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Abstract Submission Form

Poster Title: **Role of HIV-associated extracellular vesicles in HPV16 infection in the oral cavity**

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People living with HIV (PWH) have a significantly higher prevalence of oral human papillomavirus (HPV) and an increased risk of developing HPV-associated oropharyngeal cancers. Although HIV infection is a known risk factor for the development of HPV-related oral infections and malignancies, the precise mechanism underlying oral HPV acquisition, infection, and malignant transformation in the context of HIV remains poorly understood. We have reported that plasma and saliva of people with HIV as well as culture media of HIV-infected T cells contain HIV-positive extracellular vesicles (EVs) that play a crucial role in stimulating the proliferation of HPV-associated head and neck squamous cell carcinoma (HNSCC) cells. EVs are lipid bilayer-enclosed nanoparticles of endosome origin; released by various cell types for material transfer and immune regulation. HIV-associated EVs contain HIV RNA cargos and significantly promote the proliferation and migration of HPV-related HNSCC cells. These EVs facilitate the growth of HPV-related xenografts in animal models. To determine if HIV-associated EVs played a role in oral infection of high-risk HPV, we produced HPV16 pseudovirus (PsV) for infection in 3-dimentional oral organotypic cultures. HIV-associated EVs derived from culture supernatants of HIV-infected T cells significantly stimulated HPV16 PsV infection in the oral organotypic culture compared with EVs from non-HIV control T-cell culture media. HPV16 PsV failed to infect intact oral organotypic cultures, but the PsV infected oral epithelial cultures scored by pipet tips. This observation is consistent with the fact that infection by HPV occurs through microwounds of the epithelium that expose basal layer cells to viral infection. Importantly, cetuximab, a monoclonal antibody to epidermal growth factor receptor (EGFR) for cancer treatment, blocked the pro-infection effect of HIV-associated EVs on HPV16 PsV, suggesting involvement of EGFR in mediating papillomavirus infection in the oral cavity. Our results suggest that HIV-associated EVs play a role in promoting HPV acquisition and infection in the oral cavity. Further investigation of interaction between HPV and HIV-associated EVs will lead to an intervention approach to block HPV infection in people with HIV and reduce the health burning in the population.

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