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Opa-interacting protein-5 modulates Docetaxel-induced cell death via regulation of mitophagy in gastric cancer

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Damage to mitochondria induces mitophagy, a cellular process that is gaining interest for its therapeutic relevance to a variety of human diseases. However, the mechanism underlying mitochondrial depolarization and clearance in mitophagy remains poorly understood. We previously reported that mitochondria-induced cell death was caused by knockdown of *Neisseria gonorrhoeae* opacity associated-interacting (OIP) protein-5 in gastric cancer. In the present study, we show that *OIP5* loss and gain of function modulates mitophagy induced by treatment with Docetaxel, a chemotherapy drug for gastric cancer. The activation of mitophagy by *OIP5* overexpression promoted cell survival, preventing docetaxel-induced mitochondrial clearance. Conversely, short interfering RNA-mediated knockdown of *OIP5* accelerated docetaxel-induced apoptosis while increasing mitochondrial depolarization, reactive oxygen species (ROS) and endoplasmic reticulum stress and decreasing ATP production. We also found that the mitochondrial outer membrane proteins mitofusin 2 (*MFN2*) and phosphatase and tensin homolog (PTEN)-induced putative kinase-1 (PINK1) co-localized with OIP5 in mitochondria and that *MFN2* knockdown altered *OIP5* expression. These findings indicate that *OIP5* modulates docetaxel-induced mitophagic cell death and therefore suggest that this protein comprises a potential therapeutic target for gastric cancer treatment.

Biography

Seon-Jin Lee is a Senior Researcher and is currently working at the Korea Research Institute of Bioscience and Biotechnology. His major work is autophagy and biomarker in various cancer models.

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