However, the non-rejection group (n = 8) peaked already after 6 months (88 %), and then decreased rapidly to 28 %. In contrast, nearly all sera of the rejection crisis group (n = 12) remained positive after the peak at nine months for the whole period of observation. These results show a substantial difference in HLA antibody kinetics in patients with or without rejection crisis.

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M.3 The association of the specific lysis pattern of a NK line with the expression of the HLA-CW7 molecule

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The involvement of HLA molecules in the recognition and lysis by NK cells remains controversial. Some experimental models provide evidence for an association of NK lysis to the HLA-C locus and more precisely to a diallelic polymorphism based on two positions of the peptide binding cleft. All known HLA-C molecules can be divided into two families differentiated by the amino acids at positions 77 and 80. Lysis by some NK cells seems to follow allorecognition of the opposite homozygous phenotype, defined as the specificities NK-1 (Cw1, Cw3, Cw7, Cw8 sensitivity) and NK-2 (Cw2, Cw4, Cw5, Cw6 sensitivity) (Colonna et al. PNAS 89: 7983–7985, 1992). We generated a cytotoxic effector line with a $CD3^-$, $CD4^-$, $CD8^-$, $CD16/56^+$ phenotype from a normal blood donor heterozygous for this diallelic HLA-C polymorphism. The lysis pattern of this NK-like line is dependent on the expression of the HLA-Cw7 molecule. In the presence of HLA-Cw7 a target cell is not lysed whereas in the absence of HLA-Cw7 the target becomes sensitive. This phenomenon can be shown using Cw7 transfectants of HLA-class I negative cells and by segregation studies in the families. Moreover target cell recognition is influenced by EBV-associated genes which may cause either a qualitative or quantitative modulation of the molecule.

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M.4 Production of xenophile antibodies (XA) in type-I diabetic patients is strongly influenced by diabetes and/or dialysis

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Xenotransplantation of porcine islets of Langerhans is considered a promising therapy for type I diabetic patients. Hyperacute xenograft rejection, mediated by preformed XA, is one of the major immunobiological problems that has to be overcome. The question was whether diabetes and/or dialysis exert an additional effect on XA production compared to XA in healthy controls. Standard immunofluorescence staining of cryostat sections was carried out with sera from 32 healthy controls, 31 diabetic patients without dialysis (DIAB), 25 diabetic patients on dialysis (DIAB/DIAL) and 51 non-diabetic

patients on dialysis (DIAL) on porcine pancreatic tissue (Piétrain, PI, German landrace, GL, and Göttingen Minipig, GMP) in order to determine the binding pattern of XA in each serum. Results: (1) While only 60 % of all sera in the control group reacted positively on PI and GL pancreatic islet tissue with an antibody titer ≥ 1:8, the number of positive sera increased significantly in DIAB (78 %), DIAL (70 %), and DIAB/DIAL (73 %). (2) Comparing the three different pig races for human-anti-porcine islet reactivity, reactivity in DIAB, DIAL and DIAB/DIAL was significantly lower on GMP target tissue (PI 74 %, GL 73 %, GMP 59 %). However, this target tissue difference could not be detected in the sera of healthy controls (PI 61 %, GL 60 %, GMP 58 %). (3) XA in the above sera are of IgG isotype and show binding specificity for particular carbohydrate epitopes (e.g., melibiose-related oligosaccharides). Conclusions: The above data indicate, that diabetes and/or dialysis activate additional XA-producing B cell clones. However, this disadvantage can be overcome by using selected pig races or strains, e.g., GMP as islet donors.

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M.5 Distribution of extracellular matrix molecules and integrin receptors in human hepatic allografts during chronic rejection

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Recently it was demonstrated that extracellular matrix molecules and their receptors play an important role in tissue inflammation. Extracellular matrix interactions of graft cells as graft infiltrating leukocytes are unknown. The purpose of this study was to investigate the distribution of extracellular matrix molecules and their integrin receptors in human liver grafts during chronic rejection. Fifteen liver specimens diagnosed as chronic rejection were obtained at the time of retransplantation (3 months to 93 months after Ltx). Normal liver specimens were obtained from 3 liver resections and 3 cold perfused livers before transplantation. The expression of the integrin receptors VLA-1 through 6, CD51, and the extracellular matrix molecules fibronectin, collagen VI, laminin, tenascin and thrombospondin (TSP) was studied on cryostat sections using standard immunohistology. **Results:** *Expression in normal liver* – all of the molecules and integrin receptors except for TSP and VLA4 were found at the portal vascular endothelium. VLA-1, 5, CD51, fibronectin, collagen and tenascin were found on the sinusoidal endothelium. VLA-1 and 5 on the hepatocytes, VLA-2, 3, 6 and CD51 on the bile ducts. *Induction patterns on liver cells in chronic rejection* – The expression pattern at the portal vascular endothelium was the same as in normal liver, but stronger than in intensity. On the sinusoidal endothelium only VLA-2 was negative. VLA-1, 5, 6, CD51 and fibronectin were observed on the hepatocytes. VLA-2, 3, 6 and CD51 were present on the bile ducts. Portal interstitial cells and Kupffer cells showed a broad positivity for most integrin receptors except for VLA-2. *Induction patterns on graft infiltrating cells* – Enhanced leukocyte expression of VLA-4 was observed in all grafts. Infiltrating cells carrying VLA-5 in 7 grafts, VLA-6 in 7 grafts and CD51 in all grafts were observed. *Changes in extracellular matrix composition during chronic rejection.* The expression of deposition of extracellular matrix (especially of fibronectin, collagen VI) was strongly increased in the portal tracts and central vein area where infiltrating leukocytes were accumulated. High expression of TSP was found around the central vein, and homogenous extracellular