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H-2 Restriction of the Activity of Allogeneic Effect Factor

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Lack of Strain Restrictions among Allogeneic Nonresponder Donors and Recipients of GAT-Specific T Cell-Derived Suppressor Factors. Judith A. Kapp, Ph.D. The Jewish Hospital of St. Louis and Washington University School of Medicine, St. Louis, Mo. 63110.

The synthetic terpolymer of L-glutamic acid^{60}-L-alanine^{30}-L-tyrosine^{10} (GAT) fails to stimulate development of GAT-specific antibody responses in nonresponder mice but stimulates development of GAT-specific suppressor T cells that inhibit the development of normal anti-GAT PFC responses to GAT complexed to methylated bovine serum albumin. Extracts from lymphoid cells of GAT-primed but not control, nonresponder (DBA/1) mice contain a T cell factor (GAT-TsF) that also specifically suppresses responses to GAT-MBSA by normal syngeneic spleen cells. The experiments to be reported demonstrate that: 1) extracts from all GAT-primed nonresponder mice tested contain GAT-TsF; 2) non-H-2 genes do not restrict the production of GAT-TsF; 3) all nonresponder strains of mice regardless of their non-H-2 genes are suppressed by GAT-TsF from all other strains bearing the nonresponder H-2^{p,q,s} haplotypes; 4) both syngeneic and allogeneic nonresponder mice are suppressed by purified GAT-TSF that lacks immunoreactive GAT; and 5) suppression of GAT-MBSA responses by both syngeneic and allogeneic nonresponder spleen cells is mediated by a molecule encoded by the H-2 gene complex. Finally, reciprocal absorption of H-2^q and H-2^s GAT-TsF with insolubilized antisera specific for I^q or I-J^s demonstrates that suppression of syngeneic and allogeneic nonresponder mice by GAT-TsF cannot be attributed to crossreactivity between GAT-TsF determinants encoded by the I-J subregion of the H-2 gene complex. (Supported by U.S.P.H.S. Grant AI-13987.)

Cross Reactive Idiotypic Determinants on (T,G)-A--L Specific Antibodies of High and Low Responder Mice. Edna Mozes, Ruth Lifshitz and Michal Schwartz. Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel.

Mice possessing the H-2^b haplotype produce high antibody titers when immunized with (T,G)-A--L, whereas mice possessing the H-2^k haplotype are low responders to this immunogen. Following immunization with either (Phe,G)-A--L or (T,G)-A--L complexed with methylated bovine serum albumin (MBSA), low responder as well as high responder mice produce antibodies which can be titrated with (T,G)-A--L. The variable regions of antibodies produced against the above immunogens were compared utilizing guinea pig sera against (T,G)-A--L idiotypes of C3H.SW (H-2^b, Ig-1^a) mice, which appear to be allotype linked. (T,G)-A--L specific antibodies were isolated from sera of H-2^b (Ig-1^a) and H-2^k (Ig-1^a) mice immunized with (Phe,G)-A--L. These antibodies inhibited 50% of the ^{125}I-idiotype to the anti-idiotypes. In contrast, a population of antibodies isolated from the (Phe,G)-A--L specific antisera which bound only ^{125}I-modified (Phe,G)-A--L did not react with the anti idiotypes. (T,G)-A--L specific antibodies of low as well as high responder mice immunized with (T,G)-A--L + MBSA inhibited completely the binding of ^{125}I-idiotype to the anti-idiotypic sera although 3–5 fold more of these inhibitors was needed for achieving the same degree of inhibition obtained with C3H.SW anti (T,G)-A--L antibodies. It thus appears that, when appropriately triggered, the (T,G)-A--L specific B cell repertoire of low responder mice is similar to that of high responders.

H-2 Restriction of the Activity of Allogeneic Effect Factor. Terry L. Delovitch and U. Sohn. Banting and Best Dept. of Med. Res., Univ. of Toronto, Toronto, Canada M5G 1L6.

The helper activity of allogeneic effect factors (AEF) derived from mixed lymphocyte culture reactions (MLR) between activated responder cells and either *I*-region, *I*-subregion, or *Mls*-region incompatible irradiated stimulator spleen cells was analyzed. An AEF generated across either an a) entire *I*-region, b) *I-A, I-B* and *I-J*, c) *I-J* or d) *I-E* and *I-C* subregion incompatibility helps B cells of only the stimulator haplotype, or of haplotypes which carry *I*-subregions selectively expressed by the stimulator cells and not the responder cells. An AEF generated across an *Mls*-region difference provides weak help for B cells only of haplotypes which share both an *Mls* and *I*-region identity with the stimulator haplotype. The observed lack of help for B cells of the responder haplotypes is not due to a suppressor factor activity in these *H-2* restricted AEFs. These results are consistent with those obtained for another genetically restricted AEF produced by Ia negative activated responder cells and H-2 incompatible irradiated T-cell-depleted stimulator cells. This restricted AEF is predominantly a B cell derived factor which contains Ia antigens controlled by the *I-A* subregion of the stimulator haplotype, helps B cells of only its own haplotype or of haplotypes which carry an *I-A* and/or *I-B* subregion identity and possesses a putative target B cell receptor determined by *I-A*. The above data suggest that B cell activation is mediated by a specific recognition between AEF Ia antigens and Ia antigens present on the B cell surface.

Genetic Control of Immune Suppression. Sirkka Kontiainen, Elizabeth Simpson and Marc Feldmann. ICRF Tumour Immunology Unit, Zoology Department, University College London, Gower Street, London, WC1E 6BT, and Transplantation Biology Section, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.

Suppressor T cells induced *in vitro* by high concentrations of antigen release suppressor factors into their medium if incubated for 24 hours with antigen. Since there are reports that extracts of suppressor cells are related to immune response gene function, the capacity of responder or nonresponder strains to produce suppressor factor (SF) was investigated. Both responder and nonresponder strains produced SF to (T,G)-A--L and GAT. This together with differences in the target and the lack of H-2 restrictions indicates that SF is quite distinct from suppressor cell extracts, despite both having I-J controlled determinants and an antigen combining site.

The structure of SF was analysed using serological means. Rabbit and mouse antisera were raised against SF purified by absorption and elution from antigen columns. Rabbit antisera were not specific for strain or antigen specificity of SF, but did not react with helper factor, and thus defined a "constant region." Syngeneic mouse anti-SF antisera were specific for both strain and antigen specificity, but cross reacted with helper factors derived from the same strain and of the same antigenic specificity. These sera define 'idiotypic' determinants which are not H-2 linked, but have some relationship to Ig allotype. To further characterise suppressor cells and their factors, hybridomas of suppressor cells with an AKR T cell lymphoma have been produced. One has been characterised in detail and yields a SF with properties closely analogous to the material released by suppressor cells.