

## Reviews

# Cancer Stem Cells: An Old Idea—A Paradigm Shift

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Although the concept that cancers arise from "stem cells" or "germ cells" was first proposed about 150 years ago, it is only recently that advances in stem cell biology have given new impetus to the "cancer stem cell hypothesis." Two important related concepts of this hypothesis are that (*a*) tumors originate in either tissue stem cells or their immediate progeny through dysregulation of the normally tightly regulated process of self-renewal. As a result of this, (*b*) tumors contain a cellular subcomponent that retains key stem cell properties. These properties include self-renewal, which drives tumorigenesis, and differentiation albeit aberrant that contributes to cellular heterogeneity. Recent experimental evidence in a variety of tumors has lent strong support to the cancer stem cell hypothesis that represents a paradigm shift in our understanding of carcinogenesis and tumor cell biology. This hypothesis has fundamental implications for cancer risk assessment, early detection, prognostication, and prevention. Furthermore, the current development of cancer therapeutics based on tumor regression may have produced agents that kill differentiated tumor cells while sparing the rare cancer stem cell population. The development of more effective cancer therapies may thus require targeting this important cell population. (*Cancer Res* 2006; 66(4): 1883-90)