T4:104

Small molecules and their effect on osteosarcoma cell proliferation

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Osteosarcoma (OS) is a pediatric tumor that develops primarily in children and young adolescents. Poor response or resistance to conventional chemotherapy is a major problem in the treatment of this disease.
We here present a screening strategy of small molecule libraries to find new therapeutic drugs that target osteosarcoma and might be applied in addition to conventional treatments. We used automated high-throughout screening to identify compounds out of 25.000s that target OS cell proliferation. Scaled down to 300 compounds that had an effect on cell proliferation, we screened ten different cell lines (osteoblastic cells, various osteosarcoma cell lines and other tumor cell lines) and compared the effects of the selected 300 compounds on cell proliferation.
We observed differences among cell lines in regard to viability after treatment. We further selected by hierarchical clustering compounds that showed the most differential effects on cell proliferation (between 100-25% viability) in the cell lines used. This could exclude non-reproducible hits and so-called frequent hitters. From this cluster, 29 compounds were chosen, that showed high bipolarity, solubility and non-toxic reactive groups. Currently, effects of these compounds are analyzed in more detail. For this, apoptosis induction and alteration of cell morphology and mitochondria are determined as well as structural prediction of potential interaction partners.
Thus, chemical, non-toxic compounds that interfere with cell proliferation in an OS specific or a cancer cell-specific manner might be promising drugs in treatment of osteosarcoma.

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