BEZ235对肝癌细胞HepG2放射敏感性的影响

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Title: Effect of BEZ235 on radiosensitivity of hepatic cancer cell line HepG2

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摘要: 目的:评价双重PI3K/mTOR抑制剂BEZ235对肝癌细胞HepG2放射敏感性的影响。方法：通过MTT测定确定不同BEZ235浓度的生长抑制效果；焦点形成测量和克隆形成测定评估对放射敏感性的影响；通过Annexin-FITC/PI分析BEZ235对辐射诱导细胞凋亡的影响，以及Western blot分析BEZ235对缺氧诱导因子-1α（HIF-1α）蛋白水平的影响。结果：BEZ235以剂量依赖性方式抑制HepG2细胞增殖；10 nmol/L BEZ235增加HepG2细胞的放射敏感性；BEZ235与辐射组合增加了DNA双链断裂；BEZ235联合辐射与单独辐射相比，显著增加了HepG2细胞的凋亡率。BEZ235 降低了HIF-1α蛋白水平。结论：BEZ235增强了人肝癌HepG2细胞的放射敏感性，这一发现与抑制HIF-1α表达有关。提示BEZ235可能是潜在的放疗增敏药物。

Abstract: Objective:To evaluate the effect of dual PI3K/mTOR inhibitor BEZ235 on radiosensitivity of hepatocellular carcinoma.Methods:Proliferation inhibitory effects of different concentrations of BEZ235 were determined by MTT assay,effects on radiosensitivity assessed by focus formation measurements and colony formation assays,effects of BEZ235 on radiation-induced apoptosis by Annexin-FITC/PI analysis,Western blot analyed effect of BEZ235 on the level of hypoxia inducible factor 1α (HIF-1α) protein.Results:BEZ235 inhibited HepG2 cell proliferation in a dose-dependent manner.BEZ235 increased the radiosensitivity of HepG2 cells.BEZ235 combined with radiation increased γH2AX foci numbers.BEZ235 combined radiation significantly increased apoptosis rate of HepG2 cells compared to radiation alone.BEZ235 reduced HIF-1α protein levels.Conclusion:BEZ235 enhances the radiosensitization of human hepatoma HepG2 cells by inhibition of the broken DNA repair,which is related to the inhibition of HIF-1α expression.Therefore,BEZ235 may be a potential radiation therapy sensitizer.

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