

Cancer Stem Cells

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stem cell theory of cancer

- The stem cell theory of cancer proposes that among all cancerous cells, a few act as stem cells that reproduce themselves and sustain the cancer, much like normal stem cells normally renew and sustain our organs and tissues.

Normal stem cells

Rare cells within organs with the ability to self-renew and give rise to all types of cells within the organ to drive organogenesis

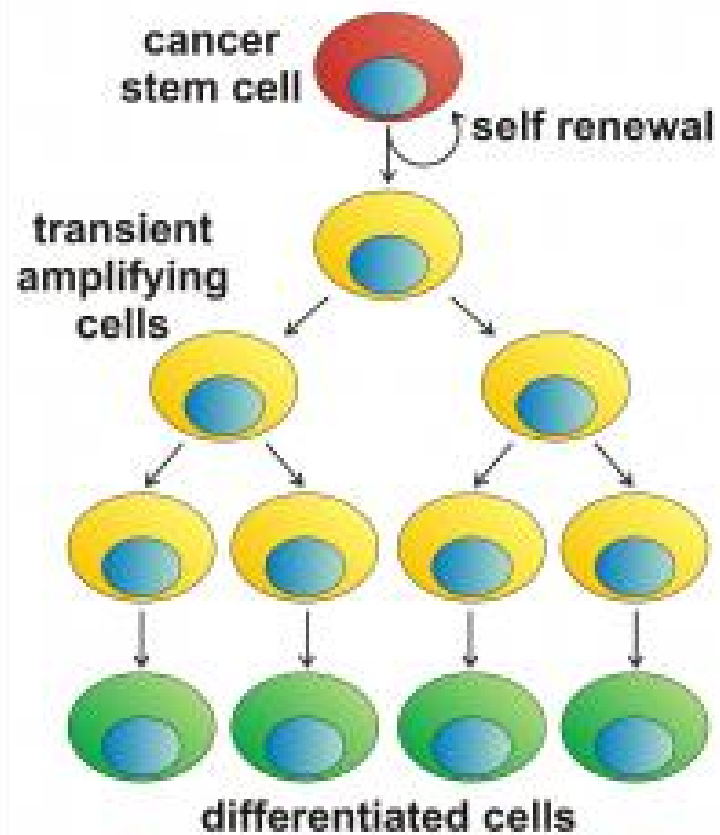
Cancer stem cells

Rare cells within tumors with the ability to self-renew and give rise to the phenotypically diverse tumor cell population to drive tumorigenesis

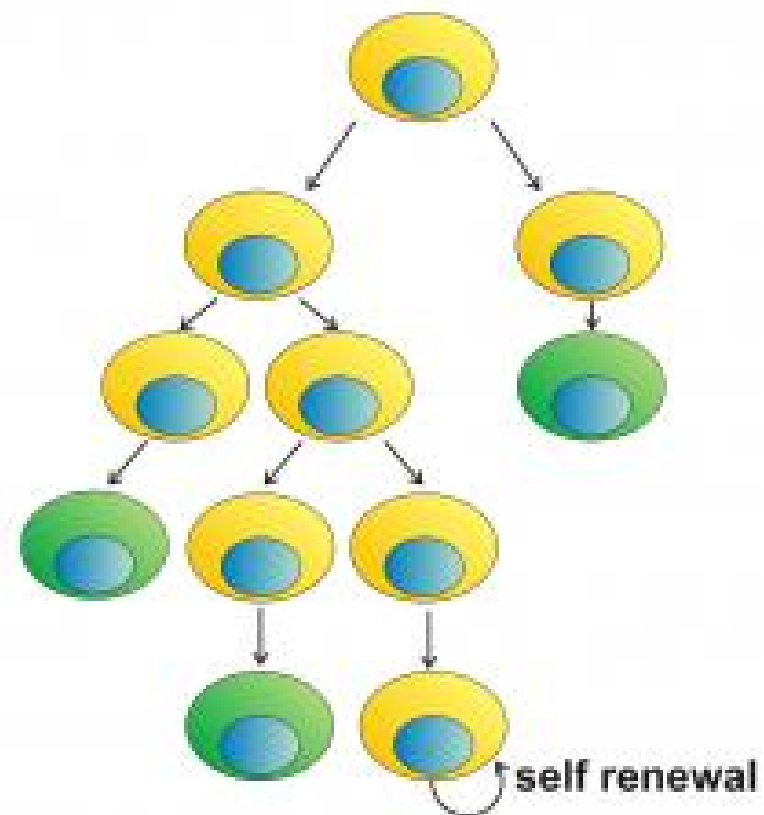
From where Cancer stem cells come from?

