(Technology Bundle) Stem cells with transiently reduced p53 to treat diabetes associated kidney disease and peripheral vascular disease

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Local delivery of endothelial progenitor cells (EPCs) may treat diabetic-related kidney disease (DKD) and peripheral vascular disease (PVD). EPCs may be obtained from a patient’s peripheral blood. The hyperglycemic state in diabetic patients causes transplanted EPCs to undergo apoptosis, creating a challenge for such therapies. By transiently silencing the apoptotic gene p53, Dr. Sen’s improved method leads to survival of transplanted EPCs to achieve formation of mature endothelial lineage cells.

Diabetes mellitus, with its vascular complications is the most common cause of kidney disease. Progenitor cells have significant regenerative paracrine properties. Also, they have the unique property of homing-in to the site that needs repair and regeneration, particularly endothelial lineage structures. The EPC-derived paracrine substances will home-in to the inflamed and necrotic areas within the host’s kidneys and help form new capillaries to improve renal perfusion. Additionally, EPCs can help form collateral vessels to overcome peripheral blood vessel blockage.

This unique technique of using p53-silenced EPCs rather than mesenchymal stem cells to treat endothelial damage in DKD and PVD is the first of its kind. In-vivo experiments with diabetic mice demonstrated the feasibility of the method. The benefits of p53-silenced EPCs post-sub capsular-renal EPC delivery in the treatment of DKD include improvement in proteinuria, diabetic polyuria, and renal blood flow by increasing angiogenesis and perfusion. Transplantation of P53 null EPCs in hyperglycemic mice with femoral occlusion demonstrate better collateral vessel formation post femoral artery occlusion setting compared to WT-EPC transplanted group.

Applications:

• Treat diabetes associated kidney disease
• Treat or prevent diabetes associated peripheral vascular disease

Advantages:

• Delays need for kidney transplant surgery
• Allows for use of patients own cells

GW is leading the patenting and licensing of these technologies on behalf of the owners, GW and Baystate Health.
Inventors

Sabyasachi Sen