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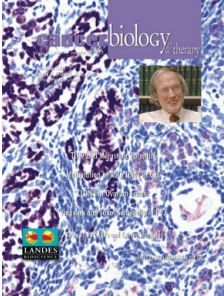
Cancer Stem Cell and Cancer Stemloids: From Biology to Therapy

Mikhail V. Blagosklonny
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It has become a cliché that cancer therapy fails because it does not target rare cancer stem cells (CSCs). Here we discuss that this is not how therapy fails and not any cancer cell with stem-like properties is CSC. Paradoxically, CSCs must be resting to explain their resistance to therapy yet must be cycling to explain their persistence in cell culture. To solve contradictions, this article introduces the term cancer stemloids (or stem cell-like cells) to describe proliferating self-renewing cells. The stem cell hierarchy (stem – proliferating – terminal cells) exists exactly to separate self-renewal (immortality) from proliferation. Cancer stemloids break the stem cell hierarchy and eventually may replace other cells. While CSC is shielded from any selective pressure and therefore unable to drive tumor progression, cancer stemloids undergo clonal selection, accumulate mutations, thus determining tumor progression and therapeutic failures. Unlike CSC, cancer stemloids are a crucial target for cancer therapy, exactly because they proliferate. Furthermore, two normally mutually-exclusive properties (proliferation and stemness) provide a means to design therapy to kill cancer stemloids selectively without killing normal stem and non-stem cells. In contrast, true CSCs are not only a difficult, but also an insufficient and perhaps even an unnecessary therapeutic target, especially in advanced malignancies.

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