

Gene-13: pediatric meningiomas are characterized by distinct methylation profiles different from adult meningiomas [Abstract]

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GENE-13. PEDIATRIC MENINGIOMAS ARE CHARACTERIZED BY DISTINCT METHYLATION PROFILES DIFFERENT FROM ADULT MENINGIOMAS

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In contrast to adulthood, meningiomas are rare among children and adolescents. However, the molecular relations between both groups have not been elucidated in detail. We have 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* mutation in Sanger sequencing (n=22) prompted whole genome sequencing of a subset (n=7). All cases exhibited bi-allelic mutation of *NF2* (combined large deletion and germline (5/7) or somatic (2/7) base exchanges/frameshifts). Subsequently, representative samples of all 37 patients were subjected to 450K DNA methylation profiling and remaining DNA to sequencing of a brain tumor specific gene panel. Loss of chromosome 22 was frequently detected (N=28, 76%), followed by loss of chromosome 1 (N=12, 32%) and chromosome 18 (N=7, 19%). Moreover, a separation into three groups was evident: One group covering all clear-cell meningiomas with enrichment for *SMARCE1* mutations, a second group dominated by atypical meningiomas, and a third group covering benign WHO grade I meningiomas, as well as rare subtypes such as rhabdoid meningiomas. Compared to adult tumors, the majority of pediatric meningiomas clustered in a separate group both by unsupervised hierarchical and clustering and t-stochastic nearest neighbor embedding. Analysis of four tumor recurrences did not reveal changes compared to the primary tumor. These data suggest that pediatric meningiomas are fundamentally different from adult counterparts.