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Transplantation of mouse induced pluripotent stem cell-derived podocytes in a mouse model of membranous nephropathy attenuates proteinuria

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Abstract

Injury to podocytes is a principle cause for initiation and progression of both immune and non-immune mediated glomerular diseases (GD) that result in proteinuria. Current advances in regenerative medicine shed light on the potential for cell-based therapy to treat several of these disorders. Thus, there is hope that generation and transplantation of podocytes from induced pluripotent stem cells (iPSCs) could potentially provide a curative treatment for glomerulonephritis caused by podocyte injury and loss. In this study, mouse model of membranous nephropathy (MN) was carried out with intravenous administration of anti-podocyte antibody (APA) after subcutaneous pre-immunization. iPSCs were derived from induced anti-podocyte nephropathy (APN) mouse tail-tip fibroblasts (TTFs) by retroviral transfection of Oct4, Sox2, Klf4, and c-Myc. We converted the iPSCs into podocytes via a series of modified differentiation procedures to obtain stage specific cell types of nephrogenic intermediate mesoderm (NIM), podocyte progenitors, and podocytes. Functional assays for iPSC-podocytes included the reorganization of F-actin cytoskeleton and contractile response to the addition of insulin and angiotensin II (AII), and the endocytosis of albumin. Then, podocyte cells were transplanted into the renal cortex parenchyma of MN mice 10 days after antibody treatment. Then, we evaluated their urine, serum, and histopathologic analyses and quantification of podocyte numbers. In this study, we generated a model of APA-induced heavy proteinuria that resembled human MN and was characterized by the presence of sub-epithelial immune deposits and podocyte loss. Thereafter, iPSCs from a mouse with proteinuria were differentiated into podocytes that showed protein marker localization and functional characteristics of podocytes. The data revealed that iPSC-podocyte transplantation (PT) decreased proteinuria and attenuated the evaluated histopathologic parameters by possibly replacing lost podocytes. These results provided evidence that iPSCs-derived renal cells could be a possible therapeutic strategy for treatment of glomerular diseases.

Biography

Reza Moghadasali has completed my PhD at the age of 35 years from Kharazmi University, Iran. I am the director/assistant professor of Royan Institute, Iran. I have over 22 publications that have been cited over 500 times, and my publication H-index is 10 and has been serving as an editorial board member of reputed Journals.

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