H-ras collaborates with Hepatitis B Viruses X gene to transform cells.

Department of Biochemistry, Yonsei University
Wang-Shick Ryu

Hepatitis B viruses (HBV), the prototype member of a hepadnaviruses, is a major cause of liver disease ranging from in severity from chronic infection of hepatocytes to liver cirrhosis and hepatocellular carcinoma. The estimated number of chronic HBV carriers exceeds 300 million worldwide. Significant subset of these chronic carriers will progress into chronic hepatitis, with high risk for liver cirrhosis and eventually liver carcinoma. Several lines of epidemiological and experimental evidence have suggested a link between development of hepatocellular carcinoma and chronic HBV infection. HBx protein, best known as a transcriptional transactivator, has long been speculated to be the viral oncogene for hepatocarcinogenesis. However, ectopic expression of HBx fails to transform either primary or immortalized rodent cells. Furthermore, except for lines produced from CD−1 mice, most transgenic mice harboring HBx do not develop liver tumors. Thus, it remains unclear whether and how HBx contributes to oncogenesis. Here, we show that HBx collaborates with activated H−ras to transform immortalized rodent cell lines. Notably, we found that HBx induced apoptosis was suppressed by activated H−ras through activation of the phosphatidylinositol−3 kinase, PI(3) K, and Akt pathway. Remarkably, nude mice injected with HBx and H−ras cotransfected REF52 cells developed tumors, whereas the mice injected with REF52 cells transfected either gene alone did not. Thus, we concluded that HBx contribute to neoplastic transformation of cells in collaboration with another oncogenes, such as H−ras, that suppress the HBx−induced apoptosis. Data presented here firmly established the oncogenic potential of HBx during multistage carcinogenesis.
연 자 악 력

1978  서울대학교 동물자원학과 졸업
1984 ~ 1989  University of Wisconsin 분자생물학 박사
1989 ~ 1992  Postdoc., Fox Chase Cancer Center (Philadelphia, USA)
1992 ~ 1996  Principal Scientist, 미국 Lucky Biotech Corp.
1994 ~ 1996  LG화학기술연구원 책임연구원
1995 ~ 1996  연세대학교 의과대학 임상의학연구센터 부교수
1996 ~ 현재  연세대학교 의과대학 생화학과 부교수

1979  가톨릭대학교 의과대학 졸업
1989  가톨릭대학교 의과대학원 박사
1991 ~ 1992  Visiting Scientist, 일본 NCI
1993 ~ 1995  Visiting Scientist, 미국 NCI
1995 ~ 2000  가톨릭대학교 의과대학 내과 부교수
2001 ~ 현재  가톨릭대학교 의과대학 내과 교수

Pei-Jer Chen
M.D., Ph.D.

1981  M.B., Departement of Medicine, Collage of Medicine, National Taiwan University(N.T.U.)
1983 ~ 1986  Ph.D., Department of Pathology, Medical School University of Pennsylvania
1986 ~ 1987  Postdoc., Graduate Institute of Clinical Medicine, Collage of Medicine, N.T.U.
1987 ~ 1993  Professor, Graduate Institute of Clinical Medicine, Collage of Medicine, N.T.U.
1992 ~ present  Attending Physician, Division of Gastroenterology and Hepatology, Departement of Internal Medicine, National Taiwan University Hospital