MS-02. TRANSCRIPTOME ANALYSIS IDENTIFIES THE PI3K/AKT/mTOR PATHWAY AS A TARGETABLE PATHWAY IN SCHWANNOMA
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Schwannomas are common benign tumors of the vestibular nerve, or arise from nerves within the spinal canal. Although benign, both Spinal schwannoma (SS) and vestibular schwannoma (VS) cause significant morbidities. The current treatment strategies for VS and SS include surgery or radiation with each treatment option having associated complications and side effects. The transcriptional landscape of schwannoma remains largely unknown.

We interrogated the transcriptome by gene-expression array analysis of 49 schwannomas and seven normal control vestibular nerves to identify tumor-specific gene expression patterns. We identified over 4000 differentially expressed genes between control and schwannoma with network analysis uncovering proliferation and anti-apoptotic pathways previously not implicated in VS. Using several distinct clustering technologies, we could not reproducibly identify VS subtypes or significant differences between sporadic and germline NF2 associated schwannomas suggesting that VS comprises of a highly similar entity. We next performed a transcript analysis comparing VS to SS. Surprisingly; we identified few differential transcripts demonstrating that schwannoma maybe a homogenous entity. Current studies are focused on DNA methylation profiling and genome wide sequencing analysis. To date our group and others have identified that inactivating mutations in NF2 is the most recurrent aberration in schwannoma. The most recurrent activated pathway in schwannoma was over-expression of PI3K/AKT/mTOR signaling pathway, which is directly druggable and we evaluated this pathway for therapeutic targeting. Testing compounds BEZ235 and PKI-587, both novel dual inhibitors of PI3K and mTOR, attenuated tumor growth in a cell line model of schwannoma. Our In vitro findings demonstrated that pharmacological inhibition of the PI3K/AKT/mTOR pathway with next generation compounds lead to decreased cell viability, and increased cell death. Future work is testing these compounds in vivo using relevant cell lines and primary cultures of schwannoma. Our findings implicate that targeting the PI3K/AKT/mTOR pathway may serve as a potential treatment strategy.