A summary of high-risk human papillomavirus in the human body and its effects.

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Introduction

The oropharyngeal tract and the anogenital tract are both affected by HPV-associated malignancies. Cervical malignancies are distinct from other HPV-related tumours in that they are almost always brought on by HPV infections. The E6 and E7 oncogenes must be expressed continuously during the ten-year period of HPV-related carcinogenesis. The cellular genome is unstable, DNA damage repair pathways are hijacked, and the cell cycle is dysregulated during this process. Due to the greater incidence of spontaneous double-strand breaks in cells expressing E6 and E7, viral oncogenes are most likely a direct factor in the loss of genomic fidelity [1].

Virtually all cases of cervical cancer are brought on by a subset of human papillomaviruses (HPVs). These so-called "high-risk" HPVs (E6 and E7) encode two important oncogenes that are required for transformation. The majority of cervical malignancies among "high-risk" HPVs are caused by HPV16, which is frequently used as a benchmark for oncogenic HPVs. By attaching to and disrupting RB, the HPV16 E7 oncogene promotes the HPV16 lifecycle and ensures that the virus has access to the cellular replication machinery. Replication stress is brought on by RB instability, which also elevates E2F1-responsive gene expression. While HPV16 E6 reduces some of the negative consequences of this replication stress by destroying p53, cells go through several adaptations to withstand the stress [2]. As HPV oncogenes interfere with the Fanconi anaemia pathway, homologous recombination, non-homologous end joining, and microhomology-mediated end joining pathways, this is probably owing to a disruption in DNA repair mechanisms. Typically receptive to platinum-based therapy, including cisplatin, HPV-related cancers are thought to have diminished capacity to repair DNA damage. Cisplatin works by generating DNA lesions, which in turn stress replication. As a result, it is possible to more precisely target tumour cells that are less likely to interrupt their cell cycle in order to repair a DNA injury.

The activation of Rad3-related (ATR) kinase and other replication stress responses, such as ataxia telangiectasia, is necessary for the HPV lifecycle. Expression of HPV16 E7 is what essentially causes this replication stress. Numerous replication stress tolerance mechanisms are triggered in cells in response to replication stress caused by HPV16 E7. Epigenetic changes to the host genome are the main method through which HPV16 E7 is known to develop replication stress tolerance. However, it is unknown to what extent cells increase TLS activity in response to HPV16 E7-associated replication stress. Our research demonstrates that TLS gene expression is frequently increased in cervical malignancies [3].

The situation is more complex in the context of cervical cancer, even while the increased expression of TLS genes presumably suggests that cells are attempting to endure replication stress. HPV16 E7 and HPV16 E6 would both be expressed in cervical cancer cells. HPV16 E6 blocks the induction of the necessary TLS polymerases, preventing the TLS pathway from allowing tolerance of replication stress. Therefore, the increased expression of TLS genes other than TLS polymerases in cervical malignancies likely denotes a futile attempt to activate the TLS pathway in response to replication stress. It has been extensively discussed how high risk -HPV can cause spontaneous DNA double strand breaks (DSB), which can lead to genomic instability. For the virus, this is a two-edged sword. While genomic instability increases the expression of host cellular DNA repair factors, which HPV needs for its own replication, it also increases the virus's risk of integrating into the host genome, which is a dead end. E7's activation of the TLS pathway may be an attempt to maintain the proper ratio of risk to reward [4,5].

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