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Meeting abstract

Lipid hydroperoxide, an intermediate product of oxidative stress, induces tumour progression-associated genes in hepatocarcinoma cells

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Hepatocellular carcinoma often develops in the liver under chronic inflammation. Oxygen radicals, produced during inflammation, attack membrane lipids and form a number of oxidized metabolites including lipid hydroperoxides. The addition of linoleic acid hydroperoxide (LOOH) to the medium of recently established human hepatocarcinoma cell line (HCC-1.2) caused dose-dependent cell loss and enhanced LDH-release. Under subtoxic conditions LOOH induced intracellular hydrogen peroxide production and a decrease of cellular GSH content. Elevated expression of protooncogene c-myc and a catalytic subunit of telomerase hTERT were observed under LOOH exposure. Myc activation is sufficient to induce cell cycle entry in the absence of growth factors. Accordingly, the cells were pushed into the S- and G_2/M-phase by LOOH. An increased expression of c-fos, c-jun, the antiapoptotic enzyme heme oxygenase 1 (HO-1) and the proinflammatory angiogenic interleukin-8 (IL-8) was detected under LOOH exposure. Pre-treatment of cells with antioxidant N-acetylcystein or with selenite, which induces the LOOH-detoxifying enzyme glutathione peroxidase, partially inhibited the expression of LOOH-induced genes implicating the involvement of oxidative stress. Application of SnPPIX, a HO-1 inhibitor, decreased the viability of HCC-1.2 cells indicating the protective role of HO-1 induction. These results show that lipid hydroperoxides may be an important driving force for carcinogenesis in the liver.