



## INSILICO MODELLING OF THE INTEGRATIVE PATHWAY OF CARCINOMA BY HPV E6 PROTEIN-PROTEIN INTERACTION

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### ABSTRACT

The Human papillomavirus (HPV) E6 protein is one of the oncoproteins encoded by the virus. In order to understand the mechanism by which E6 interacts with the host cellular proteins to trigger the cascade of cancer cell transformation. STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) is a biological database has been used to model the pathway of the protein- protein interaction and how intimately they associate to contribute to the malignancy of the HPV transformed cells. SIPA1L1, E6AP and E6BP three individual annotated pathways enable to construct a putative pathway using their annotations and in literature review. The E6 cellular target has important implications for the development of effective cancer therapeutic strategies.

**KEYWORDS:** HPV 16, E6 protein, STRING database and cancer



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## INTRODUCTION

Cancer is one of the most significant causes of morbidity and mortality and currently it is the second largest killer disease. Globally cervical cancer is the second most common cancer in women and is estimated to cause over 4,70,000 new cases and 2,33,000 deaths each year, in India, 1.5 lakh cases and 74,000 deaths are reported annually<sup>1</sup>. Human Papillomaviruses (HPVs) 16 and 18 are predominant factors for progression to cervical cancer<sup>1</sup>. They cannot replicate on their own hence they use the host cellular DNA synthesis for their lineage proliferation. Since they require more well differentiated cells which are past the cell cycle stage, to circumvent this problem the HPV E7 protein target a number of cell regulatory proteins<sup>2</sup>. However the host cell response to this unwarranted induced proliferation would be to switch to apoptosis and /or growth arrest. To evade this situation the HPV E7 proteins target also the cellular proteins involved in the terminal differentiation and antiviral mechanisms too<sup>3</sup>. The usual pathway would proceed to viral replication, resulting in production and release of

infectious virions. On rare occasions, however, the viral life cycle is interrupted and processes are initiated that lead to immortalization<sup>4,5</sup>.

## MATERIALS AND METHODS

The STRING database is a protein interaction database to identify the interaction between the proteins. E6 interacts with SIPA1L1 or E6PT1, AS or E6-AP and E6 BP. The individual pathways are mapped. The integrated pathway of the three proteins interacting with E6 is putatively elucidated based on literature review<sup>6-12</sup>.

## RESULTS AND DISCUSSION

The STRING interaction network showed below in Figure 1. indicates a coalition of E6 with E6PT1 (SIPA1L1) and E6AP which induces the ubiquitin-dependent degradation of p53 in the next network.