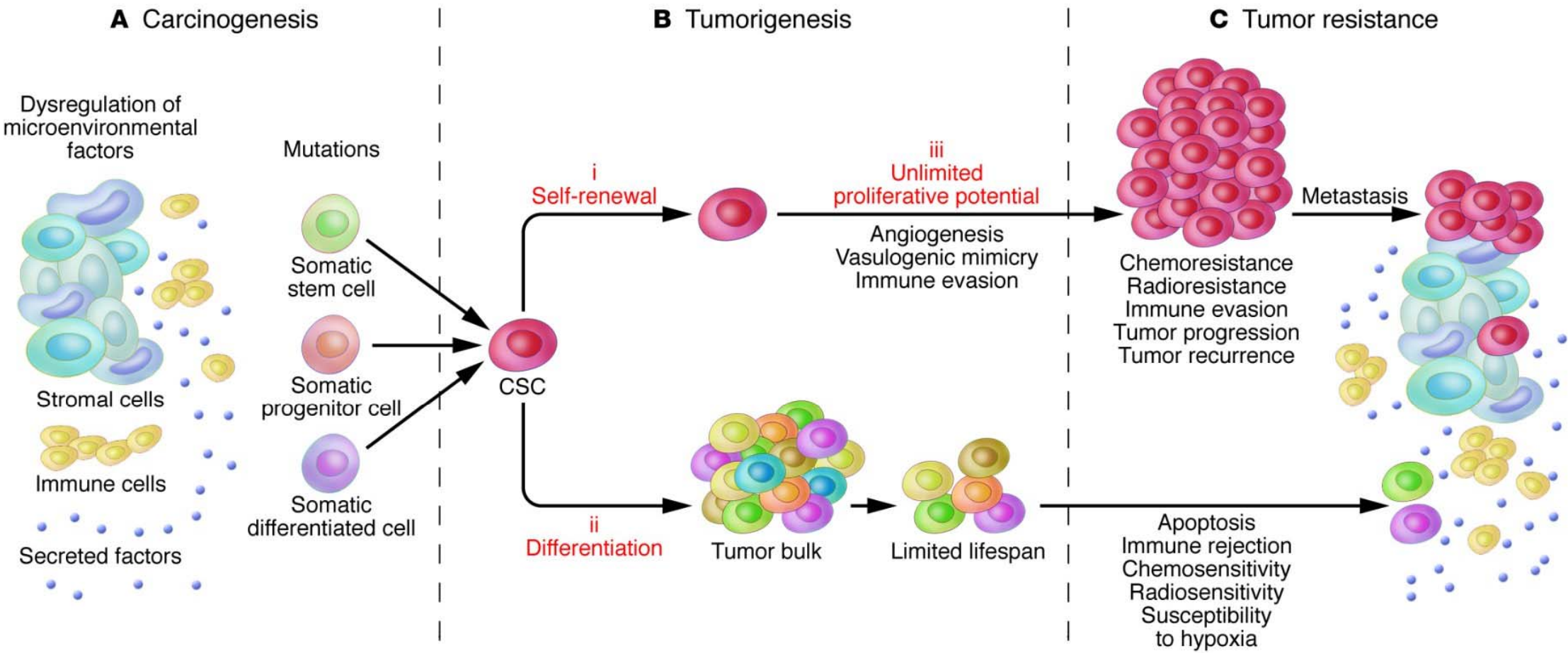
- The theory, therefore, is that cancer stem cells arise out of normal stem cells or the precursor cells that normal stem cells produce.

