



## INVESTIGATION OF THE EFFECTS OF PACLITAXEL AND OZONE USE ON HIF-1 $\alpha$ AND VASCULOGENESIS IN MAMMARY TUMOR FORMATION IN DOGS: EXPERIMENTAL MOUSE MODEL

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#### KEY WORDS

- ✓ BALB/c
- ✓ HIF-1 $\alpha$
- ✓ Mammary tumor
- ✓ Ozone
- ✓ Paclitaxel
- ✓ VEGF-A

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#### THESIS ABSTRACT

Breast tumors are one of the most common types of cancer. Triple-negative breast cancer (TNBC) does not respond to hormonal therapies because estrogen, progesterone and HER2 receptors are missing or produced at low levels. The tumor microenvironment is hypoxic due to rapid tumor growth and inadequate blood perfusion. Over time, the amount of HIF-1 $\alpha$  increases and initiates the transcription of a number of genes, including VEGF-A, which promotes vasculogenesis, which plays an important role in tumor growth and metastasis.

In a mouse model of 4T1 breast tumor, PTX and ozone administration for treatment was positively associated with anti-tumoral immune responses in high-dose ozone-treated patients, suggesting that a decrease in Ki67 expression level may suppress tumor cell proliferation. While both immune and mRNA expression of HIF-1 $\alpha$  decreased in low dose ozone, its effect on the vascular system remains unclear.

#### APPLICATION AREAS OF THE THESIS RESULTS

TNBC is a common subtype of mammary tumor with a poor prognosis in humans and dogs. It does not respond to hormonal therapy. In dogs, most treatment approaches are performed in combination with surgery and chemotherapy, but there is no standardized treatment protocol. Ozone therapy may be effective in eliminating the hypoxic environment in the tumor microenvironment and limiting tumor proliferation and may be used as an adjunctive therapy in combination with other treatment approaches.

#### ACADEMIC ACTIVITIES

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