



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Transplants and Grafts

The Identification of Matrix Metalloproteinase 3 as a Potential Diagnostic Marker Discriminating Non-severe from Severe Rejection in Face Transplantation

Vascularized composite allotransplantation (VCA) is a reconstructive strategy that offers severely injured Service members improved tissue function and aesthetic appearance compared to conventional reconstructive surgery. VCA involves the transplantation of multiple tissue types, such as a hand/limb or face, as a functional tissue graft to replace and repair irreparably damaged tissues. While VCA has been successful, numerous challenges remain preventing its wide-spread use. These include the necessity for long term immunosuppression that can lead to serious negative side effects and a high rate of acute rejection. Identification of non-invasive biomarkers for monitoring rejection episodes following VCA will improve the ability to diagnose and treat rejection in a timely fashion to improve VCA recipient outcomes.

Investigators from Brigham and Women's Hospital (Boston, MA) determined if non-invasive blood biomarkers can be identified to detect rejection earlier. Serum samples were collected from six VCA recipients that experienced no-rejection, non-severe rejection, and severe rejection. Protein expression profiling was conducted on all samples and over 1,000 proteins were analyzed. Using computational analysis, a signature of five proteins was able to discriminate severe rejection from both no- and non-severe rejection samples. Of the five proteins identified, the enhanced expression of matrix metalloproteinase 3 (MMP3) during episodes of rejection, was technically validated using a second method, confirming the utility of this protein as a diagnostic marker for the discrimination of rejection episodes. These promising results will require further evaluation using a larger independent patient cohort. The identification of novel biomarkers to predict and diagnose rejection earlier will allow for timelier clinical intervention, greater personalization of post-transplant care, and improved outcomes for VCA recipients.

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