Abstract 3087: Human Tissue-Engineered Heart Valves Based on Umbilical Cord Blood Derived Progenitor Cells as Single Cell Source

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Objective: Tissue engineering of autologous heart valves with the potential to grow and to remodel represents a promising concept. Currently we are exploring the impact of cryopre-served umbilical cord blood-derived CD133+ cells as single cell source for tissue engineering of heart valves.

Methods: Cord blood-derived endothelial progenitor cells (EPC) were obtained from the mononuclear cell fractions. After expansion and differentiation cell phenotypes of CD133+ cells were analyzed by immunohistochemistry and cryopreserved. After 12 weeks the cryopreserved, blood-derived myofibroblasts were seeded onto heart valve scaffolds (n=8) fabricated from a biodegradable polymer and subsequently coated with EPCs. Afterwards, the heart valve constructs were grown in a pulse duplicator system. After in-vitro maturation, analysis of all heart valves included histology, immunohistochemistry, electron microscopy, fluorescence imaging, biochemical and biomechanical examination.

Results: Differentiated CD133+ cells remained viable after cryopreservation and showed a myofibroblast-like morphology that stained positive for α-actin and fibroblastspecific marker as well as functional endothelial cells staining positive for CD31, VWF and VE-cadherin. The tissue engineered heart valves showed endothelialized layered tissue formation including connective tissue between the inside and the outside of the scaffold. Immunohistochemistry was positive for collagen (type I, III and IV), desmin, laminin, α-actin, CD31, VWF and VE-cadherin. The notion of an intact endothelial phenotype was substantiated by fluorescence imaging studies of cellular NO production and Ca^{2+} signaling. Electron microscopy showed that the cells had grown into the pores and formed a confluent tissue layer. Biochemical examination showed extracellular matrix formation (77±9% collagen of human pulmonary leaflet tissue (HPLT), 85±61% glycosaminoglycans of HPLT and 67±17% elastin of HPLT).

Conclusion: This study demonstrates in vitro generation of viable human heart valves based on umbilical cord blood-derived CD133+ cells. These findings suggest the potential benefit of establishing cell banks for pediatric patients diagnosed intrauterinely with congenital defects.