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Bcl-XL小发夹RNA腺病毒载体的构建及其抗肿瘤作用 [点此下载全文](#)

[胡静姿](#) [周玮](#) [王晓炜](#) [戴胜](#)

空军杭州航空医学鉴定训练中心 内科, 浙江 杭州 310013; 浙江大学医学院 附属邵逸夫医院 肛肠外科, 浙江 杭州 310016; 浙江大学医学院 附属邵逸夫医院 肛肠外科, 浙江 杭州 310016; 浙江大学医学院 附属邵逸夫医院 肛肠外科, 浙江 杭州 310016

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摘要:

目的: 构建表达Bcl-XL小发夹RNA的腺病毒载体(Ad/Bcl-XL shRNA)并探讨其抗肿瘤作用。方法: 构建、纯化重组腺病毒Ad/Bcl-XL shRNA。通过Western blotting、MTT分析验证它对Bcl-XL的下调及其杀伤肿瘤细胞的作用,并检测其处理后细胞凋亡信号的活化情况;在裸鼠皮下荷瘤模型中验证其体内抗肿瘤作用。结果: 成功构建和纯化了Ad/Bcl-XL shRNA,它能显著下调结肠癌DLD1细胞Bcl-XL蛋白的表达;与Ad/GFP、PBS组相比,Ad/Bcl-XL shRNA组明显抑制人结肠癌细胞DLD1的生长[1 000 MOI时(60.6±4.8)% vs (99.0±2.6)%、100%; 2 000 MOI时, (37.3±6.9)% vs (99.0±2.1)%、100%, P<0.01],但对正常人成纤维细胞无明显抑制作用(P>0.05); Ad/Bcl-XL shRNA组能有效诱导结肠癌细胞中凋亡信号caspase-9、caspase-3、PARP的活化。在裸鼠荷瘤模型中,与Ad/GFP、PBS组相比,Ad/Bcl-XL shRNA组显著抑制DLD1来源皮下肿瘤的生长[第29天时, (250.1±185.7) vs (880.0±286.1)、(911.0±389.1) mm³; P<0.01]。结论: Ad/Bcl-XL shRNA能显著抑制结肠癌细胞在体内外的生长,其在结肠癌治疗中具有潜在的应用价值。

关键词: [重组腺病毒](#) [Bcl-XL](#) [RNA干扰](#) [小发夹RNA](#) [结肠癌](#)

Construction of adenovector expressing small hairpin RNA targeting Bcl-XL and its anti-tumor effect [Download Fulltext](#)

[HU Jing-zi](#) [ZHOU Wei](#) [WANG Xiao-wei](#) [DAI Sheng](#)

Department of Internal Medicine, Aviation Medical Evaluation & Training Center of Airforce in Hangzhou, Hangzhou 310013, Zhejiang, China; Department of Colorectal Surgery, Sir Run Run Shaw Hospital, Affiliated to Zhejiang University, Hangzhou 310016, Zhejiang, China; Department of Colorectal Surgery, Sir Run Run Shaw Hospital, Affiliated to Zhejiang University, Hangzhou 310016, Zhejiang, China; Department of Colorectal Surgery, Sir Run Run Shaw Hospital, Affiliated to Zhejiang University, Hangzhou 310016, Zhejiang, China

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Abstract:

Objective : To construct the adenovector expressing small hairpin RNA targeting Bcl-XL (Ad/Bcl-XL shRNA), and evaluate its anti-tumor effect. Methods: Firstly, Ad/Bcl-XL shRNA was constructed and purified. Then the protein level of Bcl-XL and survival of colon cancer cells after the treatment of Ad/Bcl-XL shRNA were determined by Western blotting and MTT assay, respectively. Furthermore, the activation of apoptotic signaling was also detected by Western blotting assay. Finally, the anticancer effect of Ad/Bcl-XL shRNA in vivo was confirmed in the subcutaneous tumor model derived from DLD1 cells in nude mice. Results: Ad/Bcl-XL shRNA was constructed and purified successfully. It obviously down-regulated the Bcl-XL protein and significantly inhibited the growth of DLD1 cells (1 000 MOI and 2 000 MOI Ad/Bcl-XL shRNA group was (MOI=1 000: [60.6±4.8] vs [37.3±6.9]%, 100%; MOI=2 000: [99.0±2.6] vs [99.0±2.1]%, 100% P<0.01), but had no obvious toxicity on normal human fibroblasts. Western blotting results demonstrated that the apoptotic signal molecules including caspase-9, caspase-3, and PARP were obviously activated after the treatment with Ad/Bcl-XL shRNA. In vivo, it also dramatically suppressed the growth of subcutaneous tumors derived from DLD1 cells in nude mice (eg. 29th day Ad/Bcl-XL shRNA group was [250.1±185.7] vs Ad/GFP [880.0±286.1], PBS [911.0±389.1] mm³, P<0.01). Conclusion: Ad/Bcl-XL shRNA can down-regulate the expression of Bcl-XL and inhibit the growth of colon cancer cells in vivo and in vitro, suggesting that it may be a new strategy to treat the colon carcinoma.

Keywords: [recombinant adenovector](#) [Bcl-XL](#) [RNA interfering](#) [small hairpin RNA](#) [colon cancer](#)

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