Progression of human osteosarcoma with altered ANT1/SLC25a4 expression

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Introduction. Osteosarcoma (OS) is the most prevalent primary bone malignancy in children and adolescents. Bioinformatics analyses have identified ANT1 (encoded by SLC25A4) as part of a gene cluster implicated in the development and progression of osteosarcoma. Authors of this study investigated the expression of ANT1/SLC25A4 in clinical specimens and established OS cell lines to evaluate its potential as a prognostic biomarker and its mechanistic role in OS pathogenesis.

Methods. Immunohistochemical (IHC) analysis of ANT1 expression was performed on 63 archived human OS tissue sections (IRB-exempt). To assess functional impact, commercial MG-63 and HOS osteosarcoma cell lines were genetically modified to achieve SLC25A4 overexpression or knockdown. Cellular behavior was evaluated using proliferation, scratch wound-healing, and transwell invasion assays. In vitro numerical data were analyzed using one-way ANOVA with the LSD method for post hoc multiple comparisons. Correlations with clinical prognostic indicators were assessed using bivariate correlation analysis (SPSS v.22).

Results. IHC staining revealed that most clinical OS specimens (48/63) exhibited significantly diminished ANT1 expression compared with normal periosteal tissue. In vitro, SLC25A4 knockdown significantly accelerated cell proliferation. Conversely, SLC25A4 overexpression significantly inhibited cell migration and invasion ($p < 0.05$) compared with controls.

Conclusions. Our findings demonstrate that ANT1/SLC25A4 frequently is downregulated in clinical OS, and that its restoration suppresses aggressive cellular phenotypes in vitro. These results suggest that SLC25A4 may function as a tumor suppressor in osteosarcoma. Further research is needed to correlate SLC25A4 expression with patient survival and to define the underlying molecular pathways.