Shubei Wang
Dr. med.

Effects of viral protein E2 on the regulation of the papillomavirus type 11 activity in transgenic mice exposed to dexamethasone and ultraviolet-B irradiation---a pilot study.

Einrichtung: Deutsches Krebsforschungszentrum
Doktorvater: Prof. Dr. rer. nat. Johannes Schenkel

Papillomaviruses are a heterogenic group of pathogens with over 100 classified types. These highly species-specific viruses have gained widespread scientific interest as they are connected with a large spectrum of diseases ranging from benign skin lesions to destructive malignancies. Furthermore, the ubiquity of infection with HPV in the population deems it particularly necessary for us to study it *in vivo*.

The DNA of HPV can be divided into three different domains: the early region, accountable for essential processes such as replication and transcription regulation; the late region, responsible for cellular binding and entry; and the upstream regulatory region, containing enhancer-, promoter-regions and transcription factor binding sites. The URR also contains 'glucocorticoid response elements', which enable the interaction with hormone receptors.

In this thesis HPV 11, a 'low risk' HPV was examined. Three transgenic lines were established from 108 mice, double transgenic carrying the URR-LacZ and E2 gene, single transgenic expressing only URR-LacZ and another single transgenic model only expressing E2, which acted as a control. The mice were separated into different time groups and exposed to dexamethasone and UV-B irradiation. X-gal staining was used to examine the skin biopsies and quantify the expression of beta-galactosidase.

Although the results of this experiment were not statistically significant, the trend of the single transgenic URR-LacZ group shows an increase in the number of positive follicles 3h after application of dexamethasone and 48h after irradiation, generally concurring with results from previous experiments. This leads to the conclusion that the regulation of URR controlled gene expression of HPV 11 does exist and that this interaction can be modulated through external exposure to hormones and irradiation. Despite the presence of many other different, uncontrolled factors that are able to affect URR activity, it is presumed that a larger sample size would contribute greatly to the significance of the results.

The early protein E2 acts as an influencer on URR activity. Various *in vitro* studies have come to contradictory conclusions about the effect of E2. The results of this study hint at the possibility of E2 being an activator of transcription, as double transgenic mice in the Dex^- group consistently showed a higher level of positive follicles than the single transgenic mice.

Taken together, this study demonstrates that dexamethasone and UV-B irradiation appear to modulate the transcription of HPV-11 URR in transgenic mice. The role of the protein E2 *in vivo* remains ambiguous and requires further research.