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Engineered living blood vessels: functional endothelia generated from human umbilical cord-derived progenitors.

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BACKGROUND: Tissue-engineered living blood vessels (TEBV) with growth capacity represent a promising new option for the repair of congenital malformations. We investigate the functionality of TEBV with endothelia generated from human umbilical cord blood-derived endothelial progenitor cells. METHODS: Tissue-engineered living blood vessels were generated from human umbilical cord-derived myofibroblasts seeded on biodegradable vascular scaffolds, followed by endothelialization with differentiated cord blood-derived endothelial progenitor cells. During in vitro maturation the TEBV were exposed to physiologic conditioning in a flow bioreactor. For functional assessment, a subgroup of TEBV was stimulated with tumor necrosis factor-alpha. Control vessels endothelialized with standard vascular endothelial cells were treated in parallel. Analysis of the TEBV included histology, immunohistochemistry, biochemistry (extracellular matrix analysis, DNA), and biomechanical testing. Endothelia were analyzed by flow cytometry and immunohistochemistry (CD31, von Willebrand factor, thrombomodulin, tissue factor, endothelial nitric oxide synthase). RESULTS: Histologically, a three-layered tissue organization of the TEBV analogous to native vessels was observed, and biochemistry revealed the major matrix constituents (collagen, proteoglycans) of blood vessels. Biomechanical properties (Young's modulus, 2.03 +/- 0.65 MPa) showed profiles resembling those of native tissue. Endothelial progenitor cells expressed typical endothelial cell markers CD31, von Willebrand factor, and endothelial nitric oxide synthase comparable to standard vascular endothelial cells. Stimulation with tumor necrosis factor-alpha resulted in physiologic upregulation of tissue factor and downregulation of thrombomodulin expression. CONCLUSIONS: These results indicate that TEBV with tissue architecture and functional endothelia similar to native blood vessels can be successfully generated from human umbilical cord progenitor cells. Thus, blood-derived progenitor cells obtained before or at birth may enable the clinical realization of tissue engineering constructs for pediatric applications.

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