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

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A Thesis Submitted In Partial Fulfillment for the Degree of Master of Science in Medical Microbiology in the Jomo Kenyatta University of Agriculture and Technology

2009
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 downregulation 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.