Phospho-regulation of high-risk HPV E6 PDZ/14-3-3 interactions

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Previous studies have shown that the cancer-causing high-risk HPV E6 oncoproteins have PDZ binding potential, an activity which is important for their ability to support the viral life cycle and to cooperate in the induction of malignancy. Low-risk, non-cancer causing HPV E6 oncoproteins lack this motif, and it can therefore be considered as a marker of the viral oncogenic potential. Indeed, proteomic analysis of multiple HPV E6 oncoproteins defines a subset of PDZ domain-containing cellular proteins as being common targets for cancer-causing HPV types. However, PDZ interactions are not constitutive, and can be negatively regulated by phosphorylation with PKA or AKT within the E6 PDZ binding motif (PBM). This phosphorylation in turn confers association with 14-3-3 family members. This regulation is highly conserved between E6 proteins derived from HPV-16, HPV-18 and HPV-58. We also show that HPV-18 E6 phosphorylation occurs primarily during the G2/M phase of the cell cycle whereas HPV-16 E6 phosphorylation occurs during S phase. This phosphorylation in turn regulates the levels of E6 expression and confers enhanced interaction with multiple 14-3-3 isoforms. One consequence of E6 interaction with 14-3-3 is an alteration in the subcellular distribution of 14-3-3, which occurs in an E6 PBM dependent manner. These studies reveal unexpected differences in the regulation of HPV-16 and HPV-18 E6 function and have important implications for how phosphorylation of E6 might be expected to play a role during the respective viral life cycles and tumour development.

Biography

Chattopadhyay after completing his Masters in Biotechnology from India moved to University of Cape Town in Cape Town, South Africa to pursue his Ph.D. in human genetics, cancer biology and infectious diseases. He completed his Ph.D. in 2010 and worked as a researcher at Stellenbosch University and University of KwaZulu-Natal (South Africa) on neurogenetics, pharmacogenetics and extremophiles. After working briefly as a faculty member in genetics at University of KwaZulu-Natal he moved to the USA. Currently he is a researcher at University of Pittsburgh in Pennsylvania, USA. His expertise is in molecular genetics. He has published several papers in reputed journals and also on the editorial board for several journals.

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