COSMETIC APPROACH TO HEART VALVES TISSUE ENGINEERING

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Heart valve substitutes suffer important drawbacks and none of currently commercially available prostheses provide satisfactory long-term durability, ideal hemodynamics and remodelling performance. The attempts of Tissue Engineering for fabrication of substitutes using biological or biodegradable scaffolds, coupled with the manipulation of cells in diseases tissues (Cells Therapy) has enabled, in the mid-2000s, the development of the Regenerative Medicine approach in which the regeneration of damaged tissues is permitted by their substitution in addition to the stimulation of the body's own repair mechanisms in order to heal previously irreparable injuries [Mason 2008]. Inspite of the fact various scientists reported promising results, Regenerative Medicine of heart valves (RMHV) is still at the beginning of its evolution without any significant clinical translation. In the 2000 Hoerstrup *et al.* produced the first functional trileaflet heart valves made from a bioabsorbable polymer (polyglycolic-acid PGA) and seeded with ovine myofibroblasts and endothelial cells. The construct was implanted in pulmonary position in lambs with a maximum follow-up of 20 weeks. This synthetic scaffold was improved by Sutherland *et al.* (2005) with the addition on the mesh of poly-L-lactic acid. The graft, seeded with ovine mesenchymal stem cells, was implanted in sheep reaching a follow-up of 8 months. Up to date this result can be considered the best obtained combining the use of cells and synthetic scaffold [Gottlieb D 2010,Weber B 2011,Emmert MY 2012]. In the early 2000s the use of biological scaffolds for RMHV began with the occurrence of dramatic clinical events such as the death of paediatric patients implanted with a Synergraft engineered porcine heart valve [Simon 2003], high failure rate of bovine derived vascular grafts [Spark JI 2008] and several clinical re-intervention due to the immunological reaction of the heart valve substitute Matrix P [Rüffer A 0210].These events highlighted the need of safer biological substitutes with more exhaustive preclinical study on using animal models [Hopkins R 2009, Jordan 2012, Weymann 2012, Gallo 2012].The longest follow-up reported in literature was 15 months, and it was obtained by our research group. During the last 10 years there has been a consistent improvement in cell culture and development of new polymers, but this was coupled with an evident regression of the clinical translation of heart valve constructs. Beautiful images of *in-vitro* scaffold repopulation as well as of cell lineage differentiation as a consequence of pre-conditioning in ultra-modern bioreactors, collide with the basic requirement of reliable, safe and effective clinical application. However, biological scaffolds for HVRM provided the best results in preclinical studies. Additionally biological tissue meets important requirements allowing both to maintain several trophic factors (crucial for proper homing of cellular components) and a great time saving not requiring bioreactor pre-conditioning or cellular pre-seeding.

References

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