

C18

Hypoxia Induced Near-Native Mechanical Properties Of Engineered Heart Valve Tissue

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Objectives:

A main challenge in heart valve tissue engineering (TE) is to produce autologous valve replacements with appropriate extracellular matrix and native-like mechanical behavior that allow for systemic pressure applications. As hypoxia and insulin are known to promote matrix synthesis and hence mechanical properties, decreased oxygen tension and insulin supplements were applied to growing heart valve tissues to study their effect on tissue mechanical properties.

Method:

35x5x1 mm rapid degrading non-woven polyglycolic acid meshes, coated with poly-4-hydroxybutyrate, were seeded with human saphenous vein myofibroblasts. The obtained constructs were cultured under normoxic (20% O₂) or hypoxic (7% O₂) conditions, and incubated with or without insulin (2.5 µg/ml) supplementation for 4 wks.

Results:

Both insulin and hypoxia were associated with enhanced matrix production and improved mechanical properties, although a synergistic effect was not observed. GAG production approached native values, both under hypoxic conditions and in the presence of insulin. Collagen amounts and cross-link densities did not reach native values. Nevertheless, modulus (21.54 ± 5.32 MPa) and tensile strength (2.64 ± 0.65 MPa) of the constructs cultured under hypoxic conditions reached adult human aortic valve values, and were twice as high as values observed for normoxic controls.

Conclusions:

These results strongly indicate that oxygen tension is a key parameter to achieve desired tissue quality and integrity in TE heart valves. Engineered cardiovascular tissues of the reported strength, based on rapid-degrading polymers, have not been reported so far and are a crucial step towards systemic application of TE heart valves.