Host Adaptive Immunity Shapes Asymptomatic HPV Clearance

Inayat Bhardwaj*[1], Vanina Bouté[1], Ignacio Bravo[1], Samuel Alizon[2], and Nicolas Tessandier[1]

[1]Virostyle – Perturbations, Evolution, Virulence – France
[2]Centre interdisciplinaire de recherche en biologie – Labex MemoLife, Collège de France, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France

Résumé

Human papillomaviruses (HPVs) are among the most prevalent sexually transmitted infections and a major etiological factor in cervical cancer. More than 80% of cervical cases are caused by persistent infection with oncogenic HPV, with types 16 and 18 accounting for approximately 75% of cases. Although most HPV infections clear spontaneously within two years, persistent oncogenic infections can lead to high-grade precancerous lesions and, if untreated, invasive cervical cancer. Despite this, the host factors that enable spontaneous viral clearance are still poorly understood. In this study, we used bulk RNA sequencing data from cervical samples (n=100) from the PAPCLEAR clinical cohort to identify host transcriptomic signatures that distinguish individuals who clear asymptomatic HPV infections. Post-sample pre-processing, differential expression was assessed for samples that passed the quality assessment (n=71). Gene set enrichment analysis (GSEA) was used to identify significantly enriched biological pathways. Based on our data, HPV16-dominated infections showed upregulation of innate antiviral pathways, including type I interferon signaling. Furthermore, non-clearing infections exhibited activation of adaptive immune response, including pathways based on recombination of immune receptors built from immunoglobulin domains and downregulation of keratinocyte differentiation pathways. Strikingly, infections lasting for the longest duration were marked by negative enrichment of pathways related to tumor necrosis factor (TNF) production and regulation, leukocyte activation, and a positive enhancement of B-cell and immunoglobulin-mediated adaptive immune responses. Our analyses of host transcriptomic data from asymptomatic infections suggest that adaptive immunity is the most prominent factor distinguishing non-clearing infections.

*Intervenant