



# WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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## **Immunohistochemical quantification of the transcobalamin II protein (TCII) and receptor (TCII-R) in naturally occurring feline tumors**

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*Final report, W12-005*

Cancer cells require vitamin B<sub>12</sub> (cobalamin) for DNA synthesis, and therefore they have an absolute requirement for vitamin B<sub>12</sub> in order to grow. Cancer cells produce transport proteins such as transcobalamin II (TCII) to scavenge and shuttle vitamin B<sub>12</sub> to the cells, and they express more vitamin B<sub>12</sub> receptors (TCII-R) on their surface than do healthy cells. Vitamin B<sub>12</sub>'s TCII/TCII-R delivery system provides an effective way of targeting the delivery of diagnostic and chemotherapeutic agents to cancer cells while having little effect on healthy tissues.

The researchers' aim with this study was to develop and apply an immunohistochemical staining method to identify feline tumors with increased vitamin B<sub>12</sub> transport protein (transcobalamin II, TCII) and receptor (TCII-R) expression that may be susceptible to diagnostic imaging and treatment with vitamin B<sub>12</sub>-based tumor-targeting agents. Nitrosylcobalamin (NO-Cbl) is a novel anti-tumor drug that uses the TCII/TCII-R system to deliver a toxic dose of nitric oxide to cancer cells. Due to its tumor-specific accumulation, use of NO-Cbl is associated with minimal systemic toxicity and minimal damage to normal tissues. NO-Cbl is anticipated to begin the FDA's regulatory approval process for use in companion animals with cancer within the next year.

Three cases each of archived twelve different naturally occurring feline tumor types were evaluated, including: (1) biliary carcinoma; (2) dermal carcinoma; (3) vaccine-associated fibrosarcoma; (4) intestinal adenocarcinoma; (5) intestinal lymphoma; (6) intestinal mast cell tumor; (7) mammary adenocarcinoma; (8) nodal lymphoma; (9) oral squamous cell carcinoma; (10) soft tissue sarcoma; (11) splenic mast cell tumor and (12) transitional cell carcinoma of the bladder. An immunohistochemical protocol was developed to stain the tumors as well as their adjacent normal tissues for the presence of TCII and TCII-R.

The average age of the 36 cats in this study was 12.3 years. Every feline tumor examined stained positively for TCII and TCII-R. There was a statistically significant increase in both TCII and TCII-R expression in tumor tissues compared to adjacent normal tissues for each tumor. There was no significant association between TCII/TCII-R staining intensity and breed, age or sex. Results from this study strongly support the use of vitamin B<sub>12</sub>-based agents for both the diagnosis and treatment of feline tumors. Additionally, these study results support the investigation of other upregulated targets that might be utilized for detection and treatment of feline tumors.

*Summary prepared by Vicki L. Thayer DVM, DABVP (feline)*

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