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Injection of amniotic fluid stem cells delays progression of renal fibrosis

Introduction: Alport syndrome (AS) is a hereditary form of chronic kidney disease (CKD) and is also a valuable model for studying progressive renal fibrosis and end stage renal disease (ESRD). Herein, we investigate the therapeutic potential of amniotic fluid stem cells (AFSC), which are not only well established to possess pluripotential characteristics but also demonstrate anti-fibrotic properties that may potentially lead to better therapies for AS and/or other fibrotic diseases of the kidney.

Methods: In this study, we have administered AFSCs in a murine model of AS (Col4a5-/-) before the onset of proteinuria. Mice were sacrificed at 5 days, 1 and 2 month(s) post treatment and kidneys were harvested for molecular and histological analysis. Kidney function was assessed with serum creatinine, BUN as well as proteinuria measurements.

Results: Systemic infusion of AFSC resulted in delayed renal fibrosis and prolonged animal survival, slower progression of glomerulosclerosis and ameliorated kidney function. Treated mice presented lower myofibroblast transformation in the kidney interstitial space, accompanied with down-regulated expression of inflammatory and cytokines such as IL-1, TNFα and TGFβ. Furthermore, AFSC injected mice presented significantly less glomerulosclerosis as much as 2.5 months post stem cell treatment when compared to their untreated siblings. Injected animals exhibited decreased recruitment and activation of M1 type macrophages and an apparent preference towards M2 type macrophages; which are thought to favor tissue remodeling. AFSCs do not differentiate into podocyte-like cells and they do not stimulate the production of collagen IVa5, needed for correct glomerular basement membrane assembly and function. Our investigation supports a mechanism of renal protection through paracrine/endocrine modulation of expression of cytokines promoting fibrosis and macrophage recruitment to the interstitial space. Furthermore, injected mice manifested preservation of the number of podocytes and improved integrity of the glomerular basement membrane. These beneficial effects may be promoted by interference with the renin-angiotensin system by the AFSCs.

Conclusion: In this study, we have shown that AFSCs are capable of slowing down the progression of Alport disease by incurring structural and functional benefits to the kidney. Although injection of AFSC does not entirely reverse kidney disease, taken together, our findings suggest that a single AFSC treatment delays progression of CKD and significantly improves survival in treated AS mice. These cells may present an alternative approach to treat various medical conditions where currently therapeutic options are either limited or inadequate.

Biography

Roger E De Filippo completed his MD at the Keck School of Medicine, University of Southern California, in 1993. He completed a Pediatric Urology Fellowship in 2003 at Boston Children's Hospital, Harvard Medical School and did two years of Tissue Engineering research during his fellowship training. He is Chief of Pediatric Urology at Children's Hospital Los Angeles and Co-Director of the GOFARR Laboratory for Organ Regenerative Research and Cell Therapeutics. He has published close to 50 manuscripts in reputed journals and presently serves on the Editorial Board of the journal *Stem Cells Translational Medicine*.

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