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Indentification of cancer stem-like cells in osteosarcoma and their implications in response to chemotherapy

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Aim

There are growing evidences that tumors contain a subset of cells with stem like properties. These cells are referred as cancer stem cells (CSC) and are responsible for driving tumor growth and recurrence. We aimed to isolate and characterize putative CSCs in a human osteosarcoma cell line (MNNG/HOS) and to explore their role in response to chemotherapy.

Methods

CSCs were isolated using the sphere-forming assay in serum-free medium under non-adherent conditions and characterized for the expression of mesenchymal stem cell markers ($CD90^+$, $CD105^+$, $CD73^+$) by flow cytometry. The chemosensitity of MNNG and CSCs to doxorubicin (DOX), cisplatin (CIS) and methotrexate (MTX) was evaluated using the MTT colorimetric assay after an incubation period of 48h. Cell cycle progression was analyzed by flow cytometry with propidiun iodide.

Results

A subpopulation of tumor cells formed sphere-clusters in serum-free medium and were positive for MSC markers. These cells revealed to be more resistant to chemotherapy in comparison with MNNG/HOS cells. The half maximal inhibitory concentrations (IC_{50}) of DOX (0.66 ± 0.24 μM), CIS (13.18 ± 0.09 μM) and MTX (0.05 ± 0.01 μM) were significantly higher ($p < 0.05$) than those in MNNG/HOS cells (DOX: 0.30 ± 0.07 μM; CIS: 8.08 ± 3.78 μM; MTX: 0.006 ± 0.001 μM). All drugs induced a G2/M cell cycle arrest in MNNG/HOS cells. In opposite, no significant changes were observed in CSC.

Conclusions

We have identified a subset of tumor cells with stem-like properties in OS that are relatively resistant to conventional chemotherapeutic agents. Therefore conventional drugs might not address this subset of cells that can be responsible for tumor regrowth after therapy.

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