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International
Cancer Study & Therapy Conference

April 4-6, 2016 Baltimore, USA

Evaluation of anti-tumor activities and mechanisms of a novel Quinoline derivative 91b

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Background: Quinoline belongs to an important class of heterocyclic alkaloids. Anti-tumor activity of quinoline derivatives have been intensively investigated for the purpose of identifying novel anti-cancer agents. The purpose of this study is to evaluate the anti-tumor activities of a novel quinoline derivative 91b and identify the downstream regulatory targets.

Method: A novel quinoline derivative 91b was synthesized using the asymmetric hydrogenation reaction. MTS cytotoxicity assay was performed on the human esophageal cancer cell lines KYSE150 and KYSE450. The subcutaneous tumors of KYSE150 in athymic nude mice were also treated with 91b1 (10mg/kg/day as normal dose, and 50 mg/kg/day as high dose) via the intraperitoneal route for 1 month. The body weight and tumor volume were recorded regularly, and serums were collected to identity the changes of biochemical markers. SD rats were treated with 500mg/kg/day 91b for 7 days to examine the chronic toxicity. cDNA microarray analysis on KYSE150 cells treated with 91b was also performed to identify the downstream regulatory targets at cDNA level. One of the most down-regulated gene, Lumican, was cloned and transfected into NIH 3T3 cells for subcutaneous injection into athymic nude mice to determine its tumor transforming capacity.

Results: The MTS_{50} values ranged from 0.375 to 5.91 mg/ml for KYSE150 and 0.572 to 9.06 mg /ml for KYSE450 cell lines. Tumor volume of the treated group showed significant reduce ($p=0.007$) against the vehicle control group and the animal body weights increased significantly. ALB and ALP level were decreased compare to blank control group (ALB from 27.6 to 26.6, and ALP from 57.00 to 56.40). For the chronic toxicity test, the compound-treated group all survived. From the cDNA microarray analysis, Lumican is one of the most down-regulated genes in the 91b1 treated KYSE150 cells compared with the vehicle controls.

Conclusions: Compound 91b is a promising anti-tumor agent with high activity and low toxicity. Lumican is the most down-regulated target. The tumor transforming capacity of lumican is under investigation using the *in vitro* and *in vivo* approaches.

Biography:

Yuanyuan ZHOU is currently a PhD candidate at The Hong Kong Polytechnic University, majoring in applied biology and chemistry techniques. She completed her Masters at the China Pharmaceutical University, majoring in pharmacokinetics. She graduated with a bachelor of science also at the China Pharmaceutical University. Her research interest is on the characterization and mechanism of quinoline derivatives as novel anti-tumor agents.