Development of a novel molecular-targeted therapy for osteosarcoma

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Background

Currently, molecular-targeted therapies for osteosarcoma have not been established. GSK3β has emerged as a potential therapeutic target for other cancers we have reported. In this study, we evaluated the antitumor effects of GSK3β inhibitors used as a potential molecular-targeted therapy, in human osteosarcoma cell lines.

Materials and Methods

HOS, 143B, MG63, and Saos-2 cell lines were used in this study. FOB1.19, an osteoblast cell line, was used as a control. Expression of GSK3β was measured by Western blot. Each cell line was treated with the GSK3β inhibitors AR-A014418 and SB-216763. Cell viability and proliferation were analyzed using the WST-8 Cell Proliferation Assay and the BrdU ELISA Kits, respectively. Cellular apoptosis was measured using the TUNEL imaging assay. We used human GSK3β-specific siRNA and a negative control. After siRNA transfection, relative numbers of viable cells and the induction of apoptosis were evaluated.

Results

All osteosarcoma cells showed higher expression levels of pGSK3β^{Y216} (active form) and lower levels of pGSK3β^{S9} (inactive form) compared with hFOB1.19. Cell proliferation was suppressed in each osteosarcoma cell line after GSK3β inhibitor administration. The IC_{50} of the GSK3β inhibitors for each of the cell lines was less than 20 μM. There was a significant difference in cell proliferation between the GSK3β inhibitor-treated groups and the control group as assessed by depleted GSK3β expression.

Conclusion

GSK3β inhibitors suppressed cell proliferation and resulted in apoptosis in osteosarcoma cell lines *in vitro*. Our findings indicated that GSK3β inhibitors could have a therapeutic effect on osteosarcomas *in viv*o.