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Dual role of cytokines in tumor microenvironment

Abstract

Cytokines are immune mediators produced by innate and adaptive immune cells. Cytokines are anti-inflammatory or antitumorigenic or protumorigenic depending on tumor microenvironment. Some of the cytokines such as IL-1β, Il-6,TGF-β involved in tumor progression by activation of transcription factors such as NF-KB,STAT-3,HIf-1α and AP-1. This article briefs about the role of cytokines involved in antitumor and protumor activities.

Keywords: antitumor cytokines, protumor cytokines, NF-KB

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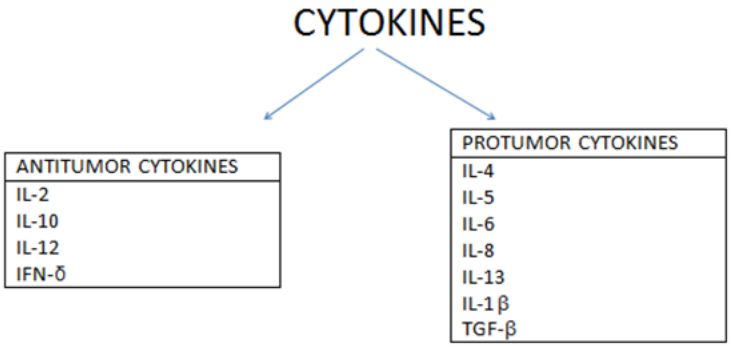
Introduction

Cytokines are molecular messengers produced by innate and adaptive immune cells, cancer cells. Most of all cancers 90 percent of cancers are due to external environmental factors such as physical or chemical or infectious agents.[1-5] Chronic inflammation is a seventh hall mark of cancer accounts 25 percent of all cancers. Chemokines brings the inflammatory cells to the site. Some of the cytokines which acts as anti-inflammatory and anti-tumorigenic and other cytokines which acts as protumorigenic and involved in tumor progression.[5-8]

Anti-inflammatory or pro-inflammatory cytokines in tumor microenvironment

IL-2, IL-10, IL-12, IFN-γ produced by innate and adaptive immune cells acts as anti-inflammatory and anti-tumorigenic. Some of the pro-inflammatory cytokines such as IL-1, TNF-α, TGF-β, IL-6, IL-8 involved in tumor progression by activating NF-KB, a key transcription factor and STAT-3 transcription factor, HIF-1α, AP-1 transcription factors involved in tumor initiation ,prompotion and tumor progression (Flow chart 1).[8-15] ROS and RNS free radicals produced by IL-1, IL-8, TNF-α involved in tissue damage and gene mutation. IL-8 involved in angiogenesis by mediated HIF-1α transcription factor.[15-21] TGF-β at initial stages of cancer acts as antitumorigenic activity and later stages of cancer acts as protumoral activity, immunemodulation and epithelial to mesenchymal transition.[22-28] Nf-Kb a key ubiquitous transcription factor located in the cytoplasm of every cell activated by proinflammatory cytokines such as IL-6,IL-1β,TNF-α results in translocation binding of NF-KB transcription factor to nuclear DNA later involved in transcription of inflammatory mediators.[28-35] NF-KB transcription factor controls more than 500 genes involved in cell proliferation by activating (cyclin D,E), cell survival by BCL-XL, BCL-2, survivin, angiogenesis by IL-8, HIF-1α, COX-2, genomic instability by ROS, RNS, AID, Immunemodulation by TGF-β, IL-4, IL-5, IL-13, IL-10 and invasion and metastasis by Mmp's 2,9 and UPA. IL-17 and IL-23 proinflammatory cytokines produced by CD4T cells involved in tissue damage (Flow chart 2).[36-44]



Flowchart 1 Antitumor or protumor cytokines in tumor microenvironment.

Flowchart 2 Cytokines in tumor micro environment involving tumor progression.

Cytokines	Transcription factor activated	Tumor progession
IL-1β TNF-α IL-6	NF-KB	Cell proliferation Cell Survival Immune modulation Angiogenesis Invasion and Metastatis
TGF-β IL-4 IL-5		Immune modulation Epithelial tomesenchymal transition
IL-17 IL-23		Tissue damage
IL-8	HIF-1α	angiogenesis

Conclusion and future perspective

Cytokines are molecular messengers produced by immune cells and cancer cells. Some cytokines such as IL-2, IL-10, IL-12 and IFN-γ acts as anti-inflammatory and anti-tumor activity where as some cytokines acts as proinflammatory and protumorigenic such as IL-6, TGF-β, IL-17, IL-23, IL-8, IL-5, IL-4, IL-13 involved in tumor progression by angiogenesis, cell proliferation, cell survival, immunomodulation, tissue damage by activation of NF-KB, STAT-3 key transcription factors. We have to understand the anti-inflammatory and anti-tumor activity or pro-inflammatory and pro-tumor activity depends on tumor microenvironment. Role of cytokines in different stages of cancer and its progression helpful for biomarkers for early detection, prognostic markers, therapeutic target cancer immunotherapy.

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None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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