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Inflammation Related Cancer - Highlights

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Abstract

Inflammation is a body response to infectious or physiological agents. During this process aggrevated chronic inflammation mediated release of various mediators such as chemokine's, cytokines and growth factors by neutrophils, lymphocytes, and macrophages are predominant abundant cells in tumor microenvironment promotes tumor progression. Myeloid derived suppressor cells are immature myeloid progenitor cells upon activation of chronic inflammatory mediators release various factors such as COX2, INOS, ROS, Arginase1 bring about immunosuppression and tumor progression. This article highlight about inflammation related cancer mediated by macrophages and myeloid derived suppressor cells.

Keywords: Inflammation; Cancer; Myeloid derived suppressor cells; Inflammatory mediators

Abbreviations

HGF: Hepatic Growth Factor; VEG: Vascular Endothelial Growth Factor; MMP-9: Matrix Mettaloproteinases-9, COX2: Cyclo-oxygenase2; INOS: Inducible Nitric Oxide Synthase; ROS: Reactive Oxygen Species; PDGF: Platelet Derived Growth Factor; EGF: Epidermal Growth Factor; FGF: Fibroblast Growth Factor; TNF-Alfa: Tumour Necrosis Factor-Alfa; IFN-Beta: Interferon Beta; IL-10: Interleukin 10; TGF-Beta: Transforming Growth Factor-Beta; CCL17: CC Chemokine ligand 17; CCL18: CC Chemokine ligand 18; CCL22: CC chemokine ligand 22; PGE2: Prostaglandin E2; IDO: Indoleamine 2,3-dioxygenase; UPA: Urokinase Plasminogen Activator; UPAR: Urokinase Plasminogen Activator Receptor; IL-2: Interleukin 2; IL-4: Interleukin 4; IL-6: Interleukin 6; IFN-Gamma: Interferon Gamma; COX-1: Cyclo-oxygenase1; COX2: Cyclo-oxygenase2, NF-KB: Neuclear Factor KB; MCP-1: Macrophage/Monocyte Chemoattractant Protein-1; M-CSF: Macrophage Colony Stimulating Factor; IL-17: Interleukin 17; CD4+ Th17: CD4+ T helper lymphocyte17; MDSC: Myeloid Derived Suppressor Cells, SR-A: The Class A Macrophage Scavenger Receptor msr1; GM-CSF: Granulocyte Macrophage-Colony Stimulating Factor; G-CSF: Granulocyte Colony Stimulating Factor; STAT3: Signal Transducer and Activator of Transcription3; bFGF-Basic Fibroblast Growth Factor; MMPS: Matrix Metallo Proteinases; HIF-1 Alfa: Hypoxia- Inducible Factor Alfa; T reg cell: T Regulatory Cell; T h1: T Helper1; Th2: T Helper 2.

Introduction

Inflammation is a physiological response to injury or infection. In this process various chemical mediators are released by recruited inflammatory cells such as cytokines, growth factors, reactive oxygen species, nitrogen species and inflammatory signals are activated as a defensive action to combat against infection and heal injured tissue [1-3].

Inflammatory mediators are released by inflammatory cells such as neutrophils, macrophages, lymphocytes. If the inflammation is persisted and aggravates chronically, results dysregulated immune system in tumor microenvironment results in initiation, promotion, progression of cancer [2,4].

Inflammatory-immune cells, stromal tissue affect malignant cells through production of chemokine's, cytokines, growth factors, prostaglandins and reactive oxygen and nitrogen species [2,3].

Infection and chronic inflammation contributes 10-20% of cancer. Preclinical and Clinical studies suggested that dysregulated immune system in Chronic inflammation is epidemiologically related to cancer [3,5,6]. Some inflammatory conditions or injury that are associated with malignancy are Lichen planus, gingivitis and chronic periodontitis associated oral squamous cell carcinoma, Sialadenitis related salivary gland carcinoma, Gastric acid associated barrett's metaplasia and reflux oesophagitis associated oesophageal carcinoma, Sjogren's syndrome and Hashimoto's thyroiditis associated mucosa associated lymphoid tissue lymphoma, UV radiation associated skin inflammation melanoma, Silica, asbestose, smoking associated silicosis and bronchitis associated lung carcinoma [7]. Neutrophils pro-tumoral activity by releasing ROS(Reactive oxygen species) and RNS(Reactive nitrogen species) induce genetic instability, promote angiogenesis by VEGF(Vascular endothelial growth factor), MMP-9 or prokinectin2 (BV8) and neoplastic cell invasion by mediators such as HGF(Hepatic growth factor) and oncostatin [8,9]. Macrophages are the predominant immune cells in tumor microenvironment contributes to tumor progression by releasing chemokine's, cytokines, growth and transcriptional factors such as VEGF, PDGF, EGF, FGF, TNF-Alfa, IFN -Beta promotes tumor growth [8]. IL-10, TGF-Beta ,CCL17, CCL18, CCL22, PGE2, ROS, IDO, B7-H1 antibody promotes immunosuppression by naïve T cell energy, Recruitment of Th2 cell, inhibition of Th1 cell and induction of Treg (T regulatory) cell. VEGFs, PDGF, EGF, FGF, TGF-Beta, MMP-9, CXCL8, ELR+ chemokine, cyclooxygenase promote angiogenesis and lymphagiogenesis. MMPs, TGF-Beta, UPA, UPAR, VEGFs, PDGF, Cathespins, TNF-Alfa, MCP-1, M-CSF, SR-A, HIF-1 promotes matrix remodeling, Cell proliferation, resistance to apoptosis, epithelial mesenchyme transition, tumor

invasion and metastasis by activating master transcriptional factor NF-KB. T lymphocytes produce cytokines such as IL-2, IL-4, IL-6, IL-10, TNF-Alfa, IFN-Gamma, COX-1 and COX2 promote malignant disease. IL-17 cytokine generated by CD4+Th17 cells produce inflammatory mediators such as TNF-Alfa, IL-6 and IL-1 Beta proinflammatory cytokines, promote tumorigenesis by production of PGE2,VEGF,Keratinocyte-derived chemokine and macrophage inflammatory protein-2 (MIP-2) angiogenic factor [10-12].

Myeloid derived suppressor cells (MDSC) are heterogeneous population of immature myeloid cells that are precursors of dendritic cells, macrophages and/or granulocytes derived from bone marrow is of two types granulocytic or monocytic. Myeloid derived suppressor cells has a potent regulatory immune response and have a major role in chronic inflammation and tumor development by activation of tumor derived mediators or cytokines such as IL-1beta, IL-4, IL-6, IL-10 and TGF-Beta induce expression of arginase-1, Inducible nitric oxide synthase (iNOS) or ROS immunosuppressive factors which can initiate apoptosis in T cells, Programmed cell death and immunosuppression of effector cells such as adaptive and Innate immune cells [13-15].

Conclusion

Expansion of Myeloid derived suppressor cells by factors such as GM-CSF, G-CSF, M-CSF, Stem cell factor and VEGF. Myeloid derived suppressor cells activates STAT3 and MMP (Matrix mettalo proteases) there by promoting angiogenesis and invasion, cell Proliferation by further activation of STAT3 induces the secretion of bFGF and VEGF. Myeloid derived suppressor cells activates matrix mettaloproteases facilitate cancer cell invasion and intravasation by disruption of endothelial cadherins, degradation of extracellular matrix, adhesion proteins or basement membrane vessels.

MDSC also facilitate epithelial to mesenchymal transition in cancer cells by using factors such as epidermal growth factor (EGF), Hepatocyte growth factor (HGF) and TGF-Beta [16,17].

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