IJAE
Vol. 123, n. 1 (Supplement): 109, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Molecular mechanisms underlying oleic acid-induced cell death of hepatocarcinoma cell lines

Federico Giulitti, Simonetta Petrungaro, Luana Tomaipitinca, Sara Mandatori, Eugenio Gaudio, Elio Ziparo and Claudia Giampietri

Sapienza Università di Roma, Dipartimento di Scienze Anatomiche, Istologiche, Medico-Legali e dell' Apparato Locomotore, Roma, Italia

Extra virgin olive oil, containing high levels of monounsaturated fatty acids such as oleic acid, has been shown to exert several protective effects on the liver, reducing hepatic steatosis, fibrogenesis and lipid peroxidation. Remarkably, oleic acid is known for its anti-cancer effects in different tumors through cell death induction [1] and autophagy modulation [2]. The aim of the present study is to investigate the effects of oleic acid on hepatocellular carcinoma. More in detail, we are investigating the effects of oleic acid treatment in two hepatocarcinoma cell lines, namely Huh7.5 and Hep3B, by evaluating lipid accumulation (through oil red staining), cell death index (through annexin and propidium iodide assay), expression of endoplasmic reticulum stress- and lipid synthesis- markers as well as analyzing autophagic flux (by Western blot assays). We found that the storage levels of neutral lipids in Huh7.5 are different than in Hep3B cell lines. This is true both under basal conditions and upon oleic acid treatment. Conversely, cell death index is increased in both cell lines upon high oleic acid concentration (300 mM). Unexpectedly, such increased cell death inversely correlates with the endoplasmic reticulum stress marker BIP, since it displays a mild reduction after high oleic acid treatment in both cell lines (300 mM). Interestingly, oleic acid treatment dose-dependently (50 to 150 mM) leads to a reduction of peroxisome proliferator-activated receptor (PPAR)-g expression in both cell lines, thus suggesting a reduction of de novo lipid synthesis at low-dose oleic acid treatments. Furthermore, reduced autophagic flux upon high oleic acid treatment (300 mM) occurs in both cell lines, as demonstrated by LC3 lipidation in the presence of bafilomycin. We are currently investigating if autophagy modulation after oleic acid treatment in these cell lines depends on phospho-glycogen synthase kinase-3 (P-GSK-3) and phospho AMP-activated protein kinase (P-AMPK). We therefore hypothesize that autophagy may have a crucial role in controlling cell death after high oleic acid treatment in the two investigated hepatocarcinoma cell lines, unrevealing new insights on the mechanisms underlying autophagy in hepatocarcinoma.

References

Carrillo C, Cavia Mdel M, Alonso-Torre SR. Antitumor effect of oleic acid; mechanisms of action: a review. Nutr Hosp 2012 Nov-Dec; 27(6): 1860-5

Mancinelli R, Carpino G, Petrungaro S, Mammola CL, Tomaipitinca L, Filippini A, Facchiano A, Ziparo E and Giampietri C. Multifaceted roles of GSK-3 in cancer and autophagy-related diseases. Oxid Med Cell Longev 2017 Dec 12.

Key words

Liver, autophagy, fatty acids.