Scientific updates in respiratory medicine

Series editor: D J Shale

Introduction

This issue of Thorax sees the start of a new feature presenting scientific updates in respiratory medicine. This will consist of a series of short reviews focusing on developments, mainly in the basic sciences, with implications for the understanding of respiratory diseases or their future management. Each review is selected by the writer, who has a research interest in the scientific area from which the review is derived. This will ensure an up to date content and relevance to respiratory medicine.

Seven reviewers will produce updates from across the spectrum of respiratory medicine, including oncology, asthma, pharmacology, molecular biology, immunology, and epidemiology. The first review, by Ron du Bois, outlines current understanding of how T lymphocytes recognise antigen and how such knowledge may lead to new options for management in interstitial lung disease. Future reviews will feature new host defence proteins and somatic gene treatment for α1 antitrypsin deficiency and cystic fibrosis.

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How T cells recognise antigen: implications for lung diseases

R M du Bois

For many years histology and differential cell counts on bronchoalveolar lavage fluid have shown the lymphocyte to be a prominent component of inflammation in the lower respiratory tract in conditions such as fibrosing alveolitis, sarcoidosis, and extrinsic allergic alveolitis. More recently lymphocytes have been implicated in diseases that affect the airways predominantly, notably asthma and bronchiectasis.

Lymphocytes can be broadly subdivided into B cells, which are responsible for antibody mediated immune responses, and T cells, which are responsible for a range of immune responses including delayed hypersensitivity, B cell “help,” and cytotoxicity. T cells have an extensive repertoire of surface receptors which often reflect functional state (for example, CD25+ cells indicate an activated state).

Perhaps not surprisingly, several lung diseases that appear to have a strong immune component have been associated with the presence of T cells, many of which are activated. Recognition of antigen by T cells is the first step in a highly complex process that results in the generation of cytokines, inflammatory cell chemotaxis and activation, and, ultimately, the release of a wide range of other mediators that are responsible for inflammation within the lower respiratory tract.

T cells recognise antigen only when it is presented by an antigen presenting cell. Antigen presented on the surface of such cells in association (as a complex) with class I major histocompatibility complex (MHC) molecules (HLA-A, B, and C) is recognised by CD8+ suppressor-cytotoxic T cells. Antigen complexed with class II MHC molecules (predominantly HLA-DR, but also possibly DP or DQ) will be recognised by CD4+ helper-inducer T cells. The MHC-antigen complex is identified by T cell antigen receptors, which are most commonly of the α/β form. This nomenclature denotes that the receptor on the T cell surface consists of two glycoprotein chains (a 40–50 kDa α chain and a 40–45 kDa β chain) linked by disulphide bonds and that it is associated with the CD3 group of molecules, present on all mature T cells and necessary for surface signal transduction. The T cell antigen receptor structure closely resembles that of an immunoglobulin molecule. Each chain consists of a variable region and a constant region. The variable region contains a hypervariable segment, which confers antigen specificity on the molecule. Both the α and the β chains of the T cell antigen receptor have many individual members, which are grouped into families (for example, Vβ1, Vβ2, etc) based on gene sequences that are common to all members of an individual family. Theoretically up to $10^{13}$ α/β T cell receptor variants could exist. Recent studies have emphasised the impor-
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