Transplants and Grafts

Biomarkers to Predict Rejection in Vascularized Composite Allotransplantation

Vascularized composite allotransplantation (VCA) offers restoration of tissue function and aesthetic appearance by substituting lost or severely damaged tissues with a composite allograft when bodily injuries are irreparable with conventional reconstructive surgery. Despite the success of VCA procedures, toxicities may result from lifelong immunosuppression regimens and there is a high frequency of acute rejection in VCA recipients. These factors remain as major barriers to wider implementation of VCA as a treatment option for injured Service members. Novel biomarkers to predict acute or ongoing allograft rejection will allow for timelier clinical interventions and minimized exposure to immunosuppression medications.

Researchers at Brigham and Women's Hospital (Boston, MA) are characterizing potential clinical biomarkers for identification of rejection in VCA recipients. Gene expression profiling was conducted on allograft biopsies collected from a face transplant recipient during suspected antibody-mediated rejection (ABMR) and T cell-mediated rejection (TCMR) episodes and non-rejection time points. Seventy-nine (79) genes were found to be upregulated and one gene was downregulated in rejection biopsies compared to non-rejection biopsies. A principal component analysis identified 31 genes that contributed most to the variability between ABMR and TCMR episodes (*Win et al. 2017*; Figure 1). An upregulation of endothelial-associated genes including intercellular adhesion molecule 1, vascular cell adhesion molecule 1, and E-selectin was observed in biopsies collected during ABMR episodes, whereas genes associated with cytotoxicity including granzyme B were upregulated during TCMR. No diagnostic criteria have been established for ABMR in VCA to date, and it may be important to develop molecular markers that can distinguish ABMR and TCMR for improved clinical management following transplant.

> Molecular diagnostics may complement existing clinical, serological, and histological examinations for diagnosing allograft rejection in individuals who have undergone VCA.

These findings offer new insights into the mechanisms underlying VCA rejection and prospective biomarkers that may be useful in guiding the clinical care of VCA recipients.

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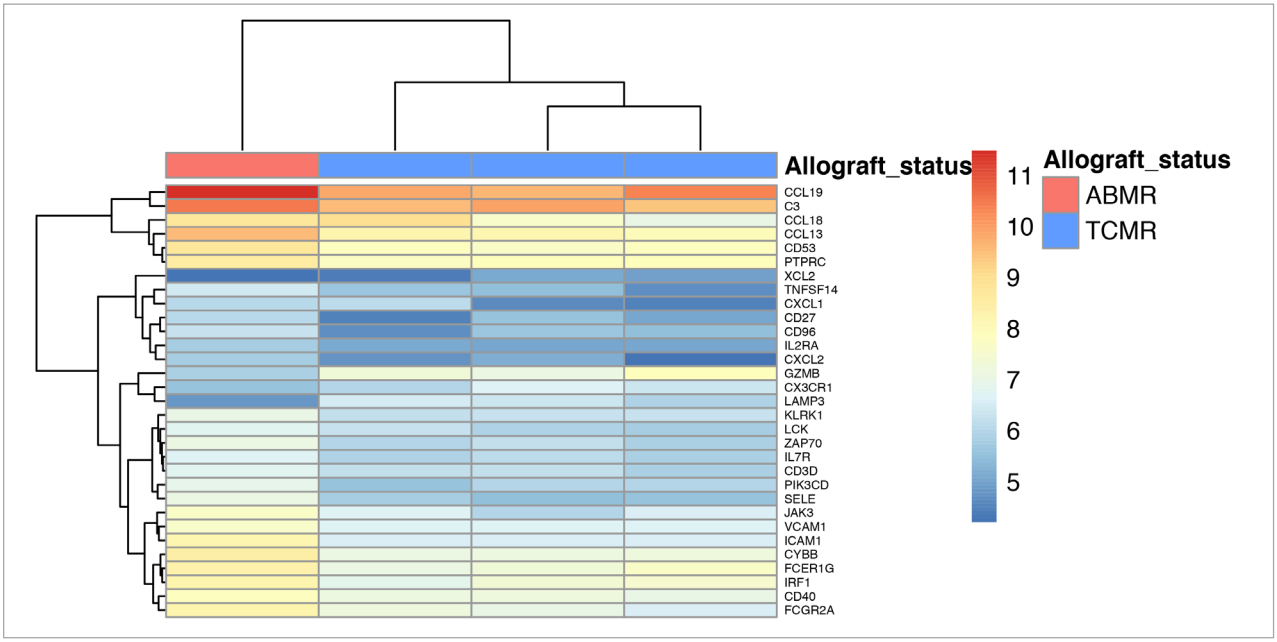

FIGURE 1: Heat map showing the expression of 31 genes that contributed most to the variability between antibody-mediated rejection (ABMR) and TCMR in a clinical face transplant. (Figure 6(B) from Toyinbo et al. (2016) used with permission from the authors)

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