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聚酰胺树形分子-脂质体介导survivin反义寡核苷酸诱导肝癌细胞的凋亡 点此下载全文

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摘要：

目的： 评价聚酰胺-胺型树枝状高聚合物（polyamidoamine，PAMAM）-脂质体复合物作为survivin反义寡核苷酸（survivin antisense oligonucleotide，survivin-asODN）载体传递系统的可行性，及其对人肝癌SMMC-7721细胞survivin表达、细胞凋亡的影响。 方法： 制备PAMAM与脂质体的复合物（PAMAM-脂质体），将survivin-asODN与PAMAM-脂质体或PAMAM混合，分别制备PAMAM-脂质体-survivin-asODN和PAMAM-survivin-asODN。透射电镜观察复合物的形态、粒径；zeta电位分析仪测定复合物的zeta电位；离心法和紫外分光光度仪测定复合物的包封率、载药率。将PAMAM-脂质体-survivin-asODN和PAMAM-survivin-asODN转染SMMC-7721细胞，测定其转染率；Western blotting检测转染后SMMC-7721细胞中survivin蛋白的表达；流式细胞术检测SMMC-7721细胞的凋亡。 结果： 成功制备PAMAM-脂质体、PAMAM-脂质体-survivin-asODN和PAMAM-survivin-asODN。PAMAM-脂质体-survivin-asODN粒径与PAMAM-survivin-asODN粒径无显著差异\[（189.33±15.42） vs (181 83±13.67) nm， P >0.05\]，包封率和载药率也无显著差异（ P >0.05），但zeta电位高于后者\[（42.83±7.14 ） vs （ 32.33±5.57) mV， P <0.05\]， PAMAM-脂质体-survivin-asODN转染SMMC-7721细胞的效率高于PAMAM-survivin-asODN \[（73.33±9.29)% vs (60.67±7.81)%， P <0.05\]，转染后SMMC-7721细胞中survivin蛋白的表达较低（24.67±11.74 vs 43 17±11.63， P <0.05），但细胞凋亡率高于PAMAM-survivin-asODN组SMMC-7721细胞\[（73.31±12.59）% vs （ 52.67±12 19）%， P <0.05\]。 结论： PAMAM-脂质体能将survivin-asODN高效递送到人肝癌SMMC-7721细胞，诱导细胞凋亡。

关键词：聚酰胺-胺型树枝状高聚合物-脂质体 反义寡核苷酸 肝癌 survivin

Survivin antisense oligonucleotide mediated by polyamidoaminedendrimer liposome induces apoptosis of hepatic cancer cells Download Fulltext

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Abstract:

Objective:To investigate the possibility of polyamidoaminedendrimer (PAMAM)-liposome for survivin antisense oligonucleotide (survivin-asODN) delivery system and explore the effects of PAMAM-liposome-survivin-asODN on survivin expression and apoptosis of human hepatic cancer cell line SMMC-7721. Methods: The liposome modified PAMAM (PAMAM-liposome) was synthesized with liposome and PAMAM. Survivin-asODN was combined with the PAMAM-liposome or PAMAM to form PAMAM-liposome-survivin-asODN or PAMAM-survivin-asODN complexes. The shape and size of the two complexes were observed under a transmission electron microscope and their zeta potentials were measured with a zeta analytical tool. The encapsulating efficiency and DNA loading level were determined by ultraviolet spectrophotometer using a centrifuging method. PAMAM-liposome-survivin-asODN and PAMAM-survivin-asODN were transfected into SMMC-7721 cells, and the transfection efficiency was measured. The protein expression of survivin in SMMC-7721 cells was measured by Western blotting, and the apoptosis of SMMC-7721 cells was assessed by flow cytometry. Results: PAMAM-liposome, PAMAM-liposome-survivin-asODN and PAMAM-survivin-asODN were successfully established. No significant difference appeared in diameter between PAMAM-liposome-survivin-asODN and PAMAM-survivin-asODN (\[189.33±15.42\] vs \[181.83±13.67\] nm, P >0.05), as well as the encapsulating efficiency and drug loading level, but the zeta potential of PAMAM-liposome-survivin-asODN was higher than that of PAMAM-survivin-asODN (\[42.83±7.14\] vs \[32.33±5.57\] mV, P <0.05). The transfection efficiency of PAMAM-liposome-survivin-asODN was higher than that of PAMAM-survivin-asODN (\[73.33±9.29)% vs \[60.67±7.81\]%, P <0.05) in SMMC-7721 cells. The expression of survivin protein in SMMC-7721 cells of PAMAM-liposome-survivin-asODN group was less than that of PAMAM-survivin-asODN group (24.67±11.74 vs 43.17±11.63, P <0.05), while the apoptosis rate was higher than that of PAMAM-survivin-asODN (\[73.31±12.59\]% vs \[52.67 ±12.19\]%, P <0.05). Conclusion: The PAMAM-liposome can delivery survivin-asODN into SMMC-7721 cells effectively and induce SMMC-7721 cell apoptosis.

Keywords:polyamidoaminedendrimer liposome antisense oligonucleotide hepatic cancer survivin

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