Cancer stem cells and self-renewal.

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Public Summary: The cancer stem cell (CSC) or cancer-initiating cancer (C-IC) model has garnered considerable attention over the past several years since Dick and colleagues published a seminal report showing that a hierarchy exists among leukemic cells. In more recent years, a similar hierarchical organization, at the apex of which exists the CSC, has been identified in a variety of solid tumors. Human CSCs are defined by their ability to: (i) generate a xenograft that histologically resembles the parent tumor from which it was derived, (ii) be serially transplanted in a xenograft assay thereby showing the ability to self-renew (regenerate), and (iii) generate daughter cells that possess some proliferative capacity but are unable to initiate or maintain the cancer because they lack intrinsic regenerative potential. The emerging complexity of the CSC phenotype and function is at times daunting and has led to some confusion in the field. However, at its core, the CSC model is about identifying and characterizing the cancer cells that possess the greatest capacity to regenerate all aspects of the tumor. It is becoming clear that cancer cells evolve as a result of their ability to hijack normal self-renewal pathways, a process that can drive malignant transformation. Studying self-renewal in the context of cancer and CSC maintenance will lead to a better understanding of the mechanisms driving tumor growth. This review will address some of the main controversies in the CSC field and emphasize the importance of focusing first and foremost on the defining feature of CSCs: dysregulated self-renewal capacity.

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