

S21 The Effects of a First or Dominant Immune Response

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A barrier to effective tumor immunity is observed almost universally once tumors become established. I suggest that the B cell response to tumor antigens is partially responsible for this barrier. A small fraction of IgG secreted by actively immunized B cells is linked to latent TGF β (IgG-TGF β). Very few B cells secreting IgG-TGF β or low threshold levels of circulating IgG-TGF β powerfully suppress CD8⁺ cytolytic T lymphocytes (CTL) responses, responses that are necessary for tumor rejection. Syngeneic MHC class I, B7*, Fc* dendritic cells (DC) are required for suppression, and suppression is prevented by antibody to active TGF β or by blocking Fc receptors. This suggests that IgG-TGF β taken up through Fc receptors is cleaved to yield active TGF β , which in turn is delivered directly to specific CD8⁺ lymphocytes interacting with antigen presenting DC. The mechanism of down regulation of CTL maybe through B7-CTLA4. Thus, down regulation of B cell responses should enhance effective CD8⁺ cell mediated tumor immunity, and this has been observed in different models using mice without B cells.

S22 Immunodominance in the Protective Immune Repertoire to Influenza Infection

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The viral envelope glycoprotein, hemagglutinin, of influenza A virus is the most well characterised of protective Ags and is a paradigm for infectious disease studies. Both neutralising antibody recognition and receptor-binding sites have been defined and assigned to 3D structure, and the principal mechanism(s) of immune evasion are now understood at the molecular level. The facility of *in vitro* selection for antigenic and/or receptor-binding virus variants, and correlating such mutations with structure, provides a relevant molecular model for viral immunity. I will consider the problem of **immunodominance** during viral infection, and the structural basis for focusing of the immune repertoire to a limited number of available antigenic sites, together with possible strategies to obviate such immunodominance for vaccines. Although immunodominance is evident for both humoral and cell mediated responses, within the individual's immune repertoire, different mechanisms may operate to select B and T cell receptor gene usage.

S23 Immunology and Aging: An Overview

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Advancing age is associated with significant declines in the function of the immune system that may make an individual susceptible to infection. Effective defense against many intracellular pathogens depends on cell mediated immunity, which in turn, is dependent upon the number of T cells that can be activated. T cells from the elderly are functionally diverse, and there is not a generalized decline in number or function. While a portion of the T cell population of the elderly is functionally similar to T cells from young individuals, a gradually increasing population fails to respond. With age, there is a diversification in cytokine production and a shift from primarily IL-2 expression to IL-4 and interferon- γ expression resulting in an increased representation of memory T cells and a relative decline in naive T cells. This shift changes CD4⁺ helper-T cell subsets from primarily Th1 to Th2 and fine tunes protective immunity to specific types of pathogens. B-cell function and the ability to make antibodies remains intact in the elderly. Nonetheless, immunization of the elderly produces lower antibody levels and the antibody is less efficacious in preventing disease. These changes are thought to be attributable to age-changes in T helper cells or their products. The increased morbidity and mortality associated with common pathogens suggests the elderly are a population that can benefit from protective immunization using vaccines specifically developed for this age group.

S24 Effect of Nutrition on Immunoresponsiveness in the Aged

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Aging is associated with a decline in several aspects of the immune system. In particular, cell-mediated immunity and selected antibody responses are impaired. Recent studies have documented the frequent occurrence of nutritional deficiencies in as many as one-third of apparently healthy elderly subjects in North America. This has led to several correlational and intervention studies. The consensus of the results from these research investigations indicates that appropriate use of nutritional supplements can enhance the beneficial effects of a good diet. The nature and amounts of various nutrients should be determined by blinded randomized control studies and dose-response curves. In addition to immune responses, morbidity due to infection should be carefully monitored. Data obtained so far suggest that nutrition is a critical determinant of immunocompetence in the aged and appropriate nutrient supplements would result in enhanced immunity and reduced illness from respiratory and other infections.