High Prevalence of *Felis catus* Gammaherpesvirus 1 in Oronasal Tissues of Domestic Cats.

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**Introduction**

Viral infections account for over 15% of the human cancer burden,(1, 2) Demonstration of viral etiology usefully identifies the subset of tumors that may be preventable through vaccination.(3, 4) Epstein Barr virus (EBV) is an oncogenic member of the gammaherpesvirus family that commonly causes asymptomatic, lifelong infections in the human host.(5) Rarely, infected individuals develop EBV-associated nasopharyngeal carcinomas.(6) *Felis catus* gammaherpesvirus 1 (FcaGHV1) is a recently discovered virus in cats.(7, 8) Serology and blood PCR studies have suggested that that up to 30% of the domestic cat population, around 200 million cats, are infected with FcaGHV1, so the impact of this virus on feline health is of great interest.(9, 10) As a first step toward understanding the natural history of FcaGHV1, we have discovered that normal feline tissues are a surprisingly common site of FcaGHV1 infection, and this is foundational for our hypothesis that FcaGHV1 could cause a subset of feline oronasal carcinomas.

**Specific Aims**

1. To establish the prevalence of FcaGHV1 in feline oronasal carcinomas vs. control tissues by PCR.
2. To explore whether FcaGHV1 is associated with specific histologically classified subsets of epithelial tumors.
3. Establish by in situ hybridization the cell specific distribution of FcaGHV1.

**Materials and Methods**

Both oronasal tumor tissue and non-tumor oronasal tissues (normal or inflamed) were tested by PCR for the presence of FcaGHV1. The data pictured above are our results on non-tumor tissues, but is similar to what we detected in tumor tissues. Amplified bands of the predicted size are present in most (8/10) samples. Viral nucleic acid was not detected in samples 3 and 4. This gel is representative of the data (in summary) that FcaGHV1 is present in both tumor and non-tumor samples. An amplified segment of GAPDH (present in all cells) serves to confirm that DNA was extracted and intact in all samples.

**Conclusion**

These results demonstrate that FcaGHV1 is more prevalent in oronasal tissues (90%) than blood (-20%) of cats in California.(8) We propose that this is a region of viral persistence, which leaves open the possibility that FcaGHV1 could contribute to oronasal cancers. By PCR analyses, there was no significant difference in viral detection between cats with or without oronasal carcinomas. PCR alone, therefore, cannot establish whether FcaGHV1 infection is oncogenic. Sorting out whether FcaGHV1 is an important etiologic agent in feline carcinomas will require further studies designed to determine which specific subset(s) of cells are infected in normal cats vs. cats with carcinomas, and whether oncogenic genes of this gammaherpesvirus are expressed in tumors. In the ongoing studies, we are testing cell specific infection by using in situ hybridization, which can determine whether FcaGHV1 nucleic acid is present within neoplastic cells. Given that the virus is so prevalent in oronasal tissue, this would be the minimum criteria for viral based oncogenesis. Future investigations comparing the viral transcription in tumor and non-tumor cells would help substantiate whether the virus is contributing to cell transformation.

**Table: FcaGHV1 prevalence by PCR amplification**

<table>
<thead>
<tr>
<th>Tumor classification</th>
<th>Positive</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous Cell Carcinoma (SCC)</td>
<td>17</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>17</td>
<td>35</td>
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</tbody>
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**References**