306a Functional Tissue-Engineered Blood Vessels Derived-from Bone Marrow Mesenchymal Stem Cells

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Cardivascular disease is the leading cause of mortality in the United States. Autologous blood vessel graft is the most intervention for coronary and peripheral atherosclerotic diseases. When autologous blood vessel grafts are not available, tissue-engineered blood vessel (TEV) may offer an option to autologous blood vessel in replacing or repairing diseased or damaged blood vessels. Functional and implantable TEVs using vascular smooth muscle cells and endothelial cells have been constructed, demonstrating significant mechanical strength and reactivity after implantation, comparable to those of native blood vessels. Bone marrow-derived mesenchymal stem cells have tremendous potential as a nonimmunogenic or autologous cell source for tissue regeneration. The repair and regeneration of damaged or diseased blood vessels using tissue engineered blood vessels generated from bone marrow mesenchymal stem cells would be of significance in improving human life and extending the acknowledge of stem cell tissue engineering. To tissue-engineer blood vessel constructs using bone marrow mesenchymal stem cells as cell resources, firstly we isolated smooth muscle cells from ovine bone marrow by transfecting bone marrow mononuclear cells with a DNA plasmid encoding EGFP under the control of a smooth muscle specific promoter and subsequently sorted EGFP positive cells by FACS; Secondly we identified these EGFP positive cells as smooth muscle cells from morphologic and phenotypic properties. Thirdly we highly expanded these bone marrow derived smooth muscle cells (BM-SM). In the end we tissue-engineered blood vessels by embedding BM-SM cells in fibrin hydrogels that were allowed to polymerize around 4-mm diameter silastic tubes. These BM-TEVs demonstrated significant reactivity to KCl and norepinephrine (NE) as compared to constructs prepared from bone marrow mononuclear cells, which did not show any reactivity to KCL and NE. Interestingly, BM-TEVs were stronger than TEVs from mature smooth muscle cells derived from ovine pulmonary veins. Notably, addition of endothelial cells in the lumen of BM-TEVs significantly increased the reactivity in response to KCl and NE, suggesting interactions between endothelial and BM-SM cells during tissue development. Our results show that BM-SM stem cells can be used in tissue engineering of functional blood vessels thus providing an autologous cell source and obviating the problem of immune rejection. The implantation of the BM-TEVs in jugular vein or carotid artery in sheep is under way.