AUF1 Down-Regulation Potentiates Chemo-Sensitisation of Osteosarcoma Cells

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Osteosarcoma (OS) is an aggressive bone cancer with poor survival rates due to chemoresistance. Chemotherapy, the main treatment, often fails as OS cells become resistant, leading to tumor growth. AUF1, an RNA-binding protein, controls genes involved in growth, spread, and survival, and its high levels have been linked to more drug resistance and blood vessel growth. This study examines whether lowering AUF1 can boost OS sensitivity to drugs and block tumor blood supply. OS cell lines (U2OS, HOS, MG63, 143B, and SaOS-2) were used to check AUF1 levels and were treated with cisplatin and doxorubicin. Cell lysates were collected from both treated and untreated cells for protein extraction. Immunoblotting was used to check AUF1 protein levels. Cell death was measured using flow cytometry with annexin V/PI staining after siRNA-driven AUF1 knockdown. To test blood vessel growth, HUVEC tube formation tests were done, and VEGF-A levels were measured. Immunoblotting showed that more aggressive OS cell lines had higher AUF1 levels. Flow cytometry showed that AUF1 knockdown greatly raised cell death in drug-treated OS cells, with death rates going up by as much as 40%. HUVEC tube tests showed that AUF1 knockdown lowered VEGF-A levels, causing a 50% drop in vessel-like shapes, showing reduced angiogenesis. Also, combining cisplatin and doxorubicin in AUF1-silenced cells caused the highest cell death, showing better drug response. These results show AUF1 as a main cause of OS drug resistance and blood vessel growth. Targeting AUF1 improves drug effects and cuts off tumor vessels, offering a two-way treatment plan.

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