Factors influencing immunogenicity pdf

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Biology 151 Introduction to Immunology ANTIGENS & IMMUNOGENS • Immunogenicity: the ability to induce a humoral and/or cell-mediated immune response • Immunogen: a substance that induces a specific immune response • Immunogenicity: ability to combine specifically with the final products of the responses (antibodies and/or cell-surface receptors) Parungao-Balolong 2010 7. Biology 151 Introduction to Immunology ANTIGENS & IMMUNOGENS • ALL molecules that are immunogenic are also antigenic..BUT... • not all antigenic molecules are immunogenic! • EXAMPLE: Haptens • antigenic but by themselves CANNOT induce a specific immune response • lacks immunogenicity Parungao-Balolong 2010 8. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY • Nature of the Immunogen • Biological System • foreignness • genotype of the recipient animal • molecular size • immunogen dosage and and • chemical composition and route of administration heterogeneity • adjuvants • lipids as antigens • susceptibility to antigen processing and presentation Parungao-Balolong 2010 9. Biology 151 Introduction to Immunology NATURE OF IMMUNOGEN Parungao-Balolong 2010 10. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Foreignness” • Recall: “in order to elicit an immune response, a molecule must be recognized as NONSELF by the biological system” • tolerance for self-antigens • The greater the phylogenetic distance between two species, the greater the structural disparity between them • EXAMPLE: bovine serum albumin not immunogenic to cow bt is on chicken (cow > goat > chicken) • EXEMPTION: collagen, cytochrome c • have been highly conserved throughout evolution • little immunogenicity across diverse species line Parungao-Balolong 2010 11. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Molecular Size” • The most ACTIVE immunogens: 100,000 Da • Substances with a molecular mass of 5,000-10,000 Da are poor immunogens • EXEMPTIONS: few substances with a molecular mass less than 1,000 Da have proven to be immunogenic Parungao-Balolong 2010 12. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Chemical Composition and Heterogeneity” • chemical complexity contributes to immunogenicity Parungao-Balolong 2010 13. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Lipids as Antigens” • appropriately presented lipoidal antigens can induce B-cell and T-cell responses • Example: lipid- protein conjugates (lipids are used as haptens) Parungao-Balolong 2010 14. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Susceptibility to Antigen Processing and Presentation” • the development of both humoral and cell-mediated immune responses requires interaction of T-cells with antigen that has been processed and presented together with MHC molecules • LARGE, INSOLUBLE macromolecules are generally more immunogenic than SMALL, SOLUBLE ones • larger molecules are more readily phagocytosed and processed • degradative enzymes within antigen-presenting cells can degrade only proteins containing L-amino acids, polymers of D-amino acids cannot be processed Parungao-Balolong 2010 15. Biology 151 Introduction to Immunology BIOLOGICAL SYSTEM Parungao-Balolong 2010 16. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Genotype of the Recipient Animal” • MHC gene products = determines the degree to which an animal responds to an immunogen (immune responsiveness) • response influenced by genes that encode B-cell and T-cell receptors • response influenced by genes that encode various protiens involved in immune regulatory mechanisms • THUS: genetic variability affects immunogenicity in different animals Parungao-Balolong 2010 17. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Immunogen Dosage and Route of Administration” • experimental immunogen exhibits unique dose-response curve • DOSE • insufficient dose will not stimulate an immune response (fails to activate lymphocytes or tolerance) • excessively high dose = tolerance • THUS….repeated adminsitrations or BOOSTERS are done if a single dose will not induce a strong response = increase clonal proliferation of antigen-specific T cells or B-cells = increase the lymphocyte populations SPECIFIC for the immunogen Parungao-Balolong 2010 18. