

## HPV 16 E6/E7 Transgenic Mice have Hyperkeratosis and Elevated ROS Related Enzyme Activities

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Human papillomavirus type 16(HPV16) has been known to be the major factor for the development of uterine cervical carcinomas. We have extended these studies to investigate the in vivo activities of HPV-16 E6/E7 when expressed in squamous epithelia of transgenic mice. Grossly, hK14HPV16E6/E7 transgenic mice had multiple phenotypes, including wrinkled skin that was apparent prior to the appearance of hair on neonates, thickened ears, and loss of hair in adults. In the transgenic mice, the wrinkled skin phenotype on the body and legs died at the age of 3~4 weeks. Histological analysis demonstrated that E6/E7 causes epidermal hyperplasia in multiple transgenic lineages with high penetrance. This epithelial hyperplasia was characterized by an expansion of the proliferating compartment and an expansion of the keratinocyte and was associated with hyperkeratosis. These transgenic mice expressed E6/E7 transgene mainly in skin, heart, pancreas and kidney. Hyperplasia was found at the skin. The enzyme activities of GR, GPx and CuZnSOD were measured from the transgene cause keratinocyte at the skin. The specific enzyme activities were significantly higher in transgenic mice skin compared to the normal mice skin. Thus these transgenic mice may be useful for the development of antioxidant enzymes or other therapies for HPV-associated hyperkeratosis.

key word) *Human papillomavirus, Hyperplasia, Hyperkeratosis, Antioxidant enzyme*