## REVIEW



## Cytokine- and chemokine-induced inflammatory colorectal tumor microenvironment: Emerging avenue for targeted therapy

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Revised: 28 February 2022

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Abbreviations: APC, adenomatous polyposis coli; CAFs, cancer-associated fibroblasts; CCL3, C-C motif chemokine ligand 3; CCR6, chemokine receptor 6; CDH1, cadherin 1; COX-2, cyclooxygenase-2; CRC, colorectal cancer; CSF1, colony-stimulating factor 1; CSF2, colony stimulating factor 2; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; CTLs, cytotoxic T lymphocytes; CXCL, C-X-C motif chemokine ligand; CXCR, C-X-C chemokine receptor; DCs, dendritic cells; ECM, extracellular matrix; EMT, epithelial-mesenchymal transition; eNOS, endothelial nitric oxide synthase; FCyR3, immunoglobulin G Fc Receptor 3; FOXP3, forkhead box P3; FRA1, fos-related antigen 1; GM-CSF, granulocyte-macrophage colony-stimulating factor; GP130, glycoprotein 130; GSK3 $\beta$ , glycogen synthase kinase 3 beta; HMGA1, high mobility group AT-hook 1; HMGB1, high mobility group box 1; IBDs, inflammatory bowel diseases; ICAM-1, intercellular adhesion molecule 1; IDO, indoleamine 2,3-dioxygenase; IL, interleukin; IL-1 $\beta$ , interleukin-1 beta; Lin"HLA-DR", lineage negative-human leukocyte antigen-DR isotype; LRG1, leucine rich alpha-2-glycoprotein 1; MAPK, mitogen-activated protein kinase; MCAM, melanoma cell adhesion molecule; M-CSF, macrophage colony-stimulating factor; MDSCs, myeloid-derived suppressor cells; MHC1, major histocompatibility complex class 1; MMP-9, matrix metalloproteinase-9; NF-xB, nuclear factor kappa-light-chain-enhancer of activated B cells; NK, natural killer; OCT4, octamer-binding transcription factor 4; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PMN, pre-metastatic niche; RNS, reactive nitrogen species; RORyt, retinoic-acid-receptor-related orphan nuclear receptor gamma; ROS, reactive oxygen species; RUNX1, runt-related transcription factor 1; SIPR1, sphingosine-1-phosphate receptor 1; SMAD4, SMAD family member 4; SNAI2, snail family transcriptional repressor 2; SNAIL, zinc finger protein SNAI1; SOCS3, suppressor of cytokine signaling 3; SOX2, SRY-box transcription factor 2; STAT3, signal transducer and activator of transcription 3; TAMs, tumor-associated macrophages; TCF4, transcription factor 4; TCGA, The Cancer Genome Atlas; TCR, T-cell receptor; TFAP4, transcription factor activating enhancer-binding protein 4; Th1, T-helper 1; TILs, tumor-infiltrating lymphocytes; TME, tumor microenvironment; TNF-a, tumor necrosis factor-a; TRAF6, TNF receptor associated factor 6; Tregs, T-regulatory cells; TRIM47, tripartite motif containing 47; TSP-1, thrombospondin-1; TWIST1, twist-related protein 1; VEGFA, vascular endothelial growth factor A; ZEB1, zinc finger E-box-binding homeobox 1; α-SMA, alpha-smooth muscle actin.

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