Creating a Working Model of a Childhood Cancer Pax3:Fkhrl Gene and Alveolar Rhabdomyosarcoma

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Introduction: Transgenic mice can be very valuable tools for understanding human cancers. When mice carrying mutations similar to the mutations in human cancers develop tumors, the first step in validation of the mouse model is to perform histological and immunohistochemical confirmation that the tumor is the expected or desired tumor. Our research deals with an aggressive form of childhood cancer, alveolar rhabdomyosarcoma. About 55-75% of the cases of this cancer share a common trait where the Pax3 gene is fused to three Fkhrl gene by a chromosomal translocation (Sorenson et al. 2002).

Methods: In effort to create a mouse model of alveolar rhabdomyosarcoma, a mouse was designed to express the Pax3:Fkhrl gene by generating a Cre-mediated conditional knock-in of Pax3:Fkhrl and replacing the Pax3 allele with the knock-in. From mice expressing Pax3:Fkhrl that generated tumors, we embedded tumors of the extremities, chest, head and neck in paraffin and sectioned them on a Reichert-Jung microtome at 3.5-4 um. We stained these slides using one of two different techniques. The first method, hematoxylin-eosin staining, dyed the DNA in the cell blue and the cytoplasm pink (Boulet et al. 2004). The other technique utilized immunohistochemistry to highlight the presence of specific muscle protein, Myogenin, within the cells. Using these staining techniques, we examined the sectioned tissue to determine whether it represented alveolar rhabdomyosarcoma.

Results: From 34 tumors, histology of 17 tumors was consistent with alveolar rhabdomyosarcoma. Of those 17 histologically verified tumors, immunohistochemistry for Myogenin was positive in all 17 cases.

Conclusion: Our histological and immunohistochemical identification of tumors from the Pax3:Fkhrl mouse line validates its utility for future for preclinical studies.