01759: Targeting Multipotency to Arrest Hemangiosarcoma Progression and Improve Outcomes

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Abstract: Hemangiosarcoma is a rapidly fatal disease. The lifetime risk is alarmingly high for some breeds like Golden Retrievers (~20% will die of this disease) and Portuguese Water Dogs (~15% will die of this disease). Furthermore, the risk of hemangiosarcoma is not limited to a single breed. In fact so many dogs are at risk to develop hemangiosarcoma that 40 Breed Clubs designated it as a research priority for 2012. Despite considerable efforts to find effective treatments, the outcome for dogs with hemangiosarcoma has changed very little over the past 30 years. We believe this is because our understanding of this disease is still rudimentary, but that is changing. Recent evidence suggests hemangiosarcoma conforms to the "cancer stem cell" model, where a defined subset of cells is responsible for initiating and maintaining the tumor. These cells are resistant to conventional therapies and they also are very adaptable, being able to survive in a variety of niches. In the case of hemangiosarcoma, the cancer stem cells also retain or acquire the potential to differentiate along several different lineages. For this project, we will use this property against the tumor by modulating factors that support the self-renewal of the stem cell compartment and by inducing their terminal differentiation along alternate pathways that have reduced malignant potential. We propose that disrupting the interactions between hemangiosarcoma cancer stem cells and their microenvironment will enhance the sensitivity of these cells to conventional and targeted therapies and improve the outcomes of dogs with this disease.

Cash: $5,000.00 Commitment

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