

Preface

For convenience, the early immune response occurring during the first few days after exposure to a foreign agent is termed innate, while the later response, after day 5, is termed adoptive. Both immune responses have defined cellular components although they vary according to different types of cells and the degree of their participation. Further, there is a balance between a necessary immune response required to protect the host versus an exaggerated response that possess unwanted and severe injury and difficulties. In both instances, the immune response causes immune-mediated tissue injury by limiting the infection through its ability to destroy infected cells, such cells are factories for manufacturing increasing infectious progeny or by reacting against self antigenic material. Thus, there needs a controlling rheostat or servo-mechanisms that can maximize the beneficial aspect as well as minimize the excessive immune-mediated injury (immunopathology) caused by cells of the immune system.

Sphingosine-1-phosphate (S1P) is a signaling lipid present at a concentration of 1–3 μM in plasma and roughly 100 nM in lymph. The majority of S1P in plasma is bound to high density lipoprotein but a small portion, approximately 15–45 nM, is unbound in the blood. Physiologically, S1P levels are under tight homeostatic control. S1P signals through specific G-coupled S1P receptors of which there are five. These receptors regulate a wide variety of signaling pathways that are specific for different cells, tissues, and organs. The purpose of this CTMI volume is to focus on S1P and its analogs in the induced sequestration of lymphocytes in secondary lymphoid organs or in microenvironment of tissues involved in infection or autoimmune disease. By this means, first, trafficking and lymphoid organization are, in part, controlled; second, migration of effect or lymphocytes, NK cells, and macrophages to distal areas where such cells might mediate immunopathologic injury leading to disease can also be restrained and; third, cytokines and chemokines regulated in the microenvironment of selected tissues. To achieve such desired therapeutics, a series of agonists and antagonists to S1P receptors have been synthesized to evaluate and control normal lymphocyte trafficking thereby employed in modulating acute infections and autoimmune disorders.

This CTMI volume illuminates this rapidly expanding field of basic and translational clinical research. Initial chapters define the pathways to understand S1P signaling from the organization of the signaling systems to the structural biology of the S1P₁ receptor to the chemical and genetic tools available and useful

to explore this area of research and therapeutics. The later chapters focus on the biology covering SIP and endothelial integrity, lymphocyte migration in the spleen, and SIP agonist in controlling immunopathologic manifestations in the lung of acute respiratory influenza virus infection and its accompanying cytokine storm as well as immunopathologic disease of the central nervous system including beginning treatments in multiple sclerosis. Also included is a chapter revealing other lipid molecules that can play a role and their use for better understanding lipid signaling and its potential in the modulation of immune responses.

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