

# A new role of glypican-3 in hepatocellular carcinoma

2 August 2010

A study group from Japan analyzed the association of glypican-3 (GPC3) expression with Wnt and other growth signaling molecules in hepatocellular carcinoma (HCC). They found altered expressions of various matrix metalloproteinases (MMPs) and growth signaling molecules, some of which were correlated with GPC3 expression, were observed in HCCs. The results suggest that GPC3, in conjunction with MMPs and growth signaling molecules, might play an important role in the progression of HCC.

GPC3 is a member of the glypican family of glycosylphosphatidylinositol-anchored cell-surface heparan sulfate proteoglycans. GPC3 is highly expressed in HCC cells and tissues. It is thought that GPC3 joins a multiprotein complex, which is composed of the ligand, receptor, GPC3, and probably other proteins. However, little is known about the association of GPC3 expression with Wnt and other growth signaling molecules. Characterization of the association is necessary to better understand the potential role of GPC3 in HCC. This is the first study to report that GPC3, in conjunction with MMPs and growth signaling molecules, might play an important role in the progression of HCC.

The potential role of GPC3 in human HCC is receiving increasing attention. However, the association of GPC3 with growth signal molecules has not been systematically analyzed in HCC.

A research article to be published on July 28, 2010 in the [World Journal of Gastroenterology](http://www.wjgnet.com/1007-9327/full/v16/i28/3521.htm) addresses this question. The research team led by Dr. Hiroyuki Yamamoto of Sapporo Medical University revealed an association of GPC3 expression with MMPs and growth signaling molecules in HCC. Using real-time RT-PCR, immunoblotting, immunostaining, and siRNA-transfection, the research team analyzed the association of GPC3 expression with Wnt and other growth signaling molecules in HCC. GPC3

was overexpressed in most HCCs at [mRNA](#) and protein levels and its serum levels were significantly higher in patients with HCC than in non-HCC subjects. Altered expressions of various MMPs and growth signaling molecules, some of which were correlated with GPC3 expression, were observed in HCCs. Down-regulation of GPC3 expression by siRNA in GPC3-overexpressing HCC cell lines resulted in a significant decrease in expressions of MMP2, MMP14, FGFR1, IGF1R. GPC3 expression was significantly correlated with nuclear/cytoplasmic localization of  $\beta$ -catenin.

In the view of the authors, further studies are necessary to clarify the direct and/or indirect interactions between GPC3 and growth signaling molecules in HCC.

Considering the tumor specific expression pattern of GPC3 together with its oncogenic function, GPC3 could be an attractive target for molecular diagnosis and/or therapy in clinical settings.

**More information:** Akutsu N, Yamamoto H, Sasaki S, Taniguchi H, Arimura Y, Imai K, Shinomura Y. Association of glypican-3 expression with growth signaling molecules in hepatocellular carcinoma. *World J Gastroenterol* 2010; 16(28): 3521-3528  
[www.wjgnet.com/1007-9327/full/v16/i28/3521.htm](http://www.wjgnet.com/1007-9327/full/v16/i28/3521.htm)

Provided by World Journal of Gastroenterology

APA citation: A new role of glypican-3 in hepatocellular carcinoma (2010, August 2) retrieved 2 August 2022 from <https://medicalxpress.com/news/2010-08-role-glypican-hepatocellular-carcinoma.html>

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