Human Papillomavirus (HPV) infections and innate immunity.

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Abstract

Human Papillomavirus (HPV) infection is the main risk factor for developing cervical cancer, which is the second most frequent malignancy in women globally. Around 40% of the HPV varieties that have been identified can infect the genital tract. HPVs are categorised as high (HR-HPV) or low risk (LR-HPV) based on their oncogenic potential, with the former being linked to anogenital cancer and the latter to genital warts or epithelial lesions. Following HPV16 in frequency of detection in cervical cancer cases is HPV18.

Keywords: HPV, Cancer, Oncogenic potential, Anogenital cancer, Epithelial lesions

Introduction

Human Papillomavirus (HPV) infection is the main risk factor for developing cervical cancer, which is the second most frequent malignancy in women globally [1]. 38 of the more than 100 HPV varieties that have been identified can infect the genital tract. HPVs are categorised as high (HR-HPV) or low risk (LR-HPV) based on their oncogenic potential, with the former being linked to anogenital cancer and the latter to genital warts or epithelial lesions. Following HPV16 in frequency of detection in cervical cancer cases is HPV18 [2].

Description

A DNA virus called HPV has a circular genome that is around 8000 base pairs long. It has two early regions that encode the early viral proteins E6, E7, E8, E1, E2, E4, E5 and a late area that encodes the late viral proteins L1 and L2, which are parts of the viral capsid. A non-encoding area involved in viral transcription and replication is known as the Long Control Region (LCR).

Since the cell differentiation programme is linked to the expression of the viral proteins, these proteins are expressed differently in the layers of the cervical epithelium [3]. E1 and E2, proteins that control viral transcription and replication are the first to be expressed. The stable binding of the E1 helicase to the LCR Ori site requires the development of an E1-E2 complex [4]. Early expressed HPV genes are regulated by E2, which also regulates the transcription of E6 and E7 viral oncogenes by binding to the LCR's four E2 binding domains.

Only a small percentage of HPV infected cervical lesions that are infected with high risk HPV type’s progress into cervical cancer and the transition stage is not frequently experienced by an HPV infection [5]. Occasionally, for as yet unknown causes, the HPV genome randomly fuses with the host DNA. The HPV DNA frequently breaks during this process at any location within the E1-E2 region. E6 and E7 are actively expressed when E2 is eliminated, increasing cervical change [6].

The immune response is crucial in clearing the majority of these infections, but some infections are resistant to treatment and last for years, increasing the risk [7].

The host's innate immune response serves as the infection's first line of defence in the early stages of an HPV infection. This study focuses on Dendritic (DC), Langerhans (LC), Natural Killer (NK), Natural Killer T (NKT) and keratinocytes, which are significant cells involved in fostering a positive adaptive immune response against HPV infection. The majority of these cell types can stimulate an inflammatory process that is mediated by cytokines and connects the innate and adaptive immune responses. Additionally, HPV infected cells can be completely eliminated by NK cells [8].

The E6 and E7 proteins, however, are primarily responsible for HPV's ability to elude the immune response. The expression of cytokines and chemo attractants can be altered, antigen presentation can be changed, IFN pathways can be downregulated and adhesion molecules can be downregulated, among other viral strategies of immune evasion [9]. For an infection to be successful, HPV must trick the immune system.

Conclusion

Thus, interrupting the HPV evasion mechanisms by activating the innate immune response with potent adjuvants has proven to be a promising therapeutic approach. It has also been helpful to comprehend the role of some innate immune cells during HPV infections.

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