48. Immunobiology in the transplanted lung: experimental and clinical evaluations

219 Late-breaking abstract: Non specific IgG replacement in lung transplantation recipients with low IgG plasma levels: Effects on survival and bronchiolitis obliterans syndrome occurrence

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After lung transplantation, IgG plasma levels < 6 g/L are recorded in more than 50% of cases resulting in adverse events (JHLT 2001;71:242; Transplantation Française du Sang-Alsace, Strasbourg, France; 3Histocompatibility Laboratory, Etablissement de Transfusion Sanguine, Strasbourg, France).

Rationale: The ex vivo pulmonary perfusion is a suitable method of evaluation of lung ischemia reperfusion injuries (IRI). The role of the Cyclosporine A (CsA) in the prevention of IRI has been shown in different organs of several animal species but not clearly evaluated in lungs. Our objective was to evaluate the effects of CsA in ex vivo reperfused pig lungs.

Methods: 10 lungs were perfused with an extracorporeal perfusion circuit, and mechanically ventilated. CsA was administered before and during reperfusion procedure (either at 1 or 30 μM).

Results: Lungs treated by 30 μM of CsA had increased capillary pressure (Pcap), pulmonary vascular resistances (PVR), lung permeability to proteins, IL-1β and TNF alpha concentrations in bronchoalveolar lavage (BAL). IgM of CsA seemed to have no effect compared to control group.

Discussion: CsA, at the concentration of 30 μM, seems to be deleterious in lung IRI. The hemodynamic effects of CsA may explain these results.

222 Comparison between SCOT-15® and Perfadex® as lung preservation solutions

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Objectives: SCOT-15® is a low K+ solution including polyethylene glycol (PEG) as a colloid for protection of endothelium. PEG was demonstrated to have immunomucocamouflage properties and has been tested for kidney, pancreas and liver preservation. This study compares the properties of SCOT-15® for lung preservation with Perfadex® as a gold standard.

Methods: Two groups of 6 pigs each were compared. After 2L cold pulmonary with either Perfadex® [P] or SCOT-15® [S], lungs were stored cold for 4 hours. Peripheral lung biopsies were taken for High Resolution Magic Angle Spinning (HRMAS) detection of colloids. Lung function was assessed in an ex vivo perfusion using a perfusion apparatus. Pulmonary arterial and resistance were calculated.

Results: PVR was significantly lower in [S] compared to [P] (p=0.04). There were no differences in PO2, mAwP, W/D (p=0.24) and W/D (p=0.006). HRMAS spectra showed presence of PEG in peripheral lung tissue in [S].

Conclusion: Anti-HLA immunization is related to early onset of BOS. Specific antibodies probably lead to humoral rejection. Non specific antibodies indicated sensitized status with increased incidence of ACR.

221 Effect of cyclosporine A in ex vivo repurified pig lungs

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Progressive epithelium degradation reached 77 ± 10% (p < 0.05). Inhibiting MSK1 is therefore a potential strategy to help combat rejection after LTx.

A new mouse model of bronchiolitis obliterans syndrome


Background: Long-term survival after lung transplantation (LTx) is hampered by Bronchiolitis Obliterans Syndrome (BOS), morphologically presented by OB. Since the pathogenesis is still not fully understood and the prognosis remains poor, a good animal model is indispensable.

Aim: The development of a new model of BOS after LTx.

Methods: C57Bl6 mice underwent LTx with BALB/C donor lungs and were sacrificed at 2, 4, 6, 10 and 12 weeks after LTx. Staining with H&E and Sirius Red (not shown) were performed.

Results: Histology showed two types of lesions. Type I lesions are characterized by lymphocytic bronch(iol)itis and functional lung parenchyma. These lesions seem to resolve over time. Type II lesions are demonstrated by fibrotic plugs growing into the airway lumen, resembling true BO lesions in humans. The surrounding parenchyma however is not functional.

Conclusions: Allograft LTx in mice mimics human histology of BO, optimisation of this model will open new perspectives to study pathogenesis of chronic rejection after LTx.

Development of a novel model of obliterative bronchiolitis following orthotopic lung transplantation in the rat

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Background: Transplantation (Tx) is the only effective treatment for several end-stage lung diseases, but long-term survival after Tx is precluded by the development of obliterative bronchiolitis (OB). The specific etiology and pathogenesis of OB are not fully understood. Animal models could be crucial to elucidate the immunological and non-immunological pathogenetic mechanisms leading to OB, to identify early markers and to test effectiveness of new treatments.

Methods:  Left lung allografts from Lewis rats were orthotopically transplanted into Fisher 344 rats [n=19]. Animals were sacrificed at day 30 [group A, n=6] or day 90 [group B, n=6; C, n=4; D, n=3] post-transplantation. In animals from group C and D, cyclosporine A (CyA) was administered from day 1 to 7 or from day 7 to 14, respectively. Following HE-staining, lung rejection was graded according to the working formulation of ISHLT. The presence of circulating donor-specific (DSA) antibodies was determined by flow cytometry.

Results: Acute rejection (AR) occurred in 25 to 33% of the animals in the different groups. OB occurred in 17% of animals in group A, in 33% of animals in group B and D, and in 75% of animals in group C. High levels of DSA IgG were observed in all cases of AR and, to a lower extent, in all animals with OB. Furthermore, early administration of CyA reduced the levels of DSA but did not prevent OB occurrence.

Conclusions: A novel model of pulmonary OB was developed in the rat. To obtain a reproducible onset of OB, short-term and sub therapeutic CyA administration appears indispensable, at least in our species combination. Furthermore, a 90-day postoperative period is required for OB to take place.

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