immunoSEQ®

CASE STUDY

TRANSPLANT

B-cell clonal expansion within immune infiltrates in human cardiac allograft vasculopathy

Moore C, *et al. (2020) American Journal of Transplantation* 5(20):1431-1438

Background

Cardiac allograft vasculopathy (CAV) remains a formidable barrier to successful long-term outcomes in heart transplantation. While previous studies have highlighted the critical role of B cells during the development of CAV, the underlying mechanisms driving the late-stage immune response remain poorly understood. Investigating dynamics of the B-cell repertoire in the context of CAV could lead to improved heart transplant outcomes. In this study, the authors characterized and compared the repertoire diversity of B-cell infiltrates across different graft sites in transplanted hearts and matched peripheral blood during CAV.

Aim

- Compare the clonality of B-cell infiltrates across different graft sites in transplanted hearts during CAV and matched peripheral blood using the immunoSEQ hsIGH Assay.
- Compare the prevalence of somatic hypermutations (SHMs) within the B-cell receptor (BCR) repertoires of different graft sites and peripheral blood.

WHY IMMUNOSEQ?

- Clonality metric quantitatively measures repertoire focusing of B-cell infiltrates that may correlate with onset and progression of immune-mediated allograft rejection
- Unbiased assessment of the B-cell repertoire allows accurate comparison of diversity metrics between samples

CASE STUDY: B-cell clonal expansion within immune infiltrates in human cardiac allograft vasculopathy—*Moore C, et al. (2020) American Journal of Transplantation 5(20):1431-1438*

Methods

1. Cardiac tissue and blood samples were collected from four patients with CAV during a second transplant procedure. Sections from the fresh tissue samples were excised from different areas of the allografts.
2. Explanted cardiac and blood samples → gDNA → **immunoSEQ hsIGH Assay**
3. Compare clonality and SHM counts between samples

Results

- Productive clonality was significantly elevated in all graft sites compared to PBMCs.
- Increased SHM counts were observed in the graft sites compared to PBMCs, suggesting antigen-driven affinity maturation.

Figure 1.

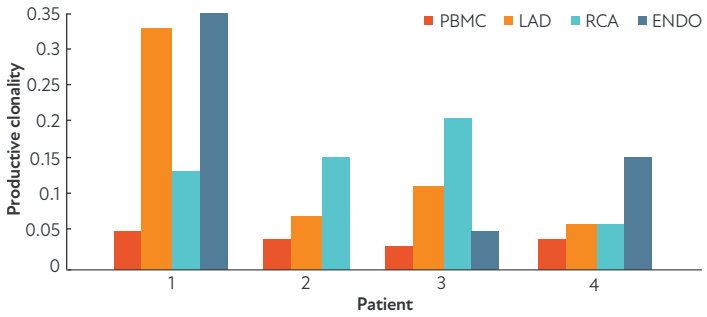

Figure 1. IGH Productive clonality of four transplant recipients across peripheral blood (PBMC) and three graft sites: ventricular endomyocardium (ENDO), left anterior descending coronary artery (LAD), right coronary artery (RCA).

Figure 2.

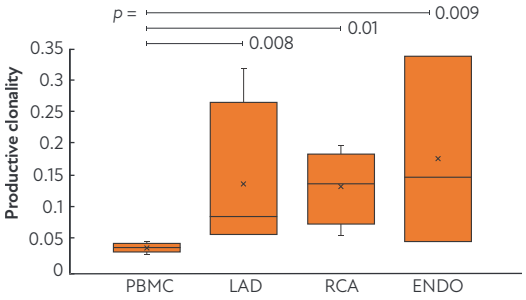

Figure 2. Box and whisker plot comparing IGH productive clonality of four transplant recipients across peripheral blood (PBMC) and three graft sites. Statistically significant differences were observed between peripheral blood and all graft sites.

Conclusions

- Significant BCR clonal expansion and increased SHM counts within patient allografts may contribute to the pathophysiology of CAV.
- Additional research is needed to fully ascertain the specific role of the B-cell mediated immune response during CAV.

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