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论文

孕激素受体拮抗剂ZXH951对乳腺癌细胞生长抑制作用及对端粒酶活性的影响

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摘要：

目的 研究ZXH951在体外对乳腺癌细胞的生长抑制作用及对端粒酶活性的影响。方法 分别用细胞生长曲线、集落形成及竞争性配体与受体结合法，测定ZXH951的体外抗肿瘤作用及其与孕激素受体（PR）、雌激素受体(ER)结合活性；用流式细胞术及多聚酶链反应-端粒重复序列扩增法探讨ZXH951对人乳腺癌T47D细胞周期及端粒酶活性的影响。结果 ZXH951对ER和PR双阳性的乳腺癌细胞T47D体外增殖有较强的抑制作用，而对ER和PR双阴性的人乳腺癌细胞MDA-MB-231无明显抑制作用；ZXH951与PR有较强结合活性，而与ER无明显结合活性；可将T47D细胞阻滞在G1期，并对端粒酶活性有一定抑制作用。 结论 ZXH951是一个有发展前景的新型抗孕激素类化合物，在体外对乳腺癌细胞有较强的抑制作用，其作用机制可能与其通过PR介导的细胞增殖及对端粒酶活性抑制有关。

关键词： 孕激素受体拮抗剂 乳腺癌 端粒酶

EFFECTS OF A NOVEL ANTIPROGESTIN DERIVATIVE ZXH951 ON PROLIFERATION AND TELOMERASE ACTIVITY OF HUMAN BREAST CARCINOMA CELL LINES

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Abstract:

AIM To investigate the antiproliferative activity of a new synthetic steroid ZXH951 structurally related to mifepristone(RU486) and its effects on cell cycle traverse and telomerase activity in human breast carcinoma cell lines. METHODS Antiproliferative activity was determined by cell growth curve， MTT reduction and colony formation. Receptor binding affinities were measured by competitive binding assay using radiolabelled ligands. Cell cycle distribution was analyzed by flow cytometry. Telomerase activity was investigated by TRAP-PCR. RESULTS ZXH951 exhibited potent antiproliferative activity in estrogen receptor and progesterone receptor positive human breast carcinoma cell lines *in vitro*, high affinity with human progesterone receptor-A, little affinity with estrogen receptor and blockade the cells in G1 phase. Moreover, when T47D cells were exposed to 0.4, 1.0 and 10 μmol.L^{-1} of ZXH951 for 72 h， the telomerase activity was significantly decreased. CONCLUSION ZXH951 is a promising progesterone receptor antagonist. It significantly inhibits the growth of estrogen receptor and progesterone receptor positive human breast carcinoma cells. Its mechanism of action may be related to its antiproliferation mediated by progesterone receptor and inhibition of telomerase activity.

Keywords: breast cancer telomerase progesterone receptor antagonist

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