THE FASEB JOURNAL

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Biochemistry and Molecular Biology

Modulation of PON2 and Proinflammatory Cytokine Genes in Rat Tissue Exposed to Combined oral Contraceptive Ethinylestradiol and Levonorgestrel

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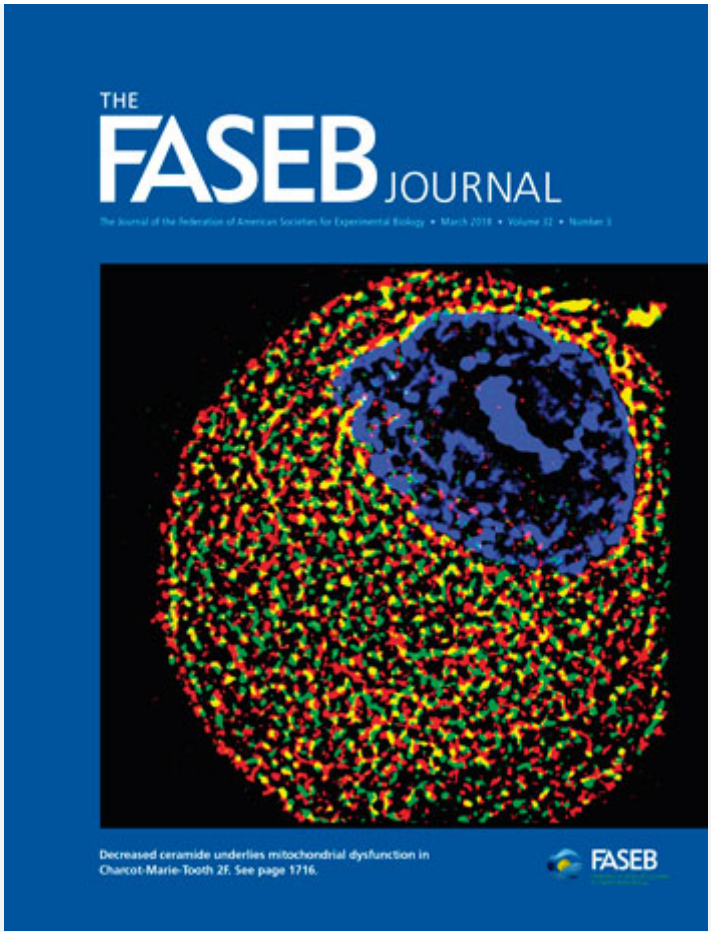
Published Online:1 Apr 2016**Abstract Number:**648.2

Abstract

Paraoxonase (PON2) was identified as a genetic risk factor for cardiovascular disease (CVD) and usage of oral contraceptive (OC) is associated with increased cervical cancer and cardiovascular risk. PON2 protect against atherosclerosis development at the cellular level and this phenomenon could be related to their antioxidative properties. Therefore, the aim of the present study was to investigate the effect of OC on the expression of PON2, pro-inflammatory cytokines interleukin one alpha (IL1α) and tumor necrosis factor alpha (TNFα) in the liver, kidney and brain of rats. Different dosage groups of eight female rats were treated with oral contraceptive (0.15mg levonorgestrel 0.03mg ethinylestradiol(A); 0.3mg levonorgestrel 0.06 mg ethinylestradiol (B) and 0.075 mg levonorgestrel 0.015 mg ethinylestradiol (C))/kg body-weight(bw)). Two groups of eight rats were included in the study for a control group (D) and ≤0.1% DMSO (drug vehicle) group (E), which were not subject to drug administration for 21days. The levels of expression of the gene were assessed using quantitative reverse polymerase chain reaction technique. Combined oral contraceptive treatment produced a significant increase($p<0.001$) in the level expression of renal IL1α and TNFα in all the groups compared to control in a dose-dependent manner but has no significant effect on PON2.

Meanwhile, OC resulted in significantly ($p<0.0001$) reduced level of expression of hepatic IL1α with no significant effect on hepatic PON2 and TNFα level. In the brain, OC resulted in significantly ($p<0.0001$) reduced level of expression of TNFα in all dose groups and IL1α level at 0.015mg/bw. Although OC treatment did increase the expression of brain PON2 significantly ($p<0.05$) at the lowest dose. Therefore, pharmacological modulation of the expression of genes could constitute a useful approach for preventing atherosclerosis



Vol. 30, No. 1 supplement

April 2016

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Publication History

Published online 1 April 2016

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FASEB
Federation of American Societies for Experimental Biology