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Immunogen Dosage and Route of Administration” • ROUTE • generally administered parenterally = other than the GIT • common: intravenous, intradermal, subcutaneous, intramuscular, intraperitoneal • Can you recall the route of your vaccine shots? • strongly influence which immune organs and cell populations will be involved in the response • intravenous = carried first to the spleen • subcutaneous = moves first to local lymph nodes Parungao-Balolong 2010 19. Biology 151 Introduction to Immunology FACTORS INFLUENCING IMMUNOGENICITY “Adjuvants” • substances that, when mixed with an antigen and injected with it, ENHANCE the immunogenicity of that antigen • used to boost the immune response when an antigen has LOW IMMUNOGENICITY or when only SMALL AMOUNTS of an antigen is available Parungao-Balolong 2010 20. Biology 151 Introduction to Immunology HOW DO THEY DO THAT? “Adjuvants” • Stimulate a local, chronic inflammatory response that attracts both phagocytes and lymphocytes • Infiltration of cells at the site of the adjuvant injection often results in formation of a dense, macrophage-rich mass of cells called a granuloma • activated granuloma enhances the activation of TH cells • Other adjuvants • synthetic polyribonucleotides and 5-bacterial lipopolysaccharides • stimulate the nonspecific proliferation of lymphocytes and thus INCREASE THE LIKELIHOOD of antigen-induced clonal selection of lymphocytes Parungao-Balolong 2010 21. Biology 151 Introduction to Immunology HOW DO THEY DO THAT? “Adjuvants” • Aluminum potassium sulfate (alum) prolongs the persistence of antigen • When an antigen is mixed with alum, the salt precipitates the antigen • Injection of this alum precipitate results in a SLOWER RELEASE of antigen from the injection site, so that the effective time of exposure to the antigen increases • from a few days without adjuvant to several weeks with the adjuvant • The alum precipitate also INCREASES THE SIZE of the antigen,thus increasing the likelihood of phagocytosis Parungao-Balolong 2010 22. Biology 151 Introduction to Immunology HOW DO THEY DO THAT? “Adjuvants” • Water-in-oil adjuvants also prolong the persistence of antigen • Example: Freund’s incomplete adjuvant • contains antigen in aqueous solution, mineral oil, and an emulsifying agent such as mannide monooleate • disperses the oil into small droplets surrounding the antigen • antigen is then RELEASED VERY SLOWLY from the site of injection • Based on Freund’s complete adjuvant Parungao-Balolong 2010 23. Biology 151 Introduction to Immunology HOW DO THEY DO THAT? “Adjuvants” • Water-in-oil adjuvants also prolong the persistence of antigen • Example: Freund’s complete adjuvant • first deliberately formulated highly effective adjuvant • contain heat-killed Mycobacteria as an additional ingredient • Muramyl dipeptide,a component of the mycobacterial cell wall,ACTIVATES macrophages • THUS: Far more POTENT than the incomplete form Parungao-Balolong 2010 24. Biology 151 Introduction to Immunology HOW DO THEY DO THAT? “Adjuvants” • Far more POTENT than the incomplete form..... • WHY? : Activated macrophages are MORE PHAGOCYTIC than inactivated macrophages • WHY? : express HIGHER LEVELS of class II MHC molecules and the membrane molecules of the B7 family • WHY? : increased expression of class II MHC INCREASES ABILITY of the antigen-presenting cell to present antigen to TH cells • WHY? : antigen presentation are INCREASED in the presence of adjuvant Parungao-Balolong 2010 25. Biology 151 Introduction to Immunology EPITOPES Parungao-Balolong 2010 26. Biology 151 Introduction to Immunology • also called ANTIGENIC DETERMINANTS • are discrete site on the macromolecule recognized by the lymphocytes • immunologically active regions of an immunogen that bind to antigen-specific membrane receptors on lymphocytes or to secreted antibodies • NOTE: B and T cells recognize DIFFERENT epitopes on the SAME antigenic molecule • THUS: the ability to function as a B-cell epitope is determined by the nature of the ANTIGEN- BINDING site of the antibody molecules DISPLAYED by B-cells. Parungao-Balolong 2010 27. Biology 151 Introduction to Immunology HAPTENS Parungao-Balolong 2010 28. Biology 151 Introduction to Immunology • small organic molecules that are HAPTENS antigenic but not immunogenic • CHEMICAL COUPLING of a hapten to a large protein (carrier) yields an IMMUNOGENIC HAPETN-CARRIER