in distribution pattern like found in normal lymphoid organs. Additionally, *in vitro* assays showed that the freshly isolated human cells from the scid-hu chimeras were able to respond to exogenous stimuli.

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M.16 Down-regulation of xenophile antibodies by specific immunosuppressive protocols to facilitate xenogeneic organ transplantation

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Xenotransplantation requires down-regulation of natural and graft-induced xenophile antibodies (NXA and XA) in the recipient to overcome hyperacute graft rejection. In the experimental combination «rat-anti-human» LEW rats received xenoantigen (5×10^6 human PBL i.p. on day 0) in combination with 15-deoxyspergualin (15-DOS: 2.5 mg/kg; 14 days), very successful in inhibiting kidney and skin allograft rejection, or with leflunomide (LF: 3 or 10 mg/kg; 10 days), a well tolerated new drug in treating experimental autoimmune diseases, or with cyclophosphamide (CY: 120 mg/kg; 6 days), known to be particularly effective in down-regulating B lymphocyte activity. Rat antibody titers were determined by standard flow cytometry. Results: (1) CY and LF, but not 15-DOS, suppress NXA in normal LEW rats (CY > LF). NXA-specific B cell clones remain immunologically responsive, as was tested by applying test xenoantigen on day +30. (2) In xenogeneically sensitized rats, in which antibody production switches from IgM to IgG, CY, LF and 15-DOS inhibit XA production significantly, when applied in close correlation to xenoantigen. CY is the most effective in down-regulating XA. (3) Repetition of the combined treatment (xenoantigen and drug) on day +30, performed with CY or 15-DOS, shows an impressive additional down-regulating effect of CY, but not of 15-DOS. This holds not only for XA, but also for NXA, which, as a product of presensitization, are known to be very difficult to suppress. Conclusions: The present approach, consisting of xenoantigen and individual drugs, appears to be very effective in down-regulating the antibody-mediated primary xenograft rejection. Further approaches should aim at combining well tolerated drugs, such as LF and 15-DOS, with a highly effective drug, such as CY in order to establish clinically attractive protocols.