European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2016; 20: 4181-4182

Letter to the Editor

Redefine staging of hepatocellular carcinoma on a "bench-to-bedside" approach

Dear Editor,

We read with great interest the paper by Dr. Cao et al[1], recently published on European Review for Medical and Pharmacological Sciences and titled ''PHACTR4 regulates proliferation, migration and invasion of human hepatocellular carcinoma by inhibiting IL-6/Stat3 pathway''. Authors concluded that Stat3 inhibitors have a promising role in the treatment of HCC and that should be considered for better pharmacokinetic design in the future. We congratulate the authors for their interesting work. Our comments focus on the clinical impact of their results. First of all, matching the down-regulation of PHACTR4, and the consequent modulation of target genes expression, with the histological grade of HCC may interestingly enrich such data. Currently, HCC severity and consequent therapeutic approach are stratified with the Barcelona Clinic Liver Cancer staging system (BCLC)[2], a multidimensional platform based on patient's performance status, liver function calculated using the Child-Turcotte-Pugh (CTP) score, and tumor's dimension[3,4]. However, high tumor grade, like other histological features, significantly influence the prognosis of HCC patients[5]. Therefore, novel tumor-specific features may be added to the currently adopted staging systems to provide a complete evaluation[6].

Moreover, it would be of great interest to clarify the role of PHACTR4 in the peri-tumoral stroma and its implications. As we previously reported in our study on the Hedgehog pathway, aggressive HCC cells modulate HSC viability via inhibition of Hh signaling mediated by the GPC3, in order to obtain a niche that permits tumor outgrowth and/or angiogenesis[7]. In other words, we believe that the complex environment of the cirrhotic liver[8] deserves more attention for the comprehension of the underlying mechanisms of tumor genesis.

In summary, studies on intracellular pathways and tumor-stroma cross-talk are needed to improve diagnosis and management of HCC, since currently adopted staging systems do not include any tumor-specific biological prognostic factor.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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