

EICOSAPENTAENOIC ACID (EPA) STIMULATES MITOCHONDRIAL BIOGENESIS THROUGH PGC-1A AND P38 MAPK PATHWAYS

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Peroxisome proliferator-activated receptor γ coactivator -1 α (PGC-1 α) is a key regulator of mitochondrial biogenesis. Our previous studies have been reported that eicosapentaenoic acid (EPA, n-3 C20:5) could increase *pgc-1 α* and TFAM gene expression and mitochondrial function. To determine whether EPA stimulated *pgc-1 α* gene transcription and resulted in elevated mitochondrial function were through the activation of the p38 mitogen-activated protein kinase (MAPK) pathway, we investigated the role of p38 MAPK in EPA-induced transcription of *pgc-1 α* and mitochondrial gene. We showed increased phosphorylation level of p38 MAPK in C6 glioma cells that treated with 25 μ M EPA and no changed levels of total-p38 (T-p38) determined by immunoblotting. Following the treatment of 25 μ M EPA increased phosphorylation level of CREB and ATF2. After treatment with 25 μ M EPA for 24 hr, the *pgc-1 α* promoter transcriptional activity was increased by reporter assay. The raised mitochondrial DNA (mtDNA) copy number was also determined in the same treated cells by real-time PCR analysis. EPA treatment could raise the expression of mtDNA encoded-ND6, but not nuclear encoded ATP synthase and succinate ubiquinol oxidoreductase. These studies supported that EPA stimulated *pgc-1 α* transcription and further resulted to augmented mitochondrial function in C6 glioma cell were mediated through the activation of the p38 MAPK pathway.

Key words:

eicosapentaenoic acid, mitochondrial function, p38 mitogen-activated protein kinase