Dear Editor,

We read with great interest the article of Pan et al. They evaluated the correlations between 17β-estradiol dehydrogenase IV (HSD17B4) and tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and proliferating cell nucleus antigen (PCNA) expression in a rat liver cancer induced. Significantly high phosphorylation level of Akt and ERK, along with the increase of HSD17B3 and PCNA expressions, was found in model group. Serum estradiol (E2) level was statistically decreased, whilst TNF-α and IL-6 were up-regulated. The authors concluded that HSD17B4 was positively correlated with TNF-α, IL-6 and PCNA expressions, suggesting its involvement in inflammation and proliferation of liver cancer cells.

The estrogen-regulated mechanisms of hepatocellular carcinoma (HCC) development and/or progression was also evaluated by Cocciadiferro et al. that investigated the expression of Merlin, the product of the neurofibromatosis type 2 (NF2) tumor suppressor gene, in non-tumoral, cirrhotic and malignant liver tissues and cells, in relation to estrogen formation and activity. NF2 expression is elevated in HCC tissues, intermediate in cirrhotic tissues and lower in non-tumoral liver cells.

Impaired sex steroid (both androgen and estrogen) receptors and their variants are one of the key factors of an increased risk for liver cancer. For this reason, the pharmacological modulation of E2 receptors with E2 may be clinically useful in preventing and/or treating HCC, as demonstrated by Jeng et al. Sanaei at al. treated HCC HepG2 cells with various concentrations of Genistein (GE) and E2. This experimental work clearly demonstrated that GE and E2 induced apoptosis and inhibited cell growth significantly.

Liver cancer is mainly associated to hepatic fibrosis due to continuous necrosis either in case of inflammations triggered by metabolic and genetic factors or in case of persistent viral replication with immune system escape mechanism. Overexpression of oncoproteins, together with pro-inflammatory factors, play a fundamental role in the process of hepatocarcinogenesis. Pharmacological therapeutics do not guarantee long term survival rate and newest therapies could be associated with severe adverse effects too. These are the reasons why research based on molecular markers could be very useful tools for the diagnosis and therapy of HCC, as demonstrated in several studies.

Abbreviations
17β-estradiol dehydrogenase IV(HSD17B4), Tumor Necrosis Factor-α (TNF-α), Interleukin-6 (IL-6), Proliferating Cell Nucleus Antigen (PCNA), Estradiol (E2), Hepatocellular carcinoma (HCC), neurofibromatosis type 2 (NF2), Genistein (GE).

Conflict of interest
The authors declare no conflicts of interest.

Comment on: Correlation between HSD17B4 expression in rat liver cancer tissues and inflammation or proliferation

Abbreviations
17β-estradiol dehydrogenase IV(HSD17B4), Tumor Necrosis Factor-α (TNF-α), Interleukin-6 (IL-6), Proliferating Cell Nucleus Antigen (PCNA), Estradiol (E2), Hepatocellular carcinoma (HCC), neurofibromatosis type 2 (NF2), Genistein (GE).
References


S. Milione1, E. Allegorico2, C. Altruda3

1Department of Medical Surgical, Neurological, Metabolic and Aging Sciences, University of Campania “Luigi Vanvitelli”, Naples, Italy
2PS/OBI A.O.R.N. Antonio Cardarelli, Naples, Italy
3Emergency Medicine, S.M. della Misericordia University, Udine, Italy