

Different signaling pathways of cholangiocarcinoma

March 4 2010

Overexpression of receptor tyrosine kinase Met has frequently been found in cholangiocarcinoma. A research group in Thailand demonstrated that hepatocyte growth factor, a Met ligand, induced invasion and motility and altered E-cadherin localization in two cholangiocarcinoma cell lines, without having any significant effects on levels of two secreted matrix metalloproteinases. However, the signaling pathways underlying HGF-induced invasiveness of the two cell lines were different.

Cholangiocarcinoma (CCA), a bile duct cancer, is one of the major cancers in Northeast Thailand. This cancer is difficult to diagnose and has high metastatic and mortality rates. [Overexpression](#) of Met, a hepatocyte growth factor (HGF) receptor, has frequently been found in CCA and is correlated with progression of this type of cancer. HGF/Met activation induces a variety of cellular processes, including cell scattering, invasion and proliferation. Although a number of studies have been reported regarding the correlation between Met expression and CCA, the molecular mechanisms by which HGF induces CCA invasion are not completely understood.

A research article published on February 14, 2010 in the [World Journal of Gastroenterology](#) addresses this question. The research team led by Dr. Suthiphongchai T from Mahidol University used two CCA cell lines overexpressing Met, KKU-M213 and HuCCA-1, to study the role of Met in CCA invasion by activating the Met pathway with HGF. HGF strongly induced invasion and motility of the two CCA cell lines and

concomitantly altered E-cadherin localization from membrane to cytosol, but did not affect the levels of secreted MMP-2, MMP-9 or uPA.

Signaling pathways responsible for HGF-induced invasion were further investigated. HGF induced ERK and PI3K/Akt pathways of both CCA cell lines but with different kinetic profiles. HGF induced sustained ERK activation in the KKU-M213 cell line, but transient ERK activation in HuCCA-1 cells. Using specific inhibitors of PI3K and ERK pathways, it was shown that HGF-induced invasion of KKU-M213 was strongly inhibited by both inhibitors, while that of HuCCA-1 was strongly inhibited by PI3K inhibitor but only weakly inhibited by ERK inhibitor. Thus, the signaling pathways responsible for HGF-induced invasiveness of the two CCA cell lines were different, in that PI3K pathway was common for both cell lines, whereas the role of ERK1/2 was likely to be dependent on the duration of ERK1/2 activation.

These results provided more information on the understanding of the signaling mechanisms responsible for HGF-induced CCA invasiveness, which may be helpful for identifying better targets for CCA therapy and for designing appropriate therapeutic strategy to suit each individual patient.

More information: Menakongka A, Suthiphongchai T. Involvement of PI3K and ERK1/2 pathways in hepatocyte growth factor-induced cholangiocarcinoma cell invasion. *World J Gastroenterol* 2010; 16(6): 713-722. www.wjgnet.com/1007-9327/16/713.asp

Provided by World Journal of Gastroenterology

Citation: Different signaling pathways of cholangiocarcinoma (2010, March 4) retrieved 19 April

2024 from <https://medicalxpress.com/news/2010-03-pathways-cholangiocarcinoma.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.