Inhibition of UCP2 Suppresses Cell Proliferation and Migration of Cholangiocarcinoma through the Regulation of Epithelial-Mesenchymal Transition

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Cholangiocarcinoma originates in the biliary tract and is usually diagnosed at advanced stages and has a high resistance to chemotherapy. The 5-year relative survival rate is about 10% for patients with cholangiocarcinoma. In order to address cholangiocarcinoma's resistance to chemotherapy, the current study focused on a protein called uncoupling protein 2 (UCP2) which is an inner mitochondrial membrane transporter. The mechanism of UCP2's effect on tumorigenesis is not clearly understood. Using cholangiocarcinoma cells, the study investigates the role of UCP2 in the metabolism of cancer cells and the epithelial-mesenchymal transition (EMT). To assess UCP2's effect on cell proliferation and migration, HuCCT 1 (Intrahepatic cholangiocarcinoma) and TFK-1 (extrahepatic cholangiocarcinoma) cell lines and their UCP2 knockdown clones were isolated and used for experimentation. HuCCT 1 and TFK-1 cells were treated with different concentrations of genipin, a specific UCP2 inhibitor, to simulate a possible treatment pathway. The study indicated that both UCP2 knockdown cells and cells treated with genipin had a significant decrease in cell proliferation and migration. The results also showed that genipin treatment increased the relative abundance of e-cadherin and decreased the relative abundance of vimentin, suggesting that genipin can regulate the EMT. Furthermore, genipin treatment sensitized cells to chemotherapy as cells treated with genipin and gemcitabine had a lower relative viable cell number compared to those treated with only gemcitabine. The study demonstrated that the inhibition of UCP2 reduced cholangiocarcinoma's ability to migrate, proliferate, and differentiate and suggested that genipin treatment could be a potential adjuvant therapy for cholangiocarcinoma.

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