A block in the expression of MHC class II genes as the molecular basis for congenital immunodeficiency ('bare lymphocyte syndrome')

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The human class II (HLA-D) genes are a multigene family whose products play a central role in the immune response. A type of congenital immunodeficiency is characterized by patients who do not possess class II histocompatiblity antigens on the surface of their immunocompetent cells. We have analyzed the class II gene expression in lymphocytes of such patients. The following observations were made:
1) The defect is due to a block in gene expression (absence of mRNA). 2) All 12 class II genes are silent. 3) Class II genes themselves are not mutated as judged by family genetics and occasional reversion of cultured lymphocytes to class II positive cells. 4) Expression of HLA-DR associated invariant chain gene is not affected. 5) The defect is found in all immunocompetent cell tested. 6) Immune interferon does not induce class II gene expression.
We conclude that the molecular defect concerns a class II-regulatory gene, located outside of the MHC which could be a target for the effect of γ interferon.

Symptomatic *Toxoplasma gondii* infection in humans is associated with imbalance of immunoregulatory antigen-specific T lymphocytes

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Infection with the protozoan *Toxoplasma gondii* causes no illness in most people. In approximately one out of five infected individuals malaise, fever and lymphadenopathy are recorded. In an effort to identify factors which separate those people who experience illness from those who do not, we examined peripheral blood T cell subsets and toxoplasma antigen-induced T cell subsets during toxoplasmosis. A total of 19 individuals were studied. Using flow cytometric analysis patients with recent symptomatic infection had significantly higher absolute numbers of T8+ cells (suppressor/cytotoxic) and lower T4/T8 (helper/suppressor) cell ratios than patients with chronic asymptomatic infection and not infected individuals. In addition, toxoplasma antigen-induced long term cultures showed prevalence of T cells with suppressor markers (T8, TQ1) and less cells with helper marker (T4) in symptomatic patients. One patient with predominantly T4+ cells in cultures had extremely high serum toxo-antibody titers. In addition, the acute symptomatic infection was accompanied by elevated numbers of monocyte/macrophages (Leu M3 +) and NK/K cells (Leu 7+). These data suggest that in patients prone to symptomatic infection toxoplasma is effective in inducing immunoregulatory T cell subsets characterized by markers and function as suppressor cells.

Bivalent vaccine strains of *Salmonella typhi* and *Salmonella typhimurium*

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The epimeraseless mutants, *S. typhi* Ty21a and *S. typhimurium* LT_2MlC, were transformed by a plasmid containing the cistron coding for the B subunit (LT-B) of the heat-labile toxin (LT) of *Escherichia coli*. LT-B was synthesized and secreted by both strains when grown in liquid culture. Immunization of mice with these strains evoked both an anti-bacterial and anti-LT immune response. Introduction of the plasmid coding for LT-B into *S. typhimurium* LT_2MIC did not diminish its immunizing capacity against a virulent strain of *S. typhimurium* in mice. These strains provide the potential to vaccinate against both the vector strain and diarrheal disease mediated by LT-related toxins.

Expression and production in *E. coli* of merozoite stage-specific polypeptide antigens from *Plasmodium falciparum*

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Certain proteins, synthesized late in the asexual blood cycle of *P. falciparum*, have been shown to be able to confer some degree of protective immunity against malaria parasite infections.
Stage-specific cDNAs were identified by differential hybridization, by screening a *P. falciparum* blood stage cDNA library with probes made from either total ring stage (early) mRNA or total schizont-merozoite stage (late) mRNA.
From a library of 10,000 clones, 150 schizont-merozoite stage-specific cDNAs were identified and these were shown to correspond to 12 different genes. These cDNAs were expressed in *E. coli* using the inducible plasmid expression vector pP131A. Hybrid fusion proteins, which contained both a portion of a vector encoded protein and the expressed portion of the parasite cDNA, were synthesized at levels of up to a few percent of the total *E. coli* protein.
Protein immunoblots and immunoprecipitation experiments confirmed that some of these cDNAs coded for proteins which cross-reacted immunologically with known protective antigens (e.g. the 200 K mol. wt merozoite protective antigen). Examination of the DNA sequences of some of these cDNA clones has shown that they have the unusual feature of containing regions of repeated units of amino acids (e.g. examples of repeat units of 4, 5 and 6 amino acids in length have been found). These unusual protein structures have been implicated as having an important role in the interaction of the parasite with its host.

***Pseudomonas aeruginosa* polysaccharide-tetanus toxin conjugate vaccine**

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Cyanogen bromide-activated polysaccharide (PS) from *P. aeruginosa* PA220 lipopolysaccharide (LPS) was linked to purified tetanus toxoid (TTXD) by use of adipic acid dihydrazide as a spacer molecule. Conjugates were composed of PS and TTXD at ratios of 1:1 to 2:1 and possessed a molecular weight greater than 350,000. Conjugates were nontoxic, nonpyrogenic and highly immunogenic in rabbits and mice. Anti-PS-TTXD antibody, elicited either in response to active vaccination, or passively transferred, were highly protective against fatal experimental *P. aeruginosa* PA220 burn wound sepsis.

Results of a vaccination campaign against hepatitis B virus in a psychiatric clinic

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In a psychiatric clinic with a known frequent occurrence of sporadic hepatitis B infections a campaign was undertaken to immunize 303 patients and 428 personnel with a killed vaccine (Hévac B). All vaccines had been tested previously for HBV-markers and individuals positive for antigens or antibodies excluded from the trial. 1 month after the last injection, 381 out of 428 personnel (89.2%) had anti-HBs antibodies, whereas of the