**Uncovering the Diversity and Clinical Significance of Myeloid-Derived Cells in the Tumor Microenvironment.**

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**Introduction.** Myeloid-derived cells (MDCs) within the tumor microenvironment (TME) play critical roles in shaping cancer progression and treatment responses. These cells exhibit remarkable plasticity, adopting distinct phenotypic and functional states that can either support or suppress tumor growth. However, the full spectrum of MDC heterogeneity across different tumor types remains incompletely understood, limiting the development of targeted therapeutic strategies.
**Aims**. To characterize MDC subpopulations across cancers, identify those linked to prognosis, and validate findings in independent cohorts.

**Methods**. We integrated scRNA-seq data from multiple solid tumors, focusing on myeloid cells. Clustering and marker analysis defined MDC subtypes. Deconvolution of bulk RNA-seq data estimated subpopulation abundance, and survival analysis identified prognostic subsets. Findings were validated in external datasets.

**Results.** Our integrative analysis identified 29 distinct MDC subpopulations across tumors, including subsets that were previously grouped together, such as TREM2+ and FOLR2+ macrophages. Several subpopulations exhibited tumor-specific expansion, suggesting context-dependent roles. We identified five MDC states with independent prognostic value, including TREM2+PD-1+ and FOLR2+PDL-2+ macrophages. Notably, TREM2 expression alone was not a reliable prognostic marker, as its association with outcome varied depending on co-expressed genes and environmental context. In ovarian and triple-negative breast cancers, high abundance of FOLR2-expressing macrophages was consistently linked to poor prognosis.

**Discussion.** This MDC atlas reveals tumor-specific and shared subpopulations with prognostic relevance. It emphasizes the need for detailed characterization beyond single markers and supports new targets for immunotherapy development.