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MESENCHYMAL STEM CELL-PRECONDITIONED MEDIUM INCREASES SURVIVAL OF HUMAN ISLETS IN HYPOXIC CONDITIONS

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Aim of Study: Islet transplantation has the potential to reverse type 1 diabetes in children. Results in adults have been encouraging, but life-long islet survival remains challenging. Mesenchymal stem cells (MSC) produce growth factors that protect islets when co-transplanted in hypoxic conditions. However, transplanting MSC into immunosuppressed patients carries neoplasia risks. This study aimed to investigate whether MSC-preconditioned media provides the same islet protection.

Methods: MSC were isolated from human adipose tissue and expanded using MEM/glutamax medium supplemented with 10% FCS. Each culture medium batch was preconditioned with MSC cultured for 2 days in normoxia (21% oxygen) or hypoxia (1%). Unused medium served as control. After harvesting MSC, cell-depleted media were frozen at -20ºC. Human islets were isolated with consent and ethical approval (n=8 pancreases) and cultured for 48-72 hours in hypoxia (2% oxygen) in either unused MEM/glutamax or MEM/glutamax preconditioned at 21% or 1% oxygen. Data were normalized to control islets in hypoxia and presented as mean ± SEM.

Main Results: Compared with controls, islet recovery increased to 117±12% (P=0.078) and 138±12% (P<0.05) when islets were cultured in medium preconditioned at 21 and 1% oxygen, respectively. Viability assessed by FDA-PI was unchanged after culture in MSC-medium either unused (59±2%), preconditioned at 21% (59±3%) or 1% (61±3%) oxygen. However, glucose-stimulated insulin release was significantly increased for islets cultured in MSC-medium preconditioned at 21% (49±30 µU/ng DNA/45 min, P<0.01) or 1% (27±9 µU/ng DNA/45 min, P<0.05) (controls 19±7 µU/ng DNA/45 min). Overall islet survival in MSC-medium preconditioned at 1% oxygen was significantly more protective (143±14%) than MSC-medium preconditioned at 21% oxygen (119±14%) or control medium (P<0.05).

Conclusions: This study demonstrates that MSC-preconditioned culture medium increases human islet survival and *in vitro* function in hypoxic conditions. This is an important novel finding that offers a safer alternative to co-transplantation with MSC.