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HUMAN AMNIOTIC FLUID STEM CELLS: A NOVEL FETAL HAEMATOPOIETIC STEM CELL SOURCE WITH POTENTIAL FOR THERAPY

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Aim of Study: The demand for haematopoietic stem cells (HSC) in clinical applications is increasing. Amniotic fluid stem cells (AFSC) serve as a potential alternative cell source for therapy. The significant haematopoietic activity of murine AFSC led us to explore the potential of human CD117/c-Kit+ AFSC to reconstitute the haematopoietic system in vivo.

Methods: Human AFSC (2nd and 3rd trimester) and cord blood HSC (CB-HSC; control) were selected for CD117 and CD34 respectively flow-cytometry. Sorted cells (104 in 200µl PBS) were injected intravenously into sub-lethally irradiated NOD-SCID/IL2rγ^{null} (NSG) mice (n=6/group). Haematopoietic engraftment of human cells (% of human CD45+ within total CD45+) and multi-lineage reconstitution (erythroid, myeloid and lymphoid) were assessed at 16 weeks in blood, bone marrow (BM) and spleen. BM mononuclear cells (MNC) from mice engrafted with human cells were used in secondary transplantation experiments (1.5x107 MNC in 200µl PBS; haematopoietic engraftment assessment 16 weeks post-transplantation; n=6/group).

Results: Human AFSC engrafted the haematopoietic system of sub-lethally irradiated NSG mice at levels similar to the ones achieved with CB-HSC (blood: AFSC 7.5±1.3% vs. CB-HSC 6.1±2.2%, p=0.6; BM: AFSC 46.3±7.9% vs. CB-HSC 38.3±8.2%, p=0.6; spleen: AFSC 39.6±9.3% vs. CB-HSC 34.7±10.5%, p=0.7). Importantly, the potential for multi-lineage haematopoietic reconstitution was comparable between groups at 16 weeks post primary transplantation. Moreover, at 16 weeks following secondary transplantation, AFSC-derived haematopoietic cells were detected in peripheral blood (8.9±1.6%) and other haematopoietic organs; engraftment levels were similar to these in the CB-HSC group (blood: 7.3±1.8%, p=0.8).

Conclusion: Human CD117/c-Kit+ AFSC have functional, multi-lineage haematopoietic potential that is similar to the current "gold-standard" stem cell source for haematopoietic transplantation. The ease of isolation during early gestation, as well as their gene-engineering and expansion potential make human AFSC a novel autologous fetal cell source for pre- and post-natal therapy of inherited haematological disorders.