

## Intensive Crosstalk between Autophagy and Intracellular Signaling Regulates Osteosarcoma Cell Survival Response under Cisplatin Stress

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**Abstract :** Autophagy has recently been linked with cancer cell survival post drug insult contributing to acquisition of resistance. However, the molecular signaling governing autophagic survival response is poorly explored. In our study, in osteosarcoma (OS) cells cisplatin shock was found to activate both MAPK and autophagy signaling. An activation of JNK and autophagy acted as pro-survival strategy, while ERK1/2 triggered apoptotic signals upon cisplatin stress. An increased sensitivity of the cells to cisplatin was obtained with simultaneous inhibition of both autophagy and JNK pathway. Furthermore, we observed that the autophagic stimulation upon drug stress regulates other developmentally active signaling pathways like the Hippo pathway in OS cells. Cisplatin resistant cells were thereafter developed by repetitive drug exposure followed by clonal selection. Basal levels of autophagy were found to be high in resistant cells to. However, the signaling mechanism leading to autophagic up-regulation and its regulatory effect differed in OS cells upon attaining drug resistance. Our results provide valuable clues to regulatory dynamics of autophagy that can be considered for development of improved therapeutic strategy against resistant type cancers.

**Keywords :** JNK, autophagy, drug resistance, cancer

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