Short Communication

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Neuroglia - Characteristics of Immunohistochemical Markers

Maksimovich N Ye, Bon L I*, Bellanage Tharushi Vihanga and Saloni Rajeshkumar Gohil

Grodno State Medical University, Gorkogo St, Grodno, Republic of Belarus

***Corresponding author:** Elizaveta I Bon, Candidate of biological science, Assistant professor of pathophysiology department named D. A. Maslakov, Grodno State Medical University; Grodno State Medical University, 80 Gorky St,230009, Grodno, Belarus

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ABSTRACT

The central nervous system's complexity is illuminated by glia markers—GFAP, OLIG2, Iba1, and S100β—serving as navigational beacons in uncovering the diverse roles and origins of glial cells. These markers are instrumental in distinguishing and exploring specific glial subtypes, offering insights into their implications across a spectrum of neurological conditions. Notably, they play roles in diagnosing traumatic brain injury and CNS tumors, while also revealing associations with inflammatory responses and neurodegenerative diseases. Beyond diagnostics, these markers hold promise for therapeutic strategies. Their nuanced functions provide a deeper understanding of glial cell involvement in brain health and pathology, paving the way for extensive research and potential interventions in diverse neurological disorders.

Keywords: Glia Markers; Brain Injury; GFAP; Olig2; Iba1; S100β

Introduction

Glia markers are particular chemicals that are employed in the central nervous system to identify various glial cell types. These markers include proteins such as S100β for different types of glial cells, Olig2 for oligodendrocytes, Iba1 for microglia, GFAP (glial fibrillary acidic protein) for astrocytes. They are essential to comprehend how glial cells interact and function in normally functioning and pathological neurological systems [1].

Functions of Glia Markers

In the CNS, glia markers function as distinguishing molecules for particular subtypes of glial cells. They are crucial for identifying and locating these cells, which helps to clarify their functions in the pathophysiology, maintenance, and development of the brain. Glia markers also aid in the investigation of glial cell-neuron interactions and their role in a variety of neurological diseases [2].

Types of Glia Markers

Numerous glia markers are employed to distinguish and describe several glial cell subtypes present in CNS. Typical glia markers consist of:

1. GFAP (Glial Fibrillary Acidic Protein): Usually utilized in the context of damage or illness to recognize and define astrocytes [3].

2. Olig2: This marker is essential in research on myelination and demyelinating illnesses and is frequently used for recognizing oligodendrocyte lineage cells.

3. Iba1 (Ionized calcium-binding adapter molecule 1): The primary function of this marker is to recognize and label microglia, the immune cells that dwell within the brain and spinal cord.

4. S100β: Several glial cell types, such as astrocytes and ependymal cells, display this marker. For these cell types, it is frequently employed as a generic marker.

These markers are crucial for comprehending the diverse roles and functions of glial cells in both normal and pathological conditions. They are also important for a number of research projects that try to clarify the intricate relationships that exist among the nervous system [2].

A) GFAP

a) Biomarkers in Traumatic Brain Injury

Found only in the astroglia cytoskeleton, glial fibrillary acidic protein (GFAP) acts as a monomeric intermediate filament protein that is exclusive to the central nervous system. Blood does not normally contain this protein; it is only released in response to damage or cell death. These features imply that GFAP might be the perfect TBI marker. It is secreted during brain injury and could be used as a TBI marker. After monitoring GFAP levels in trauma patients for 21 days, it was discovered that GFAP release was connected to higher ICP and a more severe head injury as determined by CT. As a result, GFAP might have the rare capacity to serve as a marker for both the confirmation of brain injury and any unfavorable consequences that may follow, like death [4]. Additionally, GFAP has strong diagnostic potential in predicting outcome following injury. At a 6-month follow-up assessment, lower Glasgow Outcome Scale (GOS) values were linked to higher GFAP levels. Children's serum levels of GFAP at the admission were greater in patients who died than in patients who recovered, and GFAP levels were considerably larger in children who did not recover well from their injury six months later than in those who did. GFAP was also investigated in children [3].