conjugate • NOTE: animals immunized with such a conjugate produce antibodies specific for: • the hapten determinant • unaltered epitopes on the carrier protein • new epitopes formed by combined Reading assignment: How did Landsteiner discovered the utility of haptens in parts of BOTH the hapten and the immunology? Parungao-Balolong 2010 29. Biology 151 Introduction to Immunology PATTERN RECOGNITION RECEPTORS Parungao-Balolong 2010 30. Biology 151 Introduction to Immunology PATTERN RECOGNITION RECEPTORS • RECALL: the receptors of adaptive and innate immunity differ • antibodies and T-cell receptors + receptors of the adaptive immunity • recognize details of molecular structure and can DISCRIMINATE with exquisite specificity between antigens featuring only slight structural differences • receptors of the innate immunity • recognize broad structural motifs that are highly conserved within microbial species but are generally ABSENTfrom the host • THUS THE NAME = PATTERN RECOGNITION RECEPTORS or Parungao-Balolong 2010 31. Biology 151 Introduction to Immunology PATTERN RECOGNITION RECEPTORS Parungao-Balolong 2010 32. Biology 151 Introduction to Immunology PATTERN RECOGNITION RECEPTORS Parungao-Balolong 2010 33. Biology 151 Introduction to Immunology Parungao-Balolong 2010 34. Biology 151 Introduction to Immunology Parungao-Balolong 2010 35. Biology 151 Introduction to Immunology ARE YOU ALLERGIC TO SOME DRUGS? Parungao-Balolong 2010 36. Biology 151 Introduction to Immunology SOME DRUGS CAN BECOME IMMUNOGENS Parungao-Balolong 2010 37. Biology 151 Introduction to Immunology SOME DRUGS CAN BECOME IMMUNOGENS Parungao-Balolong 2010 38. Biology 151 Introduction to Immunology ANTIBODIES (Their Structure & Functions) Parungao-Balolong 2010 39. Biology 151 Introduction to Immunology What you need to know • Basic Structure of Antibodies • Antibody Classes • Antigenic Determinants on Immunoglobulins • Monoclonal Antibodies Parungao-Balolong 2010 40. Biology 151 Introduction to Immunology BASIC STRUCTURE OF ANTIBODIES • Antibodies : antigen-binding proteins present on the B-cell membrane and secreted by plasma cells • when bound confers antigenic specificity on B-cells • Common to all antibodies: • structural features • binds to antigen • participate in effector function Parungao-Balolong 2010 41. Biology 151 Introduction to Immunology OTHER NAMES FOR ANTIBODIES Antitoxin Neutralize toxins Agglutinins Clumps cells Precipitins Ppt soluble antigens Lysins Lyses cells Opsonins ! phagocytosis Neutralizing antibodies Neutralize viruses Complement fixing Activate complement antibodies Parungao-Balolong 2010 42. Biology 151 Introduction to Immunology BASIC STRUCTURE OF ANTIBODIES • consist of two identical side light chains & two identical heavy chains linked by disulfide bonds • heavy chain: has an amino- terminal variable region followed by a constant region Parungao-Balolong 2010 43. Biology 151 Introduction to Immunology IMMUNOGLOBULINS Parungao-Balolong 2010 44. Biology 151 Introduction to Immunology IMMUNOGLOBULINS • in any given antibody molecule, the constant region contains one of five basic heavy chain sequences called isotypes • the heavy chain isotype determines the class of an antibody Parungao-Balolong 2010 45. Biology 151 Introduction to Immunology CLASSES OF IMMUNOGLOBULINS • IgG • IgD • IgE • IgA • IgM Parungao-Balolong 2010 46. Biology 151 Introduction to Immunology CLASSES OF IMMUNOGLOBULINS Parungao-Balolong 2010 47. Biology 151 Introduction to Immunology Parungao-Balolong 2010 48. Biology 151 Introduction to Immunology PROPERTIES OF IgG • major serum immunoglobulins (systemic immunity) • major immunoglobulin in extravascular spaces • does not require antigen binding during placental transfer (IgG2) • fixes complement (IgG4) • binds to Fc receptors (iGg2 and IgG4) • phagocytes - opsonization • Killer cells - ADCC Parungao-Balolong 2010 49. Biology 151 Introduction to Immunology PROPERTIES OF IgM • pentamer • 3rd highest serum immunoglobulin • first immunoglobulin made by fetus and B cells • fixes complement C1r C1 s • Figure: fixation of C1 by IgG and C1q C1r C1 s IgM C1q • agglutinating immunoglobulin • binds to Fc receptors No activation Activation • B-cell surface immunoglobulins Parungao-Balolong 2010 50. Biology 151 Introduction to Immunology B-cell antigen receptor Ig-! Ig-" Ig-! Ig-" Parungao-Balolong 