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Cytokine-chemokine network driven metastasis in esophageal cancer; promising avenue for targeted therapy

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Abstract

Esophageal cancer (EC) is a disease often marked by aggressive growth and poor prognosis. Lack of targeted therapies, resistance to chemoradiation therapy, and distant metastases among patients with advanced disease account for the high mortality rate. The tumor microenvironment (TME) contains several cell types, including fibroblasts, immune cells, adipocytes, stromal proteins, and growth factors, which play a significant role in supporting the growth and aggressive behavior of cancer cells. The complex and dynamic interactions of the secreted cytokines, chemokines, growth factors, and their receptors mediate chronic inflammation and immunosuppressive TME favoring tumor progression, metastasis, and decreased response to therapy. The molecular changes in the TME are used as biological markers for diagnosis, prognosis, and response to treatment in patients. This review highlighted the novel insights into the understanding and functional impact of deregulated cytokines and chemokines in imparting aggressive EC, stressing the nature and therapeutic consequences of the cytokine-chemokine network. We also discuss cytokine-chemokine oncogenic potential by contributing to the Epithelial-Mesenchymal Transition (EMT), angiogenesis, immunosuppression, metastatic niche, and therapeutic resistance development. In addition, it discusses the wide range of changes and intracellular signaling pathways that occur in the TME. Overall, this is a relatively unexplored field that could provide crucial insights into tumor immunology and encourage the effective application of modulatory cytokine-chemokine therapy to EC.

Keywords: Esophageal cancer, Cytokines, Chemokines, Inflammation, Tumor microenvironment, Epithelial-Mesenchymal transition, Drug targets, Immune evasion

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