Glioma Molecular Markers

The 2016 WHO Update

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Traditional Pathology: Tissue-defined disease
Advances in Sequencing

2001 WHO Hematopathology

- Old Diagnosis: Acute Promyelocytic Leukemia (FAB M3)
- New Diagnosis: Acute myeloid leukemia with t(15;17)
2008 WHO Hematopathology

- New Diagnosis: Therapy-related myeloid neoplasm
2016 WHO Hematopathology

- New Diagnosis: Acute myeloid leukemia with NPM1 mutation
WHO Neuropathology
The 2016 Update

• Seeks to approximate hematopathology naming conventions.
WHO Neuropathology

The 2016 Update

- Integrated diagnoses using, for the first time, molecular parameters in addition to histology to define tumor entities.
- Improves classification, objectivity and treatment.
- Breaks with over 100 years of tradition of defining disease based on light microscopy.
- Genotype trumps histologic phenotype (still need a pathologist for glioma diagnosis and grade).
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- Glioblastoma, IDH-wild type.
- Glioblastoma, IDH-mutant.
- Glioblastoma, NOS.
- Oligodendroglioma, IDH-mutant and 1p/19q-codeleted (even if it looks astrocytic).
- Diffuse astrocytoma, IDH-mutant (even if it looks like an oligodendroglioma).
- Oligoastrocytomas should become vanishingly rare.
All diffusely infiltrating gliomas are grouped together, so for example, diffuse astrocytoma and oligodendroglioma are more closely related than diffuse astrocytoma and pilocytic astrocytoma.
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- Diffuse midline glioma, H3 K27M-mutant.
- WHO Grade IV
- Formerly termed diffuse intrinsic pontine glioma
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- Ependymoma, RELA fusion-positive.
- Upregulates the NF-κB pathway.
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- Primitive Neuroectodermal Tumor (PNET) has been deleted, this tumor is now typically embryonal tumor with multilayered rosettes, C19MC-altered (ETMR).
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- Medulloblastoma, WNT-activated.
- Medulloblastoma, SHH-activated and TP53-mutant.
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- Review of selected cases at Saint John’s.
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• 53F with a left frontal lobe mass.
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- Oligodendroglioma, IDH-mutant and 1p/19q-codeleted.
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- 77M with a left temporal lobe mass.
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- Glioblastoma, IDH wild-type (WHO Grade IV).
- No sequencing needed in patient over 55 years old.
IDH1 R132H IHC Negative (de nova glioblastoma)
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- 32F with a right temporal lobe mass.
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• 32F with a right temporal lobe mass.
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- IDH1 R132H IHC.
- Glioblastoma, IDH-Mutant
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• 35M with a right frontal lobe mass.
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- 35M with a right frontal lobe mass.
- Diffuse astrocytoma, IDH-mutant.
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- 35M with a right frontal lobe mass.
- Anaplastic astrocytoma, IDH-mutant.
IDH Status and Survival in Gliomas
IDH Mutants Create Oncometabolite


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IDH Mutants Create Oncometabolite

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Summary

• Molecular data is guiding pathologic diagnoses, leading to better, more targeted treatment strategies.

• “Setting the stage for progress.”

• Future work: Subdivide the “NOS” categories.
