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Radio-sensitization of clioquinol and zinc ion in human cancer cells

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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.

Biography

Yunfeng Zhou is a Professor of Radiation Oncology and he was the Dean of Medical School and the President of Zhongnan Hospital, Wuhan University. From 1986 to 1991, he studied for his Oncology Diploma (DIS) in Lyon, France. He has been working at the Department of Radiation Oncology and Medical Oncology as a Director of Hubei Cancer Clinical Study Center, Hubei Key Laboratory of Tumor Biological Behaviors and Hubei Radio-therapeutic Quality Control Center. His main research fields including radiation biology which focuses on the radio-sensitivity modified by telomere/telomerase and radiation-guided gene therapy of cancer. He has published more than 100 papers in international and national journals. Due to his outstanding contributions for Sino-France medical education exchange, the French Government awarded him French Knight Badge (2006) and National Order of the Legion of Honor (2009).

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