Autoimmunity: Introduction

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The Autoimmune Process. The immune response in autoimmune disease recapitulates that of responses directed against infection, except that self antigens are, or become, the target of the adaptive immune system. These self antigens may drive a process that is localised within a specific organ, such as the thyroid gland (Grave’s disease, Hashimoto’s thyroiditis) or brain (multiple sclerosis). Or responses to them may lead to a more general inflammatory condition (e.g. systemic lupus erythematosus [SLE]).

Following initiation and trafficking, local damage can amplify disease, while the balance of this by regulation determines whether relapse or remission dominate as the disease progresses.

Autoimmune disease occurs when an immune response attacks our own tissues. Like all adaptive immune responses, it is focused on specific antigens by T-cell receptors and B cell receptors. In contrast to infection, the antigens that these cells recognise are processed from proteins within the target organ and this drives a chronic inflammatory process that disrupts the normal function of the tissue.

In human diseases the trigger for this process cannot usually be determined. There is evidence that autoimmunity can follow infection, but that more than one infection can initiate disease. Other environmental factors are also relevant but are not well defined.

There has been a lot of recent progress in understanding the influence of inheritance on autoimmune disease. A key observation is that susceptibility to autoimmune disease is influenced by a large number of polymorphic genes. These have small effects on their own, but in aggregate they determine an underlying susceptibility to autoimmunity. Many of these genes are clearly implicated in setting a threshold for an immune response, but clarifying the detail of these processes is an ongoing challenge.

The clinical course of autoimmunity is often marked by a relapsing and remitting course. This arises because there is both a continuing pro-inflammatory, disease-causing, drive (in the form of persistent antigen) and opposing this an anti-inflammatory regulatory aspect. The natural regulation of the autoimmune process is known to involve antigen-specific regulatory cells as well as anti-inflammatory cytokines such as IL-10 and TGF-beta. To date, therapies that exploit natural immune regulation have been less successful in the clinic than treatment that blocks the immune response. Blocking the immune response can be effective in autoimmunity, but is accompanied by adverse effects due to immunosuppression. This can allow the reactivation of latent infection and reduce the immuno-surveillance of transformed cells. Therefore antigen-specific immune therapy, targeted at a specific immune response, rather than general therapies targeted at the whole immune system, remains a critical goal for the treatment of these chronic debilitating diseases.