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Is there a future in vaccine development for rheumatoid arthritis?

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Rheumatoid arthritis (RA), an autoimmune disease, arises from defective innate and adaptive immunity. Synovial joint inflammation develops from enhanced migration of activated T- and B-lymphocytes, and other cells to synovial joints as well as from deregulated resident synovial fibroblast proliferation contributing to "apoptosis-resistance", subchondral bone erosion and articular cartilage destruction. Inflammation is also driven by an increase in serum and synovial fluid levels of pro-inflammatory cytokines, chemokines and adhesion proteins. The etiology of RA continues to be obscure. However, recent advances in unraveling the RA autoimmune response provided evidence for the existence of anti-cyclic citrullinated antibodies (ACPA) even before RA ensues. This suggested a potential for developing a prophylactic vaccine for RA. ACPA are pathogenic and were produced in association with the HLA-DRB1 shared epitope and the PTPN22 1858T allele. Ongoing studies have examined potential vaccine strategies for RA. These included anti-cytokine and anti-autoreactive T-cell vaccines and a vaccine construct composed of autologous immunomodulatory dendritic cells which were altered by inhibiting NF-κB and then treated with 4 citrullinated peptide antigens. This vaccine has already completed a phase-I safety trial. Another vaccine exploited the endocytic receptor, DEC205 on dendritic cells to induce immune tolerance. A category of vaccines involving pcDNA-CCOL2A1 was also tested. Normal rats were immunized with pcDNA-CCOL2A1 which caused an increase in TGF-β while decreasing interferon-γ and TNF-α. Future studies employing various immunotherapeutic vaccine strategies will be required if we are to ever incorporate such a prophylactic strategy into the overall management of undifferentiated arthritis and RA.

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Characterization of cross-reacting termite proteins and cockroach allergens

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Cockroach allergens can be a serious problem for travelers. Termites are evolutionarily related to cockroaches, co-habitate in human dwellings and represent an increasing pest problem. The Formosan subterranean termite *Coptotermes formosanus* is one of the most common species in the southern United States. Due to the evolutionary relationship between the two insects, we sought to determine if *C. formosanus* termite proteins cross-react with cockroach allergens. Termite gene sequences were searched for homology to cockroach allergens using BLAST 2.2.21 software. Whole termite extracts were analyzed by mass-spectrometry, immunoassay with IgG and scFv antibodies to cockroach allergens and human IgE from serum samples of cockroach allergic patients. Sequencing results indicate greater than 60% homology between several predicted termite proteins and German and American cockroach allergens. Peptides from whole termite extract were matched to those of the tropomyosin (Bla g 7), arginine kinase (Per a 9) and myosin (Bla g 8) cockroach allergens. Immunoblot and ELISA testing revealed cross-reaction between several proteins with IgG and IgE antibodies to cockroach allergens. In particular, anti-cockroach allergen antibodies were reactive to putative termite homologs of hemocyanin (Bla g 3) and tropomyosin (Bla g 7). We have determined that several termite proteins, including the hemocyanin and tropomyosin orthologs, cross-react with cockroach allergens. This research may have important consequences in the allergy field and especially for cockroach allergic travelers going to areas infested by termites or indulging in local cuisine that may contain termites.

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