EARLY DETECTION TO TARGET HEMANGIOSARCOMA CELLS IN DOGS:

THE SHINE ON PROJECT

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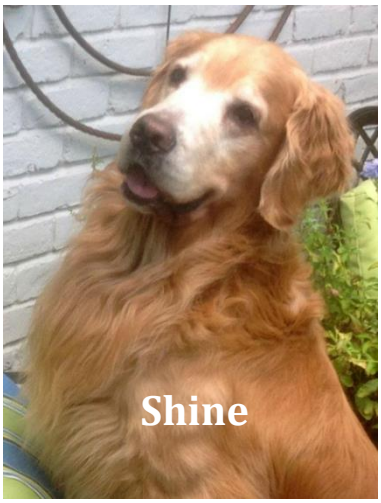
The Shine On project, led by Dr. Modiano at the University of Minnesota College of Veterinary Medicine, is designed to detect hemangiosarcoma cells in the blood at their earliest onset guide treatment with a new, targeted drug. This drug, called eBAT, was developed at the University of Minnesota with the goal to kill cells that are responsible for tumor formation, therefore arresting cancers before they start. This is the first-ever rationally designed approach to prevent cancer in dogs.

What is the project?



Canine hemangiosarcoma is an incurable disease, partly because this insidious cancer almost always grows out of sight without causing pain or obvious symptoms. This means it is diagnosed at a late stage when it is resistant to conventional therapies, and often only after it causes the death of the dog. There have been virtually no gains against the clinical outcome of this disease since chemotherapy was adopted as part of the standard of care forty years ago. However, researchers in Dr. Modiano's group at the University of Minnesota College of Veterinary Medicine have made significant strides to understand the biology and the behavior of this disease over the past decade, and these are the basis of a new approach to improve the outcomes for dogs at risk of hemangiosarcoma.

The goal of this project is to develop effective methods for early detection and for prevention of canine hemangiosarcoma. Dr. Modiano and his team will use a blood test to look for the cells responsible for establishing and maintaining the disease, and then use an experimental drug treatment that attacks those same cells in order to prevent development of the tumor. The scientists believe that reducing the number of dogs that ever get hemangiosarcoma provides the best chance to reduce the death and the suffering from this disease.

The project will have three phases and is expected to continue for at least three years.

Phase-1: test the performance of the blood test in dogs that have been diagnosed with hemangiosarcoma at the University of Minnesota Veterinary Medical Center. Healthy dogs and dogs with other tumors will also be included to define the best parameters for use of this test.

Phase-2: determine if the test can be used to predict when a dog in remission might relapse. This would allow the researchers to consider changes in the management or therapy to extend remission or prevent unexpected, life-threatening bleeding episodes. Phase-2 will re-test dogs enrolled in Phase-1 at the University of Minnesota Veterinary Medical Center.

Phase-3: establish the performance of the test in the early detection setting and implement hemangiosarcoma prevention through eradication of the tumor initiating cells with a novel targeted drug. This phase will be open nationwide, and will include pedigreed Golden Retrievers, Portuguese Water Dogs, and Boxers at risk of developing hemangiosarcoma that do not have evidence of active disease.

Each phase of the project will have specific recruitment dates and eligibility requirements. For information regarding participation, click Shine On Project

At the end of the project, the research team expects to have proof of concept that will inform how this approach can be deployed on a larger scale.

All dogs for Phases 1 & 2 will be recruited from cases being seen at the UMN Veterinary Medical Center. For more information click Shine On Project

Phase 1 is to collect blood samples for the hemangiosarcoma detection test. Phase 2 is to retest the same dogs in Phase 1 for further refinement of the hemangiosarcoma detection test. Blood samples need to be collected from dogs in the categories below, before surgery (Categories 1, 2, 3). It may not be entirely clear which category a dog will fit into until after surgery and diagnosis (for example, a dog scheduled for splenectomy may fit in Category 1 or Category 2), but once there is a definitive diagnosis, owners will be contacted to set retest schedules.

Phase-1 is designed to refine the hemangiosarcoma diagnostic blood test.

Participants must be seen at the University of Minnesota Veterinary Medical Center.

