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Serum/Plasma Viral DNA : Mechanisms and Diagnostic Applications to Nasopharyngeal and Cervical Carcinoma

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Following reports describing circulating tumor DNA, serum/plasma viral nucleic acid has shown its potential as a new diagnostic target in cancer. In the majority of examples of viral carcinogenesis, the viral genome is consistently present in certain tumors and serves as an effective marker. This article reviews recent findings, proposes possible mechanisms, and examines the potential clinical application of serum/plasma Epstein- Barr virus (EBV) DNA in nasopharyngeal cancer (NPC) and human papillomavirus (HPV) DNA in cervical carcinoma (CC). These tumors share a DNA viral etiology and present similar histopathological findings. However, plasma EBV and HPV DNA are distinct in several aspects including incidence, mechanism of release from tumor, and clinical application. Both circulating cell-free EBV and HPV DNA reveal the same viral type as their matched tumors, indicating both are derived from the neoplastic tissue. Plasma viral DNA incidence and copy number are high in NPC but low in HPV-associated cancers. Whereas much EBV DNA in NPC is episomal, the resistance to Dnase treatment and evidences confirming lytic EBV replication in NPC suggest that reasonable proportion of plasma EBV DNA is contained in virus. On the contrary, plasma HPV genomes, as in CC, integrate into host chromosome. Plasma EBV DNA copy number, by quantitative PCR, is related to tumor mass, predicts prognosis, measures immediate response to treatment and is useful in early detection of recurrence. Plasma HPV DNA on the other hand is associated with and can be considered as an early tumor marker for distant metastasis.