Disruption of Cellular Control Mechanisms by Intrinsically Disordered Viral Proteins

Intrinsically disordered viral proteins are central to the infectivity and pathogenicity of viruses. For oncogenic viruses, the presence of disordered proteins coded by the viral genome is an important part of the process of disruption of the host cell cycle that leads to cellular transformation. Examples of oncogenic viruses are adenovirus (oncogenic in rodents) and human papilloma virus (HPV). We undertook a study of the interactions of the HPV E7 protein, to elucidate the structural basis for the differences in cancer risk between high and low-risk strains. The E7 protein interacts with two major cellular control proteins, the retinoblastoma protein pRb and the CREB-binding protein CBP, forming a ternary complex with the pRb pocket domain and the TAZ2 domain of CBP. Oncogenic potential appears to be related to the affinity of the E7 protein for the TAZ2 domain. The adenoviral E1A protein also forms a ternary complex between the pRb pocket domain and TAZ2, but by a different mechanism.

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