PS176.

Rescuing Effect of Autologous Mesenchymal Stem Cells in a Model of Early Type II Diabetes

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Objectives: Repeated, low dose injections of Streptozotocin (STZ) create a model of Type II Diabetes Mellitus. We utilize this model to investigate the potential pro-repair effect of syngeneic (equivalent to autologous) bone marrow-derived mesenchymal stem cells (BMD-MSC) in Diabetes.

Methods: STZ (40 mg/Kg) was administered, daily, for five days, i.p., in C57BL6 mice (N = 12). Weekly blood glucose levels (BG) were monitored by 2-hour Glucose Tolerance Test (GTT) for five weeks after. Glucose intolerance (150 < BG < 200 mg/dL) was used as the trigger for treatment. The mice were then divided in two groups (N = 6/group). Control group received PBS and treatment group received MSC (1x10-6), by tail vein infusion. MSC were obtained by culturing BMD cells from donor mice (N = 3) in MesenCult® medium. β-cell activity was measured by immunohistochemistry, and serum level of insulin was assessed by C-peptide test.

Results: At baseline and post-STZ-induction, GTT between control and treatment group did not differ significantly. However, at week 3 the MSC treatment group's GTT normalized and the effect is sustained by week 5 (Fig). Control group continues to have significant glucose intolerance. Longer follow up is ongoing.

Conclusions: Systemic injection of a single MSC treatment improves the Glucose Tolerance in a murine model of Type II Diabetes. The findings will require confirmation in genetic murine models, yet depict a highly promising novel concept for the treatment of Diabetes.

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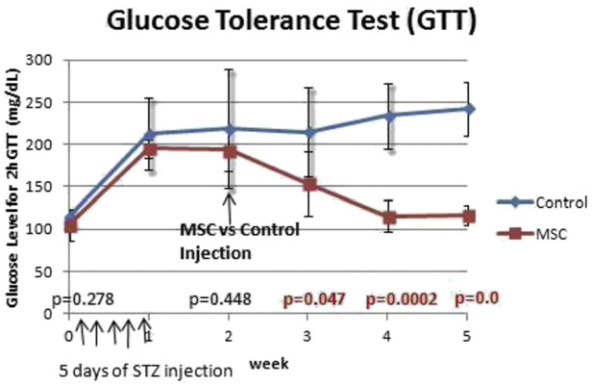

Fig.

PS178.

Supplemental Oxygen Reverses Hypoxia Induced Smooth Muscle Cell Proliferation by Modulating HIF-alpha and VEGF Levels in a Rabbit Arteriovenous Fistula Model

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Objectives: Numerous mechanisms for the formation of intimal hyperplasia have been proposed but none have been proven or accepted. Our research focuses on the potential role of Hypoxia Inducible Factors (HIFs), VEGF, and PDGF as well as the ERK, PI3-K/AKT pathway in hypoxia mediated intimal hyperplasia processes.

Methods: Rabbits were randomized into different experimental groups with varying oxygen exposure and receipt of surgery. Plasma samples were collected at designated intervals in which cytokines and smooth muscle cell proliferation were measured. In addition, cell specimens were exposed to hyperoxic, normoxic, and hypoxic environments with cytokines measured at various time points.

Results: Placement of an arteriovenous fistula resulted in hypoxia induced HIF stabilization with a concurrent increase in VEGF. Activation of VEGF receptors on smooth muscle cells through ERK1 and AKT pathways resulted in significant smooth muscle cell proliferation and migration. These effects are dramatically reduced in animals that are exposed to a hyperoxic environment of 30% oxygen.

Conclusions: Our results suggest that short-term administration of supplemental oxygen inhibits HIFs and VEGF signaling to reduce smooth muscle proliferation in the local blood vessel. These results provide strong support for the therapeutic use of supplemental oxygen following arterial surgery to reduce intimal hyperplasia. These findings also provide a nidus for future studies into the mechanisms of hypoxia induced intimal hyperplasia.

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PS180.

The Gene Expression of Adenosine Receptors in the Processes of Contrast Induced Nephropathy in Mouse Kidney

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Objectives: Contrast Induced Nephropathy (CIN) is the third leading cause of hospital acquired renal failure, which is a common complication following endovascular surgery procedures. The mechanism of CIN is not fully understood. Adenosine receptors (AR) regulate various physiological activities in kidney. We hypothesized that adenosine and its receptors may play a role in development of CIN. The objectives of this study were to investigate the expression changes of the four subtypes of adenosine receptors (A1AR, A2AAR, A2BAR, and A3AR) following administration of contrast agent in mice.

Methods: C57B1/6J mice were randomized to treatment and control groups. Iodixanol, a commonly used contrast agent, was administered to treatment groups