Medulloblastoma subgroups

While molecular subgrouping has revolutionized medulloblastoma classification, the extent of heterogeneity within subgroups is unknown.

The application of integrative genomics to an extensive cohort of clinical samples derived from a single childhood cancer entity revealed a series of cancer genes and biologically relevant subtype diversity that represent attractive therapeutic targets for the treatment of patients with medulloblastoma.

Similarity network fusion (SNF) applied to genome-wide DNA methylation and gene expression data across 763 primary samples identifies very homogeneous clusters of patients, supporting the presence of medulloblastoma subtypes. After integration of somatic copy-number alterations, and clinical features specific to each cluster, we identify 12 different subtypes of medulloblastoma. Integrative analysis using SNF further delineates group 3 from group 4 medulloblastoma, which is not as readily apparent through analyses of individual data types. Two clear subtypes of infants with Sonic Hedgehog medulloblastoma with disparate outcomes and biology are identified. Medulloblastoma subtypes identified through integrative clustering have important implications for stratification of future clinical trials [1)].

Medulloblastoma in children can be categorized into at least four molecular subgroups, offering the potential for targeted therapeutic approaches to reduce treatment related morbidities.

The data show that medulloblastomas of Group 3/4 differ metabolically as measured using Magnetic resonance spectroscopy (MRS) when compared with SHH molecular subgroups. MRS is a useful and accurate tool to determine medulloblastoma molecular subgroups [2)].

The evidence suggests that each of the four principle subgroups will likely have distinct ‘subsets’ that are biologically and clinically homogeneous as compared to other subsets from within the same subgroup. As the nature and number of subsets for each subgroup are currently unknown, the consensus classification suggests that each subset be named using a Greek letter (α, β, γ, etc.) until such time as they are sufficiently characterized to be named based on their molecular etiology [3)].

1)
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2)

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3)

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