CORRESPONDENCE

Pituitary Tumor Transforming Gene 1 in the Liver

To the Editor:

We read with interest and appreciate the paper by Fujii et al.,[1] but feel it is necessary to make the following observations.

Despite advances in our cellular and molecular knowledge, hepatocellular carcinoma (HCC) remains one of the major public health problems throughout the world. It is now known to be highly heterogeneous as it encompasses various pathological entities and a wide range of clinical behaviors, and is underpinned by a complex array of gene alterations that affect supra-molecular processes.[2]

Pituitary tumour transforming gene 1 (PTTG-1) is an oncogene expressed in various human neoplasms and cell lines.[3-8] Although its pathogenetic implications in HCC are still unknown, it has been shown that its over-expression in hepatoma cell lines negatively regulates the ability of p53 to induce apoptosis, and that its silencing by means of short interference RNA may be an efficient way of treating liver cancer.[8]

The expression of tumor-associated antigens is mainly investigated at the gene level by means of quantitative real-time PCR (qrt-PCR). However, the information provided by this approach is limited by the fact that the phenomena observed at each level of anatomical organization (*i.e.*, genes, sub-cellular entities, cells, tissues, organs, apparatuses and organisms) have properties that do not exist at lower or higher levels: qrt-PCR offers an adequate quantitative description of small-scale structures, but this is likely to be inapplicable when it comes to large-scale features.[9]

We used an immunoperoxidase-based staining assay to investigate the expression of PTTG-1 (anti-PTTG-1 polyclonal antibodies, Zymed Laboratory Inc., San Francisco, CA) in liver tissues taken from patients affected by chronic HCV-related hepatitis and primary HCC, and found that there were four immunopositive cell types: (a) hepatocytes recognized in hepatitic tissue in which the protein was located near the biliary pole (Fig. 1A); (B) Kupffer cells identified in hepatic tissue and surrounding the cancerous lesion (Fig. 1B); (c) some T lymphocytes situated in the portal spaces (Fig. 1C); and (d) a proportion of neoplastic liver cells (Fig. 1D). Primary colon cancer tissues were used as a positive control (Fig. 1E), and tissues incubated with rabbit immunoglobulin fraction (Dako, Milan, Italy) as a negative control (Fig. 1F).

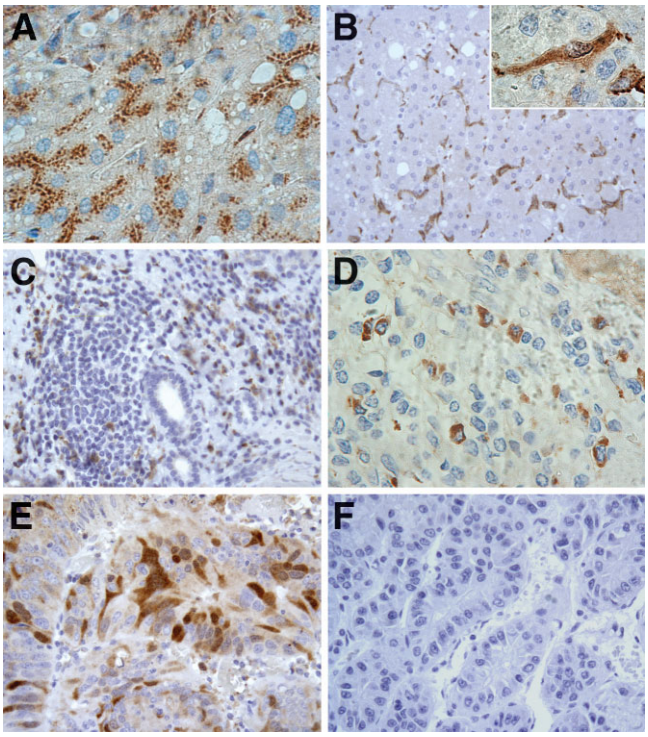

Fig. 1. PTTG-1 expression immuno-recognition in hepatocytes, in which the protein was located near the biliary pole (A), macrophagic Kupffer cells (B), some T lymphocytes sited in the portal spaces (C), and in a proportion of cancer liver cells (D). Primary colon cancer tissues were used as a positive control (E); exemplificative HCC tissue incubated with rabbit immunoglobulin fraction used as a negative control (F) (Objective magnification: A: 40×; B: 10×; C-F: 20×; inset: 63×).

All of our findings demonstrate broader PTTG-1 expression in the liver than that reported by Fujii et al.[1] Furthermore, on the basis of the above microscopic observations, it is possible to say:

1. The qrt-PCR detection of mRNA encoding PTTG-1 in HCC tissue and the surrounding non-cancerous hepatic parenchyma does not distinguish the cell types expressing the protein or its relative quantitative contribution to the total amount of detected mRNA.
2. The presence of PTTG-1 in tumoral and non-tumoral cells may actually be considered a shared characteristic that makes it possible to group different cell types in a single category.
3. The detection of PTTG-1 expression in some intrahepatic T lymphocytes extends previous findings showing its enhanced expression in circulating activated T cells.[10]

In conclusion, the paper of Fujii et al. discusses important points but, although the clinical application seems to be remarkable, we and other morphologists need additional details if we are to replicate the results.

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Potential conflict nothing to report.