

## **NFM-11: pediatric meningiomas are molecularly distinct from adult counterparts [Abstract]**

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**NFM-11. PEDIATRIC MENINGIOMAS ARE MOLECULARLY DISTINCT FROM ADULT COUNTERPARTS**

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In contrast to adulthood, meningiomas are rare among children and adolescents. Although recent papers have characterized the genomics of adult

meningiomas, the molecular profiles of childhood meningiomas have not been elucidated in detail. We analyzed 41 tumor samples from 37 pediatric meningioma patients (female: 17, male: 20; age range: 1-21 years). Atypical meningioma WHO grade II was the most frequent histological subtype (N=14, 38%). Most tumors were located at the convexity (N=18) or the skull base (N=15). Lack of SMO, AKT, KLF4/TRAF7 mutations by Sanger sequencing (n=22) prompted whole genome sequencing of a subset (n=7). All seven cases exhibited bi-allelic inactivation of NF2 (combined large deletion and germline (5/7) or somatic (2/7) base exchanges/frameshifts). Subsequently, tumor samples from all 37 patients were subjected to 450K DNA methylation profiling and targeted DNA sequencing using brain tumor specific gene panel. Loss of chromosome 22 was frequent (N=28, 76%), followed by loss of chromosome 1 (N=12, 32%) and chromosome 18 (N=7, 19%). Moreover, separation into three groups was evident: One encompassing all clear-cell meningiomas with enrichment for SMARCE1 mutations, a second dominated by atypical meningiomas, and a third group composed of benign meningiomas, as well as rare subtypes such as rhabdoid meningiomas. When analyzed with 105 adult tumors, most of pediatric meningiomas (28/37) clustered into a separate methylation group both by unsupervised hierarchical clustering and t-stochastic nearest neighbor embedding (t-SNE). Four recurrences were similar to the primary tumor. These data suggest that pediatric meningiomas are genetically distinct from adult counterparts.