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Prospective identification of tumorigenic sarcoma cancer stem cells based on high aldehyde dehydrogenase 1 activity

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Tumors contain a small population of cancer stem cells (CSC) proposed to be responsible for tumor maintenance and relapse. Aldehyde dehydrogenase 1 (ALDH1) activity has been used as a functional stem cell marker to isolate CSCs in different cancer types. This study used the Aldefluor® assay and fluorescence-activated cell sorting (FACS) analysis to isolate ALDH1high cells from five human sarcoma cell lines and one primary chordoma cell line. ALDH1high cells range from 0.3% (MUG-Chor1) to 4.1% (SW-1353) of gated cells. Immunohistochemical staining, analysis of the clone formation efficiency, and xCELLigence microelectronic sensor technology revealed that ALDH1 high cells from all sarcoma cell lines have an increased proliferation rate compared to ALDH1 low cells. By investigating of important regulators of stem cell biology, real-time RT-PCR data showed an increased expression of c-Myc, β-catenin, and SOX-2 in the ALDH1 high population and a significant higher level of ABCG2. Statistical analysis of data demonstrated that ALDH1 high cells of SW-982 and SW-1353 showed higher resistance to commonly used chemotherapeutic agents like doxorubicin, epirubicin, and cisplatin than ALDH1low cells. Using a NOD/SCID mice xenograft model, ALDH1 high cells showed a greater tumor forming capacity compared to ALDH1 low cells. The ALDH1 high tumors were significantly larger than the ALDH1 low tumors after 4-6 weeks.
This study demonstrates that in different sarcoma cell lines, high ALDH1 activity can be used to identify a subpopulation of cells characterized by a significantly higher proliferation rate, increased colony forming, increased expression of ABC transporter genes and stemness markers compared to control cells. In addition, enhanced drug resistance and a greater tumor forming capacity were demonstrated.

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