Provide an example of a medical device or biomaterial implant that failed due to the host immune response and describe why it failed.
Alternatively, discuss the issues leading to failure of transplants of a specific organ.
Very broadly, how would you modify the biomaterial device or transplant treatment to improve or reduce the host immune response?

The Synergrafte valve [1], a decellularized porcine heart valve, was launched in Europe as an innovative biological valve alternative. Implanted in four children, these valves exhibited good initial function, but three children died within a year due to valve degeneration or rupture. All explanted valves showed severe inflammation; presence of foreign body response dominated by neutrophils and macrophages, leading to structural failure and significant calcification. These outcomes suggested an initial strong inflammatory response to the xenogeneic collagen matrix, followed by a lymphocyte response.

The Scaffold could be reengineered, including:

- An improved version of the Synergrafte valve could have its surface coated to push immunoglobulins away (chemorepulsant).
- The Scaffold could be reengineered to support differentiation of the monocytes part of the pro-inflammatory reaction into M2-type anti-inflammatory macrophages which promote tissue repair and regeneration.
- Additionally, we can control how fast the valve's support structure breaks down by choosing the right types of plastic materials and adjusting their mix.
- To make the valve work better, we can add substances that attract healing cells or that encourage the growth of new blood vessels: chemotaxis could be part of the strategy to improve the Synergrafte valve by incorporating growth factors into the scaffold (VEGF), or other bioactive components to stop the influx of neutrophils. These molecules could be pre-seeded into the scaffold before the transplantation.

[1] P. Simon *et al.*, “Early failure of the tissue engineered porcine heart valve SYNERGRAFT® in pediatric patients,” *Eur. J. Cardio-Thorac. Surg.*, vol. 23, no. 6, pp. 1002–1006, 2003, doi: 10.1016/s1010-7940(03)00094-0