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TGF-β SIGNALING IS A NOVEL THERAPEUTIC TARGET FOR TREATING METASTATIC CANCERS ACQUIRED BY EMT AND CANCER STEMNESS

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TGF-β is a multifunctional cytokine involved in diverse cellular functions, including cell growth and immune responses. TGF-β signaling has emerged as a key architect of the microenvironment in poor-prognosis cancers. Disseminated tumor cells show a strong dependency on a TGF-β-activated stromal during the establishment and subsequent expansion of metastasis. TGF-β also has a positive role on the cancer stem cell (CSC) population promoting or sustaining stemness of the pool of CSCs in diverse types of malignancy. Since TGF-β signaling is dysregulation most of human cancers, thus affecting the overall progression to malignancy, TGF-β signaling has been considered a potentially novel therapeutic target for treating resistance acquired by emptying the TGF-β signaling pathway, TGF-β receptor I kinase inhibitors have shown promise in blocking the TGF-β-mediated tumor progression and metastasis and enhancing antitumor immunity in nonclinical animal models. Vactosertib, a TGF-β receptor I kinase inhibitor, has shown significant preclinical antitumor efficacy in a range of in vivo metastatic and orthotopic xenograft models and has completed phase 1 clinical trials in USA. Recent molecular classification of gastrointestinal cancer has identified a poor-prognosis transcriptional subtype associated with mesenchymal traits and genes upregulated by TGF-β in stromal cells are robust predictors of cancer recurrence and metastasis. This observation warrants the development of anti-TGF-β therapies for the treatment of poor-prognosis cancers with TGF-β response signature.

BIOGRAPHY

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