The fibroblast: sentinel cell and local immune modulator in tumor tissue

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Development and progression of epithelial malignancies are frequently accompanied by complex phenotypic alterations of resident tissue fibroblasts. Some of these changes, such as myofibroblastic differentiation and an oncofetal extracellular matrix (ECM) expression profile, are also implicated in inflammation and tissue repair. Studies over the past decade revealed the relevance of reciprocal interactions between tumor cells and tumor-associated host fibroblasts (TAF) in the malignant process. In many tumors, a considerable fraction of the inflammatory infiltrate is located within the fibroblast- and ECM-rich stromal compartment. However, while fibroblasts are known as "sentinel cells" in various nonneoplastic diseases, where they often regulate the composition and function of recruited leucocytes, they are hardly considered active participants in the inflammatory host response in tumors. This article focuses on the functional impact of TAF on immune cells. The complex network of immune-modulating effects transduced by TAF and TAF-derived factors is highlighted, and recent reports that support the hypothesis that TAF are involved in the inflammatory response and immune suppression in tumors are reviewed. The role of TAF-dependent ECM remodeling and TAF-derived peptide growth factors, cytokines, and chemokines in the immune modulation is stressed and the idea of TAF as an important therapeutic target is emphasized.