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Integrative Biology 2016: Radio-sensitization of clioquinol and zinc ion in human cancer cells - Yunfeng Zhou - Zhongnan Hospital of Wuhan University

Yunfeng Zhou
Zhongnan Hospital of Wuhan University, China

Objective: We have reported that the anticancer activity of Clioquinol and Zinc in different cancer cells, Clioquinol and Zinc can inhibit the cancer cell viability by down-regulation of NF-kb activity. Re-activation of NF-kb plays an important role in radio-resistance of human cancer cells. Here we investigated the radio-sensitization of Clioquinol and zinc in different human cancer cells.

Methods: The toxicity of 1 μM Clioquinol (CQ) and 10 μM ZnCl2 (Zn) in human cancer cells of Hep-2 and human normal cells MRC-5 was determined by MTS assay. The radio-sensitization of CQ+Zn in Hep-2 and Hela cells was detected by colon formation measure. The effect of CQ+Zn on the NF-kB activity in Hep-2 and Hela cells is measured by the luciferase activity assay. The ATM RNA and protein expression level were determined by RT-PCR and Western blot methods.

Results: The cell viability of Hep-2 and MRC-5 treated with 1 μM CQ and 10 μM Zn for 72 hours were 104.0% and 114.3% respectively compared to the control groups (Hep-2 cells: CQ+Zn vs. Control, P=0.8850; MRC-5 cells, CQ+Zn vs. Control, P=0.8204). Colon formation measure indicated that 1 μM CQ and 10 μM Zn can significantly enhance the radio-sensitivity of Hep-2 and Hela cell (Irradiation group vs. Irradiation+CQ+Zn group: P<0.001 in Hep-2 cells and P<0.001 in Hela cells), SERSF2 for Hep-2 and Hela were 1.33 and 1.75 respectively.

One μM CQ and 10 μM Zn inhibited the activity of NF-kB after 2 Gy γ-Ray irradiation in Hep-2 and Hela cells (Irradiation group vs. Irradiation+CQ+M Zn group: For Hep-2 cells, 151.10% vs. 108.60%, P<0.001; for Hela cells, 156.30% vs. 104.20%, P<0.001).

We further detected the ATM mRNA and protein expression level after 2Gy irradiation with or without pre-treatment of 1 μM CQ and 10 μM Zn for 6 hours. ATM mRNA expression level in Hep-2 after 24 hours of irradiation in the group of with the 1 μM CQ and 10 μM Zn was 67.78% of that in the irradiation along group (P=0.017). ATM protein expression level after 48 hours of irradiation in the group of with the 1 μM CQ and 10 μM Zn was 69.38% of that in the irradiation along group (P=0.039). Conclusion: Clioquinol and zinc can enhance the radio-sensitivity of human cancer cells, the inhibition of NF-kB and ATM may mediate the radio-sensitization in human cancer cells.

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