Abstract:
Macrophages are innate immune cells with well-established roles in the primary response to pathogens, but also in tissue homeostasis, coordination of the adaptive immune response, inflammation, resolution, and repair. These cells recognize danger signals through receptors capable of inducing specialized activation programs. The classically known macrophage activation is induced by IFN-gamma, which triggers a harsh proinflammatory response that is required to kill intracellular pathogens. Macrophages also undergo alternative activation by IL-4 and IL-13, which trigger a different phenotype that is important for the immune response to parasites. Here we review the cellular sources of these cytokines, receptor signaling pathways, and induced markers and gene signatures. We draw attention to discrepancies found between mouse and human models of alternative activation. The evidence for in vivo alternative activation of macrophages is also analyzed, with nematode infection as prototypic disease. Finally, we revisit the concept of macrophage activation in the context of the immune response.