

PICK1, A MITOCHONDRIAL PROTEIN, IS INVOLVED IN THE DRUG SENSITIVITY OF COLON CANCER CELL LINE SW620.

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We have previously demonstrated that PICK1 conferred resistance to chemotherapeutic agents in leukemia cells by recruiting PKC α to mitochondria. To investigate whether PICK1 is also involved in drug sensitivity in colon cancer, we first examine the expression levels of PICK1 and PKC α in various colon cancer cell lines. We found that SW620 expressed higher amounts of both proteins. PICK1 was localized to mitochondria by immunostaining. Knockdown of PICK1 significantly increased the sensitivity of SW620 cells to the killing effect of CPT-11 (Irinotecan) without an apparent effect on cell growth or viability under normal growth conditions. The response of SW620 to CPT-11 was dependent on the activity of PKC α , since treatment with a PKC α -selective inhibitor Gö6976 significantly increased the cellular sensitivity to CPT-11 as measured by trypan blue exclusion, activation of caspase 3 and formation of Bax dimers. The QSAV sequence at the extreme C terminus of PKC α has been shown to be required for interaction with PICK1. Ectopic expression of this tetrapeptide did enhance drug sensitivity of SW620 without affecting localization of PICK1. Our results suggest that PICK1 plays a role in drug sensitivity by recruiting PKC α in SW620.

Keywords:

PICK1, PKC α , Drug sensitivity, colon cancer