

(76,77,78,79). Kanazawa et al. (80) report that *peroxynitrite* is increased in airway epithelial cells and eosinophils in asthmatic patients compared with normal control subjects. To conclude, the above discloses the MOA of an inflammatory disorder. Chapter 27 describes the MOAs of various autoimmune diseases.

IX. CELLS OF THE IMMUNE SYSTEM

Cells of the immune system include DCs, T cells, B cells, NK cells, macrophages, Kupffer cells, microglia, and neutrophils. Kupffer cells (81) are resident macrophages that are part of the liver and do not circulate in the bloodstream, while microglia (82) are macrophages of the central nervous system. The term antigen-presenting cell (APC) refers to cells that can form an immune synapse with a T cell, where the APC presents an antigen once

the immune synapse is formed, and where the antigen is presented by way of the major histocompatibility complex (MHC) class I or MHC class II of the APC, to the T cell. The consequence of antigen presentation is activation of the T cell. APCs include DCs, macrophages, and B cells.

In diagrams, all of these cells may be represented as a circle. Usually though, DCs are drawn in the shape of a starfish, because of the fact that DCs have dendrites or branches (83,84). There are two lineages of DCs, the myeloid DCs and plasmacytoid DCs (pDCs). The former type of DC resembles a starfish, while the latter is round (85). The long dendrites of DCs are believed to contribute to the remarkable efficiency by which DCs take up, process, and present antigen to T cells (86).

Immune response, as it applies to infections, cancer, inflammatory disorders, and autoimmune diseases, involves the following chain of events. DCs take up antigens, and present the

⁷⁶Hebestreit H, et al. Disruption of Fas receptor signaling by nitric oxide in eosinophils. *J. Exp. Med.* 1998;187:415–25.

⁷⁷Smith AD, et al. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *New Engl. J. Med.* 2005;352:2163–73.

⁷⁸van Vliet D, et al. Prediction of asthma exacerbations in children by innovative exhaled inflammatory markers: results of a longitudinal study. *PLoS One* 2015;10:e0119434. <http://dx.doi.org/10.1371/journal.pone.0119434>.

⁷⁹Wenzel S, Ford L, Pearlman D, et al. Dupilumab in persistent asthma with elevated eosinophil levels. *New Engl. J. Med.* 2013;368:2455–66.

⁸⁰Kanazawa H, et al. Decreased peroxynitrite inhibitory activity in induced sputum in patients with bronchial asthma. *Thorax* 2002;57:509–12.

⁸¹Tomita M, Yamamoto K, Kobashi H, Ohmoto M, Tsuji T. Immunohistochemical phenotyping of liver macrophages in normal and diseased human liver. *Hepatology* 1994;20:317–25.

⁸²Rock RB, Gekker G, Hu S, et al. Role of microglia in central nervous system infections. *Clin. Microbiol. Rev.* 2004;17:942–64.

⁸³Blanco P, Palucka AK, Pascual V, Banchereau J. Dendritic cells and cytokines in human inflammatory and autoimmune diseases. *Cytokine Growth Factor Rev.* 2008;19:41–52.

⁸⁴Randolph GJ, Ochando J, Partida-Sánchez S. Migration of dendritic cell subsets and their precursors. *Annu. Rev. Immunol.* 2008;26:293–316.

⁸⁵Wu L, Dakic A. Development of dendritic cell system. *Cell Mol. Immunol.* 2004;1:112–8.

⁸⁶Swetman CA, Leverrier Y, Garg R, et al. Extension, retraction and contraction in the formation of a dendritic cell dendrite: distinct roles for Rho GTPases. *Eur. J. Immunol.* 2002;32:2074–83.