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Identifying TCR blocking HLA specific antibodies as potential therapeutics in achieving transplant tolerance

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The adaptive immune system provides highly specific responses and long-lasting protection to antigens. This is achieved by T cell mediated (cellular immunity) immune system and the antibody mediated (humoral immunity) immune system. However, the immunological paradox of transplantation implies that T cells and antibodies targeting Human Leukocyte Antigens (HLAs), termed allo-reactive T cells and allo-antibodies, are the key factors for a gradual deterioration in graft function or chronic rejection. On the other hand, some reports have shown that allo-antibodies were detected in some long-term graft survivors and suggested that they have a blocking function, decreasing T cell activation and promoting graft tolerance. From an immunological point of view, some HLA epitopes might be more immunogenic and some alloantibodies more pathogenic, thus more likely to induce graft rejection. Therefore, the role of allo-antibodies in transplantation remains unclear and more research is needed to effectively evaluate the underpinning mechanisms of graft rejection. This project focuses on elucidating the effect of HLA-specific antibodies on antigen-specific syngeneic specific T cells and HLA-specific allogeneic T cells and investigating whether these antibodies can affect TCR signaling by blocking TCR interaction with HLA. To this end, we have generated allo-reactive T-cell lines from healthy donors and specific HLA restricted T cells responding to the immunodominant epitopes of human Epstein-Barr Virus (EBV). Future work encompasses identifying the effect of anti-A*1101 monoclonal antibody on A*1101-restricted antigen-specific and allo-reactive T cells. Since successful transplantation is usually achieved by preventing the activation of T cells by administering immunosuppressive drugs, this project may inspire us how to improve transplantation outcome by using HLA-specific antibodies as potential therapeutics in achieving transplant tolerance.

Biography

Maryam Hamidinia has received her BSc in Medical Laboratory Science from Shiraz University and her Masters in Immunology, University of Jundishapour, Iran. She has then joined Shiraz Institute for Cancer Research and focused on protein biomarkers in cancer. Currently she is a PhD student in Professor Nicholas Gascoigne's lab at NUS and focusing on alloreactivity and allotransplantation.

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