**Failed valve replacement**

This module is all about how cells adhere and migrate, which are critical cell behaviors for many natural and engineered tissues. Sometimes you want to promote these behaviors to ensure cells infiltrate and remain in your scaffold while simultaneously limiting the infiltration of other cells (namely immune or cancerous cells). Below is an abstract from a clinical trial reporting the failure of a valve replacement construct. This valve failed in part because it allowed for adhesion and migration of immune cells.

**Abstract**

**Objectives:** The first tissue engineered decellularized porcine heart valve, Synergrafte (Cryolife Inc., USA) was introduced in Europe as an alternative to conventional biological valves. This is the first report of the rapid failure of these new grafts in a small series.

**Materials and methods:** In 2001, 2 model 500 and 2 model 700 Synergrafte valves were implanted in four male children (age 2.5–11 years) in the right ventricular outflow tract as a root. Two patients had a Ross operation and two had a homograft replacement.

**Results:** The cryopreserved Synergrafte valves appeared macroscopically unremarkable at implantation. Recovery from surgery was uneventful and good valve function was demonstrated postoperatively. Three children died, two suddenly with severely degenerated Synergrafte valves 6 weeks and 1 year after implantation. The third child died on the 7th day due to Synergrafte rupture. Subsequently the fourth graft was explanted prophylactically 2 days after implantation. Macroscopically all four grafts showed severe inflammation starting on the outside (day 2 explant) leading to structural failure (day 7 explant) and severe degeneration of the leaflets and wall (6 weeks and 1 year explant). Histology demonstrated severe foreign body type reaction dominated by neutrophil granulocytes and macrophages in the early explants and a lymphocytic reaction at 1 year. In addition, significant calcific deposits were demonstrated at all stages. Surprisingly pre-implant samples of the Synergrafte revealed incomplete decellularization and calcific deposits. No cell repopulation of the porcine matrix occurred.

**Conclusion:** The xenogenic collagen matrix of the Synergrafte valve elicits a strong inflammatory response in humans which is non-specific early on and is followed by a lymphocyte response. Structural failure or rapid degeneration of the graft occurred within 1 year. Calcific deposits before implantation and incomplete decellularization may indicate manufacturing problems. The porcine Synergrafte treated heart valves should not be implanted at this stage and has been stopped.

Imagine that you are a researcher in this group. Brainstorm ideas to improve this therapy; specifically, ideas that would allow the desired cells to populate your construct but limit the population of undesirable cells. Describe 1 or 2 ideas in your initial post. Be creative – your ideas don’t need to be published or validated. Think out of the box. Focus on regulation through adhesion and migration regulatory mechanisms. Do not repeat ideas that have been mentioned by your peers. Respond to at least two of your classmates.

Full article referenced in this discussion: Simon, P., M. T. Kasimir, G. Seebacher, G. Weigel, R. Ullrich, U. Salzer-Muhar, E. Rieder, and E. Wolner. "Early failure of the tissue engineered porcine heart valve SYNERGRAFT® in pediatric patients." European journal of cardio-thoracic surgery 23, no. 6 (2003): 1002-1006.