Glypican-3 (GPC3) in human cancer

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Sheep polyclonal antibody to the human GPC3 protein. Antibody recognizes the C-terminal of the GPC3 protein and with an epitope which does not overlap with the 1G12 anti-GPC3 monoclonal currently available on the market

Glypican 3 (GPC3, OCI-5; GTR2-2; MXR7; GPC3; OCI5) encodes a putative extracellular proteoglycan that is inferred to play an important role in growth control in embryonic mesodermal tissues in which it is selectively expressed It appears to form a complex with insulinlike growth factor and hence modulate IGF2 action.

Originally identified as the molecular basis for Simpson-Golabi-Behmel syndrome (SGBS) also called Simpson dysmorphia syndrome (SDYS).

The glypicans are 1 of the 2 major families of cell-surface proteoglycans, the other being the syndecans, e.g., syndecan-1. Whereas syndecans have highly conserved transmembrane-spanning regions and short cytoplasmic tails, the glypicans are anchored to the peripheral membrane through glycosylphosphatidylinositol (GPI) linkage. Glypican-3 is the human homolog of OCI-5, a GPI-linked proteoglycan first isolated from rat intestine.

The diagnostic value of glypican 3 (GPC3) immunostaining on needle biopsy specimens has now been well established. In a study of 120 liver needle biopsy specimens, including 46 from cirrhotic livers and 74 hepatocellular carcinomas (HCCs), that were immunohistochemically examined for expression of GPC3, results showed strong cytoplasmic and membranous staining in 36 HCCs (49%), among which 20 cases (56%) showed diffuse immunoreactivity. None of the 46 cirrhotic livers exhibited positive GPC3 immunostaining. Demonstrating excellent differentiation between HCC and HCV. Also, the nonneoplastic liver tissues (cirrhotic or noncirrhotic) that were present in the majority of the HCC cases were also completely negative for GPC3 expression. GPC3 is therefore a reliable immunohistochemical marker for the diagnosis of HCC by needle biopsy.

GPC3 has also been implicated in other cancers. In patients with thyroid cancer, expression of glypican 3, though scarcely expressed in the normal

thyroid gland, was dramatically enhanced in certain types of cancers: 100% in follicular carcinoma (20/20 cases) and 70% in papillary carcinoma (48/69 cases). Expression of GPC3 in follicular carcinoma was significantly higher than that of follicular adenoma ($p < 0.0019$). In contrast, GPC 3 was not expressed in 17 cases of anaplastic carcinoma.

Continued research into the role of GPC3 in human cancers demonstrates involvement in a wide range of tissues. Additional work will undoubtedly uncover other diagnostic uses for GPC3 in the future.

References:

1. Lai, J.P., et al. "Sulfatase 2 up-regulates glypican 3, promotes fibroblast growth factor signaling, and decreases survival in hepatocellular carcinoma." Hepatology 2008, 47, 1211-1222.

2. Zynger, D.L., et al. "Expression of glypican 3 in ovarian and extragonadal germ cell tumors." Am. J. Clin. Pathol. 2008, 130, 224-230.

3. Anatelli, F., et al. "Value of glypican 3 immunostaining in the diagnosis of hepatocellular carcinoma on needle biopsy." Am. J. Clin. Pathol. 2008, 130, 219-223.

4. Yamanaka, K., et al. "Immunohistochemical study of glypican 3 in thyroid cancer." Oncology 2007, 73, 389-394.

5. Filmus, J., et al. "Glypicans." Genome Biol. 2008, 9, 224.

6. Baumhoer, D., et al. "Glypican 3 expression in human nonneoplastic, preneoplastic, and neoplastic tissues: a tissue microarray analysis of 4,387 tissue samples." Am. J. Clin. Pathol. 2008, 129, 899-906.

7. Capurro, M.I., et al. "Glypican-3 inhibits Hedgehog signaling during development by competing with patched for Hedgehog binding." Dev. Cell 2008, 14, 700-711.

8. Motomura, Y., et al. "HLA-A2 and -A24-restricted glypican-3-derived peptide vaccine induces specific CTLs: preclinical study using mice." Int. J. Oncol. 2008, 32, 985-990.

9. Cheng, W., et al. "Glypican-3-mediated oncogenesis involves the Insulin-like growth factor-signaling pathway." Carcinogenesis 2008, 29, 1319-1326.

10. Stigliano, I., et al. "Glypican-3 regulates migration, adhesion and actin cytoskeleton organization in mammary tumor cells through Wnt signaling modulation." Breast Cancer Res. Treat. 2008, epub ahead of print.