Basic Research of Xenotransplantation

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【Outline of survey】

Recent progress of transplantation network, HLA typing, organ preservation technology, surgical protocol and pharmacological immunosuppression resulted in successful human to human allotransplantation medicine. Then, shortage of human donor organ becomes critical issue of transplantation medicine worldwide.

In order to overcome this issue, approach of regenerative medicine is expected in Japan. It is thus promising strategy to regenerate self organ from ES cells and to use artificial organ. However it is not yet achieved to provide clinically available donor organ by means of this strategy, and it would takes times to get goal. Alternative approach is xenotransplantation to overcome shortage of donor organ. Successful xenotransplantation would present an unlimited source of donor organs and cells for transplantation surgery.

A miniature swine attracts attention as important medical service resources for resolving a lack of donor organ. A *Clawn* miniature swine has been developed in Kagoshima University, and maturity individual weight characteristic of physiology of anatomy is nearer to humans than in comparison with in other mini-swine class. Development of a *Clawn* miniature swine with gene alteration must contribute for xenotransplantation research.

Our goal is to establish an international institute for a frontier research and education center of xenotransplantation in Japan.

【Expected results】

1) Production of *Clawn* miniature swine with gene alteration.

2) To identify *Porcine Endogenous Retroviruses (PERV)* genome and PERV Expression in *Clawn* miniature swine:

- Copy number of PERV
- How many functional clone of PERV exist in *Clawn* miniature swine
- Expression of PERV in various stage of *Clawn* miniature swine development
- Expression of PERV in various tissue or organ of *Clawn* miniature swine

【References by the principal researcher】

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(2)High mobility group protein 1(HMGB1) quantified by ELISA with a monoclonal antibody that does not cross-react with HMGB2. Maruyama I, et al. *Clin Chem*. 49:1535-1537, 2003

(3)Regulatory dendritic cells protect mice from murine acute graft-versus-host disease and leukemia relaps. Sato K, Baba M, Matsuyama T, et al. *Immunity* 18:367-379, 2003

(4)Quantitative analysis of telomerase and telomerase-reverse transcriptase gene expression in bovine nuclear transferred embryo. Yoshida M, et al. *Theriogenology*, 57:645, 2002

(5)Endothelial cells potentiate oxidant-mediated Kupffer cell phagocytic killing. Takao S, et al. *Free Radical Bio Med* 24:1217-1227, 1998

【Term of project】 FY 2005 - 2009 | **【Budget allocation】** 78,400,000 yen

【Homepage address】 none