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CML as an In Vitro Model of Allograft Reactions:

E. Goulmy and C. Mawas

THE papers summarized below reflect the increased interest in cellular events in the pre- and postrenal transplantation period.

PRETRANSPLANT PARAMETERS

Suthanthiran (New York) described an interesting approach to detect latent cellular presensitization in the potential allograft recipients. His results indicated that by chemical modification of the cell surface with NAGO or IO_4^- treatment, peripheral blood lymphocytes (PBLs) from potential allograft recipients exhibited cytolytic capacity in contrast to PBLs from normal individuals.

F. Thomas (Greenville, N.C.) reported the studies of Hoffman on pretransplant measurement of in vitro generation of specific anti-donor cytotoxic T cells. This suggests the possibility of dividing, pretransplant, the patients into low and high responders. The pretransplant CML activity seems to be predictive of the posttransplant rejection course.

The results of Kerman (Houston) showed predicting factors for prolonged allograft survival. Pretransplant nonspecific immunocompetence of the recipient, such as low active T cells, low in vitro spontaneous blastogenesis, anergy to microbial skin test antigens, and low MLC, correlated with longer allograft survival.

DONOR-SPECIFIC CML NONREACTIVITY

Goulmy (Leiden) reported on donor-specific CML nonreactivity in 39 patients

from a group of 65 unrelated donor-recipient combinations studied. The results from the Leiden group indicated a significant correlation with a good graft function and with the HLA-B locus antigen match between donor and recipient. Furthermore, they investigated whether the absence of CML reactivity of the recipients' lymphocytes towards the specific kidney donor splenocytes could be due to lack of helper cells. After stimulation of the recipients' lymphocytes towards a pool of stimulator cells, no cytolytic activity against the donor cells could be observed. However, when such pool-stimulated effector cells were tested on each cell of the pool individually as a target, an HLA-B-dependent pattern of cytolytic nonreactivity was observed.

Charpentier (Villejuif, France) reported on specific allogeneic unresponsiveness between donor and recipient pairs. He pointed out that in the case of acute cellular rejection, the number of cytotoxic T lymphocytes in the graft are much higher than those found in the peripheral blood.

CML NONREACTIVITY AND DONOR-SPECIFIC SUPPRESSOR CELLS

Kovithavongs (Edmonton Canada) described an in vitro system to detect the presence of posttransplant suppressor cells in kidney transplant recipients' lymphocytes. The mitomycin-treated recipient cells showed only a suppressive effect when added as third-party cells to the donor-specific stimulator cells.

Pfeffer (Oslo, Norway) confirmed donor-specific decreased CML activity in family transplants. As controls, the cells of healthy HLA-identical siblings were used. He found a stronger decrease in secondary CML compared to primary CML. Furthermore some data were shown on the specific suppression of the cytolytic activity. Pfeffer reported that his suppressor cell system worked only with the use of fresh cells.

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J. Thomas (Greenville, N.C.) suggested that by removing recipient-adherent cells (e.g., macrophages or monocytes) from the CML cultures on day zero of sensitizing, a loss of the donor-specific CML nonreactivity results. This experimental model suggests that the CML suppressor cell activity could be associated with an adherent cell population.

Mitchinson (London, England) suggested looking specifically for suppressor cells by cloning through limiting dilution. Several groups have focussed on the existence of suppressor cells in renal allograft recipients. Suppressing effects of the recipients' lymphocytes after renal transplantation have been observed using various protocols. Since there are so many technical variations within these clinical studies, a standardization of the techniques and assignment criteria is a primary concern.

Finally, van der Vegt (Maastricht, The

Netherlands) reported on the detection of organ-specific antigens in a canine kidney graft model. They found that cytotoxic T lymphocytes were able to recognize different antigens present on kidney cell targets and absent on PHA-stimulated lymphoblasts.

Studies from Buurman (Maastricht) demonstrated the presence of circulating "precursor" CTLs in the canine kidney graft model. After adherence of the CTLs to a monolayer of stimulator cells, the nonadherent fraction, which was devoid of CTL, seemed to be responsible for cytotoxic activity identical to the nonseparated suspensions.

In conclusion, cellular techniques have a lot to offer for the in vitro monitoring of kidney transplant recipients. Although all the results obtained in this area bring us closer to the in vivo situation, many questions are still unanswered. Better and more defined protocols are required to obtain a true in vitro correlate of the homograft reaction.