

Stem cells, signaling pathways and delivery strategies in tissue engineering



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Cell-cell interactions play a critical role in development of native and engineered tissues as well as tissue regeneration after wounding. In this context we discovered a novel role of the c-jun-N-terminal protein kinase (JNK) in cell-cell adhesion by regulating adherens junction assembly and actin polymerization. Through a combination of chemical and genetic approaches we determined the mechanism through which JNK interacts with and affects adherens junctions. To further examine cell-cell interactions in the 3D context, we developed a novel hybrid model of wound healing that is based on implantation of human bioengineered skin onto athymic mice. Using this system we evaluated the efficacy of a novel biomimetic strategy to deliver wound healing factors in a cell-controlled manner in vivo. Our findings show that cell-controlled delivery of keratinocyte growth factor doubled the rate of wound healing, suggesting that it may be useful in treatment of difficult to heal wounds such as burns or chronic ulcers.

In the last part of my presentation, I will discuss our recent efforts in vascular tissue engineering using adult stem cells. We developed a novel method to isolate smooth muscle cells from bone marrow – termed BM-SMC - using a tissue specific promoter and flow cytometry cell sorting. These cells were characterized extensively using molecular (RT-PCR, western blots, immunocytochemistry) and functional (clonogenic, karyotyping) assays. In addition, we prepared cylindrical tissue engineered vessels (TEVs) and measured significant contractile forces in response to receptor and non-receptor mediated pathways. When TEVs were implanted in the jugular veins of lambs, they integrated very well with the native vessel and demonstrated patency and similar blood flow rates. As early as five weeks post-implantation, grafted tissues displayed a confluent endothelial layer overlaying the medial layer in which BM-SMC were aligned circumferentially and synthesized significant amount of collagen. Notably, BM-SMC synthesized high amounts of elastin that was organized in a fibrillar network very similar to native vessels. Our results suggest that TEVs from bone marrow stem cells may be useful as a biological model for studying vascular development and have high potential for development of stem cell therapeutics for treatment of cardiovascular disease.



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