3 Monitoring of Heart Transplant Rejection Using a Donor-Specific Soluble HLA Class I ELISA

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Our purpose was to utilize a donor-specific sHLA Class I ELISA to monitor damage to heart allografts caused by rejection as an alternative to myocardial biopsy. A group of 21 pts (34 serum samples from 14 pts and 63 samples from 7 pts) were screened for the presence of donor-specific HLA Class I before and after cardiac transplant using an HLA-A2-specific and/or an HLA-B7 specific ELISA. The Ab pairs used in the ELISA were: MA2.1 (anti-A2, B57) and CR11-351 (anti-A2, 28) for detecting HLA-A2, and ME1 (anti-B7, 27) and MB40.2 (anti-B7, 40) for detecting HLA-B7.

The results showed: 1) consistent release of donor-type HLA class I immediately post-Tx (d.1; 15-55 ng/ml); and 2) a smaller rise (4-20 ng/ml), during biopsy-proven rejection episodes. Both HLA-A2 and HLA-B7 levels rose in tandem in patients mismatched for both antigens. Patients with no rejection showed no evidence of donor antigen above background (<3 ng/ml) after the 1st post-operative day.

The major difficulty seems to be the problem of background reactivity in patients with HLA-A9 (occasional cross-reactivity with the CR11-351 in A2 ELISA) and with certain non-B7, 27 antigens. The technique may be of clinical value in patients with low background values (<3 ng/ml) and to distinguish rejection from systemic infection which may not cause a rise in donor-specific sHLA.

4 **Peptides derived from HLA class I sequences block allorecognition in vitro and in vivo.** [1]Clayberger, C., [1]Lyu, S.C., [1]Nisco, St., [1]Vriens, P., [2]Pouletty, P. and [1]Krensky A. Departments of Cardiothoracic Surgery and Pediatrics, [1]Stanford University School of Medicine, Stanford, CA and [2]SangStat Medical Corporation, Menlo Park, CA.

We have prepared synthetic peptides corresponding to the α1 alpha helix of HLA class I molecules and tested them for effects on in vitro immune responses. Some of these peptides were potent inhibitors of T cell differentiation. We evaluated one of these peptides, corresponding to residues 75-84 of HLA-B7, designated Allotrap 07, on heterotopic heart allograft in rats. Treatment of rats with Allotrap 07 either before transplantation or at the time of transplantation caused a slight but significant delay in rejection. Animals given Allotrap 07 in combination with a suboptimal dose of cyclosporine A maintained their grafts indefinetely. When tolerant animals were given a subsequent skin graft from the donor or a third party, they accepted the donor derived graft but rejected the third party graft. Adoptive transfer studies and investigation of donor specific cytotoxic T cell precursors showed that tolerance resulted from anergy, and not from clonal deletion of suppressor cells. Tolerance could be induced if the peptide was administered intravenously, orally and to a lesser extent by subcutaneous injection. These findings indicate that synthetic peptides corresponding to HLA molecules may have important therapeutic effects in humans.