## 学位論文の要旨

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主論文の題名

Up-regulation of Glypican-3 in Human Hepatocellular Carcinoma

## 主論文の要旨

We investigated the expression and significance of glypican-3 (GPC3) in human hepatocellular carcinoma (HCC). The expression of only GPC3 was found to be markedly elevated in HCCs, compared with Syndecan. In the human HCC cell lines, GPC3 expression was consistently observed, and was mainly located in the cell membrane and cytoplasm. Immunohistochemical staining showed a tendency for overall staining of the cytoplasm of cells in the liver carcinoma tissues, but the cell membrane was preferentially stained in poorly-differentiated HCC when compared with well-differentiated HCC. Moreover, the cell membrane was preferentially stained in metastatic lesions of HCC when compared with primary HCC lesions. Non-tumor tissues and cholangiocellular carcinoma tissues were not stained. In addition, using HepG2 cells, AG490 and piceatannol, which are STAT3 inhibitors, each increased the amount of GPC3 mRNA expressed. Assay of the circulating levels of GPC3 protein in the chronic liver disease patients and HCC patients found that serum GPC3 protein levels were significantly elevated in the HCC patients. GPC3 is highly expressed in HCC, and its expression pattern differs relative to the degree of cell differentiation. In addition, the expression of GPC3 is regulated by Jak-STAT signaling. GPC3 shows potential as a tumor biomarker for HCC.