World Health Organization 2016 Classification of Central Nervous System Tumors

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KEYWORDS

• World Health Organization • Brain tumors • Neuropathology • Classification
• Molecular pathology

KEY POINTS

- The recent update of the World Health Organization (WHO) classification of tumors of the central nervous system represents a paradigm shift.
- Previous iterations of the classification relied solely on morphologic features for classification.
- In the 2016 update, for the first time, the definitions of specific neoplastic entities tumors are not exclusively subgrouped based on morphologic features but now include precise molecularly defined entities.
- This article discusses this paradigm shift, and focuses on the refinements in classification criteria, relations to previous editions, and their implication to neuropathology and neuro-oncology practice.
- The authors distinguish the criteria that were used to determine why molecular changes were included while other recent and important molecular discoveries were seemingly omitted from the classification system.
- The authors further discuss emerging and complementary efforts that aim to better harmonize the rapidly evolving genomic landscape of cancer with routine clinical practice.

INTRODUCTION

The classification of central nervous system (CNS) tumors represents a critical component of the epidemiologic, clinical, and basic-level understanding of a diverse array of neoplasms. The World Health Organization (WHO) has historically played a central role in providing guidance and a standardized set of pathologic criteria for consistent classification of these lesions at different international centers. Given their mission and widespread use, updates to these WHO guidelines require a

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prudent balance of integrating novel insights into brain tumor classification with criteria that are applicable to the international community at large. Historically, brain tumor classification was exclusively carried out based on histomorphologic features of tumors,[1] an approach compatible within the capabilities of most clinical centers throughout the world. Although emerging molecular tests could help provide support for particular diagnoses, it was thought that morphology alone was sufficient to accurately subgroup lesions into entities with common biological drivers and clinical outcomes. The maturing and evolving journey into the molecular era has, however, now dramatically improved the understanding of brain tumors since the previous morphology-centric 2007 WHO Classification of Tumors of the Central Nervous System (2007 CNS WHO). Advances in molecular understanding of brain tumors that have occurred since 2007 have driven the concept that incorporation of clinically relevant molecular markers can provide a biologic basis for classification, that, when integrated with morphologic features, may result in a classification that promotes increase accuracy and precision. As a result, the recent 2016 update of the WHO Classification of Tumors of the Central Nervous System (2016 CNS WHO) represents a revolutionary shift from previous iterations by having, for the first time, tumor classes defined not only by their histomorphologic features, but also by key diagnostic molecular parameters[2,3] (**Fig. 1**). The development of this update presented the unique challenge of embracing a growing number of molecular alterations while acknowledging the current limited accessibility and practicality of a purely molecularly driven classification system. Some of these key changes to the 2016 CNS WHO are summarized in **Table 1**[3] and allow for, where clinically applicable, incorporation of biologically based parameters into superior the classification CNS tumors.[4–7] An example of this can be seen in the emphasis, in the 2007 edition and earlier, in the primary distinction of astrocytic versus oligodendroglial tumors, on the basis of morphology. The current understanding now indicates a close biologic relationship of a subset of diffuse oligodendroglial and astrocytic tumors on the basis on IDH mutations, while other astrocytic tumors are biologically quite distinct.

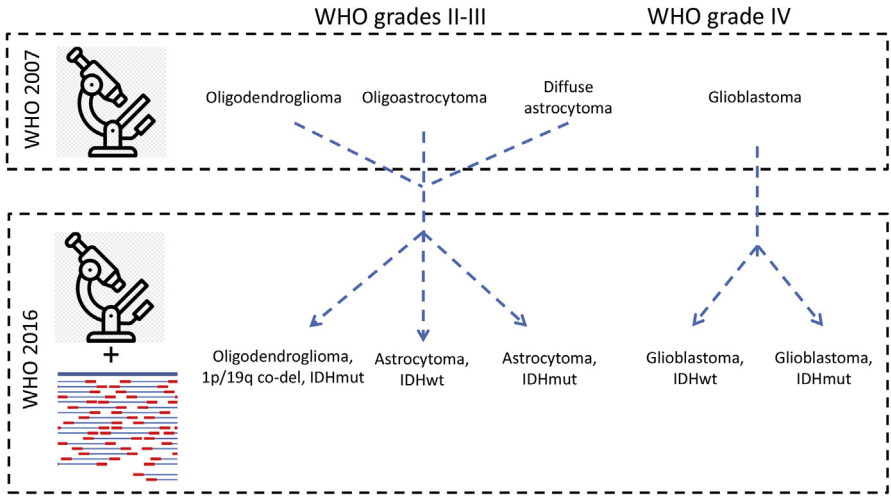

Fig. 1. The 2016 update of the WHO classification of tumors of the central nervous system represents a shift from previous iterations by adding key diagnostic molecular parameters to define tumor classes.