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研究论文

维甲酸诱导的脊柱裂小鼠的脊髓全基因组表达谱分析

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摘要:

关于维甲酸胚胎病理学的研究很多,维甲酸受体在器官发生、发育及神经管闭合过程中发挥重要作用。但维甲酸影响这些过程的机制还不清楚。在本研究中,我们发现,小鼠怀孕8天时,给予母体连续3次维甲酸灌胃,将导致胎儿脊柱裂,发生率为96.77%。本研究应用微阵列技术,在维甲酸诱导的脊柱裂小鼠胎儿的脊髓组织中发现了134个差异表达在1.5倍以上的基因。基因富集分析显示,母亲暴露于维甲酸导致的胎儿脊柱裂,与促凋亡和抗凋亡、细胞增殖、迁徙、细胞骨架成分以及细胞或局部粘附等基因功能簇相关,提示这些细胞成分和生物学的功能缺陷促使脊柱发育异常。我们的研究提供了脊柱裂的全基因组基因表达模式,有助于理解神经管缺陷的病因和病理学。

关键词: 维甲酸 脊柱裂 基因表达 微阵列 脊髓

Gene Expression Profiling of Mice Spinal Cords with Spina Bifida after Maternal Exposure to Retinoic Acid

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Abstract:

Retinoids (vitamin A and its derivatives) play important roles in the maintenance of various tissues in the adult vertebrate and are essential for diverse embryological processes. As a member of retinoids (vitamin A and its derivatives), retinoic acid (RA) has been extensively investigated in embryopathology. However, the mechanisms by which RA influences these processes are not completely understood. In the present study, we found that embryonic RA exposure via maternal treatment with gavage-fed 3 successive doses of RA on day 8 of gestation led to a high incidence (96.77%, 30/31) of rachischisis with myeloschisis, i.e., spina bifida aperta, among the surviving day 18 fetuses. Using microarray technology, we identified 134 genes in the spinal cords of mice that exhibit at least a 1.5-fold change between mice with spina bifida and control samples. Several downstream genes of RA signaling involved in lipid metabolism were regulated at the transcriptional level after maternal RA exposure. Furthermore, a gene set enrichment analysis (GSEA) implicate many altered expression of genes, involved in pro- or anti-apoptosis, cell proliferation, migration, cytoskeleton components, and cell or focal adhesion, which are associated which the spina bifida induced by the maternal RA exposure. This indicates that defective functions of these cell components and biological processes preceded the abnormal development of neural tube. Our study provides a global analysis of gene expression patterns in spina bifida and will help the understanding of the etiology and pathology of neural tube defects.

Keywords: Retinoic acid Spina bifida Gene expression Microarray

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