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JC virus early proteins: Contributions to virus-host interactions

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The ability of the small DNA tumor viruses to deregulate cell cycle progression is linked to their transforming behavior in non-permissive cells and replicating activity in permissive cells. The tumor (T) proteins of such viruses override normal G_o/G_1 to S phase transition by binding to members of the RB family of tumor suppressors through their LXCXE domain, and then causing the release of members of the E2F family of transcription factors via the co-chaperone function of their J domain. The human polyomavirus JCV expresses five regulatory proteins, TAg, tAg, T'_{135}, T'_{136} and T'_{165}, which contribute to viral replication and oncogenic activities. TAg and T′ proteins share their N-terminal 132 amino acids, sequences that include the J and LXCXE domains. We have demonstrated that these proteins interact with pRB, p107 and p130 *in vitro* and *in vivo*. Here, we show that TAg and T′ proteins cause the release of E2F-1 from RB-E2F complexes. The viral proteins exhibit differential potential to disrupt the complexes, with T'_{165} exhibiting the highest activity. By constructing the appropriate mutants, we show that the LXCXE and J domains present in JCV TAg and T′ proteins mediate the interactions with RB proteins and the release of E2F-1. Relative to wild type proteins, mutant proteins are altered in the ability to bind to and cause the degradation of phosphorylated forms of p107 and p130. Our observations suggest that JCV T′ proteins contribute to virally-induced cell cycle deregulation.