Category-1. Dogs with confirmed hemangiosarcoma. This group will include dogs that have a pathologically confirmed diagnosis of hemangiosarcoma from any anatomical site, at any stage of disease, of any pathological grade, and dogs can be of any breed, age and sex as long as samples are obtained prior to removal of gross tumor burden (primary or recurrent). Dogs in this group will be re-tested every 60 days (see Phase-2 below). About 25 dogs will be recruited into this group over the first 12-18 months of the study.

Category-2. Dogs with confirmed non-neoplastic (non-cancerous) splenic lesions. This group will include dogs that have a pathologically confirmed diagnosis of splenic nodular hyperplasia and/or splenic hematoma and/or splenic hemangioma. The disease can be at any stage and dogs can be of any breed, age and sex as long as samples are obtained prior to splenectomy. Dogs in this group will be re-tested at 6-month intervals. About 25 dogs will be recruited into this group over the first 12-18 months of the study.

Category-3. Dogs with any confirmed cancer other than hemangiosarcoma. This group will include dogs that have a pathologically confirmed diagnosis of cancer other than hemangiosarcoma, specifically malignant lymphoma (any subtype), osteosarcoma, soft tissue sarcoma, or carcinoma. The cancer can be in any anatomical site, at any stage, have any pathological grade, and dogs can be of any breed, age and sex as long as samples are obtained prior to removal of gross tumor burden (primary or recurrent). Dogs in this group will be re-tested at 6-month intervals. At least 25 dogs, and potentially up to 75 dogs will be recruited into this group over the first 12-18 months of the study.

Category-4. Healthy young dogs. This group will include young dogs (under four years of age) with no evidence of any disease recruited from our general practice well-health program and from the hospital staff pet population. At least 25 dogs will be recruited into this group over the first 12-18 months of the study.

Phase-2, check for relapse using hemangiosarcoma blood test.

Participants must be undergoing treatment for hemangiosarcoma at the University of Minnesota Veterinary Medical Center.

Phase-2 is designed to determine the ability of the diagnostic blood test to predict relapse in dogs with hemangiosarcoma that are undergoing treatment. This phase will begin shortly after recruitment for Phase-1 has started, will be limited to dogs recruited as part of Phase-1, and will be completed at the end of year-3 by re-testing dogs in the groups as described above.

Phase-3, Early detection and Prevention investigation.

Dogs nationwide that meet the criteria for participation will be eligible for testing.
Treatment will only be available at the University of Minnesota Veterinary Medical Center.

This phase is designed to determine the usefulness of the diagnostic test for early detection of hemangiosarcoma, and to confirm that the experimental drug can prevent development of the tumor. This phase will start at the end of Phase-1 and will continue through the end of year-3. It will be open to dogs at risk for hemangiosarcoma that meet the criteria below; enrollment will use a proportional formula.

In order to participate in **Phase-3 testing**, a dog must:

- be an AKC-registered Golden Retriever, Portuguese Water Dog, or Boxer. Dogs that are not registered with the AKC will be eligible if they have a pedigree to confirm they are from one of these three breeds.
- be at least 6 years old at the time of enrollment
- be any sex (intact or neutered)
- Owners must agree to submit blood samples for re-testing according to the study guidelines. Each instance of testing will involve submission of blood samples by priority (overnight) courier as described in the Informed Consent Form and in the Detailed Instructions.

Results of testing will only be provided to the licensed veterinarian that is responsible for the care of each participant. The study will cover costs to ship samples, but the family will be responsible for office visits, procedures, and any follow-up diagnostics.

In order to participate in **Phase-3 treatment** a dog must:

- have two successive positive test results
- have no evidence of a detectable tumor (based on imaging studies)
- be able to receive treatment at the University of Minnesota: experimental treatment will be offered only at the Veterinary Medical Center of the University of Minnesota; each cycle will require at least three visits over a 5-day period.

The experimental treatment will be optional, and it will not be offered to dogs that test negative. The costs of treatment will be covered by the study, but the family will be responsible for all other office visits, procedures, and any follow-up diagnostics.

Each phase of the project has specific recruitment dates and eligibility requirements. For additional information regarding participation, click Shine On Project

This information is online at the University of Minnesota, College of Veterinary Medicine Clinical Investigation Center, and is used with permission. For more information about Dr Modiano's research program, visit www.modianolab.org

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