0945

THE EXISTENCE OF T HELPER (T_μ) AND T SUPPRESSOR (T_γ) CELLS FOR THE GENERATION OF MONOCYTE THROMBOPLASTIN ACTIVITY BY LIPOPOLYSACCHARIDES.

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Human peripheral blood mononuclear cells (PBM) in response to LPS stimulation generate increased quantities of thromboplastin activity. Monocytes are the cellular source of this activity and direct lymphocyte collaboration is required for its expression. PBM were separated by adherence into monocyte and lymphocyte fractions. Lymphocytes were further fractionated into T and non-T cells by rosetting with neuraminidase treated SRBC. 1×10^5 monocytes had a basal activity of 250 mU which increased to a maximum 2850 mU when monocytes were stimulated by 10 ug LPS for 6 hrs at a T cell: monocyte ratio of 4:1. No increase in thromboplastin activity was observed when monocytes were stimulated by LPS either alone or in the presence of non-T cells. Moretta et al. have described a system in which T cells are segregated into helper and suppressor subsets according to their ability to mediate immunoglobulin synthesis in response to pokeweed mitogen (PWM) stimulation. Using this system, T cells were further subfractionated into helper (T_μ), suppressor (T_γ) and T null cells by cytoadherence to IgM or IgG coated ox RBC. 1×10^5 monocytes when incubated with increasing numbers of T_μ cells generated a maximal 4150 mU thromboplastin activity as the ratio of T_μ:monocytes approached 4:1. No increase in monocyte thromboplastin activity was observed above basal levels of 160 mU when monocytes were stimulated by LPS in the presence of either T_γ or T null cells. T_γ cells were observed to suppress T_μ helper cell function with a decrease in monocyte thromboplastin activity from 4150 mU to 1100 mU as the T_γ:T_μ ratio increased from 0:1 to 4:1. Thus, at least two populations within the T lymphocyte series the T_μ(helper) and T_γ (suppressor) fractions modulate the expression of thromboplastin activity by monocytes.

0946

COMPLEMENT-DEPENDENT ACTIVATION OF PLASMINOGEN BY ACTIVATED FACTOR B (Bb) OF THE ALTERNATIVE PATHWAY OF COMPLEMENT.

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Activated Factor B (Bb) of the alternative pathway of complement (APC) induces human monocytes and murine macrophages to spread on a glass substrate (Sundsmo and Götze (1980), Cell. Immunol., 52:1). In studies designed to investigate the effects of Bb on plasminogen activator secretion by human monocytes, it became apparent that Bb possesses innate plasminogen activator (PA) activity. PA activity of Factor Bb was determined by release of radiolabeled fibrin peptides (modified fibrin plate assay) over 4 hrs. at 37°C using purified human plasminogen, ^{125}I-labeled human fibrinogen, and 20% fresh normal human serum as a source of thrombin. Native Factor B did not express significant PA activity, however, purified Bb, or Bb in complex with cobra venom factor released, 52±8% and 79±4%, respectively, of the ^{125}I-fibrin that is released by urokinase. Intermediate complement complexes on rabbit erythrocytes (E_r) were tested for their PA activity: E_rC3b,Bb released 76±7% of ^{125}I-fibrin, and control E_r, C3, and B released <15%. Factor D was without activity. Cleavage of plasminogen by Factor B was investigated by incubating cellular complement intermediates (E_rC3b,Bb; E_sC3b,Bb,NF) 30 min./37°C with ^{125}I-labeled plasminogen; and, conducting SDS-PAGE (reducing conditions) to separate native plasminogen from the heavy and light chains of plasmin. It was found that Bb cleaves predominantly the Lys-form of plasminogen to generate fragments with apparent molecular weights of 72,000 and 30,000. As a control, ^{125}I-labeled plasminogen was incubated with E_r, C3, or D, and <10% cleavage was observed; E_sC3b or native Factor B cleaved <5%. Affinity-purified goat anti-B Ig inhibited Factor Bb-dependent plasminogen cleavage by 99%. These results suggest that activated Factor B, the central serine esterase of the APC, can serve as a plasminogen activator and raise the possibility that Factor B may play a role in initiation of fibrinolysis as well as in complement-dependent humoral and cellular mechanisms of immunity.

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