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A novel synthetic LSD1 inhibitor with anticancer activity in prostate cancer cells

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In United States during 2018 an estimated 164,690 new cases and 29,430 deaths of prostate cancer. Prostate cancer ranks as the first of new cases and the second of deaths from cancer in the US during 2018. The lysine-specific demethylase 1A (LSD1/KDM1A) is the first histone demethylase discovered and it can remove mono or di-methyl groups from lysine K4 or K9 on histone H3. LSD1 expression is increased in malignant prostate cancer. Overexpression of LSD1 enhances cell growth and cancer metastasis. Therefore, we want to treat prostate cancer by inhibiting cell growth or inducing cell death or suppressing cell migration and Epithelial–Mesenchymal Transition (EMT) through the inhibition of LSD1. We synthesized a new compound (Compound X) for LSD1 inhibition, and we compared with a well-known LSD1 inhibitor, SP2509. SP2509 can inhibit cell growth in prostate cancer cell PC3 and DU145 with micromolar GI50 value (1.34 and 2.12 μM), and Compound X can inhibit cell growth in PC3 and DU145 with submicromolar GI50 value (0.34 and 0.89 μM) by SRB assay. Our results showed that Compound X induces sub G1 phase of cell cycle arrest in a time-dependent manner and induces caspase-dependent apoptosis and inhibits migration and EMT more than SP2509 in PC3 and DU145 cells. Knockdown of LSD1 enhances Compound X-induced cell apoptosis and suppression of migration in PC3 and DU145 cells. It has been reported that N-Myc Downstream-Regulated Gene 1 (NDRG1) is a potent metastatic suppressor in prostate and colon cancer cells. Our data showed that Compound X increase NDRG1 expression, therefore we will also investigate if NDRG1 plays an important role in the inhibition of migration and EMT by treated with Compound X. These data show that our new Compound X is more potent than well-known LSD1 inhibitor, SP2509.

Biography

I-Chen Kung has completed her graduation from the Department of Medical Laboratory Science and Biotechnology, Taipei Medical University. She is a Medical Technologist in Taiwan. She is currently pursuing her Masters in the Institute of Pharmacy, Taipei Medical University and also is a Member in the Clinical Drug Discovery Lab.

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