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Targeting the EphA2 Receptor Tyrosine Kinases in Melanoma Cancer, both in Humans and Dogs

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Abstract : Background: Melanoma is the most lethal type of malignant skin cancer in humans and dogs since it spreads rapidly throughout the body. Despite significant advances in treatment, cancer at an advanced stage has a poor prognosis. Hence, more effective treatments are needed to enhance outcomes with fewer side effects. Erythropoietin-producing hepatocellular receptors are the largest family of receptor tyrosine kinases and are divided into two subfamilies, EphA and EphB, both of which play a significant role in disease, especially cancer. Due to their association with proliferation and invasion in many aggressive types of cancer, Eph receptor tyrosine kinases (Eph RTKs) are promising cancer therapy molecules. Because these receptors have not been studied in canine melanoma, we investigated how EphA2 influences survival and tumorigenicity of melanoma cells. Methods: Expression of EphA2 protein in canine melanoma cell lines and human melanoma cell line was evaluated by Western blot. Melanoma cells were transduced with lentiviral particles encoding Eph-targeting shRNAs or non-silencing shRNAs (control) for silencing the expression of EphA2 receptor, and silencing was confirmed by Western blotting and immunofluorescence. The effect of siRNA treatment on cellular proliferation, colony formation, tumorsphere assay, invasion was analyzed by Resazurin assay Matrigel invasion assay, respectively. Results: Expression of EphA2 was detected in canine and human melanoma cell lines. Moreover, stably silencing EphA2 by specific shRNAs significantly and consistently decreased the expression of EphA2 protein in both human and canine melanoma cells. Proliferation, colony formation, tumorsphere and invasion of melanoma cells were significantly decreased in EphA2 siRNA-treated cells compared to control. Conclusion: Our data provide the first functional evidence that the EphA2 receptor plays a critical role in the malignant cellular behavior of melanoma in both human and dogs.

Keywords : ephA2, targeting, melanoma, human, canine
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