What are the Issues in the Pathological Diagnosis of IDH Mutant Gliomas?

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Pathological diagnosis of tumor is about confirming a tumor, and then assigning 1. Classification; 2. Likely prognostication; and if possible 3. Likely prediction to treatment. Isocitrate dehydrogenase (IDH) mutant gliomas consists of 1p19q non-deleted oligodendrogliomas and 1p19q codeleted oligodendrogliomas. WHO Classification of 2021 assigned IDH-mutant astrocytomas which show CDKN2A/B homozygous deletion as Grade 4. The unresolved issues concerning pathological diagnosis of IDH mutant gliomas include the following:

Temozolomide treatment induces hypermutations in IDH mutant gliomas and yet does not seem to change overall survival. MGMT hypermethylation is said to facilitate hypermutation. Should MGMT, microsatellite instability or hypermutation status or status of mismatch repair genes (MMR) be mandatory tested in IDH mutant gliomas?

Why are some oligodendrogliomas showing TERTp mutation which is usually a molecular criteria for IDHwt glioblastomas?

Oligodendrogliomas are known to be ATRX non-mutated and yet a proportion show Alternative Lengthening of Telomeres (ALT) which is usually reflected by ATRX mutation.

What are the molecular events that lead to anaplastic transformation of oligodendrogliomas?

There are many unanswered questions concerning tumor microenvironment (TME) in IDH mutant gliomas which are usually in an immuno-suppressed state. Some of these information are easily tested in routine pathology laboratories.