Scientific Foundation SPIROSKI, Skopje, Republic of North Macedonia
South East European Journal of Immunology. 2025 Mar 25; 8(CITIM):063.
https://doi.org/10.3889/seejim.2025.6122
eISSN: 1857-9388
Category: *CITIM - Cancer Immunotherapy & Immunomonitoring (CITIM2025)*
Section: *Invited lectures*

Live-Attenuated Influenza Viruses Co-Expressing BPV1 E6 and E7 Peptides Eradicate BPV Infection, thus Significantly Reducing Tumour Recurrence in Horses after Surgery

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Citation: Hainisch EK, Jindra C, Wolschek M, Muster T, Brandt S. Live-attenuated influenza viruses co-expressing BPV1 E6 and E7 peptides eradicate BPV infection, thus significantly reducing tumour recurrence in horses after surgery.SEE J Immunol. 2025 Mar 25; 8(CITIM):063 https://doi.org/10.3889/seejim.2025.6122
Keywords: Papillomaviruses; Immunotherapy; Sarcoids; BPV1/2 infection ; Tumor regression
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Received: 01-Mar-2025
Accepted: 25-Mar-2025
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Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

Background, aim: It is well accepted today that papillomaviruses can induce mucocutaneous tumours in vertebrates. Given the high metastatic potential of some of these tumours in humans, and their tendency to recur following treatment, there is a need of more effective therapeutics.
Methods: Following the generation of live-attenuated influenza viruses co-expressing bovine papillomavirus type 1 (BPV1)-specific E6 and E7 peptides, we assessed the efficacy of this immunotherapeutic vaccine prototype in a natural tumour model, i.e., horses bearing BPV1 or 2-induced skin tumours termed sarcoids. So far, 21 horses with mild and moderate disease repeatedly received intralesional injections with the vaccine. Ten horses with severe disease (multiple/aggressive sarcoids; 64 in total) were treated by combined therapy, i.e., injections with the vaccine and electrosurgical tumour excision. Where possible, a follow-up was carried out by photo-documentation and BPV1/2 PCR-screening of hair roots/dandruff of the tumour sites.
Results: Nine of 21 horses with mild or moderate disease showed complete tumour regression (CR) after six months, and all samples collected from seven individuals scored BPV1/2-negative. Further nine horses exhibited partial sarcoid regression (PR) that is still ongoing, and harboured BPV1 or 2. Three horses showed stable disease and BPV1/2 infection. In one of these horses, repeated surgery and additional booster injections led to freedom from sarcoids and BPV1/2.
From the 10 severely affected horses, nine showed CR six months after combined therapy. Three recurrent lesions in two horses were eradicated by repeated immunotherapy or combined therapy. This led to 8/9 horses being tumour- and BPV1/2-free meanwhile.
Conclusion: Sarcoid recurrence following standard therapy is a common event because current treatments do not target BPV1/2 infection. Flu-BPV1-E6E7-immunotherapy was effective in 86% of mild and moderate-type sarcoids as well as eradicating BPV infection underlying the disease. Similarly, combined therapy led to CR in 9/10 cases and significantly reduced the risk of post-treatment recurrence due to eradication of BPV infection: only 3/64 treated sarcoids recrudesced, corresponding to a unique recurrence rate of only 4.7%.