Taxonomy of CNS Tumours;

A Series of Three Short Reviews on the WHO 2016 Classification and Beyond.

Editorial

Pieter Wesseling[1,2], Thomas S Jacques[3]

Affiliations:
[1] Department of Pathology, VU University Medical Center, Amsterdam, The Netherlands
[2] Department of Pathology, Princess Máxima Center for Pediatric Oncology, Utrecht, and University Medical Center Utrecht, The Netherlands
[3] Developmental Biology and Cancer Programme, UCL Great Ormond Street Institute of Child Health and Department of Histopathology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

Correspondence to: Pieter Wesseling, MD, PhD, Dept. of Pathology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

In May 2016, an update of the 4th edition of the World Health Organization (WHO) Classification of Tumours of the Central Nervous System (CNS) was officially released [1]. This revised 4th edition represents a paradigm shift as, for the first time, the definition of multiple CNS tumour entities is now partly based on particular genotypic characteristics. Additionally, compared to the 4th edition (published in 2007), some splitting and lumping of entities occurred because of new insights in the genetic underpinnings of CNS tumours and/or based on more recently published clinico-pathologic studies. As the WHO Classification of CNS tumours is the worldwide accepted standard for the diagnosis of these neoplasms and serves as an important guide for the design of studies monitoring response to therapy and clinical outcome, changes in the classification have important consequences.

Right after the *WHO 2016 Classification* was released, an authoritative review of the most salient changes was published in Acta Neuropathologica [2]. Subsequently, several other reviews discussed changes in the revised classification, some of these aiming for a readership of particular disciplines such as paediatric neuroradiologists [3]. The present series of short reviews in Neuropathology and Applied Neurobiology not only gives a concise overview of what has changed in the *WHO 2016 Classification* that was published over a year ago, but also a) provides schematic representations of what the classification of gliomas (including mixed neuronal-glial neoplasms) and embryonal tumours looks like right now, b) presents tables summarizing the most relevant molecular markers for the diagnosis of CNS tumours as well as tools that can be used to assess these markers, and c) discusses some diagnostic challenges and new perspectives.

Because the most substantial changes were made in the classification of gliomas and of embryonal tumours, these groups are addressed in two separate reviews [4,5]. The changes regarding the remaining CNS tumours, as well as some more recent developments in the pathological diagnosis of these 'miscellaneous' tumours are summarized in a third review [6].

As can be expected, after publication of the WHO 2016 Classification, further elucidation of the molecular underpinnings of CNS tumours continues at a rapid pace; see for examples of important publications regarding gliomas, medulloblastomas and meningiomas [7-9]. Of note, a consortium has now been established to determine how the most important, clinically relevant new information can be rapidly and practically incorporated into CNS tumour classification [10]. It is hoped that this series of short reviews will help the readers to appreciate the enormous progress that has been made with (WHO) classification of CNS tumours and to get a better idea of the opportunities and challenges that the near future will bring in this respect.

