kidney disease

inRegen's personalized progenitor cell therapy injects autologous kidney cells (REACT) into patients' damaged kidneys, where cells migrate and restore kidney function. The cell-based treatment is showing signs of promise in ongoing phase 2 trials.

inRegen has developed a treatment for chronic kidney disease (CKD), now in phase 2 trials, that leverages a patient's own kidney cells to repair damage and improve kidney function. The approach is an auto-transplant of progenitor cells obtained via kidney biopsy and then reintroduced back into the kidney where they migrate to damaged kidney tissue, averting disease progression. According to inRegen CEO Tim Bertram, "Our personalized, autologous cell therapy doesn't require immunosuppression, is given as a simple injection, yet has unique potential to restore renal function lost to progressive CKD, transforming treatment and outcomes by delaying or preventing end-stage kidney disease."

Kidney disease affects ~850 million people worldwide. In the USA alone, 37 million people, half of them diabetic, suffer from CKD and are at risk of progressing to kidney failure. Arnold Silva, Director of Clinical Research, Boise Kidney and Hypertension Institute, and an investigator in inRegen's clinical trials, notes, "The full impact of CKD has been underappreciated, with little in the way of new treatments in the last two decades. Current therapies typically address the effects of reduced renal function, such as anemia, acid/base imbalance and hypertension, or underlying systemic disease, like diabetes and autoimmune disorders. inRegen's cell-based therapy treats the kidney itself, and may finally offer a means to stop or even reverse CKD progression."

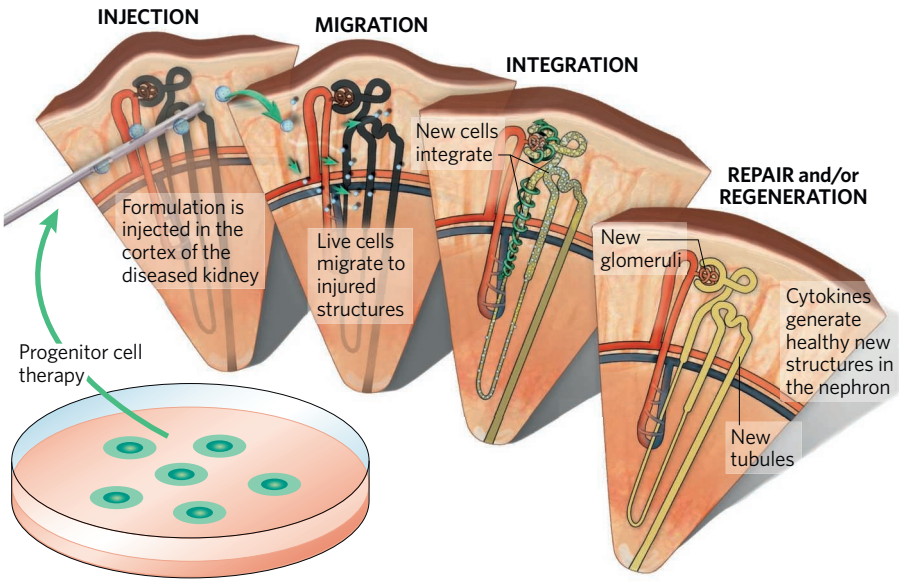

Fig. 1 | Renal progenitor REACT patient-derived cell therapy. Autologous kidney progenitor cells are injected into the kidney, where they rapidly migrate to diseased areas and integrate into nephronic structures (glomeruli and tubules), re-establishing kidney repair potential and restoring function.

Identifying kidney regeneration cells

Although kidneys are normally capable of recovering from acute injury, there is no current scientific support for the existence of a kidney stem cell. Undeterred by the decade-old challenge, with venture backing, inRegen scientists pursued a functional approach, systematically testing multiple kidney cell types in hundreds of combinations to deconvolute the activity in healthy kidneys responsible for regeneration in vivo. Their efforts ultimately succeeded in identifying a combination of cells able to form kidney tubules and Bowman's capsule in vitro. The cell mix included kidney progenitors with distinct phenotypic markers, including SIX2, OSR1, PAX2 and RET1. In preclinical studies, this combination of cells was able to induce new nephron formation, reduce disease and stabilize or improve multiple kidney functions, demonstrating long-term improvement in three different rodent models of severe CKD and a 70% nephrectomized canine model[1].

In the REACT (Renal Autologus Cell Therapy) clinical trials, patients undergo a kidney biopsy, and cells are isolated from the tissue under good manufacturing practice (GMP) conditions. The selected autologous, healthy progenitor cells are reintroduced into the kidney via injection on an outpatient basis, without the need for immunosuppression. The infused progenitor cells migrate rapidly to diseased areas, replacing damaged cells in tubules and glomeruli and regenerating new nephron structures (Fig. 1). The cells also localize in the interstitium, reducing fibrosis and inflammation, while modulating epithelial transdifferentiation. inRegen scientists hypothesize that kidney progenitor cells are programmed to heal damage, but in CKD become trapped by scars and effete from chronic inflammation, preventing normal function. This view is supported by the observation that these progenitor cells produce high levels of anti-inflammatory cytokines. By isolating and re-infusing these expert repair cells, inRegen's therapy may replenish natural reserves, allowing them to re-establish and maintain a healthy baseline function in the kidney.

Promising clinical trials

A first-in-human study with inRegen's progenitor cell-based treatment, conducted at the Karolinska Institute (Sweden), demonstrated that it was well tolerated. The therapy was granted US Food and Drug Administration fast-track status, and phase 2 trials in patients with diabetes with moderate to severe CKD were approved. Interim results of the randomized, controlled phase 2 trial showed earlier disease progression to dialysis in the control (standard-of-care) group compared with the REACT treatment group. The studies are nearing completion, with phase 3 trials slated to begin within the year. In addition, a phase 1 trial in adult patients with CKD due to congenital anomalies of the kidney and urinary tract (CAKUT) is currently enrolling in the USA and will be expanding to Mexico, where lack of surgical correction of CAKUT in childhood leads to a higher incidence of CKD in adulthood.

Kidney progenitor cells are highly sensitive to handling and prone to apoptosis. inRegen has developed proprietary methods to enable isolation, growth, formulation, and shipping of its cell-based therapy and holds extensive intellectual property (200-plus patents and patent applications) for composition, therapeutic use and methods of manufacturing. For patients in the on-going clinical trials, GMP manufacturing of autologous cell treatments is being conducted in partnership with Twin City Bio. inRegen plans to scale up clinical and commercial efforts to address the global scope of the unmet need in CKD.

1. Kelley, R. et al. *Cell Transplant.* **22**, 1023–1039 (2013).

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