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CERAMIDE-MEDIATED SIGNAL TRANSDUCTION AND c-jun GENE EXPRESSION DURING DIFFERENTIATION OF U-937 CELLS.

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Effects of ceramide on c-jun gene expression during differentiation of U-937 cells and the mechanism of ceramide-activated protein phosphatase(CAPP) pathway were studied. Ceramide induced c-jun gene expression in a time- and dose-dependent manner. The half-life of c-jun mRNA was 30 min. In contrast, inhibition of protein synthesis with cycloheximide in the absence of transcription with actinomycin D increased the half-life of c-jun mRNA in ceramide-treated U-937 cells to greater than 90 minutes. In order to investigate whether ceramide-induced c-jun gene expression is regulated through ceramide-mediated pathway, ceramide and okadaic acid were treated to the cells. Okadaic acid inhibited enhancement of c-jun mRNA induced by C_2-ceramide in dose-dependent manner. Also, in order to elucidate whether PKC-and PKA-signaling pathway are involved in c-jun gene expression by ceramide-mediated pathway, PMA and db-cAMP were added to U-937 cells exposed to okadaic acid. PMA and db-cAMP-treated group showed increased level of c-jun mRNA, but these increase could not be blocked by the addition of okadaic acid. These results demonstrated that ceramide induced c-jun gene expression during differentiation in U-937 cells and it is regulated posttranscriptionally. In addition, we suggest that the regulation of c-jun gene expression in response to ceramide might be involved the activation of ceramide-mediated pathway and this ceramide-mediated pathway is distinct from the PKA- and PKC-pathway in c-jun gene expression.

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The Mutational Study of *ultraspiracle* Gene in *Drosophila melanogaster*

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The *ultraspiracle(usp)* locus encodes a member of the nuclear hormone receptor superfamily in *Drosophila melanogaster* that interacts with ecdysone receptor(EcR) to mediate ecdysteroid-induced gene expression. Based on the genetic and molecular characterization of *usp*, it has been proposed that usp gene product funtions in at least three significant developmental pathway: embryogenesis, eye morphogenesis, and female reproduction. In order to generate muation in the *usp* gene, we mutagenized *y w* flies with EMS by standard methods. Among 4,000 chromosomes screened, the 4 *usp* mutations were isolated. We will report the molecular lesions associated with new *usp* mutants, *in situ* hybridization and immunocytochemical study in these mutant.