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# Mitochondrial DNA depletion in H1299 cells promotes radio-resistance and anti-apoptosis through activation of PI3K/Akt2

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Radiotherapy takes an important role in treatment of various cancers while the main limit for this strategy is radioresistance of cancer cells. A large number of studies have found that mitochondrial DNA (mtDNA) is not only associated with tumor development, but also affects the tumor radiosensitivity. But, the roles of mtDNA on radiosensitivity are still conflictable, and the mechanisms remain unresolved. Here, we have built a cell model with mtDNA deletion, to investigate the relationship between mtDNA and radiosensitivity and its mechanism. Human non-small cell lung cancer cells (H1299) were depleted of mtDNA ($\rho^0$) by culturing chronically in the presence of ethidium bromide, and then verified by PCR of total DNA using primer pairs specific for mtDNA. We found that loss of mtDNA decreased proliferation rate, ATP and oxidative phosphorylation. Moreover, $\rho^0$ cells regulate radio-sensitivity: (a) By inhibiting cell cycle progression at the G2/M transition leading to growth arrest and apoptosis; (b) by increasing the expression of G2/M checkpoint ATM/ATR-mitotic cyclinB1 and decrease the expression of apoptotic factors pro-caspases-3 and -8; and (c) accelerated the repair kinetics of DNA damage induced by irradiation. We further examined the phosphorylation of Akt2, mTOR and IKKs and found they all were significantly increased in $\rho^0$ cells. In keeping with these findings, suppression of the PI3K/Akt2 pathway by the small molecular inhibitor MK-2206 2HCL dramatically increased the expression of apoptotic proteins in $\rho^0$ cells. Collectively, our results indicated that mtDNA depletion resulting in downregulation of radiosensitivity, and retrograde activation the PI3K/Akt2 pathway in non-small cell lung cells.

## Biography

Fuxiang Zhou has completed his PhD at the age of 40 years old from Zhongnan Hospital of Wuhan University and Postdoctoral studies from CAL Cancer Center, University of Nice, France. He is the Director of Hubei Key Laboratory of Tumor Biological Behaviors & Hubei Cancer Clinical Study Center. He has published more than 60 papers in reputed journals and serving as an Editorial Board Member of repute.

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