Investigating an etiologic role for *Felis catus* gammaherpesvirus 1 in high grade, large cell lymphoma

Tamsen Polley MS¹, Amy Durham MS VMD², Julia Beatty BVetMed PhD, and Patricia Pesavento DVM PhD¹

¹University of California, Davis USA • ²University of Pennsylvania, USA • ³University of Sydney, Australia

tmolley@ucdavis.edu • amycd@vet.upenn.edu • julia.beatty@sydney.edu • papesavento@ucdavis.edu

**Hypothesis**

*Felis catus* gammaherpesvirus 1 (FcaGHV1) is causally-linked to post-transplant lymphoma or high grade, large cell lymphoma in domestic cats.

**Introduction**

The first gammaherpesvirus of domestic cats, FcaGHV1, was discovered in 2014.¹ FcaGHV1 is a worldwide endemic lymphoproliferative infection detected in the blood of 10-17% of cats.² Gammaherpesviruses in humans and other animals cause persistent infections that are typically clinically latent but, in circumstances such as immune dysfunction or following cross-species transmission, gammaherpesviruses can cause lymphoma and other fatal diseases.³ Lymphoma is the most common neoplasm in cats. Several prevalence studies have established that immunosuppressed cats, such as those either co-infected with feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), or organ transplant recipients, are more at risk for developing lymphoma. Emergence of any neoplasm in the context of immunosuppression is consistent with viral-associated cancer, which in humans is ~15% matched controls.

Frequently in high grade, large cell lymphomas than in tissue species is unknown. Whether FcaGHV1 plays a role in feline post-transplant lymphoma is the subject of this investigation.

**AIM:** To determine whether FcaGHV1 DNA is detected more frequently in high grade, large cell lymphomas than in tissue matched controls.

**Methods**

**Study tissue collection**

Cases were defined as post-transplant lymphoma or high grade, large cell lymphoma. Cases of high grade, large cell lymphoma were defined as those either co-infected with feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), or organ transplant recipients, are more at risk for developing lymphoma.

**PCR for GAPDH, FcaGHV1, FIV and FeLV assessment**

Positive signal for each primer set is shown with an asterisk (*). Negative control (PCR) was unhybridized DNA.

**DNA extraction**

DNA was extracted from formalin fixed paraffin embedded tissue using the Qiagen DNEasy Kit via the manufacturer’s protocol.

**PCR for GAPDH, FcaGHV1, FIV and FeLV assessment**

**A** 10 μm sections of paraffin-embedded formalin-fixed tissue

**B** PCR+ FcaGHV1 Cases

**C** In-situ diagnostics on 5 μm sections

**HE stain, tissue morphology**

**Histology**

**HCV** binds bursa epithelial materials

**IFC** binds bursa epithelial materials

**ISH**

**FcaGHV1 viral nuclear acid**

**Probe of FcaGHV1 ORF 50**

transcription activation factor

**Results**

91 domestic cats from American veterinary hospitals with high grade, large cell lymphomas were assessed.

**Discussion**

The pathology of FcaGHV1 infection is being discovered and developed, but the known risk factors for infection include age, sex, reproductive tract, haemoplasma positive, and FeLV or FIV positive status.⁴ The prevalence of potential lymphomas in domestic cats and the risk factors for infection are unknown or limited. The current study was the first assessment of potential lymphomas in domestic cats and the risk factors for infection are unknown or limited. We will focus on discussing the possible epidemiology and pathology of FcaGHV1 based on our findings.

**Future work**

The epidemiological and pathology of FcaGHV1 is continuing to be discovered, but the known risk factors for infection include age, sex, reproductive tract, haemoplasma positive, and FeLV or FIV positive status.⁴ The population for this study included cats with high grade, large cell lymphoma, providing the “risk” status. All other risk factors were unknown for most of the population. Due to the limited population and results of the current study, we will describe a descriptive study for guiding future work.

The current study was the first assessment of potential tissue specificities for FcaGHV1, specifically high grade, large cell lymphomas, since FcaGHV1 was previously characterized and studied in blood samples.⁵ Single PTL and GIT cases were positive by PCR for FcaGHV1 DNA, but the large, T-cell GIT case contained positive cells by ISH. Positive cells were large with expanded nuclei and visible nucleoli, and were part of the lymphoma population, suggesting a causal association of FcaGHV1 DNA positive lymphomas in high grade, large cell lymphomas. Only one case out of 7 total high grade, large cell GIT lymphomas were FcaGHV1 positive. Assessing for FcaGHV1 DNA presence by PCR could produce false positives, and the other 6 GIT cases will be assessed by ISH in future work.

**Low FcaGHV1 detection**

FcaGHV1 detection is also supported by the case selection criteria decreasing the infection risk factors for the study group. Cats in GIT and GIT group had assumed high quality medical care and health screening including seronegative FeLV and FIV status in decreasing risk of FcaGHV1 infection.⁶ Donor cats are additionally in optimal health and are likely screened for FeLV or FIV, decreasing the risk of being FcaGHV1 positive and subsequent transmission to the virus in recipients. The case selection criteria for GIT and GIT group is unknown, with limited overall signalment. The preliminary screens for GIT group and the unknown signalment for the other groups decreased the risk of infection with FcaGHV1, explaining the low detection in the sampled population.

Based on our findings, FcaGHV1 may be localized to high grade, large, gastrointestinal T-cell lymphomas in domestic cats.

**References**


