UNIVERSITÀ DEGLI STUDI DI MILANO

D-MEM PhD-UNIMI | Doctorate program Milan EXPERIMENTAL MEDICINE

Study of the IL7-R+ monocyte subset in infection and tumor settings

Studio della sottopopolazione monocitaria IL-7R+ in contesto infettivo e tumorale

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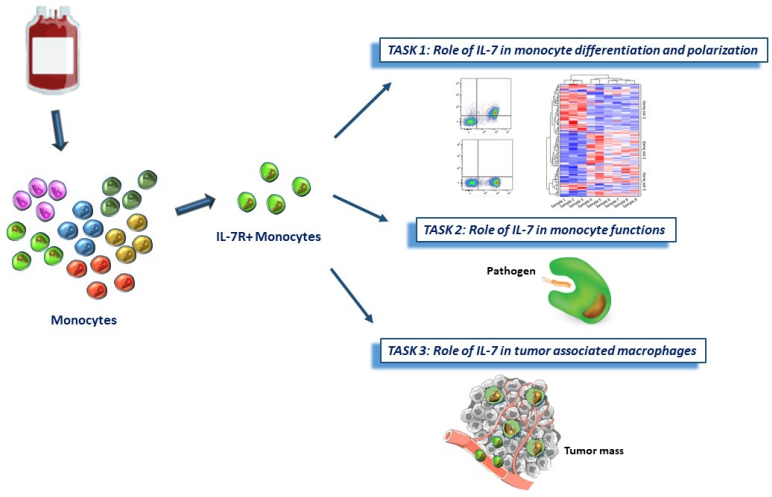
Macrophages partecipate in all stages of inflammation, homeostasis and whound healing and play critical roles in both innate and adaptive immunity. During fetal development, embryonic hematopoietic stem cells seed and differentiate into tissue-specific macrophages, while after birth precursors localized in the bone marrow originate circulating monocytes that differentiate into macrophages in steady state or during tissue inflammation. In tissues macrophages sense mcroenvironmental cues and acquire diversified functional phenotypes, conventionally classified by the two estreme of a spectrum represented by classical activated M1 macrophages and alternatively activated M2 macrophages; nevertheless, the peculiar feature of this cell type is its functional plasticity and phenotypic heterogeneity in response to different enviromental stimuli. Recently, to disclose the functional heterogeneity of monocytic cells in infection and in tumor, we conducted single-cell transcriptome analyses on human circulating monocytes from healthy subjects and COVID-19 patients and on human glioblastoma-infiltrating macrophages. These studies revealed a subset of cells positive for α-chain of the IL-7 receptor (CD127), characterized by a cytotoxic signature in both contexts. IL-7R is a heterodimeric complex consisting of CD127 coupled to the common cytokine receptor γ-chain, shared with the receptors for IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21. Most of the literature on IL-7 refers to the lymphoid compartment, where it mediates B cell progenitors and naïve and memory T cell survival. In the myeloid setting it has been reported the LPS-stimulated monocytes upregulate IL-7R on their surface membranes and IL-7 signaling in monocytic cells induces the expression of inflammatory cytokines, which has been lnked to the activation of M1 macrophages in rheumatoid arthritis. An immunoregulatory activity of IL-7 on peripheral and lung-resident monocytes in lung squamous carcinoma patients has also been reported. Overall, the role of IL-7 in the monocytes and macrophages is largely unknown.
This project will define the functional significance of IL-7R signaling in myeloid cells in infection and tumor setting.



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