The cancer stem cell model



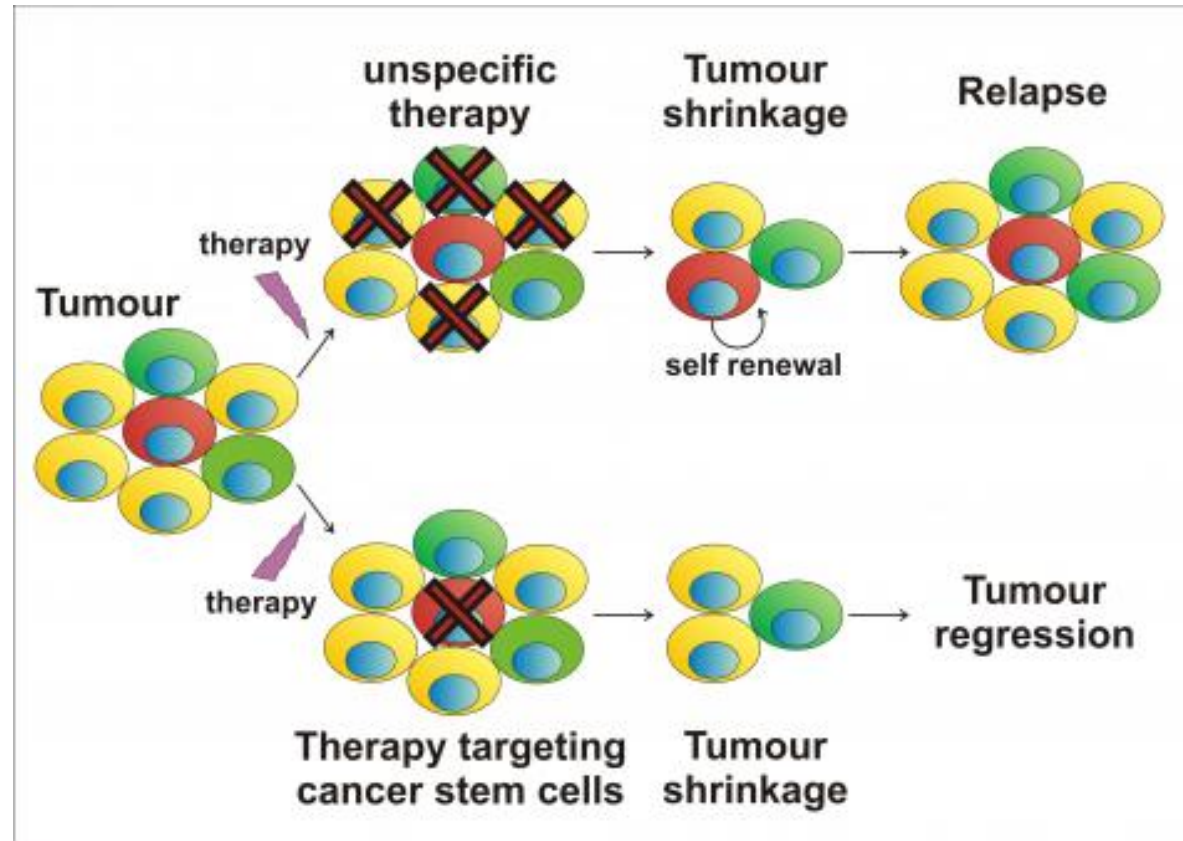
The stochastic model





Cancer Therapy

The idea that cancer is primarily driven by a smaller population of stem cells has important implications. For instance, many new anti-cancer therapies are evaluated based on their ability to shrink tumors, but if the therapies are not killing the cancer stem cells, the tumor will soon grow back (often with a vexing resistance to the previously used therapy).



An analogy would be a weeding technique that is evaluated based on how low it can chop the weed stalks—but no matter how low the weeds are cut, if the roots aren't taken out, the weeds will just grow back.

Metastasis

- Another important implication is that it is the cancer stem cells that give rise to metastases (when cancer travels from one part of the body to another) and can also act as a reservoir of cancer cells that may cause a relapse after surgery, radiation or chemotherapy has eliminated all observable signs of a cancer.

Solid Tumor Cancer Stem Cell Markers

Tumor type	Cell surface marker(s)	Reference
Breast	CD44 ⁺ CD24 ⁻ /low Lineage ⁻ ESA ⁺	Al-Hajj <i>et al.</i> (17)
CNS	CD133 ⁺	Singh <i>et al.</i> (18)
Colon	CD133 ⁺	O'Brien <i>et al.</i> (20)
	CD133 ⁺	Ricci-Vitiani <i>et al.</i> (21)
	ESA ^{high} CD44 ⁺ Lineage ⁻ (CD166 ⁺)	Dalerba <i>et al.</i> (19)
Ewing's	CD133 ⁺	Suva <i>et al.</i> (28)
Head and neck	CD44 ⁺ Lineage ⁻	Prince <i>et al.</i> (22)
Melanoma	ABC5 ⁺	Schatton <i>et al.</i> (26)
Liver	CD90 ⁺ CD45 ⁻ (CD44 ⁺)	Yang <i>et al.</i> (27)
Ovarian	CD44 ⁺ CD117 ⁺	Zhang <i>et al.</i> (23)
Pancreas	CD44 ⁺ CD24 ⁺ ESA ⁺	Li <i>et al.</i> (25)

