Down-Regulation of the Receptor for Advanced Glycation Endproducts (RAGE) by Vitamin A/Retinol is Mediated by Reactive Species

Marco Antônio Debastiani, Matheus Augusto de Bittencourt Pasquali, Daniel Pens Gelain, Marcos Roberto de Oliveira, Fábio Klamt, José Cláudio Fonseca Moreira.
CEEO – Departamento de Bioquímica – UFRGS

Vitamin A (VA) plays an important role in several biological functions. However, it is known that VA can be citotoxic, at least in part, by its ability to induce oxidative stress. Controlled clinical trials have demonstrated that VA supplementation increases the incidence of lung cancer and mortality in smokers. Other works also observed that in lung cancer patients the receptor for advanced glycation end-products (RAGE) is down-regulated. In the present work we investigated oxidative parameters and RAGE immunocontent modulation in lungs of rats that received VA supplementation (VAS) reported as therapeutic (1,000 or 2,500 UI/kg/day) or excessive (4,500 or 9,000 UI/kg/day). VAS was carried out for 28 days, being administered orally once a day. After this period, lungs were removed and total lipoperoxidation, protein carbonylation and protein thiol content were evaluated. All doses of VA increased lipoperoxidation and carbonylation, and decreased thiol content. The immunocontent of RAGE was decreased by excessive doses of VA. In addition, we also investigated oxidative parameters and RAGE immunocontent on A549 lung cancer cells that received retinol treatment at doses reported as physiologic (2 µM) or therapeutics (5, 10, or 20 µM). Retinol treatment at doses (10, or 20 µM) increases reactive oxygen species production (DCFH-DA assay), on A549 cells. These doses also decrease RAGE immunocontent. Taken together, our results indicate a prooxidant effect of VA/retinol upon adult rat lung or on A549 cells, and suggest that RAGE modulation by VA is related to modifications in the redox state. Supported by: CNPq, CAPES, FAPERGS and PROPESQ/UFRGS.