PI3Kγ抑制剂AS605240治疗小鼠胰腺癌的实验研究

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Title: **Experimental study of PI3Kγ inhibitor AS605240 in the treatment of pancreatic cancer in mice**

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摘要: 目的：探讨PI3Kγ抑制剂AS605240对于胰腺癌的治疗作用及其机制。方法：使用MTT法探索AS605240对体外胰腺癌细胞的抑制效果，同时建立胰腺癌荷瘤小鼠模型，随机分为AS605240处理组和空白对照组进行给药。处死小鼠后测量肿瘤体积，观察AS605240对于胰腺癌动物模型的抑制效果。然后使用免疫组化检测肿瘤组织Ki-67表达情况，使用TUNEL检测肿瘤组织凋亡情况，同时使用免疫荧光及RT-PCR检测肿瘤组织内CD31和VEGF的表达情况，以探讨AS605240可能的抗肿瘤机制。结果：MTT实验显示在体外情况下，不同浓度的AS605240并没有明显影响小鼠MPC-83胰腺癌细胞的活性与生长。在动物实验中，AS605240治疗组的肿瘤体积相比对照组显著缩小，差异有统计学意义（P<0.05），且治疗过程中对重要器官未表现出明显毒副作用。进一步实验结果显示：尽管AS605240没有影响肿瘤组织的凋亡或者Ki-67的表达，但AS605240能够明显降低肿瘤组织中CD31阳性细胞数量（P<0.01），RT-PCR也显示AS605240能够明显降低肿瘤组织中VEGF mRNA的表达（P<0.01）。结论：AS605240能有效抑制小鼠胰腺癌移植瘤的生长，其机制可能是减少移植瘤组织中CD31及VEGF的表达，抑制肿瘤的微血管生成，具有抗血管生成的作用。

Abstract: Objective：To explore the therapeutic effect of AS605240 which is a novel PI3Kγ inhibitor and its mechanism on pancreatic cancer.Methods：In this study，we used MTT assay to explore the inhibition of AS605240 on pancreatic cancer cells in vitro.At the same time，pancreatic tumor-bearing mice model was established and randomly divided into AS605240 treatment group and control group.The tumor-inhibiting effect of AS605240 on the animal model of pancreatic cancer was observed by measuring tumor volume after the mice were sacrificed.The expression of Ki-67 was detected by immunohistochemistry in tumor tissue.Tumor apoptosis was measured by TUNEL assay.Moreover，the expression of CD31 and VEGF was also detected by immunofluorescence and RT-PCR in tumor tissue.Results：MTT assay showed that AS605240 at different concentrations did not significantly affect the growth of MPC-83 pancreatic cancer cells in vitro.In vivo，the tumor volume of AS605240 treatment group was remarkably reduced compared with the control group (P<0.05)，and the treatment did not show obvious side effects.Although AS605240 did not affect the apoptosis of tumor tissues or Ki-67 expression，further experiment demonstrated that AS605240 could evidently reduce the number of CD31-positive cells (P<0.01).PCR also demonstrated that AS605240 could significantly decrease the expression of VEGF mRNA expression (P<0.01).Conclusion：AS605240 may be an effective drug for pancreatic cancer，of which the mechanism is relating to suppress the expression of CD31 and VEGF，and to decrease tumor angiogenesis probably through inhibiting PI3Kγ pathway.

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