
Why aren't all cells in neoplasms cancer stem cells? An evolutionary explanation for cancer non-stem cells

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Abstract

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Cancer is an evolutionary system in which tumor cells outcompete normal, somatic cells. Conventional views assume all cells in a neoplasm can propagate the tumor. Alternatively, the cancer stem cell hypothesis posits that only a fraction of the cells (the cancer stem cells) can act as tumor-propagating cells, and most of the tumor is composed of cells with limited replication potential. Here, we offer an evolutionary approach to this controversy. We used several evolutionary, computational models to investigate cancer cell dynamics and conditions consistent with the stem cell hypothesis. Our models predict that if selection acts at the cell level, neoplasms should be primarily comprised of cancer stem cells. In contrast, experimental data indicates that neoplasms contain large fractions of cancer nonstem cells. We explore several solutions explaining the paradoxical existence of cancer nonstem cells in neoplasms, including the possibility that selection acts at the level of multicellular proliferative units.

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