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论著

环磷酰胺处理雄小鼠对受精卵和二细胞期胚胎DNA甲基化和组蛋白H3K23乙酰化的影响

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摘要 **目的** 探讨环磷酰胺处理雄性小鼠对受精卵和早期胚胎DNA甲基化修饰和组蛋白H3第23位赖氨酸(H3K23)乙酰化修饰的影响。**方法** 20只性成熟的ICR雄小鼠饲喂环磷酰胺6 mg·kg^{-1} 4周。雄鼠与雌鼠交配后收集原核期受精卵和二细胞期胚胎。间接免疫荧光染色技术结合激光共聚焦扫描显微镜技术检测胚胎细胞中DNA甲基化和组蛋白H3K23乙酰化修饰的分布和水平。**结果** 与正常对照组相比，环磷酰胺组原核期受精卵和二细胞期胚胎的DNA甲基化修饰水平和分布没有明显差异；但与正常对照组（3%）相比，环磷酰胺组的二细胞期胚胎微核现象（20%）明显升高（P<0.01）；与正常对照组相比，环磷酰胺组受精卵雄原核和二细胞期胚胎细胞核的组蛋白H3K23乙酰化水平明显降低（P<0.05），且胚胎间的变化差异明显升高，其中部分原核期受精卵（58%）和二细胞期胚胎（44%）染色水平明显偏低。**结论** 长期低剂量环磷酰胺处理雄鼠可以导致部分受精卵和二细胞期胚胎组蛋白H3K23乙酰化异常，并且显著增加微核发生率。

关键词 环磷酰胺 胚胎,着床前 DNA甲基化 组蛋白乙酰化

分类号 R394.1

Effect of paternal exposure to cyclophosphamide on DNA methylation and histone 3K23 acetylation in mouse zygote and 2-cells embryo

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Abstract

OBJECTIVE To investigate effect of paternal exposure to cyclophosphamide on epigenetic characteristics of DNA methylation and histone 3K23 (H3K23) acetylation in mouse zygote and 2-cells embryo. **METHODS** A total of 20 male ICR mice of sexual maturity were *po* given cyclophosphamide 6 mg·kg^{-1} for 4 weeks. After mating with female mice, zygote at pronuclei stage and 2-cells embryo were obtained and fixed. With indirect immunofluorescence staining and laser scanning confocal microscope system, staining patterns and levels of DNA methylation and H3K23 acetylation were analyzed in mouse embryos. **RESULTS**]Although DNA methylation staining patterns and levels of zygotes and 2-cells embryos were similar between cyclophosphamide-treated group and normal control group, micronuclei were found in 20% of 2-cell embryos in cyclophosphamide-treated group, which was significantly higher than 3% in normal control group (P<0.01). Compared with normal control group, H3K23 acetylation levels in male pronuleus and 2-cells embryos in cyclophosphamide-treated group were obviously lower (P<0.05), and the variances within groups were also higher, among them there are 58% zygotes and 44% of 2-cells embryos with visible faint staining. **CONCLUSION** Paternal exposure to cyclophosphamide of low dose in a long-term can induce abnormal H3K23 acetylation in part of zygotes and early embryos, and higher micronuclei occurrences in 2-cells embryos.

Key words cyclophosphamide mouse preimplantation embryos DNA methylation histone acetylation

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