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Microbial triggers of autoimmune diseases

Microbial Triggers: It is now clear that autoimmune diseases are caused by faulty immune responses to specific microbial infections, Alan Ebringer leading the search for these triggers.

Forbidden Clones: Following Niels Jerne's epochal realization that antibodies are not built on a template of antigen, but are pre-formed in myriad diversity, awaiting selection by an antigen that fits, Macfarlane Burnet realized that it is not antibodies that are selected but the cells that make them, and that these are the lymphocytes. Burnet proposed that each lymphocyte is covered in multiple copies of a single antigen receptor to form an immunological clone, with millions of cells in a clone and millions of different clones in a person. This is his clonal selection theory of the immune response. Furthermore, he realised that multiplying lymphocyte will mutate, and if the mutation involved is in a V (variable region) gene, a new clone will be formed. Hence, his forbidden clone theory, postulating that unlucky mutations in V genes cause the autoimmune diseases. This theory has been amply confirmed in detailed studies of Graves' disease, which is caused by B lymphocyte forbidden clones, whereas T lymphocyte forbidden clones cause Type1 diabetes. The H gene theory of Adams and Knight explains all the features of the genetics of the autoimmune diseases by postulating that histocompatibility antigens, major, minor and H-Y, dictate the immune repertoire by deleting nascent complementary clones, and so altering the risk of occurrence of the various autoimmune diseases.

Specific Immunotherapy: Because unlucky somatic mutations in multiplying lymphocytes cause the autoimmune diseases, they are unlikely to recur in regenerating immune repertoires following immune ablation and autologous bone marrow cell reconstitution, as shown by Englert et al with cases of lethally severe systemic scleroderma. After isolation of its auto antigen, an autoimmune disease should be curable by selective destruction of its forbidden clone by making and using a cytotoxic auto antigen complex.

Prophylaxis: This will be possible by identifying and vaccinating against microbial triggers of the various autoimmune diseases. Johannes Salk's anterior poliomyelitis vaccine has prevented the leg paralyses that must have been a rare autoimmune complication of the virtually universal infections with the virus occurring in poliomyelitis epidemics. Ebringer has shown that rheumatoid arthritis, ankylosing spondylitis and multiple sclerosis have microbial triggers (Ankylosing Spondylitis and Klebsiella, Springer London 2012). A particular challenge is to find schizophrenia's microbial trigger, probably a virus, and vaccinate against it to prevent this distressing disease.

Biography

Duncan Adams entered Medicine with a view to doing research on the aetiology of asthma. However, Dean Sir Charles Hercus apprenticed him to work under Dr HD Purves on use of radioactive iodine in thyroid research. Attacking the cause of Grave's disease, Adams and Purves discovered the thyroid-stimulating auto antibodies. Later, in Adams' MRC Autoimmunity Research Unit, John Knight solved the genetics of the autoimmune diseases, which was confirmed at the molecular level by Alan Ebringer, who has discovered two microbial triggers, making it likely that all autoimmune diseases have microbial triggers and will be preventable by discovering and vaccinating against them. Duncan Adams has published more than 138 papers and chapters in medical science journals and books

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