

叶酸/聚酰胺-胺作为miR-7基因载体的胶质瘤靶向性研究

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Study of Targeting Ability of Folic Acid/polyamide-amine As miR-7 Vector to Glioma

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摘要 目的

检测叶酸/聚酰胺-胺(FA/PAMAM)作为miR-7基因载体的细胞转染效率及其胶质瘤靶向功能,为研发高效小分子靶向投递药物奠定基础。方法透析法制备FA/PAMAM络合物,透射电子显微镜观察粒子形貌;以其为载体转染miR-7至人脑胶质瘤细胞系U251,荧光显微镜观察络合物转染效率,qRT-PCR方法检测miR-7水平;制作去胸腺小鼠颅内U251胶质瘤模型,分别经尾静脉、颈内动脉及肿瘤原位进行络合物移植,48 h后取脑制作冰冻切片,荧光显微镜观察络合物在肿瘤内的聚集程度;蛋白印记(Western blot)法检测miR-7靶基因EGFR和细胞增殖活性抗原(PCNA)的蛋白表达。结果粒子形貌规整,与U251细胞共培养48 h后可获得高效转染,并显著提高miR-7水平。经尾静脉、颈内动脉及肿瘤原位三种途径移植后获得的冰冻切片中均可发现络合物粒子在肿瘤部位的聚集,但聚集程度为尾静脉<颈内动脉<肿瘤原位。Western blot结果显示EGFR和PCNA水平较对照组均有不同程度下降(P<0.05)。结论FA/PAMAM能够高效投递miR-7基因至体内、外胶质瘤细胞,有望成为一种新的高效小分子靶向投递药物进行胶质瘤基因治疗。

关键词: 胶质瘤 微小RNA 表皮生长因子受体 基因治疗

Abstract: Objective To explore the gene transfection efficiency of folic acid/polyamide-amine as miR-7 vector and its targeting ability for glioma,so as to lay the foundation to develop an efficient delivery of small molecule drugs targeting glioma.Methods FA/PAMAM comoles compound was prepared by dialysis method.The transmission electron microscope was performed to observe the morphology of the nanoparticles.After transfecting miR-7 gene into U251 glioma cell line,fluorescence microscope was used to detect the gene transfection efficiency,quantitative RT-PCR was used to detect the miR-7 level.The intracranial glioma model was established in de-thymus mice,the nanoparticles were transplanted by the way of vena caudalis,internal carotid artery,and tumor situ.After 48 hours,the frozen section was obtained to observe the aggregation extent.And immunocytochemistry and western blot methods were used to test the protein expression of EGFR and PCNA.Results The nanoparticle,with sphere morphology,may transfer efficiently the miR-7 gene into U251 glioma cells,and increase the miR-7 level.And it can be found in tumor situ,in spite of by different transplant ways.The aggregation extent was the vena caudalis way less than the internal carotid artery way,and furthermore less the tumor situ way (P<0.05).The protein level of EGFR and PCNA in FA/PAMAM/miR-7 group both lower than the control group(P<0.05).Conclusion FA/PAMAM can transfect effectively miR-7 into glioma both in vivo and in vitro,and is expected to become an efficient delivery of small molecule drugs targeting glioma.

Key words: Glioma microRNA Epidermal growth factor receptor Gene therapy

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