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## 组蛋白H3、H4乙酰化及H3K4甲基化对人妊娠子宫PRA/PRB的影响(PDF)

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Title: Effects of histone acetylation and H3K4 methylation on PRA/PRB in human uterine smooth muscle cells during pregnancy

作者: [罗慧](#); [陈诚](#); [梁志清](#)  
第三军医大学西南医院妇产科

Author(s): [Luo Hui](#); [Chen Cheng](#); [Liang Zhiqing](#)  
Department of Gynecology and Obstetrics, Southwest Hospital, Third Military Medical University, Chongqing, 400038, China

关键词: [组蛋白乙酰化](#); [H3K4甲基化](#); [妊娠](#); [子宫平滑肌细胞](#)

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摘要: 目的 通过组蛋白去乙酰化酶抑制剂(trichostatin A,TSA)、H3K4甲基化酶抑制剂(5'-deoxy-5'-methylthioadenosine,MTA)处理人妊娠子宫平滑肌细胞,干预组蛋白H3、H4乙酰化及H3K4甲基化水平,探讨组蛋白H3、H4乙酰化及H3K4甲基化对人妊娠子宫平滑肌细胞PRA/PRB的影响。方法 分离纯化人妊娠子宫平滑肌细胞( $n=16$ ),免疫组化定位孕激素受体(progesterone receptor,PR)及孕激素受体B(progesterone receptor B,PRB)在子宫平滑肌细胞核的表达。分别利用不同浓度TSA、MTA对其进行处理,Real-time PCR检测PR、PRA、PRB mRNA的表达;染色质免疫共沉淀技术(Chromatin immunoprecipitation,ChIP)比较处理前后PRA、PRB启动子区H3、H4乙酰化及H3K4三甲基化水平。结果 TSA可使PRA/PRB明显增高( $P<0.05$ ),使PRA启动子区H3、H4乙酰化水平明显上升( $P<0.05$ )。MTA可使PRA/PRB明显下降( $P<0.05$ ),PRA启动子区H3K4乙酰化水平明显下降( $P<0.05$ )。两种药物的干预主要通过通过对PRA的调控来调节PRA/PRB比值。结论 组蛋白H3、H4乙酰化和H3K4甲基化均可使人妊娠子宫平滑肌细胞PRA/PRB比值发生改变,可能参与“功能性孕激素撤退”机制的调节。

Abstract: Objective To determine the effects of histone acetylation and H3 lysine 4 (H3K4) methylation on the ratio of A and B isoforms of the human progesterone

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receptor (PRA/PRB) in human uterine smooth muscle cells during the course of pregnancy. **Methods** Human uterine smooth muscle cells of pregnancy were isolated from 16 full-term pregnant women receiving caesarean section, and then purified by collagenase digestion. The expression of PR and PRB was detected by immunohistochemistry in the cells and in the cells treated with different concentrations of histone deacetylase inhibitor, trichostatin A (TSA) or H3K4 methyltransferase inhibitor, 5'-methylthioadenosine (MTA). The mRNA levels of PR, PRA and PRB were detected by real-time PCR. Chromatin immunoprecipitation (ChIP) was used to analyze acetylation of histones H3 and H4, and trimethylation of H3K4 in the promoter regions of PRA and PRB. **Results** TSA treatment resulted in obviously increase in the ratio of PRA/PRB ( $P<0.05$ ) and in the acetylation of histones H3 and H4 in the promoter region of PRA ( $P<0.05$ ). While, MTA treatment led the ratio of PRA/PRB significantly decreased ( $P<0.05$ ) and reduced the trimethylation of H3K4 in the promoter region of PRA ( $P<0.05$ ). Both TSA and MTA regulated the expression of PRA to exert effect on the ratio of PRA/PRB. **Conclusion** Both the acetylation of histones H3 and H4 and the methylation of H3K4 regulate the ratio of PRA/PRB, and might be involved in the mechanism of "functional progesterone withdrawal" in the human uterine smooth muscle cells of pregnancy.

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