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Hypothesis

ROLE OF ABERRANT HLA-DR EXPRESSION AND ANTIGEN PRESENTATION IN INDUCTION OF ENDOCRINE AUTOIMMUNITY

GianFranco Bottazzo ^a ... Marc Feldmann ^b

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Abstract

Immune responses are initiated by HLA-DR⁺ cells, which present antigen to T cells. Observations that HLA-DR may be experimentally induced on thyroid epithelium and that HLA-DR occurs on thyrocytes in autoimmune thyroid diseases suggest a mechanism of autoimmunity with special relevance to organ-specific diseases. This involves the local aberrant expression of HLA-DR antigens by epithelial cells and their subsequent capacity to present autoantigens occurring on their surfaces to T lymphocytes. For autoantigens which T cells recognise infrequently because of their restricted tissue location and low concentration in the circulation, T-cell tolerance is unlikely, and so induction of autoreactive T cells would occur. Because interferon is the

...antly, and the induction of autoreactive T cells would occur. Because interferon is the best known inducer of DR antigen expression and viral infections may predate endocrine autoimmunity, the following sequence seems likely: local viral infection which causes interferon production, or other local environmental factors which would induce DR expression, presentation of autoantigens, and subsequent autoimmune T-cell induction. These T cells would activate effector B and T cells. Whether the initial induction of autoimmune T cells leads to autoimmune disease would depend on factors such as abnormalities of the suppressor T-cell pathway, reported to coexist with autoimmunity and necessary to induce autoimmune disease in mice. This mechanism of autoimmune disease induction explains vague associations with viral infections and long latency periods before disease becomes manifest and gives a simple explanation for the well-documented association between HLA-DR and autoimmune diseases in man.



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² Second Department of Internal Medicine, Osaka University Medical School, Fukushima-ku, Osaka, Japan 553.

¹ Departamento de Medicina Interna, Hospital General Valle de Hebron, Universidad Autonoma de Barcelona, Barcelona, Spain.

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