New potential instrument to fight hepatocellular cancer by restoring p53

Franklin C. Vincent 1, Marek J. Los 2, 3*

1 Interfaculty Institute of Biochemistry (IFIB), Tubingen University, Tubingen, Germany
2 BioApplications Enterprises, Winnipeg, Manitoba, Canada
3 Department of Clinical and Experimental Medicine (IKE), Integrative Regenerative Medicine Center (IGEN), Linkoping University, Linkoping, Sweden

ARTICLE INFO

Article Type:
Editorial

Article history:
Received: 7 Feb 2011
Revised: 12 Feb 2011
Accepted: 20 Feb 2011

Keywords:
Annonaceous acetogenins
HBV X protein
Hepatocellular carcinomas
Toll like receptors

Implication for health policy/practice/research/medical education:
The highlighted manuscript provides interesting information about new, plant-derived anticancer drug precursors.

Please cite this paper as:

Implication for health policy/practice/research/medical education:
The highlighted manuscript provides interesting information about new, plant-derived anticancer drug precursors.

© 2011 Kowsar M.P.Co. All rights reserved.
repression) of the p53 tumor suppressor. HBx represses the transcription of the human p53 gene through the E-box element (12, 13). As the p53 protein binds and represses the HBV enhancer/X promoter, HBx repression of the p53-promoter triggers a positive response that further represses p53 expression (14). Beside reciprocal transcriptional repression, HBx and p53 can inhibit each other by direct protein-protein interaction. The balance of the reciprocal inhibition between these two proteins may play a decisive role in the development of HBV-related malignancies. In their paper published in this issue, He and colleagues have tested the antitumor activity of desacetyluvaricin using the Hepg2.2.15 cell line. Flow cytometry analysis revealed a higher expression of p53 in desacetyluvaricin-treated cell lines when compared to untreated cell lines (15). The increase of p53 in the presence of desacetyluvaricin is very promising and may open new avenues for the therapeutic intervention of hepatocarcinoma.

Another interesting aspect of desacetyluvaricin’s activity that He and colleagues discovered is its effect on Toll-like receptors (TLRs). TLRs may promote tumor progression by acting directly on cancer cells, resulting in increased tumor cell-endothelial cell adhesion, tumor cell-extracellular matrix adhesion, and tumor cell-extracellular matrix invasion through NF-κB-mediated upregulation of β1 integrin. Additionally, reports have demonstrated that TLR signaling pathways play a key role in activating stem-cell/progenitor proliferation and conversion to cancer-stem-cell-based liver tumor formation (16). TLRs have also been found on tumor cells, but their role in these cells is still unclear. In some tumor types, TLRs promote tumor proliferation and survival, whereas in others TLR2, -3, and -9 are directly involved in apoptosis (17). In their paper, He et al. reported that the expression of TLR4 is upregulated in the presence of the drug desacetyluvaricin (15). Although they assume that in this context TLR4 helps to activate the innate and adaptive immune responses to tumors, one should not disregard the fact that TLR activation may be a double-edged sword with both antitumor and protumor consequences. It is therefore necessary to conduct comprehensive studies to assess the significance of TLR4 expression in tumor immunotherapy. Another aspect omitted from the He et al. study, and it would certainly draw additional interest to their work, is the potential effect of desacetyluvaricin on hepatocellular-cancer stem cells (18, 19). In conclusion, although the manuscript is rather preliminary, the observations made by He et al. underlines the importance of desacetyluvaricin and related compounds as potential leads for the development of new anticancer drugs.

References


Vincent FC et al.

New instrument to fight HCC
۳۰ درصد تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی

اصول تنظیم قراردادها
پروپوزال نویسی
آموزش مهارت‌های کاربردی در تدوین و چاپ مقاله