Abstract Type : Oral Presentation
Abstract Submission No. : F-008570

Single-cell RNA Sequencing Analysis of Immune Cell Population Dynamics from Peripheral Blood in Pig-to-non-human Primate Islet Xenotransplantation Treated with Clinically Applicable Immunosuppressants

Yuji Lee[1], Ji Hwan Moon[2], Jong-Min Kim[3], Daesik Kim[4], Hyun Je Kim[5], Chung-Gyu Park[5]

[1]Department of Department of Microbiology and Immunology, Seoul National University, Republic of Korea
[2]Department of Samsung Genome Institute, Samsung Medical Center, Republic of Korea
[3]Department of Department of Animal Health, Cheongju University College of Health and Medical Sciences, Republic of Korea
[4]Department of Department of Microbiology and Immunology, PB Immune Therapeutics Inc, Republic of Korea
[5]Department of Transplantation Research Institute, Seoul National University Medical Research Center, Republic of Korea

Introduction: Over the course of the last two decades, our research has been dedicated to exploring the potential of porcine islet xenotransplantation as a therapeutic option for patients with type 1 diabetes. At present, pancreatic islet xenotransplantation is on the brink of entering phase 1 clinical trials in Korea. The successful implementation of these trials relies heavily on the establishment of an effective immunosuppression protocol capable of accommodating various genetically modified pigs or islets in clinical settings. During our preclinical investigations, we have evaluated the use of Belimumab as an immunosuppressive agent, with a specific focus on inhibiting B cell activation.

Methods: In this study, porcine islets were transplanted into Rhesus monkeys (Macaca Mulatta, N=4) with an immunosuppressant regimen. Immunosuppression was induced with anti-thymocyte globulin (ATG), adalimumab, anankinra, tocilizumab, and tacrolimus. The maintenance regimen consisted of abatacept, belimumab, and tofacitinib. Blood samples were collected from the monkeys before and after the regimen. To gain a comprehensive understanding of the dynamic behavior of circulating immune cells, we have employed the single-cell transcriptome analysis method. Currently, we are actively analyzing the data gathered from this study.

Results: Following administration of Belimumab, a notable reduction was observed in the proportions of atypical memory B cells and naive B cells in the blood, while the decrease in naive B cells did not achieve statistical significance. The proportions of switched memory B cells and short-lived plasma cells remained unaffected by the Belimumab. These findings are consistent with earlier investigations utilizing Belimumab or BAFFR inhibitors in human.

Conclusion: Our findings demonstrate that the effect of Belimumab is conserved between humans and rhesus monkeys, providing further support for the use of Belimumab as a immunosuppressant for xenotransplantation. However, this result is demonstrating only the ratio of B cell subsets, and further analysis of the qualitative modification in each subset is needed.