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Selected Abstracts for the 1991 Annual Meeting
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ALLERGY/IMMUNOLOGY

1

DEVELOPMENT OF LYMPHOMAS OF HUMAN ORIGIN IN MICE WITH SEVERE COMBINED IMMUNODEFICIENCY (SCID): ROLE OF EPSTEIN-BARR VIRUS (EBV) AND INTERLEUKIN-6 (IL-6).

David Nadal, Boris Albini, Erika Schläpfer, Pearay L. Ogra - Departments of Pediatrics and Microbiology, State University of New York at Buffalo School of Medicine and Biomedical Sciences, and Division of Infectious Diseases, The Children's Hospital, Buffalo, New York 14222, and The Children's Hospital of Zürich, Switzerland.

SCID mice were inoculated intraperitoneally with 50×10^6 human tonsillar lymphocytes (hu-TOL) per animal. Five to eleven weeks later, 29.4% (10/34) of mice injected with hu-TOL from EBV seropositive donors, but none of 34 animals receiving hu-TOL from EBV seronegative donors, developed intraabdominal and/or intrathoracic tumors ($p=0.002$). In situ hybridization identified all tumors to be of human origin and to possess EBV genome. The EBV bearing tumor tissues stained for human kappa and/or lambda chains in poly- or oligoclonal patterns. High levels of human IL-6 were detected in the serum of animals with human lymphomas. No human IL-6 activity was detected in other animals. These observations suggest that EBV and IL-6 play an important role in the evolution of human B cell lymphoma. The use of SCID mice may serve as a unique model to study the effects of lymphokines on virus-induced human lymphoproliferative disorders.

2

Engagement of the monocyte antigen CD14 induces a state of IL-2 unresponsiveness in T cells

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CD14 is a 52 kD phosphatidylinositol-anchored protein expressed on mature monocytes. We have recently shown that engagement of CD14 by monoclonal antibodies (mAb) induces an increase in LFA-1/ICAM-1-dependent adhesiveness of the monocytes. We studied the role of CD14 in monocyte-T cell interaction by testing the effect of a panel of anti-CD14 mAbs on T cell proliferation.

The proliferation of human T cells induced by antigens, mitogens, and anti-CD3 mAbs was inhibited by anti-CD14 mAbs, but not by isotype-matched control mAbs. Inhibition by anti-CD14 mAbs was epitope-dependent, and required physical contact between monocytes and T cells. CD14 engagement did not affect IL-2 receptor expression, nor IL-2 synthesis, but induced a state of unresponsiveness to IL-2. These data indicate that CD14 plays an important role in monocyte-T cell interactions.

3

Anti-Endothelial Cell Antibodies in Renal Allograft Rejection

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5-10 % of HLA identical, living related kidney grafts are lost due to immunological rejection revealing the importance of non-HLA-antigens in transplantation. The observation that mixed lymphocyte culture inhibiting antibodies do not inhibit mixed lymphocyte endothelial cell culture responses pinpointed alloantigens on endothelial cells. 41 sera without detectable HLA antibodies from patients with rejected renal allografts and 29 sera of highly sensitized subjects with HLA antibodies were screened for the presence of anti-endothelial cell antibodies. A double immunofluorescence technique was applied after blocking HLA class I antigens. Anti-endothelial cell reactivity was demonstrated in 7 % of sera from unsensitized and 76 % of sera from highly HLA-sensitized patients. Successive serum samples of one unsensitized patient contained anti-endothelial cell antibodies before and six months after transplantation. Conclusion: We identified anti-endothelial cell antibodies to a non-HLA-antigen system in sera from unsensitized and highly sensitized patients with rejected kidney allografts.

4

INFLUENCE OF INFLUENZA A VIRUS, PARAINFLUENZA VIRUS TYPE 3 (P3) AND RESPIRATORY SYNCYTIAL VIRUS (RSV) ON HISTAMINE RELEASE (HR) AND CYSTEINYL LEUKOTRIENE (CYSTEINYL-LT)-SYNTHESIS FROM HUMAN BASOPHILS.

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Viral infections of the airways have been demonstrated to produce wheezing in infants and children and facilitate enhanced bronchial responsiveness. As an explanation for these effects virus-induced enhancement of mediator release from inflammatory cells has been suggested. The aim of the present study was to verify this hypothesis. Washed human leucocytes (10^7 cells/ml) were incubated (2 h, 37 C) with different concentrations of influenza A antigen, P3 and RSV (n=6 and control group). After further incubation (8h, 37 C) basophils were stimulated (40 min, 37 C) with anti-IgE. Histamine was determined by an automated fluorometric technique, cysteinyl-LT's were measured by means of radioimmunoassay.

Results: 1) Preincubation with influenza A virus led to a statistically significant ($p < 0.01$) enhancement of HR and cysteinyl-LT-synthesis compared to controls. 2) In contrast preincubation with P3 and RSV did not lead to an enhancement of HR and cysteinyl-LT-synthesis.

From our data we conclude that enhancement of mediator release from leucocytes by viral antigens is not a general phenomenon but seems to be limited to specific viruses (i.e. influenza virus A).