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Epithelial to mesenchymal transition (EMT), as a targeted therapy for multidrug resistance in epithelial ovarian cancer

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Worldwide, over 230,000 women are diagnosed with ovarian cancer each year, and about 140,000 women die from the disease. In the USA, estimated new cases 22, 240 and 14, 030 deaths from ovarian cancer in 2013. Resistance to anticancer drugs is a major obstacle towards a successful treatment of ovarian cancer. Multidrug resistance (MDR) is cross-resistance of tumor cells to several structurally unrelated chemotherapeutic agents after exposure to a single cytotoxic drug. Drug resistance mechanisms in ovarian cancer cells have been explored, but they are still unclear. It has been shown that, Cisplatin-resistant COC1/DDP, which is derived from its parental ovarian cancer cell line COC1 by stepwise selection in vitro using cisplatin, and can also display cross-resistance to other anticancer drugs such as adriamycin, mitomycin C, and 5-fluorouracil, is a useful cell model for investigating the mechanisms underlying MDR in ovarian cancer. It is not clear whether resistance is due to subpopulations of resistant cells, possibly with stem cell properties, already existing in the tumor before treatment, or is induced by mutations or epigenetic changes caused by chemotherapeutic drugs. Epithelial to mesenchymal transition (EMT) -related pathways provide targets for chemoresistant ovarian cancer therapy. Inhibition of integrin-linked kinase (ILK) increases the sensitivity of mesenchymal cells to EGFR-target therapy. In addition, Src kinase inhibitors effectively inhibit the growth of cells undergoing EMT. Furthermore, the inhibition of hedgehog signaling can prevent cancer cells from acquiring tumor-initiating property and undergoing EMT. RNA interference and microRNA are new technologies in drug development. Silencing of Snail by shRNA induces MET and reduces *in vivo* tumor growth. Specific silencers of endogenous miRNAs, antagomirs, shown to silence specific miRNAs *in vivo*. It follows that, microRNAs associated with EMT such as the miR-10b and miR-200 family could be a therapeutic target. In addition, the tumor microenvironment, which contributes to the maintenance of EMT, could be targeted. Furthermore, reducing EMT could also lessen the occurrence of anticancer drug resistance and effectively improve the efficacy of conventional cytotoxic therapy, to eradicate cancer cell, and cause minimal toxicity to normal cells. Further studies are needed to develop preclinical epithelial ovarian cancer models that mimic clinical cytotoxic drug resistance mechanisms related to epithelial to mesenchymal transition (EMT) in order to discover efficacious targeted therapy.

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