5 - 58 Tigecycline Combined with Carbon Ion Irradiation Induces Mitochondrial Dysfunction and Inhibits Proliferation of Lung Cancer Cells

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Mitochondrial dysfunction is receiving considerable attention due to irreplaceable biological function of mitochondria. Ionizing radiation and tigecycline (TIG) alone can cause mitochondrial dysfunction, playing important role in tumor therapy. However, prior studies fail to investigate combined mechanism of carbon ion irradiation (IR) and TIG on tumor proliferation inhibition[1]. The study aimed to explore the combined effects of both on autophagy and apoptosis. Results showed IR combined TIG inhibited cells proliferation by increasing apoptosis in both cells and enhancing autophagy in H1299 cells (Fig. 1). Additionally, combination treatment induced the most severe mitochondrial dysfunction by sharply reducing ATP, mitochondrial membrane potential (MMP) and increasing Ca^{2+} level of mitochondria. Up-regulation and down-regulation of mitochondrial translation proteins (EF-Tu, GFM1 and MRPS12) expression affected apoptosis and autophagy, while the level of p-mTOR was consistent with their expression in both cell types. In A549 cells, p-AMPK level decreased while p-Akt and p-mTOR increased after combination treatment. Overall, our results showed that p-Akt and p-AMPK antagonistically targeted p-mTOR to regulate mitochondrial translation proteins to affect autophagy and apoptosis[2, 3]. Furthermore, this study suggests that combination of carbon ion and TIG is a potential therapeutic option against tumors.

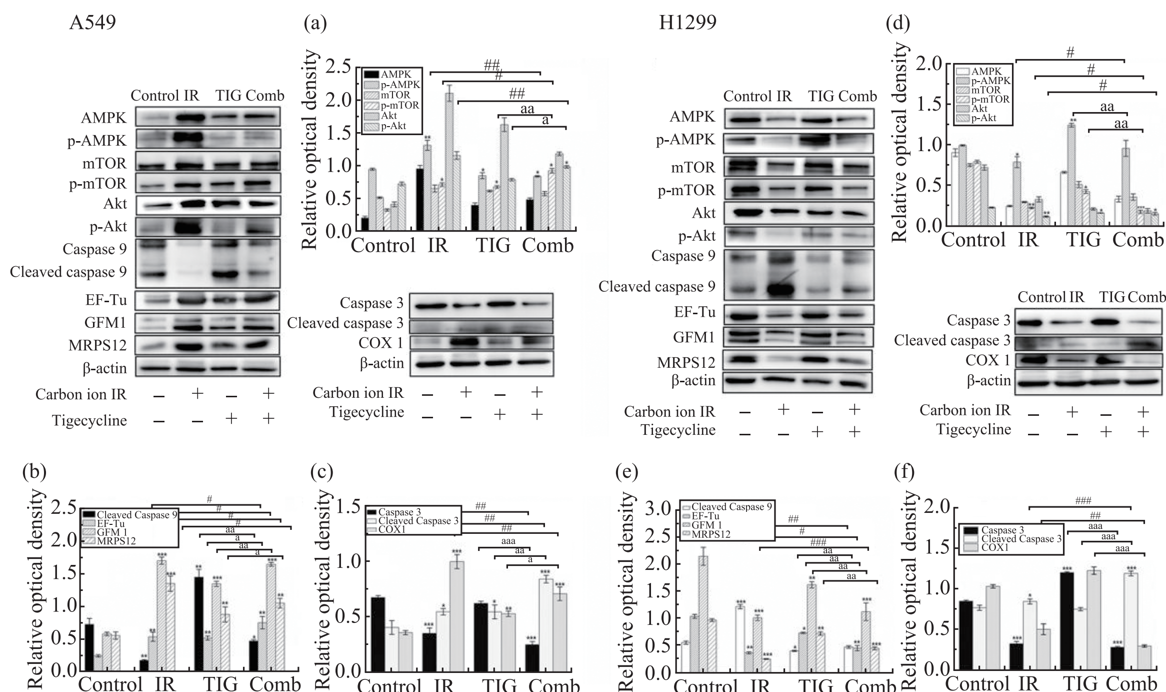

Fig. 1 The Akt/AMPK/mTOR pathway was involved in regulating mitochondrial function in the interplay of IR and TIG. Representative western blot results showed the expression levels of related proteins in A549 and H1299 cells after 24 h of stimulation with CI, TIG or both. Upper panel (a) and (b) showed protein expression level of mTOR signaling proteins (AMPK, phosphorylation level of AMPK, mTOR, phosphorylation level of mTOR, Akt and phosphorylation level of Akt), cleaved caspase 9 and mitochondrial translation proteins (EF-Tu, GFM1 and MRPS12). The protein expression level of caspase 3, cleaved caspase 3 and COX1 in A549 cells were analyzed in the panel (c). Corresponding results in H1299 cells were presented in (d), (e) and (f). Results are shown as the mean ± SEM. $*P<0.05$, $**P<0.01$, $***P<0.001$ *versus* the control group. # $P<0.05$, ## $P<0.01$, ### $P<0.001$ *versus* IR group. $_{a}$ $P<0.05$, $_{aa}$ $P<0.01$, $_{aaa}$ $P<0.001$ *versus* TIG group. TIG: tigecycline; IR: ionizing radiation.

