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Modulation of Immunosuppression for Long-Term Graft Survival in Lamellar Pig-to-Monkey Corneal Xenotransplantation from the Genetically Engineered Pig Model

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Introduction: In this study, the following study was conducted to find out whether immunosuppression control through antibiotic eye drops and subconjunctival injection in partial thickness corneal transplantation using different types of medi pigs could affect the difference in graft survival.

Methods: The transgenic donor pigs used were Gal-knockout (GTKO)+membrane cofactor protein (CD46) in one recipient and GTKO + CD46 + thrombomodulin (TBM) in the other. For minimal immunosuppression subconjunctival injection of dexamethasone (1.5 mg/0.3 ml) was done immediate postoperatively and eyedrops of 0.5% levofloxacin and 1% prednisolone acetate were applied 4 times a day for 1 week, gradually tapered and once a day after 1 month. Subconjunctival injections such as dexa were additionally administered to subjects with corneal opacity and rejection. No eye drops were applied after 2 months.

Results: Compared to the GTKO group, the GTKO+CD46 group tended to increase the corneal graft survival rate, whereas the GTKO+CD46+TBM group showed a tendency to decrease the corneal graft survival rate. In particular, in each NHPs that showed a long-term survival rate, graft survival tended to increase in individuals who received a lot of subconjunctival injection, and corneal opacity such as graft rejection was observed in the GTKO+CD46 group than in the GTKO+CD46+TBM group showed a decreasing trend. In addition, in the GTKO+CD46 group, the inflammatory response in graft tissue cells was not severe in the long-term surviving individuals.

Conclusion: Therefore, it is thought that controlling immunosuppression through eye drops with antibiotics requires subconjunctival injection or systemic immunosuppressive control rather than weak immunosuppression. Although our teams partial layer survival results hold the worlds longest transplant survival record, it is necessary to develop various knock-in suitable source animals such as CD46 based on GTKO and control immunosuppression through continuous experiments and research. It is thought that this may affect transplant long-term survival.