In Silico Binding Site Analysis of E6 Oncoproteins from High-Risk European HPV variants.

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Cervical cancer is the most studied oncopathology associated with Human Papillomavirus (HPV), which is present in all the studied cases of the disease. HPV of type 16 is the most prevalent, representing 70% of cases of cervical cancer worldwide. The SNPs throughout the virus gene gave rise to viral variants, such as European variants of HPV type 16 oncoprotein E6 (HPV16-E6V). In the last two decades, several studies investigated the relationship of SNPs in oncoprotein E6 and the differences in oncogenic potential of virus, rising E6 oncoprotein status to a potential therapeutic target. The aim of this work was to predict and evaluate, through the use of *in silico* methods, the differences between the binding sites of four European variants of HPV's oncoproten E6. The binding site prediction was performed using the metaPocket 2.0 server. Based on the predicted coordinates of the binding site, we performed measurements of area and volume, along with electrostatic potential and hydrophobicity analysis of the studied region through the computational software USC CHIMERA. Our results showed that the binding site includes both zinc-binding domains and the α-helix that connects them. All variants displayed the same binding site region, but with meaningful differences in their respective area and volume. We did not find relevant differences between the electrostatic potential or hydrophobic profile of the binding site of different variants. To the present day, we have no knowledge of non-invasive therapeutic routines against HPV infection. The interaction between oncoprotein E6 with different tumor-suppressor proteins is directly related to the immortalization and uncontrolled growth of epithelial cells, which can lead to cervical cancer. By thoroughly uncovering the structural properties of the binding sites of E6, we can hopefully contribute to the future development of anti-HPV drugs.

Área: (3) Proteins and Proteomics