References

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5 - 59 Effects of HLY78 on Apoptosis Induced by Irradiation in HeLa Cells*

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The Wnt/β-catenin signaling pathway is involved in many biological events including cell differentiation, cell proliferation, invasion, and apoptosis[1, 2]. It is an important regulatory pathway during cell development. Accumulating evidences indicate that the Wnt/β-catenin signaling pathway is involved in the tumorigenesis and propagation of numerous cancers. During normal adult stage, the Wnt signaling pathway is inactive or silent. However, once the body is stimulated by inflammation and cancer, Wnt signaling becomes dysregulated[3]. The activation of Wnt signal helps tumor proliferation and metastasis, while the inhibition of Wnt signal blocks the stemness of tumors and induces cell senescence. The standardized Wnt signaling pathway is indispensable for the pathogenesis and progression of tumors.

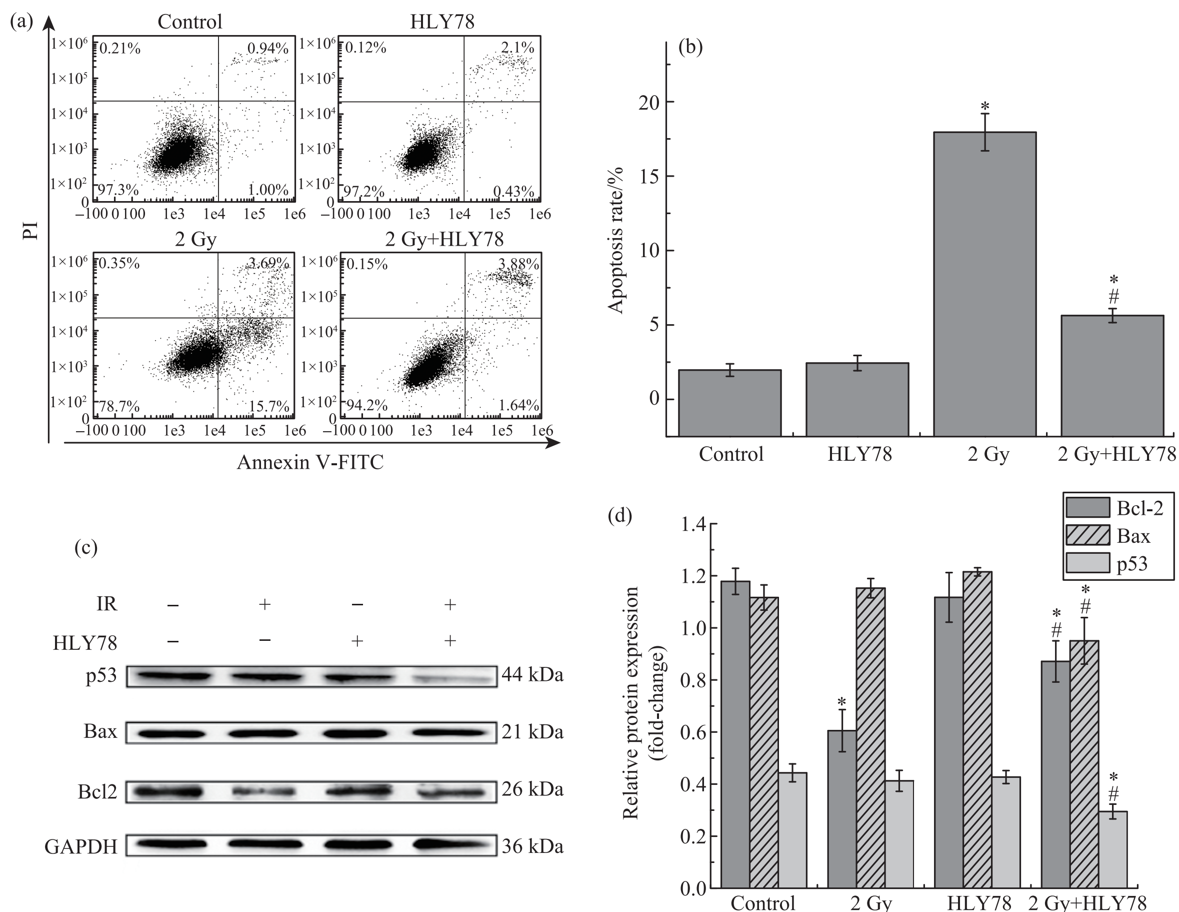

Fig. 1 HLY78 effectively inhibits irradiationinduced apoptosis in HeLa cells. (a) Cells were cultured under various treatments for 24 h, and cell apoptosis was assessed using Annexin VFITC and PI doublestaining flow cytometry, (b) Quantitative analysis of cell apoptosis percentages when treated with $^{12}C^{6+}$ radiation alone, or combined with HLY78 in cells, (c) Bcl-2, Bax and p53 expression levels were assessed by western blotting in cells. GAPDH was used as a loading control, (d) Bar chart representing the quantification of western blotting protein signals. Data are presented as the mean ± SEM from three independent experiments. *$P<0.05$ (vs. the control group). #$P<0.05$ (vs. the radiation group). Bcl-2, B-cell lymphoma-2; Bax, Bcl-2 Associated X protein.