The infection by high-risk human papillomaviruses is involved in causing cancers. The extreme carboxy terminus of high-risk α-HPV E6 protein contains a PDZ domain-binding motif. The E6 protein of high-risk HPV binds by PDZ domain-binding motif to cellular proteins containing PDZ domain, which participate in the maintenance of the cell polarity, in the stabilization of cell-cell junctions or in the regulation of cellular signaling pathways, e.g. hDlg (human homologue of Discs large protein), hScrib (human homologue of Drosophila tumor suppressor Scribble). Binding of E6 with cellular proteins prevents the induction of apoptosis and influences the enhancement of growth rate of infected cells, degradation of tight-junctions, regulation of cell polarity and vesicular transport. The interaction between E6 and cellular proteins increases the stability of E6 protein and protects E6 from proteasomal degradation. PDZ domain-binding motif of E6 high-risk HPV contributes to the development of malignant tumors.