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Beta HPV38 oncoproteins act with a hit-and-run mechanism in ultraviolet radiation-induced skin carcinogenesis in mice

Cutaneous beta human papillomavirus (HPV) types are suspected to be involved, together with ultraviolet (UV) radiation, in the development of non-melanoma skin cancer (NMSC), the most common form of human cancer. However, findings support a different scenario than the one observed for the mucosal high-risk HPV types in the genital tract. Indeed, beta HPV types may be required only at an initial stage of skin carcinogenesis, and may become dispensable after full establishment of NMSC.

A new study by researchers from the International Agency for Research on Cancer (IARC) and the German Cancer Research Center (DKFZ), published today in *PLoS Pathogens*,[1] used a transgenic mouse model in which the expression of beta HPV38 oncogenes can be modulated in the skin. They found that loss of viral gene expression before long-term UV radiation prevents skin cancer development, whereas deletion of the viral oncogenes after the development of UV-induced skin lesions did not affect the growth of the tumour. Importantly, whole-exome sequencing showed that chronic UV irradiation of beta HPV38 E6/E7 transgenic mice resulted in accumulation of a large number of UV-induced DNA mutations, which resembles the mutation pattern detected in human NMSC, with the highest mutation rate in the *p53* and *Notch* genes.

Together, these findings support the concept that beta HPV types act only at an initial stage of carcinogenesis, by potentiating the deleterious effects of UV radiation. These results open exciting new avenues for the development of preventive strategies, for example prophylactic vaccination, against the development of NMSC in high-risk populations, such as organ transplant recipients.

[1] Viarisio D, Müller-Decker K, Accardi R, Robitaille A, Dürst M, Beer K, et al. (2017). Beta HPV38 oncoproteins act with a hit-and-run mechanism in ultraviolet radiation-induced skin carcinogenesis in mice. *PLoS Pathog*, Published online 11 January 2018; http://dx.doi.org/10.1371/journal.ppat.1006783

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