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Sommario/riassunto

The innate immune system has evolved means to recognize and react suitably to foreign entities such as infectious agents. In many cases infectious microorganisms threaten the integrity and function of the target organs or tissues; therefore, consequent to their recognition the immune system becomes activated to ensure their elimination. Toll-like receptors (TLR) constitute a family of receptors specialized in the recognition of molecular patterns typically associated with infectious agents. Different TLRs exist, each selective for molecular entities and motifs belonging to a specific pathogen group. Consequently, it is thought that the molecular nature of invading microorganisms activates specific TLRs to drive adequate anti-infectious immunity. For instance, nucleic acid-specific, intracellular receptors (TLR3/7/8/9) are used to sense viruses and drive antiviral immunity, while other receptors (such as TLR2 and TLR4) recognize and promote immunity against bacteria, yeast, and fungi. Yet, it is becoming evident that activation of TLR pathways trigger mechanisms that not only stimulate but also regulate the immune system. For instance, TLR stimulation by viruses will drive antiviral interferon but also immunoregulatory cytokine production and regulatory T cell activation. Stimulation of TLRs by bacteria or using molecular agonists can also trigger both immune stimulatory and regulatory responses. TLR stimulation by infectious agents likely serves to activate but also control anti-infectious immunity, for instance prevent potential immunopathological tissue damage which can be

caused by acute immune defense mechanisms. Previous work by us and others has shown that the immunoregulatory arm of TLR stimulation can additionally help control autoreactive processes in autoimmune disease. Hence, it is becoming established that gut commensals, which also play a crucial part in the control of autoimmune disease, establish immune regulatory mechanisms through activation of particular TLRs. In sum, it appears that TLRs are key immune players that not only stimulate but also regulate immune processes in health and disease. In this Research Topic, we wish to review the dual role of TLRs as activators and regulators of immune responses. We aim to motivate data-driven opinions as to the importance of context of TLR agonism for determining immune activation vs. regulation. The presentation of ongoing original works, as well as data and opinions around other innate immune receptors pertaining to this topic, are also encouraged.