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Mini Review

Potential roles of cytokine signaling

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Abstract: Cytokines are signaling proteins that are vital to numerous brain functions and have well-established roles in infection, pregnancy, and the function of bones, muscles, and the cardiovascular system. Signaling proteins called cytokines were initially identified as elements of the immune response, but they have now been shown to have a variety of pleiotropic effects on other bodily functions in both health and illness. Numerous cells release them, and they are widely utilized in intercellular connections to generate a variety of activities, including complex processes involved in ontogenetic development. This brief review covers recent research on cytokine signaling pathways during development as well as aspects involved in the control of many diseases. Given the evidence currently available that cytokines play a part in the development and management of several illnesses, these molecules and their signaling pathways may be the focus of therapeutic intervention.

Keywords: Cytokines; signaling pathways; human diseases

Background

A single cell type releases cytokines, which are a class of proteins that regulate an organism's response to infection or inflammation. By binding to particular receptors, cytokines affect the activity of other cells. Cytokines carry signals from one cell to another in an organism. Their interactions with receptors, which either inhibit or stimulate the activity of particular genes within the cell, result in secondary signals. The majority of cytokines are specific to the cells that created them, in contrast to endocrine hormones, which have a broad variety of effects. Glycoproteins known as cytokines act as intercellular mediators, promoting the growth, differentiation, proliferation, or death of target cells[1-7].

They function by binding to specific receptors on the surface of target cells and initiating an intracellular signalling cascade based on phosphotyrosine, which is initiated by kinases and then spread and impacted by transcription factors with SH2 domains. The intensity and duration of cytokine signalling are strictly limited due to its proliferative and often inflammatory nature. By modifying associated signalling pathways such proliferation, growth, metastasis, and apoptosis, cytokines can either promote tumour growth (oncogenic cytokines) or inhibit tumour growth (anti-oncogenic cytokines). The majority of cytokines are small, 150–200 amino acid helical tubular proteins that fall into one of two groups based on receptor patterns. Class I cytokines are arranged in an up-up-down-down sequence with four helices. While their shape is sustained, some of them, such as IL5, are dimers. Two lengthy loops are anticipated to create up-up and down-down sets because of the peculiar up-up-and-down-down structure. In class II cytokines, one or both of these loops are modified by an extra helix, producing roughly five to six antiparallel helices. Numerous cell types emit cytokines, which have a big impact on how the body responds to invasive infections or cellular damage. The production of TH1 cytokines is mediated by two important processes. IL-12 signalling activates Stat4 through its receptor, increasing the production of IFN-gamma. However, IFN-gamma stimulates Stat1, which in turn stimulates T-bet, the most important TH1 transcription factor, increasing IFN-gamma synthesis[2, 3, 8-17].

Cytokines and human diseases: Covid-19 is an infectious human disease that is spread throughout the world. According to a number of studies, people who are really sick have higher levels of pro-inflammatory cytokines, namely interleukin (IL)-6, than patients who are only mildly unwell. It has long been thought that cancer patients are far more vulnerable to viral infections, most likely as a result of compromised immune systems. Early in the COVID-19 infection, a number of cytokines were elevated, including as interleukin (IL)-6, IL-1ß, tumour necrosis factor-a (TNF-a), and interferons. The microtumor environment may profit from the virus protein's ability to activate important inflammatory pathways by triggering a variety of signals. The disruption of the signalling pathways will lead to immunosuppression, altered cellular communications, decreased apoptosis, altered metabolism, and increased angiogenesis. Viral proteins and inflammatory mediators onco-modulate the tumour microenvironment, increasing the likelihood of cancer survival and progression. In human disorders, changes (genetic changes, aberrant signalling pathways, and epigenetic modifications) at various levels can lead to changes in cell destiny[2, 4, 18-23]. Cellular signalling and connectivity may

be impacted by changes in proteomics and epigenomics. Cytokines are released by host cells as a defensive reaction to internal stressors, such as cancer or microbial infection, and are essential for cell metabolic reprogramming. The cause could be squamous cells, mucus, or any other lung cell[3, 21, 24-33].

Tumour spread is controlled by several signalling channels and epigenetic mechanisms. Chronic inflammation brought on by lung infections causes pro-inflammatory cytokines to build up, the TME to change, and cancer to spread. Macrophages release pro-inflammatory cytokines (including TGF-, IL-6, IL-10, and TNF-) that help tumour cells proliferate and survive by giving them characteristics of stem cells. In lung malignancies, prolonged exposure to all of these cytokines triggers several inflammatory pathways, such as TNF, enhanced TGF-signaling network activation, and STAT3 pathway stimulation through overexpression of IL-6. Patients infected with COVID-19 are more prone to the systemic weakened immune responses of the cancer patients or the anticancer treatment they are undergoing may be the cause of this[2, 34-37]. Since lung cancer patients already have chronic pulmonary inflammation due to the underlying TME and lung pathology, they may be in a more difficult condition. Understanding the impact of the tumour microenvironment can be gained by compiling a systematic list of genes whose expression is either upregulated or downregulated in response to infection. Lung cancer and COVID-19 infection are associated with mutations in a number of genes or proteins that may either activate or suppress specific signalling pathways and epigenetic mechanisms that promote tumour growth.

Cytokines are important inflammatory mediators that play a significant role in inflammatory and autoimmune disorders. Beyond their well-established activities in the immune system, the cytokines most relevant to rheumatic disorders also play significant roles in a variety of non-immune cell types, such as fibroblasts, osteoblasts, osteoclasts, and endothelial cells. In addition to helping us better understand the pathogenetic mechanisms of conditions like rheumatoid arthritis, osteoarthritis, and systemic lupus erythematosus—diseases in which cytokines are crucial—advances in our understanding of cytokine biology are also propelling the creation of novel treatment approaches. Numerous studies are currently being conducted to evaluate the effectiveness of cytokine signalling modulation in disease, and this rapidly evolving field of study is seeing noteworthy success with techniques that target cytokine-mediated processes[3, 31, 38-43].

Future perspectives and conclusions: Cytokines have dual roles in normal physiology and the pathophysiology of illnesses like cancer, and they are essential in controlling immune responses and cellular behaviour. These molecules can affect the tumour microenvironment, promote or inhibit tumour growth, and affect the effectiveness of cancer treatments. They include chemokines, interleukins, interferons, tumour necrosis factors, and growth factors like TGF-β, VEGF, and EGF. Recent developments in focussing on these pathways have demonstrated encouraging therapeutic potential, providing fresh approaches to immune system modulation, tumour progression inhibition, and treatment resistance. The present knowledge and therapeutic implications of focussing on cytokine and chemokine signalling pathways in cancer were compiled here. We emphasised the creation of new therapeutic drugs targeted at modifying these pathways in order to fight cancer by investigating the functions of these molecules in tumour biology and the immune response. The review explained how cytokines can either promote or suppress carcinogenesis, depending on the situation, and the potential and problems this poses for therapeutic intervention. Examining the most recent developments in targeted therapies—such as receptor inhibitors, fusion proteins, monoclonal antibodies, bispecific antibodies, and synthetic cytokine variants—and their effects on tumour growth, metastasis, and the tumour microenvironment is essential. In order to overcome resistance and enhance patient outcomes, it may also be worthwhile to assess the possibility of combining these targeted medicines with other forms of treatment. should concentrate on the ongoing studies and clinical trials that are essential to improving our knowledge and use of cancer treatments that target cytokines and chemokines.

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