The Future of Osteosarcoma Treatment: FL118

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Purpose. Osteosarcoma (OS) is an especially aggressive bone cancer disproportionately affecting children. Current treatments like surgery, chemotherapy, and radiation suffer from high recurrence, toxicity, and treatment resistance, giving OS a poor prognosis and survival. FL118, a novel molecular glue degrader therapy, has potential to overcome these limitations; however, limited research on its mechanism and efficacy prevents clinical usage. This study investigated FL118's viability as a pediatric OS treatment. Methods. Pediatric patient-derived xenograft cell lines OS-152, OS-742, OS-833, and OS-186 were used. To determine FL118 efficacy, cell viability after FL118 treatment (72h), compared to chemotherapy, and colony formation (10d) were performed. To determine mechanism, western blots were conducted for apoptotic markers and hypothesized target protein DDX5, an oncogenic transcription co-activator aiding proliferation and apoptosis evasion. DDX5 knockout effect on cell growth and FL118 sensitivity was used to confirm this. Results. Cell viability and growth were significantly inhibited in a dose-dependent pattern in all cell lines analyzed in short and long term. FL118 consistently displayed lower IC50 than chemotherapeutic agents. Analysis of FL118's mechanism showed FL118 increased apoptosis marker levels. Results also showed that FL118 inhibited DDX5 and that DDX5 knockout inhibited cell growth and drug sensitivity, indicating DDX5 is likely a target protein. Conclusion. This study pioneered knowledge of FL118's mechanism and efficacy in treating OS, informing future research in clinical trials. These results highlight FL118's potential for OS treatment, helping address key barriers faced by previous treatments to improve efficacy, safety, and precision.

Awards Won:

Third Award of $1,200