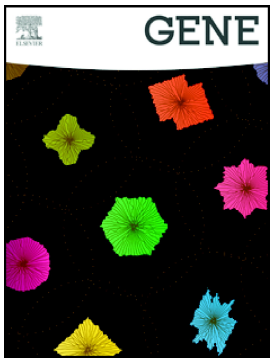
Accepted Manuscript



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PII: S0378-1119(18)30264-6
DOI: doi:10.1016/j.gene.2018.03.026
Reference: GENE 42648

To appear in: *Gene*

Received date: 18 November 2017
Revised date: 5 March 2018
Accepted date: 8 March 2018

Please cite this article as: Murali Aarthy, Deepak Kumar, Rajanish Giri, Sanjeev Kumar Singh , E7 oncoprotein of human papillomavirus: Structural dynamics and inhibitor screening study. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Gene(2017), doi:10.1016/j.gene.2018.03.026

E7 Oncoprotein of Human Papillomavirus: Structural Dynamics and Inhibitor Screening Study

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Running Title: Structure based docking and dynamics studies on E7 oncoprotein

Abstract

Human papillomavirus (HPV) has been the primary causative agent of cervical cancer, the most threatening cancer affecting millions of women worldwide. HPV, a small non enveloped DNA virus of high and low risk types contain intrinsically disordered region and it also plays significant role in the development of cervical cancer. HPV E7 contains an ordered Zinc finger motif that binds to pRB and alters its function. It utilizes both disordered N-terminal and structured C-terminal regions for cellular transformation. In this study, we have focused extensively on the evolutionary relationships of E7 among various HPV types and generated a 3D homology model of full length E7, since the structure have not been solved till date. We also analysed the stable conformation and atomic flexibility of modelled E7 through molecular dynamics simulation at 100ns. To understand the disordered based binding sites of E7 oncoprotein, Molecular recognition features (MoRFs) analysis was carried out on the E7 oncoprotein. The validated model was taken forward for the identification of potential lead compounds and the most prominent compounds were selected for the molecular dynamics simulation of the 100ns for the stability analysis. Overall, this study highlights the holistic E7 regions including important disordered based binding sites analysed through the MoRFs. The potential inhibitor compound that targets the structured C-terminal region of E7 oncoprotein were subjected for the pharmacological properties analysis and further validates the binding modes of the compounds with the target structure. This study helps in providing a better intuition to develop a potent anti-HPV agent.

Abbreviations List: