

Title (en)

PREVENTION OF HYPERACUTE REJECTION IN PIG TO PRIMATE ORGAN TRANSPLANT

Title (de)

VERMEIDUNG DER HYPERAKUTEN ABSTOSSUNG VON ORGANTRANSPLANTATEN VON SCHWEIN ZUM PRIMATEN

Title (fr)

PREVENTION DU REJET HYPERAIGU DANS LES GREFFES D'ORGANES PORC-PRIMATE

Publication

**EP 0759763 A4 19970730 (EN)**

Application

**EP 95919185 A 19950512**

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Abstract (en)

[origin: WO9531209A1] The invention provides a method to prevent or ameliorate a hyperacute rejection reaction which would normally occur after transplant of a pig organ to a primate recipient, including a human recipient. Normally, anti-pig antibodies in the blood of the recipient will bind to pig antigens on the endothelial cells of the grafted pig organ, and activate the complement cascade causing necrosis of the pig organ within minutes to hours. The invention method involves passing at least 2-3 plasma volumes of the primate recipient's plasma over a sterile and pyrogen-free column coupled to protein which binds to and thereby removes immunoglobulin from the recipient's plasma, and then transplanting a pig organ to the primate recipient. The column treatment is preferably repeated on several days before and after transplant, and thereby prevents or ameliorates the hyperacute rejection reaction by removing anti-pig antibodies from the recipient's plasma. The method can remove greater than 99 % of the primate recipient's total IgG and greater than 99 % of the recipient's total IgM. The method also effects a 50-500 fold reduction in anti-pig immunoglobulin, and a 15-60 % reduction in potential complement activity. This invention also provides immunoglobulin-depleted human plasma suitable for infusion to a human recipient of a pig organ transplant.

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Citation (search report)

- [X] WO 9303735 A1 19930304 - ALBERTA RES COUNCIL [CA], et al
- [X] EP 0269279 A2 19880601 - IMRE CORP [US]
- [E] WO 9531727 A1 19951123 - BAXTER INT [US]
- [X] SHAPIRO R. ET AL.: "Immunodepletion in Xenotransplantation", JOURNAL OF INVESTIGATIVE SURGERY, vol. 3, no. 1, 1990, pages 39 - 49, XP000673902
- [X] ORIOL R ET AL: "Carbohydrate antigens of pig tissues reacting with human natural antibodies as potential targets for hyperacute vascular rejection in pig -to-man organ xenotransplantation.", TRANSPLANTATION (BALTIMORE) 56 (6). 1993. 1433-1442, XP000674259
- [X] NEETHLING F A ET AL: "Protection of pig kidney (PK15) cells from the cytotoxic effect of anti- pig antibodies by alpha-galactosyl oligosaccharides.", TRANSPLANTATION (BALTIMORE) 57 (6). 1994. 959-963, XP000674257
- [DX] DANTAL J ET AL: "Effect of plasma protein absorption on protein excretion in kidney-transplant recipients with recurrent nephrotic syndrome.", NEW ENGLAND JOURNAL OF MEDICINE 330 (1). 1994. 7-14, XP000674269
- [A] PALMER A ET AL: "REMOVAL OF ANTI-HLA ANTIBODIES BY EXTRACORPOREAL IMMUNOADSORPTION TO ENABLE RENAL TRANSPLANTATION.", LANCET 1 (8628). 1989. 10-12, XP002031721
- [DA] LOVELAND B E ET AL: "CD46 MCP CONFER PROTECTION FROM LYSIS BY XENOGENETIC ANTIBODIES.", XIVTH INTERNATIONAL CONGRESS OF THE TRANSPLANTATION SOCIETY, PARIS, FRANCE, AUGUST 16-21, 1992. TRANSPLANT PROC 25 (1 BOOK 1-2). 1993. 396-397, XP000673901
- [A] FISCHEL R J ET AL: "CARDIAC XENOGRAFTING IN THE PIG-TO-RHESUS MONKEY MODEL MANIPULATION OF ANTIENDOTHELIAL ANTIBODY PROLONGS SURVIVAL.", J HEART LUNG TRANSPLANT 11 (5). 1992. 965-973, XP000673900
- [A] BENSINGER W.: "Plasma exchange and immunoabsorption for removal of antibodies prior to ABO incompatible bone marrow transplant", ARTIFICIAL ORGANS, vol. 5, no. 3, August 1981 (1981-08-01), pages 254 - 258, XP000673998
- [PX] LEVENTHAL J R ET AL: "Removal of baboon and human antiporcine IgG and IgM natural antibodies by immunoabsorption: Results of in vitro and in vivo studies.", TRANSPLANTATION (BALTIMORE) 59 (2). 1995. 294-300, XP000674258
- See references of WO 9531209A1

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