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T-type calcium channel blocker, KCP10043F inhibits G_1 cell cycle phase and induces apoptosis in caspase-dependent pathway on lung adenocarcinoma

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KCP10043F (3,4-dihydroquinazoline derivative) is a selective T-type Ca^{2+} channel blockers and other studies showed that selective Ca^{2+} channel bloackers could inhibit the growth of cancer cells such as ovarian, lung, and pancreatic cancer cells. we now investigated that KCP10043F induced G_1 arrest dose-dependently and cyclins and CDKs are regulated at protein expression level. In addition, KCP10043F made synergic effect on cell death with Etoposide, a novel anti-cancer agent. Then we continuously studied that KCP10043F induced apoptosis at high dose, detected by Annexin V-FITC / PI staining assay, and this cell death was dependent on caspase-activation, both capsase-3, 8 and -9. moreover, Bcl-2(anti-apoptotic protein), was down-regulated and Bax(pro-apoptotic protein) was up-regulated by this agent. This pathway was confirmed by using z-VAD-FMK, pan-caspase inhibitor, blocked the cell death induced by KCP10043F. Co-treatment with etoposide in low-dose also activated caspase-8,9. So our results suggested pathway how KCP10043F makes synergic effect on A549 cell line and it has possibility to be a potential anti-cancer agent reducing chemoresistance of lung cancers that show the lowest viability among many cancers.

Biography

Jeong hun Lee majored in Oriental Pharmacy at Kyunghee University, and now studying on master course, belonging to Department of Life and Nanopharmaceutical Science, Kyunghee University. He has studied about cancer biology, especially related with apoptosis and cell cycle arrest in cancer cells and how apoptosis is induced in specific cancer cells, like lung carcinoma, by using derivatives of natural product or chemical compositions.

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