recipients for HLA-DR *alleles,* exactly defined on the DNA level, rather than for HLA-DR *typings* would significantly improve graft survival in clinical transplantation. This is not possible when using the conventional method. We reported recently on a new technique for the rapid DNA-typing of HLA-DRB1 alleles. The method is based on the amplification of alleles or groups of alleles with sequence-specific PCR primer sets, which are designed to hybridize at the 3'-nucleotide(s) only to the desired alleles. The specificity of the typing system is thus part of the amplification process in that all other alleles are refractory to amplification. In the present study we designed primer sets for the serologically defined specificities DR51, DR52, DR53, and DQ1-9. The complete system thus enables the definition of all serologically defined HLA-class II alleles in all homozygous and heterozygous combinations. The results of an ongoing quality control study with blinded DNA samples of individuals which were reference typed by a highly standardized PCR-SSO technique show essentially no typing error. DNA typing by nested PCR-SSP was performed in the time of 3 hours, including DNA extraction and interpretation of the results. We conclude that this novel technique is most suitable for replacing HLA-class II serology.

Dept. of Medicine, University, 4400 Münster, Germany

A.8 Enhanced TNF-α and IL 6 production by isolated monocytes during chronic rejection of renal allografts

S. Heidenreich, D. Lang, and J. Crout

Long-term kidney allograft survival is primarily limited by chronic rejection (c.r.). For evaluation of immunological rather than hemodynamic mechanisms we isolated monocytes (MΦ) from 17 renal allograft recipients with histologically confirmed c.r. and for control from 22 patients with stable graft function (s.f.). Basal and stimulated cytokine production was measured by culturing MΦ for 20 h *in vitro.* Basal TNF-α synthesis in s.f. patients was 0.7 ± 1.8 ng/ml and was triggered to 11.5 ± 14.6 ng/ml TNF-α (range 0.03–59.8 ng/ml) by 100 ng/ml LPS. During c.r., basal TNF-α amounts of 7.0 ± 24.1 ng/ml were markedly enhanced by LPS up to 154.9 ± 242.7 ng/ml TNF-α (range 14–1002 ng/ml, $p < 0.001$ vs. s.f.). Similarly, significant differences were detected for LPS-elicited IL 6 production by MΦ: 12.08 ± 12.50 ng/ml in s.f. vs. 33.12 ± 12.85 ng/ml IL 6 in c.r. ($p < 0.01$). Additional stimulation of MΦ in s.f. patients by 25 U/ml IFN-γ enhanced LPS-triggered TNF-α production by 67 % whereas in c.r. patients there was no increase of TNF-α synthesis by IFN-γ detectable. These results indicate that during c.r. elevated T cell-derived IFN-γ may be responsible for increased monokine production.

We conclude that immune processes are involved in progression of chronic renal allograft rejection and that stimuli such as LPS should be therapeutically blocked to prevent an initiation of the immune cascade.

Institute of Immunology, University, 2300 Kiel, Germany

A.9 The human cell-mediated response to xenogeneic (porcine) transplantation antigen depends on the stimulator cell compartment

A. Heiser, K. Ulrichs, V. Eckstein, and W. Müller-Ruchholtz

Because xenogeneic cell-mediated immunity (CMI) has been claimed to be weaker than allogeneic CMI, we examined the *in vitro* response of human responder peripheral blood

lymphocytes to porcine stimulator lymphocytes of different lymphatic compartments in the mixed lymphocyte culture (MLC) and of porcine pancreatic islets in the mixed lymphocyte islet culture (MLIC).

Results: (1) Porcine stimulator cells induce a significant response in the xenogeneic MLC and xenogeneic MLIC. Its strength depends on the stimulator cell compartment studied. (2) Different responders develop significantly different reaction profiles against stimulator cells in the MLC, similar to the allogeneic response. (3) The extent of the MLC response correlates with the number of antigen-presenting cells, e.g., MHC class II-positive monocytes/macrophages, in the stimulator cell compartment. (4) The strength of the cellular response to porcine islets depends on islet purity. Handselected islets are significantly weaker stimulators than the crude islet preparation.

Conclusions: (1) The strength of the human cellular response in the MLC/MLIC is determined by the selection of the porcine stimulator cell compartment. It follows, that each xenogeneic cell compartment in question (here isolated porcine islets) should be investigated separately for cellular immunogenicity. (2) The selection of the human responder influences the type and strength of the MLC response. Individual pretransplant testing of the potential graft recipient, e.g., the insulin dependent diabetes mellitus patient, may be considered to establish a suitable immunosuppressive treatment protocol. (3) To reduce graft immunogenicity as much as possible transplantation of porcine pancreatic islets requires not only careful purification from exocrine tissue fragments, but also elimination of intraislet antigen-presenting cells.

Dept. of Virology, University, 7900 Ulm, Germany

A.10 IFNγ, but not TNFα, restores defective antigen presentation of MHC class I molecules by cytomegalovirus early genes

H. Hengel, T. Ruppert, and U. H. Koszinowski

Murine cytomegalovirus (MCMV) early (E) genes interfere with the MHC class I antigen processing and presentation pathway of the host cell by blocking the transit of peptide charged and correctly assembled MHC class I complexes to the cell surface. This transport inhibition of MHC class I complexes is specific and prevents the L^d mediated presentation of pp89, an immediate-early protein of the virus. Here we report that two T cell derived factors, TNFα and IFNγ, which were selected because of their influence on MHC class I expression, exert differential effects on the antigen presentation capacity of MCMV E genes expressing cells. While IFNγ fully restored pp89 presentation could TNFα not compensate the MCMV early gene effect. This action of IFNγ did not result from the suppression of cytomegalovirus E genes and was not restricted to presentation of pp89, since other antigens became also detectable for CTL. IFNγ strongly increased MHC class I synthesis and β_2m association and restored transport to the cell surface. In addition, the quantification of endogenous processed pp89 peptides revealed a significant higher efficiency in antigen processing when compared with pp89 synthesis and stability. This profound effect of IFNγ may reconcile the paradoxical finding that pp89 presentation is abolished during permissive infection *in vitro* whereas $CD8^+$ T lymphocytes with specificity for pp89 protect against lethal MCMV infection *in vivo*.