Characterization of a Chimeric MmuPV1 Genome with HPV-16E6E7

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Background/Objectives: Papilloma Viruses (PVs) are double-stranded DNA viruses that infect cutaneous and mucosal epithelium. In humans, there are over 100 types of PVs. HPV-16 is a high-risk type that causes ~50% of cervical cancers and ~70% of oropharyngeal cancers by expressing viral oncogenes E6 and E7 in replicating keratinocytes. The mouse PV, MmuPV1, displays species tropism and causes neoplastic lesions. Its discovery in 2011 introduced the opportunity to study PVs from early stages of infection to cancer development. Such an *in vivo* model of HPV-16 could uncover novel mechanisms for treatment intervention and disease prevention. Our study aims to characterize a small-animal infection model using a chimeric MmuPV1 genome with HPV-16 E6 and E7 in place of mouse E6 and E7 (MmuPV1-16E6E7). The goal of our study is to investigate the genome's ability to express the HPV-16 oncogenes *in vitro* and to cause tumors *in vivo*.

Methods: To increase selective pressure *in vitro,* we replaced the MmuPV1 L1 and L2 genes with a neomycin cassette (MmuPV1-16E6E7neo). We packaged these genomes into infectious quasiviruses using a HEK 293TTF viral packing cell line. After isolating quasiviruses, we infected two donor human foreskin keratinocytes (HFK) cell lines. Forty-eight hours post infection, we isolated mRNA for qPCR to quantify HPV-16 E6 expression. To investigate whether MmuPV1-16E6E7 can cause tumors in *in vivo*, we infected athymic nude (N/J) mice orally with quasiviruses to evaluate infection and viable genome persistence.

Results: HPV-16 E6 cDNA was detected in three HFK isolates.

Conclusions/Future Directions: The presence of HPV-16 E6 cDNA indicates that the gene can be successfully transcribed from MmuPV1-16E6E7neo in HFKs. Future studies will assess the this ability in primary mouse keratinocytes. If tumors are observed, we can use this model to study the efficacy of antiviral compounds to inhibit HPV16 E6 *in vivo*.