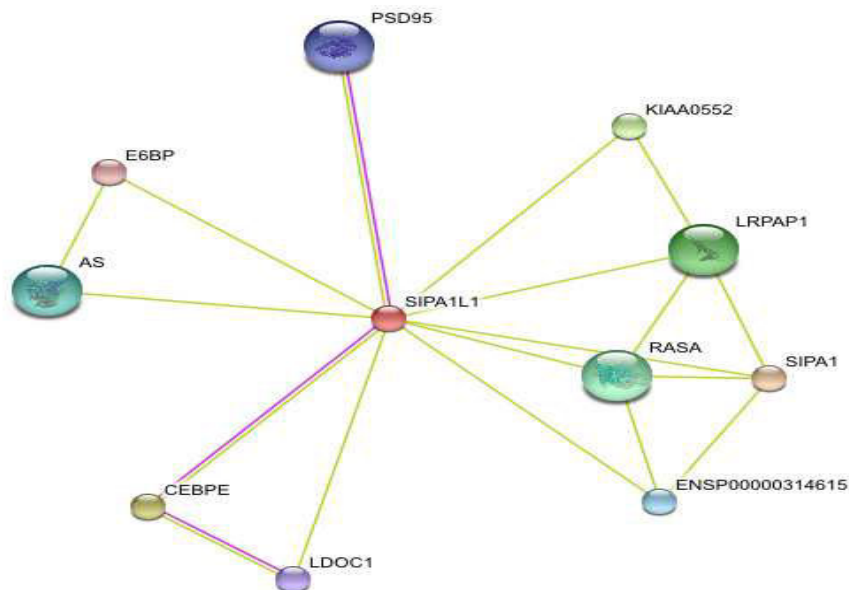
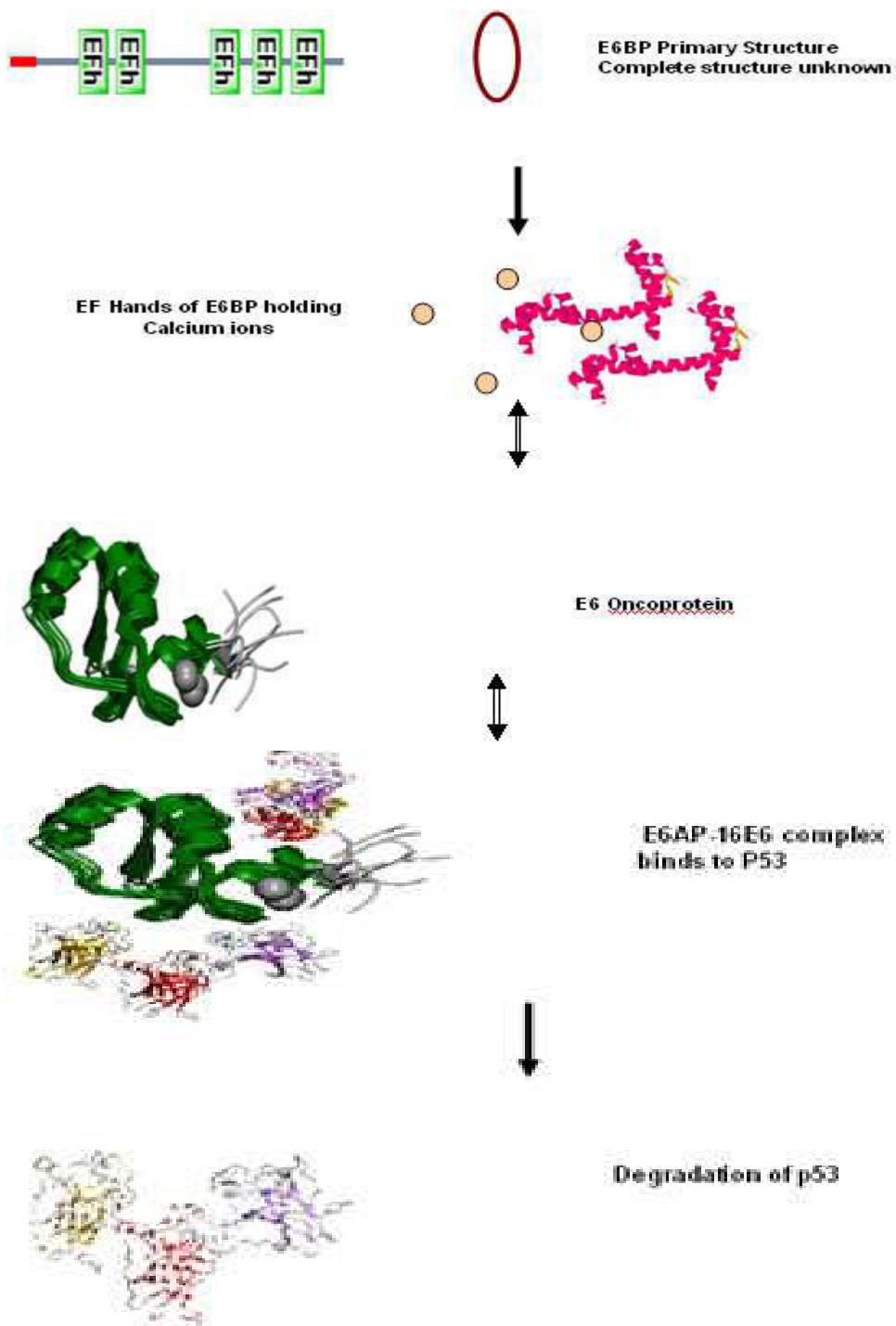
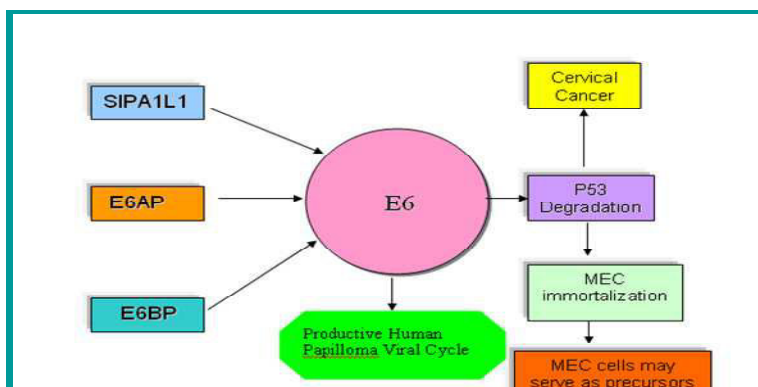


Figure 1

**Figure 2**  
**The E6BP protein- protein interaction pathway**





**Figure 3**  
*Integrated Pathway network*

The above insilico results show that E6 protein interacts with three more crucial proteins to lead to triggering P53 degradation. The individual pathways lead to the construction of the hypothetical pathway to better understand the protein- protein interactions.

## CONCLUSION

During HPV infection E6 plays multiple roles, interfering with several cellular pathways. The insilico results using STRING database prove that E6 protein interacts with three vital proteins which eventually lead to cascade of chain reactions causing p53 degradation. The study of the E6 cellular targets pathway mapping has important implications for the development of effective therapeutic strategies.

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