

论著

微矩阵基因芯片筛选抗抑郁剂地昔帕明相关基因的研究

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摘要 目的 研究抗抑郁剂相关基因, 探讨其可能作用机制。方法与结果 以高浓度皮质酮 (Cort) $10 \mu\text{mol} \cdot \text{L}^{-1}$ 或 Cort 与三环类经典抗抑郁剂地昔帕明 (DIM) $5 \mu\text{mol} \cdot \text{L}^{-1}$ 共同处理 PC12 细胞 3 d 分别作为对照组和实验组, 按 Trizol 一步法提取细胞总 RNA 并纯化 mRNA, 将等量的对照组与实验组 mRNA 以逆转录法分别标记荧光素 cy3 和 cy5, 合成 cDNA 探针并等量混合, 与小鼠 2048 点微矩阵基因芯片杂交, 扫描荧光信号图像并分析比较二组差异表达基因, 发现 DIM 与 Cort 共孵 PC12 细胞 3 d 可以诱导 259 个基因表达水平发生改变。其中 163 个基因表达降低, 如葡萄糖调节蛋白 78 ku、葡萄糖激酶 (GA)、细胞骨架蛋白、转化性生长因子 β 受体结合蛋白、细胞色素 C 氧化酶、锂盐敏感性内消旋肌醇-1-磷酸酯酶等; 有 96 个基因表达水平升高, 如神经元生长分化因子-9 (GDF-9)、锌指蛋白 216、细胞色素 P450、睾丸特异基因-1 等。随机选取二个差异表达基因—GA 和 GDF-9, 以细胞原位杂交方法验证, 取得与基因芯片评价一致的结果。结论 抗抑郁剂 DIM 作用可能与能量代谢、细胞骨架、营养因子、酶等多层次、多水平的基因表达改变有关。本研究利用基因芯片技术对抗抑郁剂相关基因进行了初步探索, 为深入研究抗抑郁剂作用机制和药物筛选芯片的研发提供了线索与依据。

关键词 [抗抑郁剂](#) [地昔帕明](#) [基因表达](#) [基因芯片](#) [细胞, PC12](#) [皮质酮](#)

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Screening studies on the antidepressant desipramine related genes using microarray gene chip

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Abstract

AIM To study the antidepressant related genes and explore the possible action mechanism of antidepressants.

METHODS and RESULTS PC12 cells were treated with corticosterone (Cort) $10 \mu\text{mol} \cdot \text{L}^{-1}$ for 3 d in the absence or presence of desipramine (DIM) $5 \mu\text{mol} \cdot \text{L}^{-1}$ and the mRNA was extracted, and then labeled with fluorescein cy3 or cy5 respectively using reverse transcription. The labeled probes were mixed equally and hybridized with the mouse 2048-gene dot microarray gene chip. After scanning and analysis, it was found that DIM induced 259 gene expression changes in Cort treated PC12 cells, in which 163 gene expression down-regulated (for example, glucose regulated protein 78 ku, glucokinase (GA), cytoskeleton tubulin or actin, transforming growth factor- β receptor binding protein, cytochrome C oxidase, lithium-sensitive myo-inositol monophosphatase A1, etc.) and 96 gene expression up-regulated (for example, growth differentiation factor-9 (GDF-9), zinc finger protein 216, cytochrome P450 subfamily IV B, testis specific gene-1, etc.). Using hybridization *in situ*, the effect of DIM on the GA or GDF-9 expression in Cort treated PC12 cells was also detected and the gene expression changes were consistent with results of gene chip detection. **CONCLUSION** It was indicated that the effect of DIM is associated with the gene expression changes at the levels of energy metabolism, cytoskeleton, neurotrophic factors, enzyme, etc.. The antidepressant related genes were elementarily studied with microarray gene chip and clues for further studies were provided.

Key words [antidepressive agents](#) [desipramine](#) [gene expression](#) [gene chip](#) [cells](#) [PC12](#) [corticosterone](#)

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