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论著

木犀草素联合卡介苗治疗膀胱癌的协同效应及其机制

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摘要：

目的：研究木犀草素(Luteolin，Lu)联合卡介苗(bacillus calmette-guerin，BCG)抑制膀胱癌BIU-87细胞增殖
的作用及其机制。方法：体外培养膀胱癌BIU-87细胞株，分别用不同浓度的Lu(20，40，60，80，100，160 μmol/L)
单独及联合BCG(100，200 mg/L)处理BIU-87细胞，作用6，12，24，48 h。采用Hoechst 33258核荧光染色观察细胞形
态学变化，MTT法检测Lu和BCG对BIU-87细胞增殖的抑制作用和半数抑制率IC50，流式细胞术分析肿瘤细胞的凋
亡及细胞周期，比色法测定caspase-3蛋白活性，Western印迹分析磷酸化c-Jun氨基末端激酶(phosphorylated c-Jun
N-terminal kinases，P-JNK)的表达。结果：Hoechst 33258核荧光染色提示Lu可诱导细胞凋亡，并增强BCG诱导的细
胞凋亡。MTT法检测显示Lu及BCG对BIU-87细胞增殖均有明显抑制作用，且呈浓度和时间依赖性；Lu与BCG联合
作用对BIU-87细胞的增殖抑制具有显著的协同效应(P<0.05)。流式细胞术提示Lu及BCG均诱导细胞周期阻滞及细
胞凋亡，并具有明显的协同增敏效应(P<0.05)。Lu及BCG均可上调caspase-3活性及P-JNK表达水平，二者联合作用
明显增强(P<0.05)。结论：Lu与BCG均可抑制BIU-87细胞增殖，诱导细胞凋亡，并呈浓度依赖性，二者具有明显
的协同增敏作用；Caspase-3蛋白活化及JNK的激活是其可能的分子机制，Lu可作为BCG免疫治疗的有效增敏剂用
于对膀胱肿瘤的治疗。

关键词： 膀胱癌细胞 木犀草素 卡介苗 半胱氨酸天冬氨酸蛋白酶-3 磷酸化c-Jun氨基末端激酶 协同作用 凋亡

Anticancer activity of Luteolin and its synergism effect with BCG on human bladder cancer cell line BIU-87

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Abstract:

Objective: To investigate the anticancer activity of Luteolin (Lu) and its synergism effect with bacillus calmette-guerin (BCG) on human bladder cancer cell line BIU-87.
Methods: Cultured BIU-87 cells were treated with different concentrations of Lu alone or the combination of Lu with BCG. MTT assay was used to measure the cell proliferation inhibition, and IC50 was calculated. Cell cycle and apoptosis were analyzed by flow cytometry with propidium iodide (PI) staining and Annexin-V FITC/PI dual parameter markers to clarify the mechanism of
inhibiting cell proliferation and inducing apoptosis. Caspase-3 and phosphorylated c-Jun N-

terminal
kinases (P-JNK) expression were measured to detect the apoptosis signal pathways of Lu in cancer cells.
Results: Both Lu and BCG apparently inhibited the cell proliferation and induced the apoptosis
dose-dependently, and microscope observation showed morphological changes in the apoptosis. Flow
cytometry indicated that Lu arrested the cell cycle at G2 phase (P<0.05). It sensitized BCG-induced
cytotoxicity and cell apoptosis, and upregulated expression of caspase-3 and activation of JNK (P<0.05).
Conclusion: As an effective anticancer agent, Lu can sensitize the effect of BCG by inducing the
cell cycle arrest and apoptosis. This synergism effect is achieved by activation of caspase-3 and JNK.
Combination of Lu with BCG may be one of the potential treatment for bladder cancer.

Keywords: human bladder cancer cell line Luteolin BCG caspase-3 P-JNK drug synergism apoptosis
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