Familial Tumor Syndrome

Several Familial Tumor Syndromes of the Central Nervous systems are characterized by increased meningioma risk, and the genetics of these syndromes provides mechanistic insight into sporadic disease. The best defined of these syndromes is neurofibromatosis type 2, which is caused by a mutation in the NF2 gene and has a meningioma incidence of approximately 50%. This finding led to the subsequent discovery that NF2 loss-of-function occurs in up to 60% of sporadic tumors. Other important familial diseases with increased meningioma risk include nevoid basal cell carcinoma syndrome, multiple endocrine neoplasia 1 (MEN1), Cowden syndrome, Werner syndrome, BAP1 tumor predisposition syndrome, Rubinstein Taybi syndrome, and familial meningiomatosis caused by germline mutations in the SMARCB1 and SMARCE1 genes. For each of these syndromes, the diagnostic criteria, incidence in the population, and frequency of meningioma are presented to review the relevant clinical information for these conditions. The genetic mutations, molecular pathway derangements, and relationship to sporadic disease for each syndrome are described in detail to identify targets for further investigation. Familial syndromes characterized by meningiomas often affect genes and pathways that are also implicated in a subset of sporadic cases, suggesting key molecular targets for therapeutic intervention. Further studies are needed to resolve the functional relevance of specific genes whose significance in sporadic disease remains to be elucidated [1)].

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Kerr K, Qualmann K, Esquenazi Y, Hagan J, Kim DH. Familial Syndromes Involving Meningiomas Provide Mechanistic Insight Into Sporadic Disease. Neurosurgery. 2018 Dec 1;83(6):1107-1118. doi: 10.1093/neuros/nyy121. PubMed PMID: 29660026; PubMed Central PMCID: PMC6235681.