High density lipoproteins inhibit oxidative stress-induced prostate cancer cell proliferation

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Recent evidences suggest that oxidative stress can play a role in the pathogenesis and the progression of prostate cancer (PCa). Reactive oxygen species (ROS) are normally generated within cell metabolism and can be produced within tumor microenvironment by xenobiotics or infiltrating inflammatory cells. Interestingly, ROS generation is higher in PCa cells with respect to normal prostate epithelial cells and this increase is proportional to the aggressive phenotype. High density lipoproteins (HDL) are known to prevent atherosclerosis through different mechanisms, including their antioxidant properties. Aim of the study was to assess whether HDL were able to reduce oxidative stress in two PCa cell lines (LNCaP and PC-3) and the consequent impact on cell proliferation.

HDL isolated from plasma of healthy human volunteers significantly reduced basal and H2O2-induced oxidative stress in LnCaP and PC-3 cell lines. ROS production decreased when HDL were given in combination with or before H2O2. The antioxidant effect of HDL was independent from androgen receptor, scavenger receptor BI and ATP binding cassette G1 transporter. When both cell lines were grown in the presence of H2O2, an increase of cell proliferation rate was observed that was completely blunted by the concomitant addition of HDL. Anti-proliferative effect of HDL was due to their capacity to prevent the H2O2-induced shift of cell cycle distribution from G0/G1 towards G2/M phase. Synthetic HDL made of apolipoprotein A-I and phosphatidylcholine, the main protein and lipid components of HDL, retained the ability of plasma-derived HDL to inhibit ROS production in LNCaP and PC-3 cell lines.

In conclusion, HDL exert antioxidant activities on PCa cell lines, thus limiting cell proliferation induced by ROS. Interestingly, HDL were effective not only on androgen-dependent PCa cells, but also on castration-resistant ones. Synthetic HDL, which are under clinical development as anti-atherosclerotic agents, retained the antioxidant effects of plasma-derived HDL. Overall, the present data indicate a possible role of HDL against PCa progression.