

Targeting human cancer stem cells with monoclonal antibodies

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Cancer stem cells (CSCs) constitute a distinct subpopulation of tumor cells that exhibit self-renewal and tumor initiation capacity and the ability to give rise to the heterogenous lineages of cancer cells that comprise the tumor. CSCs possess various intrinsic mechanisms of resistance to conventional chemotherapeutics, novel tumor-targeted drugs and radiation therapy, permitting them to survive current cancer therapies and to initiate tumor recurrence and metastasis. Different cell surface and transmembrane proteins expressed by CSCs, including CD44, CD47, EpCAM (CD326), CD123, CD133, GD2, Lgr5, insulin-like growth factor receptor I (IGF-IR), and members of the Notch and Wnt signaling pathways, have been identified and mainly used for the characterization of CSCs in experimental settings. Recently, monoclonal antibodies and antibody constructs such as Triomabs and BiTEs raised against these CSC proteins have shown efficacy against CSCs in human xenograft mice, and some of them have been demonstrated to induce tumor regression in clinical trials.

Since current cancer therapies fail to eliminate CSCs, ultimately leading to cancer recurrence and progression, selective targeting of CSCs with mAbs and antibody constructs reviewed herein may represent a novel and promising therapeutic strategy to eradicate cancer.

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