

Human papillomavirus type 16 genetic variants: phylogeny and classification based on E6 and LCR

Abstract:

Naturally occurring genetic variants of human papillomavirus type 16 (HPV16) are common and have previously been classified into 4 major lineages; European-Asian (EAS), including the sublineages European (EUR) and Asian (As), African 1 (AFR1), African 2 (AFR2), and North-American/Asian-American (NA/AA). We aimed to improve the classification of HPV16 variant lineages by using a large resource of HPV16-positive cervical samples collected from geographically diverse populations in studies on HPV and/or cervical cancer undertaken by the International Agency for Research on Cancer. In total, we sequenced the entire E6 genes and long control regions (LCRs) of 953 HPV16 isolates from 27 different countries worldwide. Phylogenetic analyses confirmed previously described variant lineages and subclassifications. We characterized two new sublineages within each of the lineages AFR1 and AFR2 that are robustly classified using E6 and/or the LCR. We could differentiate previously identified AA1, AA2, and NA sublineages, although they could not be distinguished by E6 alone, requiring the LCR for correct phylogenetic classification. We thus provide a classification system for HPV16 genomes based on 13 and 32 phylogenetically distinguishing positions in E6 and the LCR, respectively, that distinguish nine HPV16 variant sublineages (EUR, As, AFR1a, AFR1b, AFR2a, AFR2b, NA, AA1, and AA2). Ninety-seven percent of all 953 samples fitted this classification perfectly. Other positions were frequently polymorphic within one or more lineages but did not define phylogenetic subgroups. Such a standardized classification of HPV16 variants is important for future epidemiological and biological studies of the carcinogenic potential of HPV16 variant lineages