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Sommario/riassunto	<p>Activation of innate immune system underlies both pathological and physiological inflammatory responses and is critical for the host. Regulated innate immune response is thus essential not only for the elimination of invading pathogens but also for the restoration of tissue homeostasis. The innate immune system relies on the expression of families of highly conserved Pattern Recognition Receptors (PRRs) by specialised immune cells such as macrophages or dendritic cells. Engagement of PRRs by microbial or host-derived danger signals coordinates the cellular innate immune response. While some receptors such as Toll-like Receptors (TLRs) and C-type Lectin Receptors (CLRs) are membrane bound, others like the Retinoic-acid-Inducible Gene I (RIG-I)-Like Receptors (RLRs), Nucleotide-binding Oligomerization Domain (NOD)-Like Receptors (NLRs) and several DNA receptors (e.g. AIM2, cGAS) are expressed in the cytosol. Moreover, several molecules released by innate immune cells including complement proteins and members of the pentraxin family act as soluble PRRs. Activation of PRRs initiate specific signal transduction cascades, which lead to transcription and secretion of inflammatory mediators, thereby facilitating inflammation. Furthermore, some PRRs can form large oligomeric protein complexes called inflammasomes that instigate proteolytic maturation of members of the IL-1 family of cytokines, thereby driving inflammatory programmed cell death. Current research</p>

on immunomodulation is focused on understanding the fundamental mechanisms that control the activation and regulation of innate immune cell function. This includes exciting advances in understanding signals that can polarize innate immune cells into different functional states, for instance from a more inflammatory to a more tolerogenic profile. However, this response of innate immune cells critically depends on several intrinsic and extrinsic factors such as their own biological status and their microenvironmental context, respectively. For instance, it is known that the extracellular matrix or biomaterials can modulate macrophage behavior and that autophagy flux is a critical regulator of inflammation. Consistent with this, there has been an increase in the development of novel drugs and biomaterials aimed at inducing immunomodulatory responses in targeted innate immune cell populations to be used in the context of tissue regeneration, cancer, autoimmune disease etc. Thus, a thorough understanding of immunomodulatory mechanisms of innate immune cells will guide the development of novel therapeutic strategies aimed to control inflammation-mediated pathologies. In this Research Topic, we aim to highlight recent advances in our understanding of the fundamental mechanisms controlling activation of innate immune cells and document new strategies to study and manipulate their immunomodulation.
