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Transcriptional repression of p21^{waf1} promoter by hepatitis B virus X protein via a p53-independent pathway

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X-gene product of hepatitis B virus (HBx) has been implicated in HBV-mediated hepatocellular carcinoma through its ability to induce liver cancer in some transgenic mice and to transactivate a variety of viral and cellular promoters. In this study, we demonstrated that the level of p21^{waf1} RNA was decreased in the HBx-expressing cells and this effect was due to the transcriptional repression of p21^{waf1} gene by HBx via a p53-independent pathway. As the Sp1 binding sites of p21^{waf1} promoter was sufficient to confer HBx responsiveness to a previously nonresponsive promoter, we suggested that HBx represses the transcription of p21^{waf1} by down-regulating the activity of Sp1. Because the tumor repressor p21^{waf1} protein is a universal inhibitor of cyclin-CDK complexes and DNA replication that induces cell cycle arrest at the G1-S checkpoint, the repression of p21^{waf1} by HBx might play an important role in a HBV-mediated pathogenesis.