



## Developing tumor infiltrating lymphocytes as a future treatment for canine osteosarcoma

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**Introduction to this study:** Immunotherapy based on the use of immune cells known as T lymphocytes found within the patient's tumor has proven to be effective in treating human patients with metastatic melanoma. These tumor infiltrating lymphocytes (TILs) are a mixed population of T cells that target many different proteins producing a broad anti-tumor immune response. Adoptive cell therapy using TILs requires access to fresh tumor tissue so that tumor-specific T cells can be expanded to large numbers and transferred back into the patient (**Fig. 1**). These T cells are expected to seek out and destroy tumor cells that remain in the body following surgery, thus delaying or preventing metastatic disease.

Osteosarcoma (OS) is an aggressive bone tumor that disproportionately affects middle to older aged Greyhounds and other large breed dogs. Current standard of care treatment consists of amputation of the affected limb and follow up chemotherapy to prevent metastatic disease. Despite this,

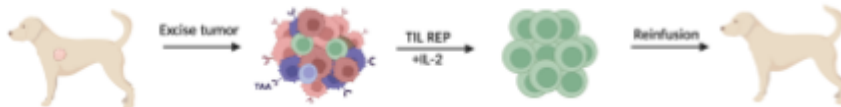


Fig. 1: General schematic of canine TIL therapy.

most patients will succumb to metastatic disease within one year of diagnosis. Importantly, OS has been shown to be “immune responsive” with therapies aimed at stimulating the patient's immune system showing benefit in some patients. Moreover, recent data indicates that patients who have tumors that are enriched in immune cells (suggesting their immune system is attempting to control the tumor) have prolonged survival compared to those with tumors that have minimal immune cell infiltrates. Together, these findings support the hypothesis that adoptive cell therapy with TILs might be beneficial in delaying or preventing metastatic disease when administered after definitive surgery in dogs with OS. However, before this hypothesis can be tested, it is necessary to i) generate a robust method to expand TILs from canine OS lesions and ii) demonstrate that expanded TILs can recognize and kill OS tumor cells.

### Overview of the study

Here, with the generous support of the Greyhound Health Initiative, we propose to leverage the passion and commitment of GREYt owners whose pets are diagnosed with OS and undergo standard of care amputation to begin researching the feasibility of a new cellular immunotherapeutic approach for dogs with osteosarcoma. Owners whose GREYs are diagnosed with OS and elect to undergo amputation will receive a tumor-collection set and pre-paid overnight posting. Fresh tumor samples will be collected within the operating room and shipped overnight to the Mason laboratory at UPENN where they will undergo processing. Tumor infiltrating lymphocytes (TILs) will be subject to different expansion protocols and assessed for tumor reactivity.

### We need your help

- One of the greatest obstacles to rapid advancement of research into cellular therapies to treat tumors is access to fresh tissues from the operating room.
- Unfortunately, Greyhounds are very prone to developing bone cancer (osteosarcoma) and their GREYt owners are amongst the most committed to help find new and more effective ways to treat this

disease. If you have elected for your GREY to undergo amputation for the treatment of his/her osteosarcoma, we are asking you to help us find a better treatment for bone cancer for our dogs.

### **What am I being asked to do?**

- We are asking you to allow a small portion of your dog's tumor (taken from the amputated limb) to be sent to the laboratory of Dr. Nicola Mason at the University of Pennsylvania for early TIL studies.
- If you are interested in having a part of your dog's tumor sent for further studies that may help to combat OS in the future, we will send a tumor-collection packet to your veterinarian. It will contain a tube holding transport liquid that will help to keep the tumor and immune cells alive during overnight shipping and a short consent form.
- When you arrive at the veterinarian on the day of your dog's amputation, you will be asked to sign the consent form to allow a portion of your dog's tumor to be sent to UPenn for further studies.
- After amputation, your veterinarian will take a small piece of tumor from the amputated limb, place it in the transport liquid and ship it overnight to the Mason lab.
- It is important to note that at this early stage, **participation in this study will not provide any treatment for your dog at this time.** Providing consent for sharing a portion of your dog's tumor will not provide a new therapy for your dog but it will help us learn how we might be able to attack these tumors more effectively and might help dogs in the future with this disease. This is a very early pilot study to see if we can grow and analyze the function of immune cells from osteosarcoma tumors. We are hopeful that in the future, because of this work, there may be an option to develop a new treatment for osteosarcoma. This is the very first step and we need GREYt help to get started!