Genome polymorphisms in HPV6s from benign respiratory and genital lesions

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Complete genomes of HPV6s from respiratory papillomatoses and from a genital condyloma (single episode) were determined and compared to published genomes.

Three adult onset respiratory papillomatoses (one solitary and two recurrent papillomas with two and six episodes) were HPV6b positive and five HPV6vcs (in the condyloma, in two juvenile papillomatoses with four and five recurrences and in two adult onset papillomatoses with seven and twelve episodes) were found, HPV6a was not encountered.

In HPV6b, 25 polymorphisms were identified, 17 to 21 polymorphisms in a genome. Ten were virus-specific and fifteen were characteristic to the intratypic variant group. All three HPV6b genomes clustered separately from the prototype into three different groups. Five, two and two polymorphisms were found in E1, E5a and E6 ORFs, respectively, of which those of E5a were unique. These two resulted in amino acid alteration (E39D and P78S), others were silent. Other early ORFs were conservative. Late ORFs L1 and L2 contained four and five conservative polymorphisms, respectively. In the noncoding region one, in the long control region (LCR) six polymorphisms were detected.

In HPV6vc, 22 polymorphisms were found, three to seven polymorphisms in a genome. Only one was present in all five genomes, one in three; 20 were unique. All five genomes clustered to the same large group as the reference genome, but all to different subclusters. ORFs E1, E2, E4, E5a and E6 carried three, five, one, one and two polymorphisms, respectively, of which, in contrast to HPV6b, all except two (in E1 and in E5a) were unique. Four of them led to amino acid replacement, all in the E2-E4 ORF (T116N, S144T, S246A and E340D in the E2; S246A corresponded to a S68R change in E4 ORF, the others were in the region belonging solely to E2). ORFs E5b and E7 were the same as the reference. Late ORF L1 contained one polymorphism common to all five genomes and five unique alterations. The common polymorphism led to a Y219D change. Three of the five unique polymorphisms were silent, one led to F441L and one to K449E amino acid replacement. In the noncoding region one unique, in the LCR two unique polymorphisms were detected.

HPV6vc showed considerably higher variability with multiple non-silent polymorphisms in E2-E4, while coding regions of the three HPV6bs, though different from the prototype, were more similar. LCR, in contrast, was more variable in HPV6b. These suggest that HPV6bs differ mainly in LCR activity, while in HPV6vc polymorphisms of replication proteins may be more important.

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