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Overexpression of Smac/DIABLO in Hep-2 cell line: possible role in potentiating the sensitivity of chemotherapeutic drugs

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ABSTRACT

Aims and background. The major obstacles for tumor chemotherapy are drug resistance and/or adverse effects on the host. In the present study we investigated the role of the second mitochondria-derived activator of caspase (Smac/DIABLO) in the action of cisplatin (DDP), 5-fluorouracil (5-FU), and the combination of both in Hep-2 cells.

Methods and study design. Hep-2 laryngeal carcinoma cells exposed to DDP, 5-FU and the combination of both were investigated. Cell viability was determined by MTT assay. Apoptosis was measured by Ho.33342 and PI double staining and flow cytometry. The expression of Smac/DIABLO at the mRNA and protein level was assayed by RT-PCR and Western blotting.

Results. DDP, 5-FU and the combination of both drugs reduced the cell survival rates in a concentration- and time-dependent manner. The drug combination not only exerted a stronger inhibitory effect, but also at a lower concentration compared with the single drugs. Apoptosis was concomitant in a caspase-dependent manner. The expression of Smac/DIABLO increased significantly at both mRNA and protein levels after cell exposure to the combination compared with single drugs.

Conclusions. Smac/DIABLO plays a pivotal role in attaining a synergistic effect in Hep-2 cells in response to this combined strategy. **Free full text available at www.tumorionline.it**

Key words: Smac/DIABLO, Hep-2 cells, chemotherapy, synergistic effect.

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