Survivin基因沉默下调血管形成相关因子表达抑制视网膜母细胞瘤侵袭性及其分子机制研究

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Title: **Effects of Survivin-shRNA on tumor invasive capacity and expression of angiogenesis related factors of HXO-RB44 cell**

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摘要: 目的:研究基因沉默Survivin对视网膜母细胞瘤HXO-RB44细胞凋亡、侵袭以及血管内皮生长因子（VEGF）、基质金属蛋白酶 2（MMP-2）、基质金属蛋白酶9（MMP-9）活性的影响。方法：培养视网膜母细胞瘤HXO-RB44细胞，构建Survivin-shRNA载体。按照处理不同分为Survivin-shRNA组、GFP组和CON组。分别检测三组HXO-RB44细胞凋亡指数、细胞侵袭能力以及VEGF、MMP-2、MMP-9、CAS-3蛋白的表达水平。结果：流式细胞术结果表明，与CON组和GFP组相比，Survivin-shRNA组细胞凋亡率增加，差异有统计学意义（P < 0.05）；Transwell侵袭小室实验显示Survivin-shRNA能明显降低HXO-RB44细胞的侵袭能力；Western blot结果发现，Survivin-shRNA可降低VEGF、MMP-2、MMP-9蛋白的表达水平，并提高CAS-3的表达水平。结论：Survivin-shRNA可诱导HXO-RB44细胞凋亡，抑制细胞侵袭能力，下调血管形成相关因子VEGF、MMP-2、MMP-9的表达，进而抑制肿瘤新生血管的形成。

Abstract: Objective:To explore the effects and molecular mechanisms of survivin -shRNA on tumor apoptosis,invasive capacity and Expression of Angiogenesis Related Factors of HXO-RB44 cells.Methods:HXO-RB44 cells were cultured in DMEM medium and recombinant adenovirus vector Survivin-shRNA and negative control rAd5-GFP were transfected into HXO-RB44 cells.Positive stable transfectants were selected and expanded for further study.The clone in which the rAd5-Survivin-shRNA virus vectors transfected was named as Survivin-shRNA group,the negative control vectors transfected was named as GFP group and HXO-RB44 cells were named as CON group.Flow cytometry detected apoptosis index.Transwell invasion assay detecteded cell invasive capacity.Western blot assay determined the protein expression level of VEGF,MMP-2,MMP-9 and CAS-3.Results:After Survivin-shRNA was transfected into HXO-RB44 cells,it was found that knockdown of Survivin markedly increased the apoptotic index of HXO-RB44 cells compared with GFP group and CON group indicated by flow cytometry.Transwell invasion assay showed that the cell invasive capacity in treated groups was markedly HXO-RB44 lower than the control group.Western blot assays performed that the protein expression level of VEGF,MMP-2,MMP-9 was decreased,while CAS-3 expression was increased in treated group compared with the CON group.Conclusion:Survivin-shRNA could induce apoptosis,inhibit invasive capacity,down-regulate the expression of angiogenesis related factors such as VEGF，MMP-2，MMP-9，and then inhibit angiogenesis of HXO-RB44 cells.

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