

Inflammation and cancer

Different types of inflammation contribute to tumour development in different ways; chronic inflammation leads to mutations, genomic instability, angiogenesis and tumour development; tumour associated inflammation leads to genomic instability, angiogenesis, immunosuppression, metastasis and tumour growth; inflammation caused by environmental exposure leads to mutations, genomic instability, angiogenesis and tumour promotion; therapy induced inflammation leads to antigen presentation. Chronic inflammation is associated with cancer to a greater extent than acute inflammation.

Cancer-enabling inflammation

Infiltrating cancers provoke a chronic inflammatory reaction, causing systemic signs and symptoms such as anaemia, fatigue, and cachexia. Inflammatory cells, also modify the local tumour microenvironment to enable the hallmarks of cancer, these effects may stem from direct interactions between inflammatory cells and tumour cells, or through indirect effects of inflammatory cells on other resident stromal cells, particularly cancer associated fibroblasts and endothelial cells.

Cancer enabling effects of inflammatory cells-

- Release of factors that promote proliferation. Infiltrating leukocytes and activated stromal cells secrete growth factors, such as EGF, and proteases that can liberate growth factors from the ECM.
- Removal of growth suppressors. The growth of epithelial cells is suppressed by cell-cell and cell-ECM interactions, proteases released by inflammatory cells can degrade the adhesion molecules that mediate these interactions, removing a barrier to growth.
- Enhanced resistance to cell death. Detachment of epithelial cells from basement membranes and from cell-cell interactions can lead to a form of cell death called anoikis. Tumour-associated macrophages prevent anoikis by expressing adhesion molecules such as integrins that promote direct physical interactions with tumour cells. Stromal cell-cancer cell interactions increase the resistance of cancer cells to chemotherapy.
- Inducing angiogenesis. Inflammatory cells release numerous factors, including VEGF, which can stimulate angiogenesis.
- Activating invasion and metastasis. Proteases released from macrophages foster tissue invasion by remodelling the ECM, while factors such as TNF and ECM may directly stimulate tumour cell motility. Other factors released by stromal cells, such as TGF-beta, may promote epithelial-mesenchymal transitions, a key event in the process of invasion and metastasis.
- Evading immune destruction. A variety of soluble factors released by macrophages and other stromal cells contribute to the immunosuppressive T regulatory cells or suppress the function of CD8+ cytotoxic T cells. Advanced cancers contain alternatively activated macrophages which produce cytokines that promote angiotensin, fibroblast proliferation and collagen deposition.
- Inhibition of tumor growth by antigen presentation, cytokines and reactive oxygen/nitrogen intermediates.
- Induction of DNA damage by the generation of free radicals.