Single-cell rna sequencing in osteosarcoma: applications in diagnosis, prognosis, and treatment

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Abstract

Background: Osteosarcoma is the most common primary malignant bone tumor in children and adolescents, characterized by high heterogeneity and complex tumor microenvironment (TME). Despite advances in multimodal treatment approaches, survival rates remained stagnant for decades, highlighting the need for novel therapeutic strategies. Single-cell RNA sequencing (scRNA-seq) has emerged as a powerful tool to dissect tumor heterogeneity, identify key populations, and uncover tumor progression and immune evasion mechanisms.

Objective: This systematic review aims to critically synthesize the role of scRNA-seq in osteosarcoma research. The primary objective is to explore its utilization in uncovering the TME and reveal novel biomarkers that could influence clinical prognosis and treatment strategies.

Methods: A comprehensive review of the literature was conducted until January 2024 across PubMed to evaluate the contributions of scRNA seq to the understanding of osteosarcomagenesis. A total of 102 key studies were analyzed to highlight the identification of tumor subpopulations, signaling pathways, diagnostic and prognostic biomarkers, and therapeutic assessments.

Results: Our analysis highlights the critical role of scRNA-seq in uncovering osteosarcoma TME complexity. Studies have identified distinct subpopulations of non-immune and immune cells, revealing key players including TXNIP+ and IFIT1+ macrophages, KAZALD1, EGFL7, TNFSF11, and TRAIL receptors as potential therapeutic targets. Moreover, it facilitated the identification of resistance mechanisms in osteosarcoma progression and metastasis, including CD24 expression as a promising therapeutic target. It also helped discover diagnostic and prognostic biomarkers, such as specific immune and stromal cell signatures within the TME, and enabled the identification of novel therapeutic strategies, including the targeting of Tregs via CXCR4 inhibition, CAFs through LOX and SERPINE1 modulation, and MCL1 in metastatic niches. Additionally, it uncovered promising drug candidates like etoposide, mevastatin, oxfendazole, HDAC inhibitors, and TIGIT blockade, alongside immunotherapeutic strategies leveraging PD-1 inhibition and adoptive CD8+ T cell therapy.

Conclusion: scRNA-seq has revolutionized our understanding of osteosarcoma by revealing key cellular interactions and potential therapeutic vulnerabilities. Although some challenges persist in applying and interpreting this technology, it holds promise for developing more effective and personalized treatments, ultimately improving patient outcomes and survival rates.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.