# The role of TAp73 protein in dedifferentiation of hepatocellular carcinoma

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**Statement of the Problem:** Hepatocellular carcinoma (HCC) is a highly complex and heterogeneous type of liver cancer. Hepatocyte dedifferentiation is one of the important steps in the development of HCC. However, molecular mechanisms of the hepatocyte dedifferentiation are not well known. As a member of the tumour suppressor gene p53, p73 has been extensively studied in cancers. However, the status of p73 isoforms in tumours is not clear and the data on the potential roles in cancer malignancy is controversial. In this study, we aim to revaluate p73 expression in HCC and exploration of potential roles of p73.

**Methodology & Theoretical Orientation:** Expression profiles of p73 and patient clinical data were collected from the Genomic Data Commons (GDC) data portal and the TSVdb database, respectively. Global gene expression profiles were determined by pan-genomic 54K microarrays. The Gene Set Enrichment Analysis method was used to identify TAp73-regulated gene sets. The effects of TAp73 isoforms were analysed in monolayer cell culture, 3D-cell culture and xenograft models in zebrafish using western blot, flow cytometry, fluorescence imaging, real-time polymerase chain reaction (RT-PCR), immunohistochemistry and morphological examination.

**Conclusion & Significance**: This study clearly demonstrates that TAp73 isoforms are overexpressed in a large set of HCC tumours. This observation contradicts early claims that DNp73 isoforms are overexpressed in this cancer. This clinical observation strongly suggests that TAp73 promotes but does not suppress HCC malignancy. Also, TAp73 overexpression caused landscape expression changes in sets involved in a variety of cellular processes such as cell cycle, growth signalling, stress response, metabolism, development. At the cellular level TAp73 overexpression provoked major changes in HCC cells including attenuation of cell proliferation with maintained survival, dedifferentiation from a hepatocyte-like phenotype towards cholangiocyte-like phenotype possibly by activation of YAP protein. Moreover, TAp73 induced activation of Epithelial to mesenchymal transition (EMT). Based on these observations, we claim that TAp73 can promote HCC malignancy primarily by inducing hepatocellular dedifferentiation.

## Biography

Iscan Evin is a scientist at the Izmir Biomedicine and Genome Center. She is also a lecturer at the Dokuz Eylul University. She is an expert in hepatocellular carcinoma and translational cancer scientist focusing on intervention with pro-oncogenic cell signalling machinery in hepatocellular carcinoma. She has studies on determining targets specific to liver cancer and determining them as drug targets.