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Production of transgenic cloned mini-pigs expressing Human Leukocyte Antigen-G1(HLA-G1) gene by Nuclear Transfer

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Human natural killer(NK) cell-mediated response plays an important role in xenograft rejection. In the case of pig to human xenotransplantation, it has been suggested that NK cells are involved in delayed-type rejection, which is characterized by pig endothelial cell(PEC) activation, direct lysis, and secretion of proinflammatory cytokines. NK cell activation can be a direct barrier to the potential use of pig organs for human xenograft transplantation. Therefore, the importance of suppressing NK cell activity on pig-to-human xenografts. Expression of HLA-G1(non-classical major histocompatibility complex class I molecules) inhibits the cytotoxic activity of NK cells and has been proposed as a potential solution to overcome NK cell-mediated xenogeneic cytotoxicity in PEC.

In this study, we transfected the HLA-G1 gene into mini-pig fetal fibroblasts to produce two HLA-G1 clonal cell lines. The presence of the HLA-G1 gene in clonal cell line was confirmed by PCR, flow cytometry, Western blot, Immunohistochemistry assay. We used these cell lines to produce cloned pigs by nuclear transfer(NT). Porcine fibroblasts derived from 35 day cloned fetus also showed characters similar with those of clonal cell lines. The rate of NK 92MI cytotoxicity of porcine fibroblast was significantly reduced to 33.1% ± 10.0% compared to the control 95.6% ± 16.5%.

In conclusion, transgenic cloned pigs expressing HLA-G1 were produced by NT for the first time. It is expected that these pigs would be used to overcome the NK cell-mediated rejection in xenotransplantation.

Key words: *NK cell, HLA-G1, Nucler transfer(NT), transgenic*