

ROLE OF MITOCHONDRIAL IMPAIRMENTS IN HUMAN GASTRIC CANCER PROGRESSION

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In the past decade, high incidence of somatic mitochondrial DNA (mtDNA) mutation and mtDNA copy number change has been reported in several human primary cancers. In our previous studies, we identified somatic mtDNA mutations in Taiwanese gastric cancer patients and found most of these mutations could potentially lead to mitochondria dysfunction. In addition, we also found the decrease of mtDNA copy number of gastric cancer was correlated with poor prognosis. To address the role of mitochondrial impairment in gastric cancer progression, we used different mitochondrial inhibitors to study phenotype changes in human gastric cancer cell-lines. We found that gastric cancer cells with partial mtDNA depletion caused by ethidium bromide treatment or OXPHOS inhibition caused by oligomycin exhibited increased resistance to doxorubicin- and cisplatin-induced cytotoxicity in human gastric cancer SC-M1 cells. Moreover, after oligomycin treatment, cell migration and invasion were increased in two human gastric cancer cell lines. Interestingly, the oligomycin-enhanced cell migration could be effectively prevented by N-acetylcysteine pretreatment, which suggested that reactive oxygen species generated from impaired mitochondria might be highly involved in the induction of cell migration of human gastric cancer cells. Taken together, we suggested that mitochondrial impairments in gastric cancer cells could be important in promoting cancer malignancy.