Xenotransplantation: Prevention of Human Natural Killer Cell-Mediated Immune Responses

Summary / Zusammenfassung

Pig-to-human xenotransplantation has the potential to overcome the current organ shortage in human allotransplantation. However, immunological barriers are not easily overcome in this species combination. The role of humoral immunity in causing hyperacute rejection of such discordant xenografts has been studied extensively, emphasizing the importance of human natural antibodies (nAb) directed mainly against Gal alpha1-3Gal (a-Gal), a carbohydrate epitope present on all porcine cells but not on human cells. Prolonged xenograft survival has been achieved by strategies to circumvent hyperacute rejection. These experiments demonstrated that cellular responses also play an important role in xenograft rejection which is in part characterized by recognition, infiltration, and damage of grafts by various leukocyte subsets. An increasing body of evidence indicates that polymorphonuclear neutrophils, natural killer (NK) cells and cytotoxic T lymphocytes all are involved in the rejection of xenogeneic grafts. The goal of this study is to prevent cellular immune responses mediated by human NK cells against porcine endothelial cells (EC), the primary location of immune responses against vascularized grafts. Employment of strategies aimed at preventing NK cell-mediated xenograft responses in combination with other strategies aimed at preventing hyperacute rejection and T cell-mediated responses may lead to the clinical feasibility of pig-to-human xenotransplantation.

Weitere Informationen unter http://www.dim.uzh.ch/lti/research.html

Publications / Publikationen

Forte P*, Lilienfeld BG*, Baumann BC, Seebach JD. Human NK cytotoxicity against porcine cells is triggered by NKp44 and NKG2D. *Both first authors contributed equally
Rieben R, Seebach JD. Xenograft rejection: IgG1, complement, and NK cells team up to activate and destroy the endothelium.
Matter-Reissmann UB, Sonntag KC, Gilli UO, LeGuern C, Schneider MK, Seebach JD. Human Fas-ligand expression on porcine endothelial cells does not protect against xenogeneic NK cytotoxicity.
Matter-Reissmann UB, Forte P, Schneider MK, Filguiera L, Groscurth P, Seebach JD. Xenogeneic NK cytotoxicity against porcine endothelial cells is perforin/granzyme B dependent and not inhibited by Bcl-2 overexpression.


Brander C, Matter-Reissmann UB, Jones NG, Walker BD, Sachs DH, Seebach JD. Inhibition of NK cell-mediated cytotoxicity by exposure to ammonium chloride.

Matter-Reissmann UB, Forte P, Seebach JD. Human NK cells lyse porcine endothelial cells via the perforin/granzyme B pathway.

Weitere Informationen unter http://www.dim.uzh.ch/lti/publications.html

Keywords / Suchbegriffe
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http://www.dim.uzh.ch/lti/index.html

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