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Mart Ustav, born in 1949, received his B.Sc. in organic and bioorganic chemistry in 1972 and the degree of candidate (Ph.D.) in 1980 in Molecular Biology. He was awarded the Estonian State Prize for his research into the biosynthesis of proteins in 1980 and for his research in the field of papillomaviruses in 1996. He held a postdoctorate at the University of Uppsala from 1982-1985 and was a visiting scientist at the Cold Spring Harbour Laboratory, NY, USA from 1989 to 1992. He has been working at the University of Tartu since 1992 as the Professor of Microbiology and Virology. His research interests lie in molecular biology, virology and diagnostics, also gene therapy and vaccination.

Research from 2000

Mechanisms of papillomavirus DNA replication during the viral life cycle

The p53 protein is a transcriptional regulator of genes involved in growth control, and it plays a central role in modulating the processes that lead to apoptosis and DNA replication. We have shown with transient replication assays that the p53 protein specifically blocks the amplificational replication of bovine (BPV1) and human (HPV11, HPV18) papillomavirus origins. This inhibitory effect can be detected in the number of cell lines. Domain mapping by point mutations and deletions showed that the central core domain and oligomerization domain are necessary and sufficient for p53 replication suppression activity. Cell cycle analysis of the transfected cells showed that this activity is not an indirect consequence of a p53-dependent cell cycle block or apoptosis, nor is the phenomenon mediated by transactivation or transrepression activities of p53 protein. We tested the effect of p53 on papillomavirus and Epstein-Barr virus latent origin replication. We showed that both latent replication modes are insensitive to p53 action, which suggests that the inhibitory effect of p53 is specific to the type of DNA replication mode represented by papillomavirus amplification. Papillomavirus genomes are maintained as multicopy nuclear plasmids in transformed cells. We found that plasmids of BPV1 origin are tightly associated with chromatin throughout the cell cycle. We showed that the minichromosome maintenance element (MME), composed of oligomerized E2 binding sites, is the only cis element required for this activity. Our data show a perfect correlation between episomal maintenance and the ability of these plasmids to associate with chromatin. We identified by mutational analysis the specific pocket in the E2 transactivation domain that is responsible for binding of the E2 to the metaphase chromosomes. Our data suggest that E2-mediated MME chromatin association provides the mechanism for partitioning and segregating the plasmids in the dividing cells during latent papillomavirus infection.

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