

The Fatty Acids of CLA-enriched Egg Yolks may Activate the Peroxisome Proliferator-activated Receptors (PPARs) in Breast Cancer Cells

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Background: Conjugated linoleic acids (CLAs) are a family of at least 28 isomers of linoleic acid found mainly in the meat and dairy products derived from mammals called ruminants. Among these compounds two isomers *cis*⁹,*trans*¹¹ and *trans*¹⁰,*cis*¹² have received considerable attention. In our previous research we have demonstrated that fatty acids' extract obtained from egg yolks enriched naturally with the CLA isomers may exhibit a strong tendency to inhibit proliferation of breast, prostate and melanoma tumor cell lines. Until now it has been also reported that the CLA isomers may regulate gene expression as ligands of peroxisome proliferator-activated nuclear receptors: PPAR α , PPAR δ and PPAR γ , which are thought to be transcription factors with potential anticancer activity. **Objectives:** The aim of this study was to determine the impact of fatty acids of CLA-enriched egg yolks on transcription efficiency of genes regulated by the peroxisome proliferator-activated receptors (PPARs). **Material and Methods:** Experiments were performed using breast cancer cell line T47D treated with fatty acids of CLA-enriched egg yolks as well as pure *cis*⁹,*trans*¹¹ and *trans*¹⁰,*cis*¹² CLA isomers. Genes potentially regulated by CLA-liganded PPARs were selected by bioinformatic identification of peroxisome proliferator responsive elements (PPREs, AGGTCANAGGTCA), which were found in 5' promoter regions of the genes. PPAR-mediated transactivation of the genes was measured with Real-Time PCR method. **Results:** Our bioinformatic study allowed for identification of some genes involved in carcinogenesis, which PPRE consensus sequences have not been reported before. We recognized these elements at 5' side of genes such as *BCAR3*, *LZTS*, *SLC5A*, *TCF20*, *WT1*, *ZNF621*, *THRB* (TR β 2 isoform), indicating possible involvement of the genes in PPAR-mediated cellular response. Real-Time PCR measurements revealed that among these, TCF-20, WT-1 and TR β 2 isoform showed the greatest changes in the mRNA levels after treatment with CLA isomers. Fatty acids of CLA-enriched egg yolks resulted in raising the mRNA level of PPAR α , PPAR δ , PPAR γ as well as TR β 2, TCF-20 and in decreasing the level of WT-1 in T47D breast cancer cells. This was accompanied by significant inhibition of proliferation of the cells, measured by BrdU proliferation test. Moreover, a positive correlation was observed between the mRNA level of PPARs, TR β 2 and TCF-20 after treatment with the CLA compounds. In case of WT-1 transcripts, there was no correlation between WT-1 mRNA and PPAR level that may result from a complex regulation of the WT-1 transcription. **Conclusions:** These results demonstrated that fatty acids of CLA-enriched egg yolks may increase transcription levels of genes regulated by the PPAR transcription factors, that may be at least in part responsible for the observed anti-proliferative effects of the CLAs.