References
1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison DW, Figarella-Branger D, Perry A, Reifenberger G, Deimling A von. WHO Classification of Tumours of the Central Nervous System. IARC Press, Lyon 2016
2. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016 ; 131: 803-20
3. Chhabda S, Carney O, D'Arco F, Jacques TS, Mankad K. The 2016 World Health Organization Classification of tumours of the Central Nervous System: what the paediatric neuroradiologist needs to know. Quant Imaging Med Surg 2016; 6: 486-489
4. Wesseling P, Capper D. WHO 2016 classification of gliomas. Neuropathol Appl Neurobiol 2016; in press
5. Jacques T, Hawkins C, Pietsch T. WHO 2016 classification of embryonal CNS tumours. Neuropathol Appl Neurobiol 2016; in preparation
6. Sahm F, Reuss DE, Giannini C. WHO 2016 classification: Changes and advancements in the diagnosis of miscellaneous primary CNS tumours. Neuropathol Appl Neurobiol 2017; in press
7. Korshunov A, Capper D, Reuss D, Schrimpf D, Ryzhova M, Hovestadt V, Sturm D, Meyer J, Jones C, Zheludkova O, Kumirova E, Golanov A, Kool M, Schüller U, Mittelbronn M, Hasselblatt M, Schittenhelm J, Reifenberger G, Herold-Mende C, Lichter P, von Deimling A, Pfister SM, Jones DT. Histologically distinct neuroepithelial tumors with histone 3 G34 mutation are molecularly similar and comprise a single nosologic entity. Acta Neuropathol 2016;131: 137-46
8. Cavalli FMG, Remke M, Rampasek L, Peacock J, Shih DJH, Luu B, Garzia L, Torchia J, Nor C, Morrissy AS, Agnihotri S, Thompson YY, Kuzan-Fischer CM, Farooq H, Isaev K, Daniels C, Cho BK, Kim SK, Wang KC, Lee JY, Grajkowska WA, Perek-Polnik M, Vasiljevic A, Faure-Conter C, Jouvet A, Giannini C, Nageswara Rao AA, Li KKW, Ng HK, Eberhart CG, Pollack IF, Hamilton RL, Gillespie GY, Olson JM, Leary S, Weiss WA, Lach B, Chambless LB, Thompson RC, Cooper MK, Vibhakar R, Hauser P, van Veelen MC, Kros JM, French PJ, Ra YS, Kumabe T, López-Aguilar E, Zitterbart K, Sterba J, Finocchiaro G, Massimino M, Van Meir EG, Osuka S, Shofuda T, Klekner A, Zollo M, Leonard JR, Rubin JB, Jabado N, Albrecht S, Mora J, Van Meter TE, Jung S, Moore AS, Hallahan AR, Chan JA, Tirapelli DPC, Carlotti CG, Fouladi M, Pimentel J, Faria CC, Saad AG, Massimi L, Liau LM, Wheeler H, Nakamura H, Elbabaa SK, Perezpeña-Diazconti M, Chico Ponce de León F, Robinson S, Zapotocky M, Lassaletta A, Huang A, Hawkins CE, Tabori U, Bouffet E, Bartels U, Dirks PB, Rutka JT, Bader GD, Reimand J, Goldenberg A, Ramaswamy V, Taylor MD. Intertumoral Heterogeneity within Medulloblastoma Subgroups. Cancer Cell 2017; 31: 737-754

9. Sahm F, Schrimpf D, Stichel D, Jones DTW, Hielscher T, Schefzyk S, Okonechnikov K, Koelsche C, Reuss DE, Capper D, Sturm D, Wirsching HG, Berghoff AS, Baumgarten P, Kratz A, Huang K, Wefers AK, Hovestadt V, Sill M, Ellis HP, Kurian KM, Okuducu AF, Jungk C, Drueschler K, Schick M, Bewerunge-Hudler M, Mawrin C, Seiz-Rosenhagen M, Ketter R, Simon M, Westphal M, Lamszus K, Becker A, Koch A, Schittenhelm J, Rushing EJ, Collins VP, Brehmer S, Chavez L, Platten M, Hänggi D, Unterberg A, Paulus W, Wick W, Pfister SM, Mittelbronn M, Preusser M, Herold-Mende C, Weller M, von Deimling A. DNA methylation-based classification and grading system for meningioma: a multicentre, retrospective analysis. Lancet Oncol 2017; 18: 682-694

10. Louis DN, Aldape K, Brat DJ, Capper D, Ellison DW, Hawkins C, Paulus W, Perry A, Reifenberger G, Figarella-Branger D, Wesseling P, Batchelor TT, Cairncross JG, Pfister SM, Rutkowski S, Weller M, Wick W, von Deimling A. Announcing cIMPACT-NOW: the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy. Acta Neuropathol 2017; 133: 1-3