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论著

雷公藤甲素对Wistar大鼠免疫毒性相关基因表达的影响

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摘要 目的 应用基因芯片技术研究雷公藤甲素对大鼠胸腺全基因表达谱的影响, 从基因水平探讨雷公藤甲素引起免疫抑制毒性的潜在分子作用机制。方法 Wistar大鼠, 连续28 d ig给予雷公藤甲素0.5和1.0 mg·kg^{-1}以及环孢素A 20 mg·kg^{-1}(阳性对照), 进行T细胞依赖抗体反应检测、免疫器官组织病理学检查和胸腺组织基因芯片实验。结果 与溶媒对照组相比, 雷公藤甲素0.5和1.0 mg·kg^{-1}组和环孢素A组大鼠血清中T细胞依赖抗体应答水平均受到了显著抑制。组织病理学检查发现, 雷公藤甲素1.0 mg·kg^{-1}使胸腺皮髓质淋巴细胞数量轻度减少, 环孢素A使胸腺髓质皮质化。基因芯片检测结果显示, 雷公藤甲素1.0 mg·kg^{-1}给药第7天引起422个显著差异表达基因, 其基因功能主要涉及DNA依赖的细胞转录调节、核转运、微管蛋白复合体装配、核小体装配、线粒体DNA转录、氨基酸转运和线粒体DNA复制等。KEGG通路分析发现差异表达基因主要参与移植排斥和自身免疫性疾病等多个与免疫抑制相关的基因表达调控途径。结论 雷公藤甲素1.0 mg·kg^{-1}能够引起大鼠胸腺基因表达谱的显著性改变, 其免疫毒性的主要机制可能是通过下调免疫毒性相关基因的表达, 抑制淋巴细胞的增殖。

关键词 雷公藤内酯 胸腺 免疫 毒性作用 基因表达谱

分类号 R992

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本文作者相关文章
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Effect of triptolide on immunotoxicity-related gene expression in rats with microarray

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Abstract

OBJECTIVE To explore the effect of triptolide on the gene expression profiles in rat thymus with microarray and to further investigate the molecular mechanism of its immnuosupression toxicity. **METHODS** Wistar rats were ig given triptolide 0.5 and 1.0 mg·kg^{-1} and cyclosporin A 20 mg·kg^{-1} (positive control), once daily, for 28 d. T-cell-dependent antibody response assay, histopathology examination of immune organs and microarray test of thymus were performed respectively. **RESULTS** Compared with vehicle control group, T cell dependent anti-keyhole limpet hemocyanin(KLH) specific antibody response level significantly decreased in triptolide 0.5 and 1.0 mg·kg^{-1} groups and ciclosporin A group. Histopathology examination showed that the number of lymphocytes in thymus cortex and medulla was slightly reduced in triptolide 1.0 mg·kg^{-1} group and the area of thymus medulla was moderately reduced in cyclosporin A group. In microarray test, about 442 down-regulated genes were remarkably altered in triptolide 1.0 mg·kg^{-1} group. The functions of these differentially expressed genes were associated with regulation of transcription, nuclear transport, tubulin complex assembly,

nucleosome assembly, transcription from mitochondrial promoter, translation, amino acid transport, and mitochondrial DNA replication. KEGG pathway analysis results showed that these differentially