THE HARTWELL FOUNDATION

2018 Individual Biomedical Research Award

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Acoustic Device to Prevent Antibody Mediated Organ Transplant Failure

Solid organ transplantation has benefitted over 50,000 children in the U.S. since the late 1980s. Alarmingly, in an era of immense scarcity of available organs, 50% of transplanted organs are lost by 10 years post-surgery due to antibody-mediated rejection. There is currently no effective way to prevent this type of rejection. Most children requiring transplantation present with congenital malformations leading to organ failure in infancy and early childhood and therefore, undergo numerous medical interventions before transplantation. After transplantation, the adverse development of detrimental donor specific antibodies occurs over time. The antibodies permanently damage the transplanted organ, resulting in organ failure and a 70% increased risk of mortality. A more effective approach to limit antibody-mediated rejection is needed to increase the life span of recipients, reduce re-transplantation rates, and increase access to life-sustaining organ transplantation. Moreover, any approach must consider that infants and young children with solid organ transplantation are chronically immunosuppressed and particularly vulnerable to potentially life-threatening complications. Existing methods to limit antibody-mediated rejection focus on antibody removal and are based principally upon apheresis, a blood exchange device in which the plasma is first removed from the body, with the antibodies removed in a secondary step by filtration or as a result of their affinity to certain materials, before the treated plasma is returned to the donor. However, in children the large required extracorporeal volume of blood in current apheresis machines can cause low blood pressure and require a blood transfusion that will stimulate unfavorably, more antibody production; where exposure to synthetic materials may increase the risk of allergic reactions; and where because the methodology is not targeted to donor specific antibodies may remove other desirable antibodies protective against infection. To overcome these limitations for pediatric applications, I discovered a way to deploy sound waves to separate antibody and blood cell components in a scalable device that requires a very small volume of blood (e.g., 10 mL), and that will remove effectively only donor specific antibodies. The device will be tested using pediatric human and rat blood samples with high levels of antibody, as well as in a living rat transplant model with elevated levels of donor specific antibodies. I will evaluate two approaches for presentation of donor specific antigens to the circulating blood to "trap" donor specific antibodies, including removal of donor specific antibody from pediatric transplant recipients that have experienced antibody-mediated rejection and thus harbor elevated antibody levels. If I am successful, my acoustic apheresis device will transform the lives of hundreds of thousands of children with solid organ transplantation by providing the means to overcome antibody-mediated rejection.