

## **Circulating Exosomal microRNA as Biomarkers of Medulloblastoma Progression, Metastasis, and Recurrence**

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Abstract: Medulloblastoma is the most common malignant pediatric brain tumor resulting in the death of nearly one-third of affected children despite aggressive therapy. Metastatic disease and recurrent tumors are highly resistant to therapy thus necessitating earlier detection and identification of novel therapeutic targets. Our primary objective is to noninvasively identify molecular determinants of tumor progression including metastasis and tumor recurrence. Specifically, we seek to determine whether exosomal microRNA isolated from plasma or cerebral spinal fluid (CSF) from medulloblastoma patients can serve as surrogates for tumor tissue for the identification of potentially targetable oncogenic pathways and for monitoring disease status following treatment. Our team proposes a combination of studies that incorporates tumor-specific exosomal microRNA isolation and profiling, as compared to tissue microRNA profiling, through high-resolution genomics and computational analysis using a novel genetically relevant mouse model of sporadic medulloblastoma. We will use this preclinical model to identify tumor-specific exosomal microRNA profiles of medulloblastoma from plasma and CSF during tumor evolution (**Aim 1**) and in the setting of tumor recurrence following radiation therapy (**Aim 2**). We will correlate our results with analogous analyses of tissue and exosomal microRNA profiles of human medulloblastoma including patients with metastatic disease both at initial diagnosis and following standard radiation therapy (**Aim 3**). We predict our studies will aid in identifying metastatic and/or recurrent disease earlier in medulloblastoma patients resulting in earlier treatment initiation, higher treatment intensity, or potential use of novel experimental therapies in order to improve outcomes.