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靶向抑制GLUT1对糖尿病视网膜病变中视锥细胞的

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Title: Target inhibition of glucose transport-1 protects cone photoreceptors in diabetic retinopathy mice

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关键词: 葡萄糖转运蛋白-1; RNA; 小分子干扰; 糖尿病视网膜病变; 视锥细胞

Keywords: glucose transporter type-1; siRNA; diabetic retinopathy; cone photoreceptors

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摘要: 目的 观察抑制视网膜上葡萄糖转运蛋白-1（glucose transporter-1,GLUT1）对糖尿病视网膜病变中视锥细胞的影响。 方法 27只8周龄C57BL/6小鼠按随机数字表法分为正常对照组、糖尿病对照组和GLUT1小干扰核糖核酸（siRNA）治疗组。腹腔注射链脲佐菌素建立糖尿病模型后，GLUT1 siRNA治疗组予以玻璃体腔注射靶向GLUT1的siRNA，正常对照组和糖尿病对照组注射等量非靶向性siRNA，以上操作每2周重复注射1次，共注射9次。建模第18周3组小鼠行明适应视网膜电图检查视锥细胞功能，免疫荧光共定位法和免疫印迹法检查视网膜GLUT1的表达，测定比较视网膜含糖量，通过免疫荧光共定位法检查视锥细胞的密度及形态改变。 结果 与糖尿病对照组相比，GLUT1 siRNA治疗组小鼠视网膜GLUT1表达明显下调，较正常对照组下降68.51%（$P<0.01$）。尽管糖尿病对照组和GLUT1 siRNA治疗组视网膜组织含糖量均高于正常对照组，但GLUT1 siRNA治疗组小鼠视网膜含糖量比糖尿病对照组低42.67%，差异有统计学意义（$P<0.01$）；糖尿病对照组和GLUT1 siRNA治疗组小鼠的明适应视网膜电图的a波及b波振幅均低于正常对照组，但GLUT1 siRNA治疗组较糖尿病对照组分别高47.59%和42.61%，差异有统计学意义（$P<0.01$）；形态学检查发现糖尿病对照组较GLUT1 siRNA组视锥细胞排列稀疏，外节形态更为短小。 结论 GLUT1 siRNA通过抑制GLUT1表达，限制转运葡萄糖进入视网膜，降低视网膜局部含糖量从而对光感受器视锥细胞产生保护作用。

Abstract: Objective To determine the effect of glucose transporter-1(GLUT1)

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suppression on cone photoreceptors in diabetic retinopathy in mice. Methods Twenty-seven 8-week-old C57BL/6 mice were divided into normal control, diabetic control and GLUT1 siRNA treatment group. Diabetic model was established by intraperitoneal injection of streptozotocin. GLUT1 siRNA treatment group received intravitreal injection of siRNA-mediated GLUT1, and the other 2 groups received equal amount of non-specific siRNA. The intravitreal injection procedure was repeated every 2 weeks for 9 times in all. In 18 weeks after diabetic induction, photopic electroretinography (ERG) was performed to evaluate cone photoreceptors function, and immunofluorescence assay and Western blotting were carried out to examine the expression of GLUT1. The glucose concentration was determined in the retina. Immunofluorescence colocalization was employed to determine the density and morphological change of cone photoreceptors. Results The expression of GLUT1 was notably down-regulated in GLUT1 siRNA treatment group than diabetic control group, and was lower by 68.51% compared with normal control groups (P<0.01). Retinal glucose concentration was obviously higher in the diabetic control and GLUT1 siRNA treatment group than the normal control, but GLUT1 siRNA treatment group was decreased by 42.67% compared with diabetic control（P<0.01）. A-wave and b-wave amplitudes in photopic ERG were lower in diabetic control and GLUT1 siRNA treatment group than the normal control, but GLUT1 siRNA treatment group was increased by 47.59%（P<0.01）and 42.61%（P<0.01）compared with diabetic control, respectively. Morphology examination showed that density of cones were decreased significantly and had a shorten outer-segment appearance in diabetic control group. Conclusion GLUT1 siRNA controls the glucose transport into the retina by suppressing the expression of GLUT1, reduces the glucose concentration in retinal environment, and thus protects cone photoreceptors in diabetic retinopathy.

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