Table 2

Cell surface phenotype of CSC identified in solid tumors

Table 1

Cell surface phenotype of CSC identified in hematological malignancies

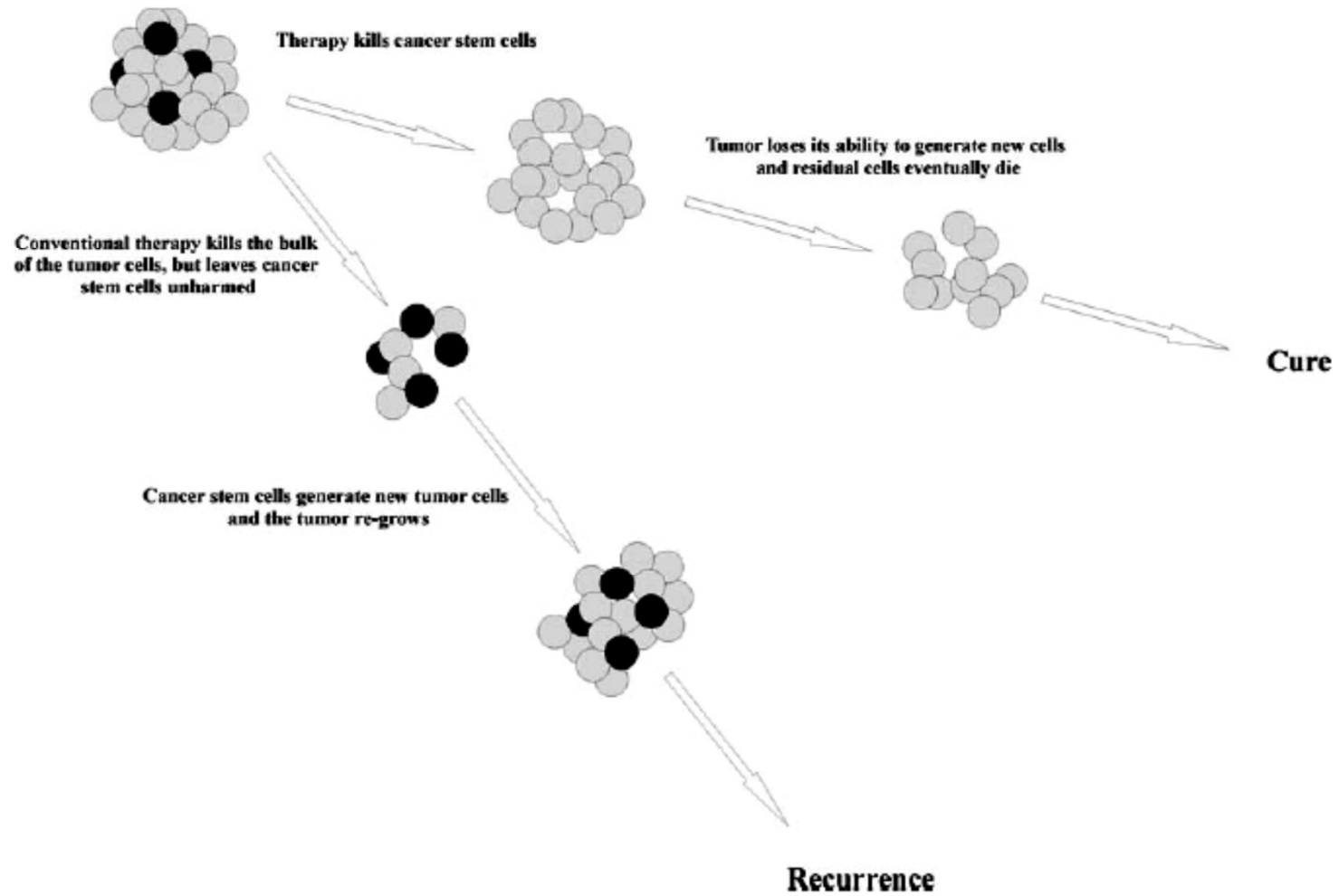
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia.

^aSerial xenotransplantation into secondary mouse recipients unsuccessful or not performed.

Tumor type	Cell surface markers	Reference
AML	^a CD34 ⁺ CD38 ⁻	Lapidot <i>et al.</i> (46)
	CD34 ⁺ CD38 ⁻	Bonnet and Dick(11)
	CD34 ⁺ CD38 ⁻	Ishikawa <i>et al.</i> (15)
B-ALL	CD34 ⁺ CD10 ⁻ /CD34 ⁺ CD19 ⁻	Cox <i>et al.</i> (13)
	CD34 ⁺ CD38 ⁻ CD19 ⁺	Castor <i>et al.</i> (12)
Multiple Myeloma	^a CD34 ⁻ CD138 ⁻	Matsui <i>et al.</i> (16)
T-ALL	CD34 ⁺ CD4 ⁻ /CD34 ⁺ CD7 ⁻	Cox <i>et al.</i> (14)

Targeting Cancer Stem cells

- Cancer stem cells, are thought to account for relapses following seemingly successful treatments, because their **slow turnover** and **capacity for expelling anti-tumor drugs** leave them untouched by conventional treatment regimens.
- Targeting of cancer stem cells by virotherapy, which use viruses that replicate in all type of cancer cells even in CSC.
- Viruses enter cells through infection and might therefore not be sensitive to stem cell resistance mechanisms.



Thank you