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Meeting Abstract

Toll-like receptors, cancer, and inflammation

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Abstract

The interaction of the inflammatory mediators and innate and immune effector cells with carcinogenesis and tumor progression is complicated and results in effects that either favor or impede tumor progression. The simple concept that early inflammation is necessary for carcinogenesis whereas inflammatory and immune response would prevent, when successful, tumor progression has been replaced by a more subtle understanding that the degree of inflammation and the type of inflammatory/immune response are responsible for tilting the balance between tumor progression and regression. Furthermore, it is becoming evident that the processes that the organisms use for resistance to infections are derived and shared with the mechanisms essential for tissue homeostasis and morphogenesis. Innate resistance is mediated not only by specialized cells but most stromal and parenchyma cells participate in the process and they may express and utilize many of the receptors also utilized by "immune" cells with similar signaling and physiological responses. Similarly, in cancer biology, it is becoming manifest that what used to be considered the defensive mechanisms of innate resistance and inflammation are indeed manifestations of tissue homeostasis and control of cellular proliferation that have many pleiotropic effects on carcinogenesis as well as on tumor progression and dissemination.

The Toll-like receptor (TLR) family has been recognized as having a central role in the recognition of molecular pattern on pathogens and other self and non-self products and in the induction of inflammation/innate resistance. Although initially the TLR have been studied mainly as receptors expressed on hematopoietic cells, particularly on phagocytes and dendritic cells, it is clear that some of them are widely distributed on other cell types, including epithelial, endothelial, stromal cells and also on tumor cells. Although TLR have been described to recognize products of foreign organisms (pathogenic or not) they might also participate in the regulation of inflammation by recognizing endogenous ligands (e.g. heat shock proteins and low mol wt hyaluronan for TLR4, antibody-DNA complexes for TLR9 and RNA from necrotic cells for TLR3) that are present in inflamed tissues. Importantly, the cellular response to TLR ligands is not only production of pro-inflammatory mediators but also cellular differentiation, proliferation, and apoptosis. In this lecture I will briefly summarize data on the tissue distribution of TLR and on the role that TLR expressed on hematopoietic infiltrating cells and on tissue or tumor cells may have on tumor initiation and progression as well as in cancer immunotherapy.