

P023 Sumoylation of papillomavirus E2 proteins

Yu-Chieh Wu, Adeline Deyrieux, and Van G. Wilson

Dept. of Microbial & Molecular Pathogenesis, Texas A&M Health Science Center, College Station, TX, USA

The papillomavirus E2 proteins are major transcriptional regulators that control viral gene expression and also affect host gene expression. Examination of the amino acid sequences of several papillomavirus types indicated that E2 proteins had 1 or more predicted sumoylation sites. Both *in vitro* and in an *E. coli* system, bovine papillomavirus (BPV) E2 and human papillomavirus 18 (HPV) E2 proteins were efficiently sumoylated with SUMO1. Consistent with these results, HPV18 E2 was demonstrated to bind Ubc9 in an *in vitro* pull-down assay. However, *in vivo*, E2 was preferentially modified by SUMO2 or SUMO3, and not SUMO1. With either SUMO2 or SUMO3, a single predominant sumoylated species of E2 was observed, and the sumoylated form could be eliminated by overexpression of SENP1. In addition, overexpression of Ubc9 and either SUMO2 or SUMO3, but not SUMO1, resulted in a dramatic stabilization of E2 levels *in vivo*. We have also recently shown that during keratinocyte differentiation there is increased expression of SUMO2/3, but not SUMO1. These results suggest that increased levels of SUMO2 or 3 in the upper layers of stratified skin would lead to more stable E2 and could account for the increased E2 levels seen in infected suprabasal cells. Lastly, E2 reduced the levels of sumoylation of a binding partner, the cellular transcription factor C/EBP beta, suggesting that sumoylation changes in differentiating keratinocytes have complex effects on viral-host interactions.