Human papillomavirus oncoproteins induce a reorganization of epithelial-associated γδ T cells promoting tumor formation

D. Van hede1,2, B. Polese1, C. Humblet1, A. Wihlarm2, V. Renoux1, P. Delvenne1, C. Desmet1, F. Bureau1, D. Vermijlen2 and N. Jacobs1

1Giga-R, University of Liège, Belgium, 2Faculté de Pharmacie, University of Bruxelles, Belgium, 3Institute of Immunology, Hannover Medical School

Significant statement

Of all tumor-infiltrating leukocytes, T cells bearing γδ T cell receptors have been associated with the most favorable prognosis. However, we show here, in a mouse model of carcinogenesis induced by human papillomavirus (HPV)-oncoproteins, that γδ T cells promoted the development of HPV-induced lesions. Indeed, HPV-oncoprotein expression induced an infiltration of γδ T cells producing IL-17A, a proangiogenic cytokine, and a decrease density of anti-tumor Vγ5+ γδ T subsets. Supporting the clinical relevance of our observations, IL-17A+ γδ T cells were detected in human cervical cancer, where HPV-oncoproteins are highly expressed, but not in less advanced cervical lesions. These results support the notion that viral oncoproteins can induce a switch from antitumoral to pro-tumoral γδ T subsets in solid tumors.

1. γδ T cells accelerate HPV-induced lesions development

2. Skint1 expression and density of resident Vγ5+ γδ T cells are reduced in mice expressing HPV oncoproteins in epidermis

3. HPV-oncoprotein expression in epidermis leads to infiltration of non-Vγ5 γδ T cells expressing CCR2

4. γδlow T cells produce IL-17A in epidermis of HPV oncoprotein-induced lesions

5. γδ T cells promote HPV oncoprotein-induced angiogenesis in the skin

6. Human cervical squamous cell carcinoma (SCC) contains IL-17A producing γδ T cells

Contact: n.jacobs@uliege.be

Reference: Van hede et al, PNAS vol 114, E9056.