Human papillomavirus 57 positivity in periungual squamous cell carcinoma eradicated by topical tirbanibulin

To the Editor: In a previously published case report, tirbanibulin 1% ointment eradicated a periungual squamous cell carcinoma (SCC) at the location of a recalcitrant wart.[1] To confirm the presence of human papillomavirus (HPV), we sent the specimen for polymerase chain reaction (PCR) analysis. We were specifically questioning, whether HPV-16 was associated, since it is the most common HPV type associated with SCC on the finger. HPV typing by nested PCR with PGMY-GP+ PCR was utilized (Fig 1). The obtained putative HPV-PCR product was purified, cloned, and sequenced. The acquired sequencing data was evaluated using the Basic Local Alignment Search Tool of the National Center for Biotechnology Information, and HPV type 57 was detected (Fig 2). HPV-57 is an alpha HPV that is often associated with common warts and phylogenetically similar to HPV-2 and HPV-27. Comparative and phylogenetic analysis of amino acid sequences using the Jotun-Hein algorithm indicate a close relationship of HPV-57b oncogenes E5 and E7 with corresponding HPV-16 and HPV-18 oncogenes. As one of the more studied HPV types, prototypical HPV-16 oncoproteins upregulate the non-receptor tyrosine kinase (Src) family kinases.[2] These are modulated with the E6 and E7 oncoproteins, which interact with cellular regulatory proteins to promote viral replication and upregulation of cellular proliferation in high-risk HPV types.[2] Since not all SCC contain HPV, HPV oncogenes may be important in initiating keratinocyte oncogenesis rather than tumor progression. Most commonly associated with common warts and oral papillomas, HPV-57 has also been associated with SCC on the chest and esophageal SCC.[3] Since tirbanibulin works through inhibition of tubulin polymerization and Src kinase signaling,[4] HPV-57 positivity in the SCC suggests that tirbanibulin might impact the HPV pathway and diseases with HPV DNA incorporated into the host genome through Src. Activation of Src kinase occurs through a disruption of the negative regulators, particularly modification by phosphatases and kinases.[5] Further mechanistic and clinical studies with tirbanibulin on HPV and SCC are warranted to evaluate its effect on these pathways.

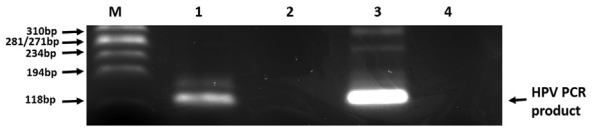

Fig 1. Human papillomavirus (HPV) polymerase chain reaction (PCR) result obtained by the PGMY-GP+ nested PCR assay. Lanes M, fx174 RF DNA marker; 1, patient DNA; 2, negative control DNA; 3, positive control SiHa cell DNA; 4, reagent control.

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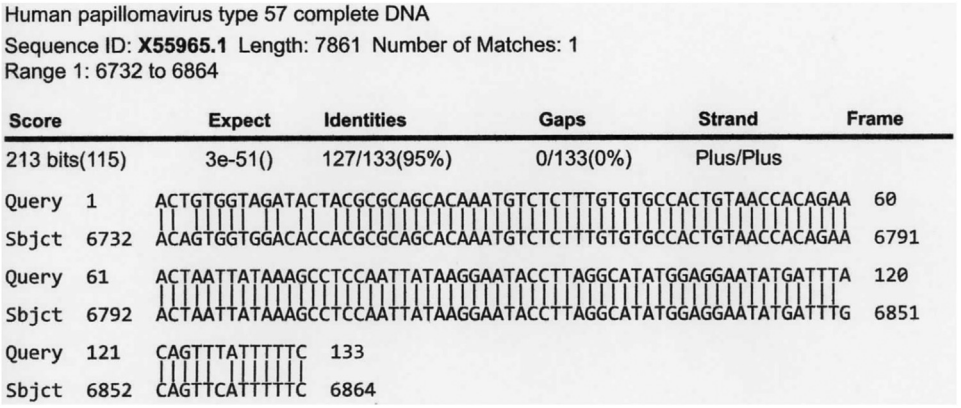

Fig 2. Alignment of sequencing data obtained from the human papillomavirus (HPV) polymerase (PCR) product using the Basic Local Alignment Search Tool (BLAST) of the National Center for Biotechnology Information (NCBI). The sequence data obtained from patient's sample ("Query") showed 95% similarity to the prototype HPV-57 DNA sequence (accession number, X55965) in the NCBI GeneBank ("Sbjct").

Conflicts of interest

Dr A. Moore has received research funds and honoraria from Almirall. Author S. Moore and Dr Tyring have received research funds from Almirall, LLC. Drs He and Rady have no conflicts of interest to declare.

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