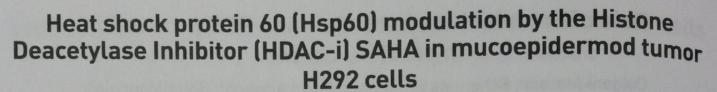
P09 Posters



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Objective

Hsp60 is a mitochondrial chaperone essential for mitochondrial protein folding. Hsp60 over-expression has an important role in cancer development and progression. HDACi are epigenetic drugs that modulating gene expression induce cell death in different tumor models. Treatment with HDACi can result in hyperacetylation of chaperones including Hsp90 and Hsp70, but no data are available about their effects on Hsp60. In this study, we investigate the effects of the HDACi SAHA on Hsp60 in H292 tumor cell line.

Materials and Methods

H292 cells were treated with different doses of SAHA for 24h. MTT test and flow cytometry cell cycle analysis were conducted. Mitochondrial membrane potential was evidenced using a JC-1 assay. Hsp60 expression and acetylation state were evaluated using western blot and immunoprecipitation. Hsp60 localization was analyzed by immunofluorescence. Cells were treated with SAHA and the proteasome inhibitor MG132 to elucidate whether Hsp60 undergoes proteasomal degradation under the SAHA effect.

Results

After SAHA treatment dose-dependent reduction of cell viability was observed, after 24h the cells were arrested in the G2/M phase, whereas pre G0/G1 peak appeared at 48 h indicating DNA fragmentation. Moreover SAHA determined a loss of mitochondrial membrane potential and preliminary results seem to indicate that this event is most likely correlated with new Hsp60 localization. Treatment with SAHA reduced significantly Hsp60 levels and seemed to favour its acetylation. Instead, Hsp60 levels did not change after combined treatment with SAHA and MG123.

Conclusion

SAHA induces growth suppression of H292 cells and decreases the level of Hsp60. This reduction could be due in part to Hsp60 proteolitic degradation in part to its externalization from the mitochondia and possible extracellular export. This hypothesis will be further investigated. SAHA seems to interfere with the pro-tumoral role of Hsp60 which could be then considered as a novel target in cancer therapy.