ATW 2022 Nov. 17(Thu)~19(Sat), 2022
CONRAD SEOUL, Seoul, Korea

Submission No.: PG12-9999
Session : Postgraduate Course 12 (Basic)
Date & Time, Place : November 17 (Thu), 15:00-16:30, Room 6F-1
Session Title : Immunology of Xenotransplantation

Macrophages in xenotransplantation

Shuji Miyagawa, Takuji Kawamura, Hiroomi Okuyama, Akira Maeda
Dep. of Surgery, Osaka University Graduate School of Medicine, Japan

At the end of 2021, three pig kidney transplants were performed, and pig heart transplant was performed in 2022, beginning the clinical practice of new xenotransplantation.

Initially, the reaction of the complement system, a liquid factor of innate immunity, and part of the coagulation system attracted attention, and now gene-edited pigs, such as "10-GE", have been created to express complement regulatory factors (CRPs) and anticoagulation factors, which have overcome hyperacute rejection. The next issue is to regulate the innate immune cells, such as natural killar (NK) cells, monocytes/macrophages,and dendritic cells, etc.,one of which, NK cells have been the focus in the past, with studies on regulation by HLA class-Ib molecules and remodeling of the cell surface glycoantigens. In this review, we focus on the regulation of macrophage, because,it is well known that macrophages mediate robust immune responses in xenografts. On the other hand, macrophages also express various inhibitory receptors that regulate their immune function.

Recent studies,including ours, have shown that overexpression of inhibitory ligands on porcine cells leads to phosphorylation of tyrosine residues on intracellular immune receptor tyrosine-based inhibitory motifs (ITIMs) on macrophages, leading to the suppression of xenogenic rejection by macrophages. In general, the focus of this field has been on the regulation of CD47-SIRP , but there are still many problems and little further progress has been made. Therfore, we have focused on the ITIM-containing receptors, such as CD200R, NKG2A, ILT2/4, CD155, etc., which are involved in inhibitory signaling in macrophages. We believe that suppressing the innate immune response by macrophage will lead to the creation of new type of the genetically engineered pigs.