Enhanced expression of a proto-oncogene, Pim-3, with serine/threonine kinase activity, in various types of tumors

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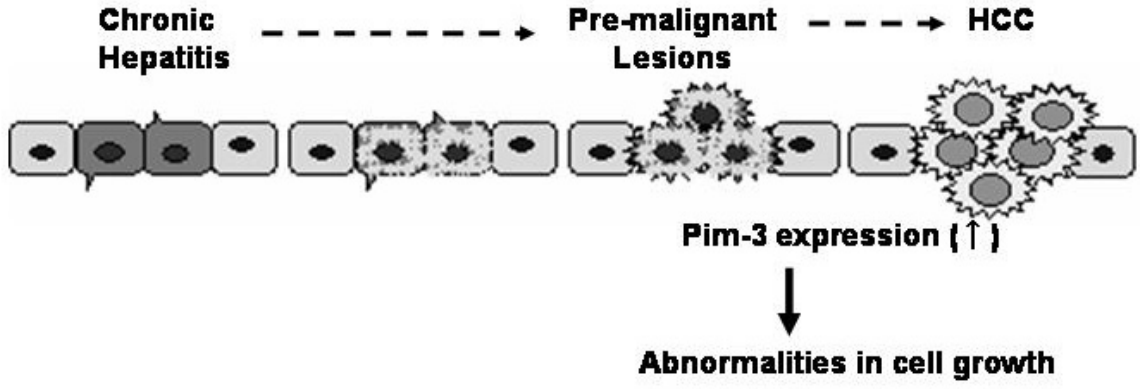
Most cases of human hepatocellular carcinoma develop after persistent chronic infection with human hepatitis B virus or hepatitis C virus, and host responses are presumed to have major roles in this process. To recapitulate this process, we have developed the mouse model of hepatocellular carcinoma using hepatitis B virus surface antigen transgenic mice. In order to identify the genes associated with hepatocarcinogenesis in this model, we compared the gene expression patterns between pre-malignant lesions surrounded by hepatocellular carcinoma tissues and control liver tissues by using a fluorescent differential display analysis. Among the genes which were expressed differentially in the pre-malignant lesions, we focused on Pim-3, a member of a proto-oncogene *Pim* family. Due to the unavailability of the nucleotide sequence of full-length human Pim-3 cDNA, we cloned full-length Pim-3 cDNA, consisting of 2,392 bp, which encodes a predicted open reading frame consisting of 326 amino acids. Pim-3 mRNA was selectively expressed in human hepatoma cell lines, but not in normal liver tissues. Moreover, Pim-3 protein was detected in human hepatocellular carcinoma tissues and cell lines but not in normal hepatocytes. Furthermore, cell proliferation was attenuated and apoptosis was enhanced in human hepatoma cell lines by the ablation of Pim-3 gene with RNA interference (reference). These observations suggest that aberrantly expressed Pim-3 can cause autonomous cell proliferation and/or prevent apoptosis in hepatoma cell lines.



We recently observed that Pim-3 expression was enhanced selectively also in human pancreas cancer tissues and pancreatic cancer cell lines, but not normal pancreas tissue. Moreover, similarly to human hepatoma cell lines, cell proliferation was attenuated and apoptosis was enhanced also in human pancreatic cancer cell lines by the ablation of Pim-3 gene with RNA interference. Thus, Pim-3 is aberrantly expressed in various types of tumors and can counteract apoptosis process, thereby contributing to carcinogenesis. Therefore, Pim-3 may be a good molecular target for treating tumors, which exhibit the enhanced expression of Pim-3.

Reference

Fujii C, et al. Intl. J. Cancer 114: 209, 2005.