b) Molecular Genetic Testing

Clinical access to GFAP genetic testing is possible. Certain services restrict their decoding to the 9 GFAP exons of the primary GFAP isoform; however, the discovery of a splice site mutation that causes AxD suggests including some DNA bordering each exon. Similarly, sequencing that region should be recommended in light of the revelation of a potential mutation that causes disease in the occasionally spliced section of intron 7 of the typical GFAP species. Sequence analysis frequently uses blood DNA, however given the finding of a chimera patient who tested positive with buccal DNA but negative with blood, buccal swabs might be a preferable source [5]. Because new cases of GFAP mutations are reported at a rapid pace, it is frequently unclear how well a novel coding change is a disease-causing mutation or a benign polymorphism. Further proof that a specific coding alteration may induce AxD pathology in such cases may come from familial genetic analysis (best achieved by screening both parents), comparing it to reference chromosomes, or assembling of improperly produced GFAP protein in cell cultures. Since that the disease seems to be caused by increase of activity rather than diminished function, in silico assumptions of the impact of a mutant on GFAP arrangement is dubious [5].

B) OLIG2

a) OLIG2 and Brain Tumor Origins

Although recent developments in the study of medulloblastoma have demonstrated that a neural precursor cell is most likely the cell of origin, the prevailing theories on the cell of origin of diffused gliomas in the cerebral cortex of adults have been diverse and wide-ranging. Among the suggested cells of development included the following

1) Dedifferentiated glia

2) Proliferative multipotent adult neural progenitor cells located within the adult subventricular zone

3) Glial-Restricted Precursor Cells (GRP)

4) Oligodendroglial progenitor cells

Even less is known about the cell of genesis for several additional brain cancers, including central neurocytoma and DNET, which also resemble oligodendrocytes morphologically. Our findings add to the increasing amount of evidence that gliomagenic cells are progenitor-like cells. It's feasible that aberrant OLIG2 expression (due to genomic instability or rearrangements, for example) has no bearing on gliomagenesis in terms of lineage [6]. Given the abundance of other developmentally adequate brain progenitor markers found in these tumors, we believe this to be implausible. Among astrocytic, neuronal, primitive lineage tumors, the expression of an oligodendroglial lineage marker like OLIG2 varies and is heterogeneous, which supports the theory that some brain tumors originate from real multipotent neural progenitor cells. The lack or irregular manifestation of OLIG2 in some classes of these cancers may be due to the progenitor cells' capacity to select specific cell fates in adaptation to the brain environment, specific growth regulators, age, or distinct genetic alterations that initiate the process. This theory is undoubtedly supported by the latest finding of stem-like cells inside human brain tumors, which also opens up fascinating new research directions [6]. To confirm a glial component, other markers of oligodendroglial development must be studied in cancers currently classed as neuronal, including DNET or central neurocytoma. Olig2 expression in these tumors shows divergent differentiation throughout these malignancies. Furthermore, the varied expression of Olig2 in several tumor classes (e.g., ependymoma and central neurocytoma) raises the prospect that Olig2 may disclose novel tumor subtypes, the clinical importance of which would require additional research [7].

b) OLIG2 as a Marker of CNS Tumors

Technically speaking, OLIG2 is a reliable marker for easy identification of diffuse gliomas because of its,

1) Widespread expression in most tumor types

2) Location of the nuclear facility

3) Preservation in conventional clinical material encased in paraffin,

4) In neuroectoderm and neuroectodermal malignancies, limited expression occurs.

