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Cancer Stem Cells in Sarcomas

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Solid tumors are composed of a heterogeneous population of cells with different in vitro proliferative capacities; only a minority have the ability to initiate tumor formation in immunodeficient mice. This observation led to the concept of cancer stem cells (CSC), which have the ability to self-renew and differentiate. By manipulating these characteristics, CSCs have been postulated to be responsible for driving the growth of tumors and the recurrence of neoplasms after therapy. Although many cancers are maintained by tumor initiating cells (TICs), until recently this had not been demonstrated for mesenchymal tumors, in part due to the lack of unique surface markers that identify mesenchymal progenitors. We previously identified a subpopulation of cells in sarcomas with stem-like or tumor initiating cell (TIC) capacity which can be identified based on a functional biologic assay of their exclusion of Hoescht dye. There was a positive correlation between the percentage of TICs and the grade of the tumour, suggesting a potential prognostic factor. These stem-like cells or TICs preferentially formed tumours upon serial transplantation into immunodeficient mice. Specific signaling pathways appear to be critical for tumour self-renewal as blockade decreases the proportion of stem-like cells and prevents serial transplantation of xenografts. This new data suggests that therapeutically targeting this subpopulation of TICs could be used to improve patient outcome. For undifferentiated pleomorphic sarcoma (UPS), we identified a gene expression signature for TICs that predicts clinical outcome when applied to unsorted patient tumour specimens. This data further supports the clinical relevance of the TIC concept in sarcoma.

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