Oncology and Translational Medicine
DOI 10.1007/s10330-016-0161-9
June 2016, Vol. 2, No. 3, P97–P98

EDITORIAL

Progress in the molecular pathology of glioma

Changshu Ke (✉)

Department of Pathology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

Changshu Ke, Associate Professor of Pathology, Masters Supervisor, Associate Director of the Department of Pathology, Tongji Hospital, Tongji Medical College of HUST, China. Prof. Ke graduated from The Fourth Military Medical University in 1986 and obtained his Master's degree in the Department of Pathology, PLA General Hospital (Beijing), in 1989. In 1995, he received a fellowship for training in surgical pathology supported by the Hong Kong Division of the International Association of Pathology, which was held at the Department of Anatomical and Cellular Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong. From 1997 to 2001, he studied in the Faculty of Medicine, The Chinese University of Hong Kong, and obtained his doctorate in 2001. He is now in charge of clinical services at the Department of Pathology, Tongji Hospital, Tongji Medical College, HUST. In addition, he teaches the pathology courses for medical students, and overseas medical students and graduate students (neuropathology courses). His research is mainly focused on brain edema, the surgical pathology of CNS tumors, and experimental studies in tumor biology. His current academic activities include: member of the editorial board of the Chinese Journal of Clinical Neurosurgery, member of the Neuropathology Group of the Pathological Society of the Chinese Medical Association, member of the Standing Committee of Onco-pathology Specialty of Chinese Anti-Cancer Association, and vice chairman of the Standing Committee of Onco-pathology Specialty of Hubei Anti-Cancer Association.

Glioma represents the most common primary tumor in the central nervous system (CNS). Along with the increased incidence of brain tumors, there was a 194% increase in brain tumor-related mortality in China in 2008 compared with that of the 1970s [1]. Malignant glioma, as the main pathological subtype of brain tumor, often leads to a fatal outcome because of its invasive nature and resistance to currently available treatments, posing great challenges to public health.

For the past century, the classification and pathological diagnosis of glioma has been primarily based on microscopic morphology, including analysis of hematoxylin and eosin-stained slides, immunohistochemical staining, and ultrastructural features, when compared with the putative cells of histogenesis and their presumed differentiation. According to the World Health Organization (WHO) classification of CNS tumors (2007 edition), glioma can be divided into four grades: Grade I (benign), Grade II (low malignant potential), Grade III (malignancy), and Grade IV (high-grade malignancy). The last two decades of molecular research have provided valuable and encouraging information about tumorigenesis. Along with the development and accumulation of molecular pathological data, it is now possible to define different entities of glioma, and other brain tumors, by integrating both histological and molecular parameters, as introduced in the updated WHO Classification of CNS tumors (2016 edition) [2]. In this new classification, the diffuse gliomas include astrocytic tumors (Grades II & III), oligodendrogliomas (Grades II & III), glioblastoma (Grade IV), as well as diffuse glioma in children, presenting the molecular phenotypes of the IDH-mutant, IDH-wild type, and NOS categories. Other astrocytomas with distinct genetic features usually show a circumscribed tumor margin, lack *IDH* gene alterations, and bear the frequent *BRAF* gene alterations (seen in pilocytic astrocytoma, pleomorphic xanthastrocytoma) and the *TSC1/TSC2* mutation (seen in subependymal giant cellastrocytoma), etc. The previous astrocytoma entities protoplasmic astrocytoma and fabrillary astrocytoma were abandoned because of their overlapping genetic characteristics. The entity "gliomatosis cerebri" has also been removed, which has been considered as one of the most widespread invasive tumor growth patterns consistently observed in many diffuse

✉ Correspondence to: Changshu Ke. Email: kecs@hust.edu.cn

astrocytomas. Glioblastoma can be divided into glioblastoma with the IDH-wild type (*de novo* variant) and glioblastoma with the IDH-mutant (secondary variant). Furthermore, the diagnosis of oligodendroglioma and anaplastic oligodendroglioma now requires screening for *IDH* mutation and 1p/19q co-deletion. In ependymoma and anaplastic ependymoma, only one genetic subtype was accepted: RELA fusion-positive subtype.

There are several intracellular signaling pathways of focus in glioma research, because of their important roles in glioma cell growth and maintenance of malignancy, including the receptor tyrosine kinase/Ras/phosphatidylinositol 3-kinase pathway, TP53 pathway, and RB pathway [3]. In the angiogenesis of gliomas, the related signaling pathways include upregulation of angiopoietin-2 (ANG-2)/tyrosine kinase with immunoglobulin-like and epidermal growth factor homology (TIE-2), promotion of vessel disruption, followed by vascular endothelial growth factor (VEGF) binding to the VEGF receptor (VEGFR), which activates intracellular signaling cascades transduced by the RAS/MAPK and PI3K/AKT pathways, leading to enhanced proliferation of endothelial cells. This detailed information of signaling pathways has now made it possible to select and design molecular targeted therapy of gliomas.

In general, the molecular pathology of gliomas has progressed considerably within the last two decades, highlighting the bright future of the application of molecular technology in clinical and experimental research on gliomas. It is reasonable to hope that the integration of histopathological and molecular parameters in glioma diagnosis and classification may help to reveal more information of the biology of human gliomas and the impact on molecular targeted therapy; meanwhile, this progress is expected to motivate and inspire a new generation of investigators in this field.

References

1. Hou L, Jiang J, Liu B, *et al*. Smoking and adult glioma: a population-based case-control study in China. Neuro Oncol, 2016, 18: 105–113.
2. Louis DN, Perry A, Reifenberger G, *et al.* The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol, 2016, 131: 803–820.
3. Wang H, Xu T, Jiang Y, *et al.* The challenges and the promise of molecular targeted therapy in malignant gliomas. Neoplasia, 2015, 17: 239–255.

DOI 10.1007/s10330-016-0161-9
Cite this article as: Ke CS. Progress in the molecular pathology of glioma. Oncol Transl Med, 2016, 2: 97–98.