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Immunome Research

Perspective

Significance of Myeloid Antigen-Presenting Cells

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DESCRIPTION

Myeloid progenitors also give rise to a group of phagocytic cells (monocytes, macrophages, and dendritic cells) that have the professional function of Antigen-Presenting Cells (APCs). Myeloid APCs are considered cellular bridges between the innate and adaptive immune systems because they make contact with a pathogen at the site of infection and communicate this encounter to T lymphocytes in the lymph node ("antigen presentation"). Each APC can respond to pathogens and secrete proteins that attract and activate other immune cells. Each can engulf pathogens through phagocytosis, cleave pathogen proteins into peptides, and then present these peptide antigens on their membrane surfaces. Each can be induced to express a set of stimulatory molecules required for optimal T cell activation. However, it is likely that each plays a different role during the immune response depending on its location and its ability to respond to pathogens. In particular, dendritic cells play a primary role in antigen presentation and activation of naïve T cells. Macrophages and neutrophils are particularly efficient at eliminating pathogens as well as damaged host cells and may provide the first line of defense against pathogens.

Monocytes

Monocytes comprise about 5% to 10% of white blood cells and are a heterogeneous group of cells that migrate into tissues and differentiate into a diverse array of tissue-resident phagocytic cells, including macrophages and dendritic cells. During hematopoiesis in the bone marrow, granulocyte-monocyte progenitor cells differentiate into pro-monocytes, which leave the bone marrow and enter the blood, where they further differentiate into mature monocytes. Two broad categories of monocytes have recently been identified. Inflammatory monocytes rapidly enter tissues in response to infection. Guard monocytes, a smaller group of cells that slowly crawl along blood vessels, provide a reservoir for tissue monocytes in the absence of infection and may suppress rather than initiate immune responses. Monocytes that migrate into tissues in response to infection can differentiate into tissue-specific macrophages.

Macrophages

Similar to monocytes, macrophages can play several different roles. Some macrophages are long-term residents of tissues and play an important role in regulating tissue repair and regeneration. Other macrophages participate in the innate immune response and undergo a number of key changes when stimulated by pathogen encounters or tissue damage. These are referred to as inflammatory macrophages and play a dual role in the immune system as efficient phagocytes that can contribute to the removal of pathogens from tissue, as well as antigen-presenting cells that can activate T lymphocytes. Osteoclasts in bone, microglial cells in the central nervous system and alveolar macro e-specific examples of macrophages with these properties.

Activated inflammatory macrophages are more effective than resting macrophages in eliminating potential pathogens for several reasons. They exhibit greater phagocytic activity, increased ability to kill ingested microbes, increased secretion of inflammatory and cytotoxic mediators, and ability to activate T cells. Activated macrophages also function more effectively as antigen-presenting cells for helper T cells (TH cells), which in turn regulate and enhance macrophage activity. Thus, macrophages and TH cells facilitate mutual activation during the immune response.

Many macrophages also express receptors for certain classes of antibodies. If the antigen (eg: bacteria) is coated with an appropriate antibody, the antigen-antibody complex binds to the antibody receptors on the macrophage membrane more readily than the antigen alone, and phagocytosis is enhanced.

Dendritic cells

Dendritic cells are critical for initiating the immune response and get their name because they are covered in long membrane extensions that resemble the dendrites of nerve cells and dynamically expand and retract, increasing the surface area available for viewing by lymphocytes. They are a more diverse population of cells than previously thought and appear to originate from both myeloid and lymphoid lineages of hematopoietic cells. Functional differences between these diverse cells are still being elucidated and are likely to be critically important for tailoring immune responses to different pathogens and targeting the corresponding cells to distinct tissues.

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