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论著

# 司坦唑醇激活ERα调节雌激素受抑的青春期大鼠生长板软骨细胞的增殖和分化

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摘要 目的： 探讨司坦唑醇（ST）对离体培养的促性腺激素释放激素拟似物（GnRHa）处理后青春期大鼠生长板软骨细胞的增殖和分化的影响；研究ST是否经由雌激素受体α（ERα）介导软骨细胞增殖和分化，以探讨ST促进骨生长/成熟生物效应的机制。方法: MTT法和免疫组化法检测软骨细胞在不同浓度、不同时间ST处理后增殖细胞核抗原（PCNA）表达；Western blotting分析ST作用后ERα的变化；分子动力学模拟方法预测ST与ERα的相互作用方式。结果: (1)ST以时效和量效作用方式分别对雌激素受抑的离体青春期大鼠生长板软骨细胞的增殖呈双相型影响，在合适的剂量和疗程时，细胞增殖效应可达最好效果。(2)ST 作用后磷酸化ERα（p-ERα） 水平随时间增加而上调，于10 min时达峰值，后渐减。增加ST 浓度，p-ERα 水平渐强，并在10-9 mol/L-10-8mol/L 时达峰值，后渐弱。阻断ERα和MAPKK, ST所致的p-ERα水平较未阻断时减弱。(3)分子动力学模拟结果：ST与17β-雌二醇一样均能与ERα的2个氨基酸残基（Glu353、His524）发生较强的氢键作用。ST和17β-雌二醇与ERα的结合力相当。结论: ST是雄激素的衍生物，但本研究结果显示其作用经ERα介导，包括了经典ERα的受体途径和MAPK途径，实现其促长骨生长板软骨细胞生长和成熟的生物效应。分子动力学研究证实了ST能与ERα产生特异性、稳定性结合。

关键词 软骨细胞 司坦唑醇； 受体,雌激素

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# Stanozolol regulates the proliferation and differentiation of growth plate chondrocytes in the estrogen- inhibited adolescent rats through activation of ERα

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**Abstract**

<FONT face=Verdana>AIM: (1) To observe the effect of stanozolol (ST) on the proliferation, maturity and differentiation of the growth plate chondrocytes cultured in vitro of adolescent rats treated with gonadotropin releasing hormone analogue (GnRHa). (2) To study if ST mediates the proliferation/differentiation of chondrocytes via the estrogen receptor α (ERα), and to investigate the mechanism of the biological effects in ST promoting bone growth/maturity in molecular level. (3) To predict the interaction mode of ST with ERα through molecular dynamics simulation, and to investigate the similarities and differences of the interaction mode between ERα with ST and estradiol. METHODS: Immunohistochemical staining of PCNA and MTT were conducted. Prediction of the interaction mode of ST with ERα was through molecular dynamics simulation. RESULTS: (1) Duplex effects of ST in time- effect and dose-effect modes were observed, respectively. With the appropriate dose and period of treatment, the proliferation of the growth plate chondrocytes presented the best effect. (2) After ST action, the expression of p-ERα was up-regulated with the increase in time, and up to the peak value at 10 min, then gradual down-regulation. With increase in ST concentration, the expression of p-ERα became gradually strong, and up to the peak value at 10-9 mol/L-10-8mol/L, then gradually weakened. After ERα and MAPKK were blocked, the expression of p-ERα induced by ST was weakened. (3)Like 17 β-estradiol, ST induced a stronger

reaction of the hydrogen bonding with the two amino acids residues (Glu353, His524) of ERα. The bonding capacity of ST to ERα was almost the same as 17 β-estradiol. CONCLUSION: ST is a derivative of androgen, but the results of this study show that its action is ERα-mediated, including the classic ERα receptor pathway and MAPK pathway, resulting in the promoting growth and maturation of the long bone growth plate chondrocytes. Molecular dynamics study confirms that the ST can specifically and stably bind to ERα. </FONT>

**Key words** Chondrocytes Stanozolol Receptors estrogen

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