Identifying Antigens Responsible for Antibody-Based Graft Rejection in Human Transplant Recipients

Bryan Ballif  
Biology

Antonio DiCarlo  
Surgery

Abstract:  
Successful tissue transplants are a wonder of modern medicine and can increase patient lifespans by several decades. Still, roughly one quarter of transplant recipients exhibit signs of graft rejection, due in part to antibody-mediated rejection (AMR). At the heart of AMR is the variability in the molecular makeup between the donor and recipient; the recipient rejects the transplant due to molecules (typically protein variants or their modifications) on the graft that the recipient doesn’t have. Thus, the recipient recognizes the graft as “non-self” and generates antibodies to these “foreign” antigens—ultimately the graft fails. Several proteins are known to cause rejection and are the basis of pre-screening protocols to match donors and recipients. However, AMR is also caused by unknown antigens that if identified could produce more powerful screening methods and anti-AMR therapies given AMR-dependent graft failure can take years, while antigen identification may, in some cases, take only months. It is proposed to use pre-transplant and post-transplant sera from ten graft recipients showing signs of AMR to enrich for and identify by mass spectrometry the proteins harboring the antigens responsible for the rejection. This is a novel collaboration between UVM PIs Ballif (Biology) and Di Carlo (Surgery).