Knockdown of SET protein sensitizes HNSCC-HN12 cells to UCN-01

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UCN-01 (7-hidroxystaurosporine) has been considered for clinical use against several forms of cancer, including head and neck squamous cell carcinoma (HNSCC). Its antiproliferative action has been correlated with inhibition of kinases, which regulates the cell cycle such as a checkpoint kinase-1 (CHK1) of cyclin-dependent kinases (CDKs) and increased levels of inhibitors of cyclin-dependent kinase (CKIs) as p21Cip1/WAF1 and p27KIP1. SET cooperates with p21 to inhibit cyclin B activity and to arrest cell cycle. Here, three cell lineages of HNSCC (HN6, HN12 and HN13) were selected to evaluate whether knockdown of the protein I2PP2A (SET) associated with UCN-01 treatment is able to promote a cooperative response in the loss of cell viability, once these tumor cells have SET protein constitutively increased. HN6 and HN13 cells were sensitive to treatment with UCN-01, through the same mechanisms described in previous reports (increased p21 and dephosphorylation of the pRb). However, the treatment of HN12 cells with UCN-01 did not show significant reduction of cell viability, although there was increase of p21 and cell cycle arrest in G1/S. HN12 cells showed cell cycle distribution with higher number of cells in S phase and lower level of p21 compared to HN6 and HN13 cells. Furthermore, knockdown of SET in HN12 cells become UCN-01 more efficient as antitumor therapy by reduction of cell viability, similarly as for HN6 and HN13 cells. This data suggest that SET is involved in HN12 cell resistance to death induced by UCN-01 and suggest another mechanism for UCN-01, independent of p21.

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