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VEGF及EGFR抑制剂联合放疗对裸鼠鳞状细胞癌增殖的抑制作用

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Therapeutic Efficacy of VEGFR and EGFR Inhibitor Combined with Radiotherapy for Squamous Cell Carcinoma in Nude Mice

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摘要

目的

探讨VEGF及EGFR抑制剂ZD6474联合放疗抗肿瘤效果，并探讨其对肿瘤微血管生成，细胞增殖及凋亡影响的机制。方法 建立裸鼠鳞状细胞癌荷瘤模型，随机均分成4组：对照组、放疗组（RT）、ZD6474组、联合治疗组（ZD6474+RT）观察肿瘤大体增殖情况，用免疫荧光法检测肿瘤组织CD34表达、细胞增殖相关抗原Ki67，凋亡抗原capase-3表达，计数微血管密度(MVD)，肿瘤增殖及凋亡。 结果 VEGF及EGFR抑制剂同步联合放疗组相较于单药治疗及单纯放疗明显延迟肿瘤增殖时间，同时通过针对CD34、Ki67、caspase-3免疫荧光染色，显示明显减少微血管密度，降低肿瘤增殖、提高细胞凋亡（$P<0.05$）。结论 VEGF及EGFR抑制剂与放疗同步，从机制上抑制肿瘤新生血管形成，抑制肿瘤增殖，从而增进放疗疗效。

关键词： 血管内皮生长因子 表皮生长因子 放疗 裸鼠模型

Abstract:

Objective

To evaluate the antitumor efficacy of a combination of vascular endothelial growth factor receptor (VEGFR) and epidermal growth factor receptor (EGFR) tyrosine kinase activity inhibitor—ZD6474 and radiotherapy for human tumor xenograft model (FaDu，squamous cell carcinoma) and to investigate whether the effects of the treatments were related to changes in tumor microvessel density，proliferation and apoptosis.MethodsTumor-bearing nude mice received either vehicle or ZD6474 with or without irradiation (4 treatment-groups:control;ZD6474 alone;radiotherapy (RT) alone;ZD6474 + RT).The antitumor efficacy of the different treatment modalities was evaluated by the tumor sizes.For the different treatment-groups the tumor vascularisation was evaluated by immunofluorescence analysis of CD34 positive vessel segments (tumor vascular density) and the proliferative capacity and apoptotic degree of the tumor tissue were analysed by the quantification of Ki67 positive nuclei and capase-3 positive cell.ResultsThe tumor growth delay induced by the combined treatment (ZD6474 + RT) was more significant than that induced by ZD6474 or radiotherapy alone.ZD6474 clearly reduced neoangiogenesis.Moreover，proliferative and apoptosis of the tumor tissue was significantly decreased and increased,respectively by ZD6474($P<0.05$).ConclusionWhen irradiation combined with VEGFR and EGFR blockade，significant enhancement of antiangiogenic，antivascular，and antitumor effects were observed.These data provided supports for clinical trials of biologically targeted and conventional therapies in the treatment of cancer.

Key words: Vascular endothelial growth factor Epidermal growth factor receptor Radiotherapy Nude mice model

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