ONCOGENES AND TUMOR SUPPRESSOR GENES IN VETERINARY MEDICINE:
Canine Mast Cell Tumor and Feline Lymphoma

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OBJECTIVES

Bibliographic review on **oncogenes and tumor suppressor genes** in dogs and cats, focusing on the most relevant/prevalent types of tumors in each species and other **important aspects of veterinary oncology**.

ACTUAL SITUATION: MOST PREVALENT NEOPLASMS

DOGS

Cutaneous or Subcutaneous

33,33%

Malignancy ⬆

20-40%

CATS

Lymphatic System

25%

Malignancy ⬆

50-65%

⬆ Level of animal health & care ➡ ⬆ Life Expectancy

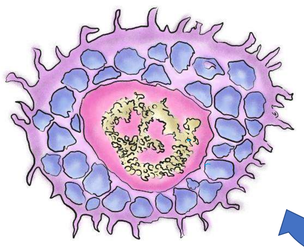
Better diagnostic techniques ➡ ⬆ Case Detection

Recent advances in the knowledge of tumor biology, But limited application in clinical practice

CANINE MAST CELL TUMOR

EPIDEMIOLOGY

Prevalence ⬆ 7-30% of cutaneous neoplasms; ⬇ 6% of all



Mast cells:
Pro-inflammatory cells, bioactive molecules releasers

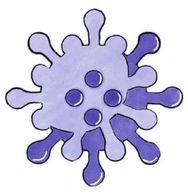
ETIOLOGY

c-kit	Encodes a growth factor receptor (KIT).	Activating mutation in yuxtamembrane domain.
p-53	Encodes the P53 protein, whose regulatory protein is MDM2.	⬇ Expression of P53 (or ⬆ expression of MDM2).
CD25	IL-2 receptor subunit.	Expressed by tumor cells. Expression of receptor and lligand ➡ anti-tumor immune response modulation.
GNB1	Encodes G proteins, related to signal integration.	Mainly associated with TKIs therapy's resistance.
JAK/ STAT	Cytokine signaling pathway.	⬆ Expression of pSTAT3 = ⬆ metastasis. ⬆ Expression/activation of JAK1 = ⬆ survival.

Masitinib mesylate (TKI)

These alterations' discovery has generated an enormous interest and effort to develop more individualized **novel therapeutic approaches**.

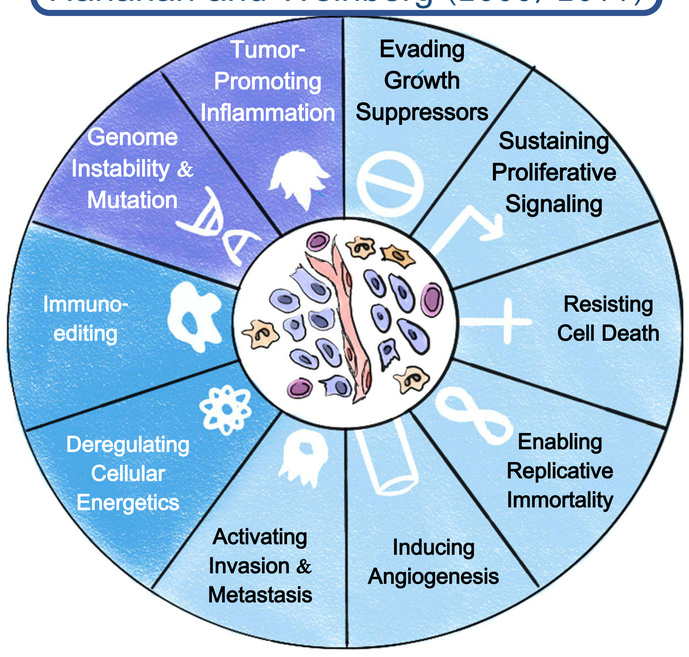
Oncolytic viruses ➡



Diagnosis by cytological and histological evaluation → **Treatment** by traditional and/or novel therapies → **Prognosis** can be difficult to predict

CLINICAL FEATURES

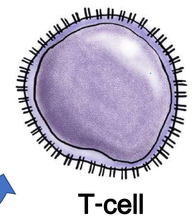
THE HALLMARKS OF CANCER
Hanahan and Weinberg (2000, 2011)



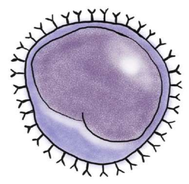
*Oncogene (*gain of function*) or related to it.

*Tumor Supressor Gene (*loss of function*) or related to it.

FELINE LYMPHOMA



T-cell



B-cell

Lymphocytes:
White blood cells belonging to the Immune System

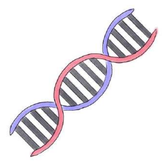
EPIDEMIOLOGY

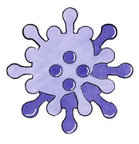
Prevalence ➡ Influenced over time by FeLV

33,33% of all (upward trend) ⮌

ETIOLOGY

FeLV	FIV
• Gammaretrovirus • ⬆ Risk of lymphoma x60 • Predominant T-cells	• Lentivirus (retrovirus) • ⬆ Risk of lymphoma x5-6 • Predominant B-cells
Direct oncogenesis: Modulation of oncogenes and TSG's expression by genomic insertion.	**Indirect oncogenesis:** Deregulates the IS, altering anti-tumor immunity.





⬆ Infectious Factors

Genetic Factors ➡

P27, P16	CDKIs encoders. Related to cell cycle control. P16 participates in RB pathway.	⬇ *P27* expression. Genetic and epigenetic alterations in *P16*.
P53	Same as in canine mastocitoma.	⬇ Expression. Only in 10% of cases.
BCL-2	Anti-apoptotic protein encoder.	⬆ Expression➡ tumor cells survival and CT resistance.

Diagnosis by FeLV/FIV tests and histological evaluation → Limited knowledge about **treatment** and **prognosis**

CLINICAL FEATURES

CONCLUSIONS

1. All neoplasms present the **same hallmarks** (2 enabling characteristics and 8 acquired capabilities), but their **aetiology can vary hugely**.
2. Alterations in **oncogenes and TSGs** are **strongly linked** to some of the acquired capabilities and they are **very frequent** in animal neoplasms.
3. In **canine mast cell tumor** there have been detected alterations in **oncogenes**, **TSGs** and even in other genetic elements like **mtDNA**.
4. In **feline lymphoma**, **viral infections** stand out as potential etiologic agents, either producing direct or indirect oncogenesis. Even so, alterations in **genetic factors** have also been reported.
5. Due to the great variability of alterations that can take place, and, given that **not all of them** can be treated with **traditional therapies**, more and more effort is being given to the research and development of new, more **individualized therapeutic approaches**.

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