The Society for Pediatric Research announces the results of the 3rd Annual Young Investigator Award for pediatric research.

The winner is Alan M. Krensky, M.D., Assistant Professor of Pediatrics, Stanford University Medical Center, Stanford, California, for his study on "human allogeneic cytolytic T lymphocytes".

This presentation will be made during the Thursday morning plenary session on May 9, 1985.

THE HUMAN CYTOLYTIC T LYMPHOCYTE RESPONSE TO TRANSPLANTATION ANTIGENS.
Alan M. Krensky, Department of Pediatrics, Stanford University Medical School, Stanford, CA 94305.

In order to study the effector and target cell antigens involved in the human cytolytic T lymphocyte (CTL) response, long term CTL lines and clones were generated. Human allogeneic CTL can recognize not only Class I major histocompatibility complex (MHC) antigens (HLA-A,B,C) but also Class II MHC antigens (HLA-DR, DC, SB). Whereas Class I specific CTL express and use CD8 (OKT8, Leu2) in antigen recognition, Class II specific CTL express and use the CD4 (OKT4, Leu3) cell surface molecule. These findings suggest that CD8 and CD4 may be receptors for monomorphic determinants on Class I and II MHC molecules, respectively.

To identify additional cell surface molecules involved in the CTL-target cell interaction, mice were immunized with a CTL line and the monoclonal antibodies (mAb) derived were screened for their ability to inhibit cytolysis by the CTL line used as the immunogen. Cytolysis was inhibited by mAb which recognized three distinct cell surface molecules, designated lymphocyte function-associated antigens (LFA) - 1, 2, and 3. LFA-1 (177kd, 95kd) is a leukocyte specific molecule which is involved in the general process of cell-cell adhesion. LFA-2 (49kd), the sheep erythrocyte receptor, is a T cell specific antigen which appears to mediate a calcium dependent T cell activation pathway. LFA-3 (60kd) is a broadly distributed cell surface molecule which inhibits function by binding to the target cell rather than the effector cell. Monoclonal antibodies to any of the LFA molecules inhibit CTL mediated cytolysis, natural killer cells, and T cell proliferative responses.

The studies above involved T cell recognition of B lymphoblast target cells as a model for transplantation. Although lymphoid targets are experimentally convenient and have provided new insights into the CTL-target cell interaction, endothelial cells may be pathophysiologically more relevant tissues to study as allogeneic targets. CTL derived by stimulation with human preputial capillary endothelial cells are specific for non-MHC antigens, and, although they utilize LFA-1 and LFA-3, they appear not to utilize any of the other cell surface structures identified in lymphoblastoid systems.

These findings are relevant to the further development of immunotherapeutic modulators for use in the inhibition of particular CTL-target cell interactions.

Much of this work was performed in the laboratory of Dr. S.J. Burakoff at the Dana-Farber Cancer Institute. The LFA project was carried out in collaboration with Dr. T.A. Springer and colleagues.

Recognition is given to the following individuals whose outstanding research accomplishments qualified them for consideration for this award.

James F. Casella
John T. Curnutte
Margaret K. Hostetter
David G. Oelberg
Jeffrey L. Platt
Ronald J. Sokol