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## P.8 The new immunosuppressant Leflunomide appears to be a potent inhibitor of humoral xeno-sensitization

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Success in organ transplantation between phylogenetically discordant species is primarily limited by the presence of natural xenophile antibodies (NXA). Therefore the aims of our study were (a) to further analyze the kinetics of NXA in the xenogeneic model «rat-anti-human» and (b) to manipulate their production by the new B-lymphocyte immunosuppressive drug Leflunomide (LF). Antibodies (IgG, IgM) binding to human peripheral blood lymphocytes (PBL) were quantitated by immunofluorescence (FACS-analysis). Results: (1) Normal LEW rats contain detectable amounts of NXA against human PBL (IgM > > IgG). (2) NXA production strongly increases and switches from IgM to IgG after sensitizing LEW rats with $2 \times 10^7$ human PBL (i.p.). (3) Three mg/kg LF, given from day −4 to day +10 (daily i.p.) suppress NXA production in sensitized LEW rats ($2 \times 10^7$ human PBL on day 0) in a dose-dependent manner. This significant suppression is maintained during the period of drug application. Conclusions: (I) LF appears to be very potent new immunosuppressive drug for prevention of NXA production after xenogeneic sensitization. (II) Presumably LF-treatment for suppression of the xenograft-elicited production of NXA can be combined with the elimination of pre-existing NXA, thus eliminating a major barrier for xeno-transplantation.

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## P.9 Effects of cyclosporine administration to CB17 scid/scid reconstituted with human mononuclear leukocytes

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CB17 scid/scid *(scid)* mice accept human peripheral blood mononuclear cells (huMNC) and which remain functional in the animals for about 25 weeks after transfer. It is possible to detect human immunoglobulins (2–3 mg/ml) in the sera of the mice subsequent to the transfer. In order to determine the influence of immunopharmacological agents we tested this system using the known immunosuppressive agent Cyclosporine A (CyA). After i.v. injection of CyA the serum level of human immunoglobulins show a significant decrease compared to untreated animals. Therefore, it seems that the huMNC transferred to *scid* underlie functional regulation and that this system is useful for studying immunopharmacological effects of drugs.