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Regulation of Toll-Like Receptors Expression in the Lower Genital Tract of Adolescent Young Women Infected With *Human Papilloma Virus*

J. K. U. A. T. LIBRARY

Ibrahim Ismail Daud

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ABSTRACT

Cervical cancer is one of the most prevalent types of cancer in women. Every year approximately 0.5 m women are diagnosed with the disease worldwide. Cervical cancer development is linked to the persistent infection by high-risk mucosal human papillomaviruses (HPVs) types. To elucidate the role of Toll-like Receptors (TLRs) in the persistence and clearance of HPV, the association between Toll-like Receptors (TLRs) expression and HPVs (HPV type 16, 18, 51 or 6) infection among young women who either had persistent or cleared HPV infection were investigated. Messenger expression of *TLR1*, *TLR2*, *TLR3*, *TLR4*, *TLR6*, *TLR7*, *TLR8*, and *TLR9* was measured by quantitative RT-PCR using endocervical specimens collected before and following viral acquisition in a cohort well-characterized for HPV DNA infections. HPV16 infections that persisted were significantly associated ($p<0.05$) with downregulation of Toll-like receptor (TLRs) *TLR2*, *TLR3*, *TLR7*, *TLR8* and *TLR9* upon viral acquisition. In contrast, HPV type 18, which are known to persist less competently in the host than HPV16 showed down-regulation of only Toll-Like Receptors (TLRs) 1 ($p<0.005$). No significant associations were found with clearance versus persistence of HPV 6 or HPV 51. This study unravels a novel mechanism used by HPV16 to suppress the host immune response by deregulating the TLRs transcripts, providing evidence that abolishing innate responses may be a crucial step involved in the carcinogenic events mediated

by human papillomaviruses. Understanding the mechanism involved in reversing this down-regulation could lay the foundation for new therapies.