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Recognition of foreign antigens and the development of immune response

Rozpoznanie obcych antygenów i rozwój odpowiedzi immunologicznej

The function of the immune system is to protect the body from micro-organisms such as bacteria, viruses and fungi. Any foreign molecule that induces an immune response is called antigen and since all micro-organisms have many different molecules on their surfaces, they therefore also have many potential antigens. When a microbe enters the body, the injured tissues initiate an inflammatory response. This serves as a danger signal to the immune system and attracts cells to the source of infection. Among these cells will be antigen presenting cells, such as dendritic cells and macrophages, whose role is to phagocyte the micro-organisms, process them into small fragments of cell peptides and present them to helper T lymphocytes. The role of these cells is to recognise the peptides presented by the antigen presenting cells and then provide help to the effector cells of the immune system. Helper T lymphocytes only recognise antigen when it is presented as a peptide inside the groove of an HLA (Human Leukocyte Antigen) molecule on the surface of an antigen presenting cell. The helper T lymphocytes provide help by secreting molecules called cytokines which act as growth factors and modulate the activities of other cells, such as effector cells. Effector cells are cells of the immune system which directly attack and destroy micro-organisms. These include B lymphocytes which secrete antibodies, cytotoxic T lymphocytes which kill infected cells and macrophages/neutrophils which phagocyte micro-organisms. Antibodies are particularly important in immunity against bacteria, cytotoxic T lymphocytes in immunity against viruses, neutrophils in immunity against bacteria and fungi, and macrophages in immunity against microbacteria. The cocktail of cytokines secreted by helper T lymphocytes in response to a particular microbe will activate the most appropriate immune response to eliminate that particular microbe. Helper T lymphocytes can be crudely divided into two sub-types depending on the cytokines they secrete: T helper 1 lymphocytes secrete cytokines such as interferon-gamma and intereukin-2 which help cellular immunity while T helper 2 lymphocytes

secrete cytokines such as interleukin-4 and interleukin–1 — which help antibody mediated immunity.

The relationship between the immune system and tumours is a long studied but still incompletely understood one. In the majority of malignancies, the immune system appears to allow the tumour to grow without intervening to a significant degree. Exceptions to this are virally-induced tumours, such as EBV-lymphoma and some spontaneously regressing tumours. There are many theories as to why most tumours grow uninterrupted: (i) anergy — the immune system does not recognise the tumour as a threat, (ii) evasion — the tumour hides from immune system by downregulating antigens on its surface, (iii) suppression — the tumour suppresses the immune system by secreting suppressive substances or by direct cell-to-cell contact, (iv) help — the tumour cells secrete anti-apoptotic autocrine growth factors such as cytokines.

The research interests of our group are: (i) to break the anergy between the immune system and the tumour by stimulating patients' dendritic cells with tumour antigen and stimulating an immune response, (ii) to study the down-regulation of important molecules on T lymphocytes in patients with tumours, and (iii) to study cytokines which may act as anti-apoptotic growth factors for tumour cells. The disease of interest in our studies is B cell chronic lymphocytic leukaemia (B-CLL) and our long term aim is a vaccine/immunomodulatory strategy for such patients.