Circulating tissue specific exosome profiles for noninvasive monitoring of immunologic rejection in transplantation

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Statement of the Problem: Organ/tissue transplantation remains the only life-saving, curative therapy in patients with end stage diseases of the heart, liver, kidney, and lungs. Transplant patients are placed on obligatory immunosuppressive medications to prevent organ rejection, thus placing them at higher risk for malignancies and infectious complications. Rejection and immunosuppression-related complications remain the primary causes of morbidity and mortality in transplant patients. Yet to this date, there is a critical need for development of biomarkers for noninvasively monitoring rejection. We proposed that circulating exosomes, microvesicles carrying tissue-specific nucleic acids and proteins, reflect condition specific changes imposed on the transplanted tissue. If so, transplant tissue specific exosome profiling would constitute a novel biomarker platform for monitoring transplant rejection. We studied this concept in animal models of islet, heart, and lung transplantation, and further validated its translational potential in clinical setting.

Findings: In animal models of islet and heart transplantation, we demonstrated that circulating transplant tissue specific exosome quantitative and cargo profiles are significantly decreased early in the acute rejection process. This change was noted to occur in a time sensitive manner, before histological evidence of rejection/ injury to the transplanted tissue. Further, in clinical islet transplantation, transplant islet specific exosomes were reliably tracked in 4 patients over long term follow-up of over 5 years, suggesting that transplant exosomes can be utilized for noninvasive surveillance in the clinical setting. In addition, in heart transplant patients (n=5), we demonstrated that circulating donor heart specific exosomes can be reliably tracked in the perioperative setting.

Conclusions & Significance: Circulating transplant tissue specific exosomes accurately herald early acute rejection in animal models of transplantation. These potential noninvasive biomarkers can also be reliably tracked in the clinical setting. Further investigations may reveal the noninvasive diagnostic potential of transplant tissue specific exosome platform.

Speaker Biography

Prashanth Vallabhajosyula received his Bachelor of Science and Masters of Science in molecular biophysics and biochemistry, along with his Doctor of Medicine degrees from Yale University, New Haven, CT. He completed his residency in general surgery at Johns Hopkins Hospital, Baltimore, MD. During this period, he did a clinical fellowship in upper gastrointestinal surgery at Oxford-Radcliffe Hospitals, Oxford, United Kingdom. He attended the Hospital of University of Pennsylvania for a fellowship in cardiothoracic surgery, and completed a sub-specialization year in aortic surgery, along with endovascular and minimally invasive techniques. His surgical interests are in aortic surgery, endovascular surgery and thoracic organ transplantation.

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