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Title: Artificial sodium channel amine ligands suppress growth and invasion in prostate cancer cells *in vitro*

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关键词: 电压门控性钠离子通道; 钠离子通道胺类配体; 前列腺癌; PC3细胞; 肿瘤侵袭

Keywords: voltage-gated sodium channels; sodium channel amine ligands; prostate cancer; PC3 cells; neoplasm invasiveness

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摘要: 目的　研究人工合成钠离子通道阻断剂(sodium channel amine ligands，SCALs)对前列腺癌细胞株（PC3细胞、DU145细胞）生长及侵袭的影响，以筛选高效的抗肿瘤药物。　方法　四甲基偶唑氮（MTT）法检测SCALs对肿瘤细胞的存活率的影响；Transwell侵袭实验检测SCALs干预后肿瘤细胞体外侵袭能力的变化；流式细胞仪检测SCALs促进细胞凋亡及阻滞细胞周期的能力，蛋白免疫印迹实验检测SCALs对钠离子通道蛋白α亚基Nav 1.7 蛋白表达的影响。　结果　7种SCALs中的3种（S1127、S1169、S1180）对前列腺癌细胞敏感，在低浓度时对肿瘤细胞具有杀伤效应，且其抑制率与药物浓度呈剂量-效应关系，其中S1180对PC3和DU145细胞的IC_{50}分别为2.9 μmol/L和2.5 μmol/L，在10 μmol/L时能促进12.89%的肿瘤细胞凋亡、抑制75.53%的细胞侵袭，并具有阻滞细胞周期的能力，以及能下调Nav 1.7 蛋白的表达水平。　结

论　　合成的钠离子通道阻断剂中3种SCALs尤其是S1180具有显著杀伤前列腺癌细胞效应，将来可能成为治疗肿瘤的一类新型药物。

Abstract: Objective To determine the effect of artificially synthesized sodium channel amine ligands (SCALs) on the growth and invasion of prostate cancer cell lines. Methods SCALs compounds, S1127, S1156, S1169, S1170, S1178, S1180, and S1182 were synthesized and confirmed. Prostate cancer cell lines, PC3 and DU145, were used in this study. The cell viability was assessed by MTT assay in the cells after the treatment of SCALs respectively. The cell apoptosis and cell cycle progression were assessed by flow cytometry. The cancer cell invasion was assessed by Transwell chamber assay. The protein expression of prostate cancer sodium channel α subunit, Nav 1.7 was determined by Western blotting. Results Three compounds, S1127, S1169, and S1180, inhibited the growth of tumor cells in a dose-dependent manner. S1180 was found to be the most potent among the 7 compounds. The IC_{50} values of S1180 were 2.9 and 2.5 μmol/L respectively for PC3 and DU145 cells. At 10 μmol/L, S1180 improved cell apoptosis in 12.89% PC3 cells, and suppressed the cell invasion in 75.53% cells, and exerted significant effects on cell arrest, and down-regulated Nav 1.7 protein expression. Conclusion Three SCALs compounds, especially S1180, have obvious anti-tumor effect on prostate cancer cells, and might be a potential therapeutic agent for prostate cancer.

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