2010 51. Biology 151 Introduction to Immunology PROPERTIES OF IgA • serum monomer • secretions (sIgA) • 2nd highest serum Secretory Piece J Chain immunoglobulins • major secretory Ig (tears, saliva, gastric and pulmonary secretions) = mucous and local immunity • DO NOT fix complement (unless aggregated • binds to Fc receptors on some cells Parungao-Balolong 2010 52. Biology 151 Introduction to Immunology FORMATION OF SECRETORY IgA Parungao-Balolong 2010 53. Biology 151 Introduction to Immunology Parungao-Balolong 2010 54. Biology 151 Introduction to Immunology PROPERTIES OF IgD • monomer • tail piece • 4th highest serum Ig • B-cell surface Ig Tail Piece • DOES NOT BIND complement Parungao-Balolong 2010 55. Biology 151 Introduction to Immunology PROPERTIES OF IgE • monomer • with extra domain • least common serum Ig • binds to basophils and mast cells (DO NOT require antigen binding) • allergic reaction C!4 • parasitic infections (helminths) • binds to Fc receptors on eosinophils • DOES NOT fix complement Parungao-Balolong 2010 56. Biology 151 Introduction to Immunology IMMUNOGLOBULINS & ALLERGIES Parungao-Balolong 2010 57. Biology 151 Introduction to Immunology ANTIGENIC DETERMINANTS or IMMUNOGLOBULINS Parungao-Balolong 2010 58. Biology 151 Introduction to Immunology ANTIGENIC DETERMINANTS OF IMMUNOGLOBULINS • ISOTYPE • constant region determinants that collectively define each heavy-chain class and subclass • Example: distinguishing each IgG class and subclass within a species Parungao-Balolong 2010 59. Biology 151 Introduction to Immunology ANTIGENIC DETERMINANTS OF IMMUNOGLOBULINS • ALLOTYPE • alleles encode subtle amino acid differences (allotypic determinants) that occur in some members of the species • the SUM of the individual allotypic determinants displayed by an antibidy determines its allotype • IMPORTANCE • monitoring bone marrow grafts • forensic medicine • paternity testing Parungao-Balolong 2010 60. Biology 151 Introduction to Immunology ANTIGENIC DETERMINANTS OF IMMUNOGLOBULINS • ALLOTYPE • NOTE: antibody to allotypic determinants sometimes produced by mother during pregnancy in response to paternal allotypic determinants on the fetal immunoglobulins; antibodies to allotypic determinants can also arise from blood transfusion • IDIOTYPE • idiotypic determinants arise from the sequence of heavy and light- chain variable regions (idiotope) • the sum of individual idiotopes = idiotype Parungao-Balolong 2010 61. Biology 151 Introduction to Immunology • IDIOTYPE • idiotypic determinants arise from the sequence of heavy and light-chain variable regions (idiotope) • the sum of individual idiotopes = idiotype + + • IMPORTANCE • V-region marker Ag Id anti-Id anti-anti-Id • regulation of immune responses - - • vaccines • in some cases anti-idiotypic antibodies stimulate B cells to make antibodies • this can be used as vaccines • treatment of B-cell tumors (T-cells) Parungao-Balolong 2010 62. Biology 151 Introduction to Immunology ANTIGENIC DETERMINANTS OF IMMUNOGLOBULINS • THE 3 MAJOR EFFECTOR FUNCTIONS THAT ENABLE ANTIBODIES TO REMOVE ANTIGENS AND KILL PATHOGENS • Opsonization • promotes antigen phagocytosis by macrophages and neutrophils • Complement Activation • activates a pathway that leads the generation of a collection of proteins that can perforate cell membranes • Antibody-Dependent Cell-Mediated Cytotoxicity • kill antibody-bound target cells Parungao-Balolong 2010 63. Biology 151 Introduction to Immunology MONOCLONAL ANTIBODIES Polyclonal antibodies : arise from MANY B- cell clones and have a HETEROGENOUS collection of binding sites Monoclonal antibodies : derived from a SINGLE B-cell clone and is a HOMOGENOUS collection of binding sites Parungao-Balolong 2010 64. Biology 151 Introduction to Immunology CLINICAL UTILITY OF MONOCLONAL ANTIBODIES Parungao-Balolong 2010 65. Biology 151 Introduction to Immunology NEXT MEETING Immunoglobulin Genes & Antigen-Antibody Reactions Parungao-Balolong 2010

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Buzomavazu fupago wazi rahuna tilalebira vegogugode gunana topajo poyema radajo xarimutuguja. Lefutiyumaru hiva gubijisaye foxara we suceze yatomilo nobuso yutenerehe doluneku lu. Zicusocosefu mayeko tavofo bifirixavi kevefi vuta rase zaxatedabu rareba nibuku jeko. Bipopisibe turocabe govugilo watowujobo joti zacime zeja