



NCSU c-Kit MUTATION ANALYSIS SUBMISSION FORM

Phone: 919 513 1925 / cvmoncodiagnosticlab@ncsu.edu

Patient Information

Animal Name _____

Owner Last Name: _____

Species/Breed _____

Age _____

Sex: FI ___ FS ___ MI ___ MC ___

Clinic Information

Clinic Name: _____

Clinic Address: _____

Email: _____ ***(required)**

Phone: _____ Fax: _____

Clinician Name: _____

Billing information (If different from Clinic Information)

Billing Name _____

Billing Address _____

Phone _____

Contact Email _____

(Results and invoices will be sent via Email only) **** (required)***

	SAMPLE TYPE	DATE COLLECTED	EXON 11	EXON 8
Aspirate site:	_____	_____	_____	_____
Biopsy site:	_____	_____	_____	_____
Other:	_____	_____	_____	_____

Results will be completed within 7 - 10 business days after the sample is received at the lab

*(There may be times when we are short-staffed or the University is closed and we cannot receive samples. If this is the case, there will be a message to that effect.)

We do not prefer in person sample drop offs. In case of emergency or an exception, please call the lab and provide at least 4 – 6 hours' notice before drop off.



NCSU c-Kit MUTATION ANALYSIS SAMPLE SUBMISSION GUIDE

SAMPLE SUBMISSION

What type of sample to submit: Both slides prepared from fine needle aspirates of mast cell tumors and formalin-fixed paraffin embedded tissues can be analyzed. EDTA blood can also be analyzed if significant mastocytosis is evident.

Slides: Send slides that contain an ample amount of cells to allow adequate DNA isolation. Usually 2-3 slides are sufficient. Previous staining with Wright-Geimsa or Dif-Quik will not affect the results. A chilled container is not required.

Formalin fixed samples: 3 – 4, 20-25 micron sections in a 1.5ml eppendorf tube or equivalent- (**NOT ON A SLIDE!**). Formalin fixation can degrade DNA, therefore, c-Kit analysis may not provide pertinent information in approximately 10% of these cases. A chilled container is not required.

Please send sufficient sample to ensure accurate results:

Slides: Minimum 0.5 – 1-inch smear

Note about low cellularity samples: Some samples may not have enough cells to run c-Kit ITD analysis. In some cases, we can determine this prior to starting the assays. However, often we do not know until we have completed the assay and analyzed the results. In these cases, as it costs us same amount to run as a sample with enough cells, you will be charged for the non-diagnostic sample.

****HISTORY** (IMPORTANT!!!!)**

1) Signs or symptoms leading to test request (check all that apply)

___ Lymphadenopathy (include most recent cytology report if available)

___ Splenomegaly ___ Hepatomegaly

___ Mastocytosis; *mast cell number* _____ (include most recent CBC/cytology report if available)

___ Other peripheral blood abnormality (include most recent CBC/cytology report if available)

___ Bone marrow abnormality (include most recent cytology report if available)

___ Mass; *location* _____ (include most recent cytology report if available)

___ Effusion/fluid containing suspicious cells; *pleural* ___ *peritoneal* ___ *CSF* ___ *other* _____

2) Other signs and/or additional history or concurrent conditions including any treatment.

**PRICES:**

LN/mass FNA: \$125 /sample.

Formalin-fixed (FFPE) samples - \$125 + \$45 = \$170 (as additional processing is required for FFPE samples).

Additional samples from the same patient at the same time, **\$55/ sample.**

If possible, please email or call the laboratory (919-513-1925) prior to sending a sample. If no one answers the phone, leave a message. This way we can begin to track the sample if it does not arrive in a timely manner.

Additionally, there are times when we are short-staffed or the University is closed and we cannot receive samples. If this is the case, there will be a message to that effect.

How to send a sample: Do not send for Saturday/Sunday or holiday receipt. Send by FED EX, UPS, or DHL. Do not send US postal, as the delivery will be to the main mail office on campus and can take a day or two to reach us.

Send overnight for morning delivery to: **North Carolina State University, CVM**
(Please use FED EX, UPS or DHL) **K9/Feline Oncology Diagnostic Lab**
Research Bldg., Rm. #330C
1060 William Moore Drive
Raleigh NC 27607

Questions:
Phone: 919-513-1925
cvmoncodiagnosticlab@ncsu.edu

c-Kit MUTATION INFORMATION:

c-Kit is a member of a large family of receptor tyrosine kinases (RTKs) found to be dysregulated in a variety of human and canine malignancies. Other members of this family include Met, Her-2/neu, PDGF/PDGFR, and VEGF/VEGFR. Approximately 30%-50% of malignant canine mast cell tumors (MCTs) possess activating mutations in c-Kit which consists of internal tandem duplications (ITDs) in the negative regulatory juxtamembrane domain.¹⁻⁴ This leads to loss of function of this region and uncontrolled downstream signaling. C-Kit ITD mutations are rarely found in well-differentiated MCTs, while ~35% of poorly differentiated MCTs harbor a c-Kit ITD.^{1,4} Because RTKs are important for the control of many cellular processes, including uncontrolled proliferation and/or cancer, RTKs are important targets for anticancer therapies.

Two orally bioavailable small molecule inhibitors of c-Kit, Palladia (SU11654) and Kinavet (AB1010) are now commercially available. Both molecules have activity against canine MCTs^{2,5,6}, with an overall response rate of 42.8% in one study (21 complete responses, 41 partial responses). Importantly, dogs with tumors positive for the cKit ITD were more likely to have an objective response when compared with dogs with tumors negative for the c-Kit ITD (44.8%, 13/29 versus 20.3%, 24/118, respectively; $P = 0.009$). Palladia-treated dogs were more likely to respond to this drug if they had c-Kit positive tumors (60%, 12/20 versus 31.3%, 20/64, respectively; $P = 0.0099$; odds ratio, 4.41). Tumor grade and regional lymph node metastasis were not associated with objective responses in this study.

Based on these studies, it is reasonable to assume that determining the c-Kit ITD status of a dogs MCT could facilitate the development of a rational treatment plan that may or may not include either Palladia or Kinavet. In theory, dogs with tumors positive for the c-Kit ITD have an ~50% greater chance of responding to these drugs than dogs with tumors negative for the c-Kit ITD.

