TARGETING CANCER STEMNESS PATHWAYS

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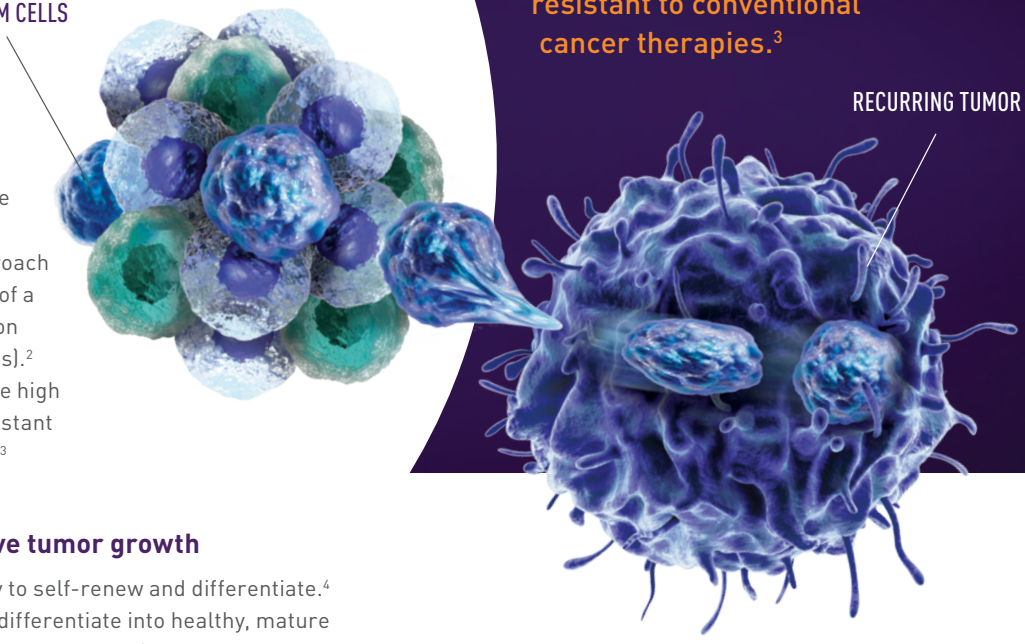


Not all cancer cells within a tumor are equal

Despite current advances in cancer therapy, tumor recurrence and metastases remain clinical challenges.[1] A potential new approach to address these is the targeting of a subset of the tumor cell population known as cancer stem cells (CSCs).[2] CSCs are highly tumorigenic, have high metastatic potential, and are resistant to conventional cancer therapies.[3]

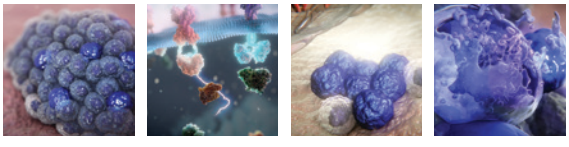
Stemness of CSCs may drive tumor growth

Stemness is defined by the ability to self-renew and differentiate.[4] Unlike normal stem cells, which differentiate into healthy, mature cell types, CSCs differentiate into cancer cells.[4] The stemness of CSCs is maintained by various signaling pathways that are overactivated, including JAK/STAT, Wnt/ß-catenin, Nanog, and Notch, depending on the tumor type.[5-9]

Stemness may enable CSCs to metastasize and regrow tumors.[3] This makes CSCs phenotypically different from non-stem cancer cells and may confer therapy resistance.[3] Stemness can be acquired by non-stem cancer cells as they dedifferentiate in response to multiple stimuli, possibly including conventional cancer therapies.[10,11]

The CSC model may help explain tumor recurrence

In the clonal evolution model, all cells within a malignant tumor have similar tumorigenic activity.[12] By contrast, in the CSC model only a subset of tumor cells, CSCs, have tumor-initiating capability.[2] This may help to explain why early tumor shrinkage is often poorly predictive of overall survival.[13,14] While conventional therapies kill the bulk of non-stem cancer cells, resulting in tumor shrinkage, CSCs may remain viable and later reestablish the tumor, leading to relapse.[4]



A key implication of the CSC model for cancer treatment is that both CSCs and non-stem cancer cells should be targeted to reduce tumor recurrence and metastasis.[15,16] The next generation of cancer therapeutics is in development with investigational agents designed to inhibit stemness pathways.[1]

Targeting Stemness

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Boston Biomedical is developing the next generation of cancer therapeutics with drugs designed to inhibit cancer stemness pathways. Clinical trials are underway with the goal of reducing recurrence and metastasis.

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