Minimally Invasive Prognostic Tests for Osteosarcoma in Children

Project proposal to identify prognostic markers that inform therapeutic strategies for osteosarcoma (20170056)

Osteosarcoma (OS) is the most common form of malignant bone tumor in children, affecting 400 to 800 kids, teens, and young adults annually. With the best therapies available, about 50-60% of patients that did not have metastasis at diagnosis will survive longer than 10-years. But at present, there are no reliable methods to determine the long-term outlook for any individual patient. Development of accessible tests to predict cancer behavior would be a valuable tool to personalize the type and intensity of treatment in order to reduce therapy-related toxicity, improve quality of life, and enhance the probability of survival.

TECHNOLOGY BACKGROUND

Dogs develop OS at increased rates compared to humans, and thus can serve a useful model for certain aspects of the disease. Jaime Modiano’s lab at the University of Minnesota has studied OS in dogs and developed tumor xenograft models that faithfully recapitulate the disease. A platform was developed based on these models to identify disease signatures from blood samples. This model has been successfully applied to pinpoint diagnostic markers of OS in dogs and is now being employed to isolate prognostic markers of OS in children.

POTENTIAL FOR TRANSLATION TO HUMANS

Using his successes in dogs as proof-of-concept and a guide, Dr. Modiano is applying this platform to learn more about OS in humans. Translating the xenograft models for use with human tumors has the potential to yield biomarkers that will inform cancer behavior and relapse on a patient-by-patient basis. This type of precision medicine may not only save lives, but also money, effort and physical pain expended on inadequate or unnecessary treatments.

PROPOSED PROJECT SUMMARY

Funds will enable the identification of prognostic markers of osteosarcoma in children using approaches that have been previously validated in dogs. This project will use xenograft models (in mice), apply a proprietary method for biomarker identification, and employ machine learning algorithms to create signatures indicative of tumor identity and behavior. The genetic signatures will be derived from exosomes released into the bloodstream, which can be captured by a simple blood sample. This method allows for precise identification of biomarkers that are intrinsic to the tumor, as well as those that are associated with the patient’s response. Prognostic signatures will be validated using serial blood samples obtained at diagnosis and during treatment of patients with known outcomes.

UNIQUELY POSITIONED TO SUCCEED

Osteosarcoma is a rare disease, which can hinder research progress. However, the University is at the leading edge of OS research. Not only is the U of M home to the Biology of Osteosarcoma (BOOST) Registry and Biobank, but it also houses the only NCI-funded Children’s Oncology Group phase 1 program in Minnesota. As a hub of expertise in OS, the University of Minnesota is well equipped to support this work. Furthermore, Dr. Modiano’s group specifically has developed intellectual property around the proposed platform of biomarker discovery, which is able to reliably measure mRNA signatures from blood samples.

FUTURE ADVANCEMENTS

Dependent on the successful completion of this project, the next anticipated development step would be to validate the findings in patient samples from the Children’s Oncology Group (COG). Subsequently, the technology could be licensed to industrial partners for further validation and development as an FDA approved diagnostic for wide-spread, clinical use, and as a platform for additional biomarker discovery.

Strategically Aimed Objective
Identify prognostic markers indicative of the identity and behavior of osteosarcoma tumors that can be obtained using minimally invasive procedures and inform treatment.

Primary Inventors
Jaime Modiano, VMD, PhD
Milcah Scott, BS
John Garbe, PhD

Status
Feasibility demonstrated in a mammalian species (dog)

Requested Funds
$300,000 - $350,000

Potential Risks and Mitigation
While multiple experimental approaches increases the chance of success, there is never a guarantee. In the event that the objectives are not met, this work will still yield vital information on the best path forward to further understand the pathology and treatment of osteosarcoma.

Contact
BJ Haun
Technology Licensing Officer
haunx003@umn.edu