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EDITORIAL

Brain Pathology

# The WHO classification of tumors of the central nervous system-finally here, and welcome!

The publication of the fifth edition of the WHO classification of tumors of the central nervous system, first online at the end of 2021 and in print at the beginning of 2022, was a much awaited event in the brain tumor community. The remarkable pace of scientific advances that has increasingly refined our diagnostic approach to the various tumor types seems to have impacted the perceived time regarding expectations. The fourth edition was published in 2007 while a "revised" (not technically a new) edition was published in 2016, but so many advances have made the roughly 5 year wait seem a very long time. Fortunately, the timely publication of seven cIMPACT-NOW series, which has developed in the interim [1], and a preliminary summary of the WHO Classification proper [2] have supported diagnostic neuropathology practice to the benefit of the medical community and brain tumor patients. Tumors are organized in 13 major categories reflecting in part prior classifications (Figure 1). However, the effort of incorporating major molecular genetic drivers pioneered in the 4th classification (2016) has progressed and in particular, the input of epigenetic profiling chiefly obtained from methylation arrays has provided another important layer of information.

In the minisymposium published in this issue of Brain Pathology, four practical review articles optimally illustrated and with useful guiding tables provide updates in the classification of major tumor categories relevant to diagnostic neuropathology as specified in the new WHO Classification. Whitfield BT et al., [3] discuss the current classification of diffuse gliomas in adults, including the role of ancillary molecular testing in identifying distinct tumor types (e.g., *EGFR* amplification, *TERT* promoter mutation, and +7/−10 in glioblastoma, IDH wildtype) and grading (homozygous *CDKN2A/B* homozygous deletion in IDH mutant astrocytomas). Bale TA et al., [4] summarize and address the challenges inherent to the expanding group of low-grade glial and glioneuronal tumors that affect children, another category of tumors where molecular diagnostics has played an important role in outlining new types. Kresbach C. et al., [5] cover important advances in the classification of ependymal

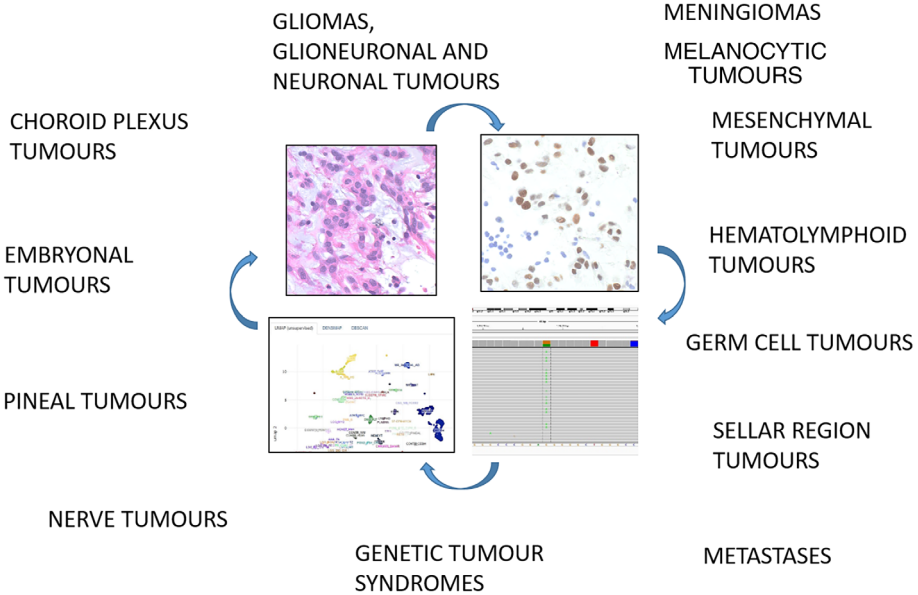


**FIGURE 1** The fifth edition of the WHO classification of Tumors of the central nervous system. Central nervous system tumors are still organized in 13 broad categories. The efforts to cohesively incorporate phenotypic and molecular genetic data in major integrated diagnostic categories that was pioneered in the fourth edition has accelerated. Integration of epigenetic data through methylation profiling in particular has played a novel role and is one of its distinguishing features.

neoplasms, a tumor group that best illustrates the updated model of the WHO classification, merging anatomic, histologic, immunohistochemical, sequencing, and epigenetic data into a powerful classification approach that has significantly improved prognostication. Finally, Meredith DM et al., [6] address the dual topics of embryonal neoplasms and non-meningothelial mesenchymal neoplasms. The latter group has been particularly timely, given that specific tumor types which may have counterparts in the broader field of soft tissue tumors have been teased out from historical CNS groups.

Certainly, this minisymposium does not encompass all tumor groups and updates of the new WHO classification. Important topics such as pediatric high-grade gliomas and meningiomas are covered in other reviews [7] and even complete minisymposiums [8]. Additionally, challenges intrinsic to all molecular-based classifications remain, specifically difficulties in platform and bioinformatic standardization, as well as accessibility of novel diagnostic tests in underdeveloped, and sometimes even developed countries. In the spirit of the prior WHO, "not otherwise specified" options and long diagnostic comments are still available when thorough profiling resulting from large-scale groundbreaking studies are not possible in the individual case. Therefore, creativity in the design of surrogate markers and practical diagnostic approach guidelines should continue to be encouraged at the present time.

## KEYWORDS
CNS, minisymposium, WHO classification of tumours

## CONFLICT OF INTEREST
None.

## AUTHOR CONTRIBUTIONS
Fausto Rodriguez: wrote manuscript and approved in final form.

## DATA AVAILABILITY STATEMENT
None.

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## REFERENCES
1. Louis DN, Aldape K, Brat DJ, Capper D, Ellison DW, Hawkins C, et al. cIMPACT-NOW (the consortium to inform molecular and practical approaches to CNS tumor taxonomy): a new initiative in advancing nervous system tumor classification. Brain Pathol. 2017;27(6):851–2.
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. Neuro Oncol. 2021;23(8):1231–51.
3. Whitfield BT, Huse JT. Classification of adult-type diffuse gliomas: Impact of the World Health Organization 2021 update. Brain Pathol. 2022:e13062. https://doi.org/10.1111/bpa.13062
4. Bale TA, Rosenblum MK. The 2021 WHO Classification of Tumors of the Central Nervous System: An update on pediatric low-grade gliomas and glioneuronal tumors. Brain Pathol. 2022:e13060. https://doi.org/10.1111/bpa.13060
5. Kresbach C, Neyazi S, Schüller U. Updates in the classification of ependymal neoplasms: The 2021 WHO Classification and beyond. Brain Pathol. 2022:e13068. https://doi.org/10.1111/bpa.13068
6. Meredith DM, Alexandrescu S. Embryonal and non-meningothelial mesenchymal tumors of the central nervous system – Advances in diagnosis and prognostication. Brain Pathol. 2022:e13059. https://doi.org/10.1111/bpa.13059
7. Viaene AN, Santi M, Hawkins C. Pediatric glial tumors. Pediatr Dev Pathol. 2022;25(1):46–58.
8. Sahm F, Mawrin C. Introduction to the mini-symposium "molecular neuropathology of meningioma". Brain Pathol. 2022;32(2):e13055.