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Inhibition of Guinea Pigs Infection with Pseudomonas Aeruginosa by siRNA Targeting rhlI Gene

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英文关键词:siRNA biofilm Pseudomonas aeruginosa

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中文摘要:

目的 探讨靶向rhlI基因的siRNA分子对豚鼠体内铜绿假单胞菌生物膜感染的抑制作用。方法 应用气管注入法制备铜绿假单胞菌生物膜感染豚鼠模型，18只豚鼠模型随机分成3组，分别经尾静脉注射siRNA分子(50 μg·mL^{-1})与脂质体混合物(siRNA组)、乳酸环丙沙星(环丙沙星组)或生理盐水(对照组)。检查肺和支气管组织病理改变。取左肺组织匀浆和支气管肺泡灌洗液(BALF)进行细菌学检查。结果 siRNA组豚鼠肺和支气管组织结构未见明显异常，环丙沙星组和对照组豚鼠肺和支气管组织结构异常，表现为肺组织实质变性伴炎性细胞浸润，支气管黏膜脱落，管壁变薄。siRNA组豚鼠左肺和BALF的细菌总数均显著低于环丙沙星组(P<0.001)，siRNA组豚鼠体内分离的铜绿假单胞生物膜形成能力均显著低于环丙沙星组(P<0.001)。结论 靶向rhlI基因的siRNA分子能够破坏豚鼠体内的铜绿假单胞生物膜，减少感染组织内细菌总数，使病变组织结构恢复正常，有望成为治疗细菌生物膜感染的新一代药物。

英文摘要:

OBJECTIVE To investigate the inhibiton of small interfering RNA(siRNA) aimed at rhlI gene on guinea pigs infection by Pseudomonas aeruginosa biofilm. METHODS After guinea pigs model with Pseudomonas aeruginosa biofilm infection being made by trachea injection, 18 of model guinea pigs were randomly assigned to three groups, which were injected through tail vein by mixture of siRNA(50 μg·mL^{-1}) and liposome (siRNA group), ciprofloxacin lactate (ciprofloxacin group), or 0.9% NaCl(control group). Histopathological changes in lung and bronchial tissue were investigated. Bacteriologic test were examined in lung tissue and bronchoalveolar lavage fluid (BALF). RESULTS In siRNA group, the histology structure of lung and bronchial tissue showed no obvious abnormal. In ciprofloxacin group and control group, the structure of lung and bronchial tissue showed abnormal changes such as consolidations with inflammatory cells infiltration, bronchus mucosa degeneration with thin wall. The total bacteria number in left lung and BALF samples from siRNA group guinea pigs were significantly less than that in ciprofloxacin group(P<0.001). The biofilm formation ability of Pseudomonas aeruginosa isolated from siRNA group guinea pigs was significantly lower than that in ciprofloxacin group(P<0.001). CONCLUSION siRNA aimed at rhlI gene is able to damage biofilm in Pseudomonas aeruginosa in vivo, reduce total number of bacteria, promote diseased tissue get right, and is likely to be a new generation of drugs for bacteria biofilm infection cure.

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