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Session Title : Immunology of xenotransplantation

The immunosuppression protocol for xenotransplantation of Gal KO/hCD55-59 porcine islets reverse the diabetic rhesus

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The immunosuppression protocol for xenotransplantation of GTKO/hCD55-59 porcine islets reverse the diabetic rhesus Wei Wang The Institute for Cell Transplantation and Gene Therapy, Central-South University **Background** The safety and efficacy of wildtype porcine islet xenotransplantation has been proved in our produced clinical trials 1999-2005 and 2012-2017. Efficacy data was shown partial function of islet graft, but not shown insulin independent result. Some groups have shown insulin-independent results in the diabetic primate models via large-dose gene-edited porcine islets. There must be solutions to 3 critical issues before the initiation of porcine islets clinical trial: Safety donor pig, Clinical-approved immunosuppression protocol, Reasonable range of porcine islets dose. **Material and Method** Ethics and Regulatory： The project was approved and funded by The National Ministry of science and technology Donor pigs were adult GTKO/hCD55-59 gene-edited pigs (Xenolife, China), originated from the PERV-C negative pig, XENO-1 DPF pigs were qualified by National Institute for Food and Drug Quality Control Animals were treated as the Chinese Animal Welfare Regulation Quality of Islets and diabetic rhesus model Four male rhesus diabetic models were induced with STZ, 3 months before pig islet transplantation. Average insulin dose: 14 IU/day. Quality of adult porcine islets product Islets yield: 3000 IEQ±293/g pancreas, viability: 89±8.3 %, Purity: 77±11.7 % Pig islets were infused into diabetic rhesus via catheterized portal vein. Two rhesus monkeys（lower dose group) were transplanted with 12,750 IEQ /kg, and 15,700IEQ/kg adult porcine islets. Another 2 rhesus monkeys （higher dose group) were transplanted 39,750 IEQ /kg, and 41,400 IEQ/kg adult porcine islets respectively. Immunosuppressive Protocol **Results** The lower dose group showed a partial function of graft, with average insulin requirement reduced by 70%, and HbA1C returned to normal. The higher dose group got insulin-independent results, normalized HbA1C, and porcine C peptide was detected (710 pmol/L, 30 days post-Tx) . The body weight of recipient monkeys kept stable, or a little bit increase. All recipients survived until to end of the research(more than 360 days). No infectious disease or neoplasm happened in all recipients. PERV-C was tested in all recipients on the 100th day and the 360th day post-Tx. A negative result was shown in all recipients. **Summary** The adult GTKO/hCD55-59 gene-edited porcine islets xenotransplantation could

reverse the hyperglycemia condition of the diabetic rhesus, result was number dependent. This clinical immunosuppressive protocol could get insulin-independent results in the high-dose group with a practicable number of islet graft. No xenotransplantation-related complications occurred.