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Nuove opportunità di trattamento per i carcinomi tiroidei scarsamente differenziati: studio su modelli preclinici.

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One of the major events involved in the pathogenesis of undifferentiated carcinomas is the loss of cell-cycle checkpoints, often due to the loss of p53 activity. The purpose of our study was to evaluate the potential of SP600125 as anticancer drug with special attention to p53 status. The experiments, executed on 6 different thyroid cancer cell lines, show that SP affects the replication of the p53-mutated cell lines with minor effects on the null ones and no effect on the wild type cell. It is able to induce nuclear translocation of the mutated p53 and consequent p21 overexpression thus causing cell cycle arrest and to affect tubulin morphology and stability thus causing alteration in mitosis progression and cell morphology. All these aberrations block mitosis progression and finally induce cell death by a specific event called mitotic catastrophe. Therefore, SP600125 represents a promising perspective for the medical treatment of undifferentiated thyroid cancer carrying p53 point mutations, selectively acting against those features which confer growth advantage and drug resistance to cancer cells.

CELL PROLIFERATION IN RELATION TO P53 STATUS