Nuclear IKKalpha confers HBx-mediated migration of Hepatoma cells

Hepatitis B virus (HBV) X protein (HBx) has been implicated in HBV-associated carcinogenesis through activation of IκB kinase (IKK)/nuclear factor kappa B (NF-κB) signaling pathway. Besides activating NF-κB in the cytoplasm, IKKα was found in the nucleus to regulate gene expression epigenetically in response to various stimuli. However, it is unknown whether nuclear IKKα plays a role in HBx-associated tumor progression. Moreover, the molecular mechanism underlying IKKα nuclear transport also remains to be elucidated. Here, we disclosed HBx as a new inducer of IKKα nuclear transport in hepatoma cells. HBx induced IKKα nuclear transport in an Akt-dependent manner. HBx-activated Akt promoted IKKα nuclear translocation via phosphorylating its threonine-23 (Thr23). In addition, IKKα ubiquitination enhanced by HBx and Akt also contributed to the IKKα accumulation in the nucleus, indicating the involvement of ubiquitination in Akt-increased IKKα nuclear transport in response to HBx. Furthermore, inhibition of IKKα nuclear translocation by mutating of its nuclear localization signal and Thr23 diminished IKKα-dependent cell migration. Taken together, our findings shed light on the molecular mechanism of IKKα nuclear translocation and provide a role for nuclear IKKα in mediating HBV-related hepatocellular carcinoma (HCC) progression.