These characteristics imply that OLIG2 might be a useful marker for both the non-diffuse glioma pilocytic astrocytoma and positive identification or efficient identification of diffuse glioma tumor cells. Our findings also unequivocally demonstrate that OLIG2 level of expression is neither unique nor restricted to diffuse gliomas, oligodendrogliomas, or even gliomas in general. IHC and microarray research revealed highly significant variations in the pattern and expression levels of OLIG2 between diffuse glial tumors and neuronal cancers, primitive neuroectodermal malignancies, and other non-glial malignancies [8]. On the other hand, examination of single tumors in these groups as well as mysterious tumors such dysembryoplastic neuroepithelial tumors (DNET) revealed expression levels that were identical to those found in single diffuse gliomas. This result implies that OLIG2 is more probable to be beneficial when evaluated in context alongside other biomarkers and the histologic nature of its expression, thus ruling out the use of OLIG2 expression individually for the precise diagnosis of glial class malignancies [8].

C) Iba1

Ionized calcium-bound adaptor molecule 1, or Iba1, is a protein that is mostly present in microglias, which are the immune cells that make up CNS. Iba1 is frequently utilized as a marker in both healthy and sick brain tissue to detect and investigate microglia. The brain's immunological responses and the preservation of neuronal health depend on the activation, migration, and phagocytosis of microglia, all of which are regulated by Iba1. Iba1 is widely used by researchers to investigate the role of microglia in a variety of neurological conditions, including brain trauma, neurodegenerative illnesses, and inflammatory responses in the brain [9]. Iba1 level variations usually correlate with changes in microglia activation state. An elevated Iba1 level is frequently associated with increased microglia cell activation or proliferation, which can be a reaction to a number of neurological disorders, including neuroinflammation, brain injury, and neurodegenerative illnesses. The elevated expression of Iba1 could indicate an immunological response in motion or an effort to fix harm to CNS. Increased levels of lba1 can result from conditions such multiple sclerosis, stroke, traumatic brain injury, and several infections or inflammatory conditions of the brain. Decreased activation or a decline in the quantity of microglia within the brain is indicated by a lower level of Iba1 [10]. This drop may indicate a decline in the presence of microglia as a result of a variety of events, including a cessation of inflammation, cell death, or altered immunological activity in neurological diseases. It may also reflect an inhibition of the immune response inside the central nervous system. In addition to this, a drop in Iba1 levels may indicate a change in the microglia state from highly activated to less active, or resting. Evidence suggests that diseases including Alzheimer's, Parkinson's, and Huntington's disease are associated with lower Iba1 levels [10].

D) S100β

S100β, sometimes referred to as S-100 protein subunit beta, is a calcium-binding protein that belongs to the S-100 protein family. S100β, which is mostly present in astrocyte cytoplasm, stimulates neurogenesis and fosters communication between the immunological and neurological systems of the brain. Biological fluids often have minimal or no detectable levels of S100β. The amount of S100β in cerebral fluid has been discovered as a credible biomarker of active neurological injury because high S100β has been identified in a range of neuropathological disorders. However, S100β is not brain distinct and additionally rises in liver, kidney, or GIT injury. According to reports from adult traumatic brain injury studies, the S100β level is rising, becoming more specific in cases of head trauma and reflecting the severity of the injury [11]. Serum levels of S100β are linked to several forms of traumatized intracranial lesions. In addition, S100β has been identified as a biomarker of disruption to the blood-brain barrier. Serum S100β amounts has been linked to a stroke patient's degree of brain damage. Although it comes from CNS as well as is more prevalent in the cerebrospinal fluid following an injury, it is still unclear if elevated serum S100β levels indicate blood barrier malfunction or neuronal tissue damage. An elevated level of S100β was observed during heart surgery, which is thought to be related to cerebral emboli. Following heart surgery and head trauma, there is a clear correlation between the intensity and length of these increased levels and cognitive results [12].

Where S100β is a biomarker for a number of brain illnesses, its levels and distribution in neural tissue have a direct bearing on those disorders. Acute brain damage like stroke and trauma are among them, as are neurodegenerative diseases like Alzheimer's [13], Parkinson's, multiple sclerosis, and amyotrophic lateral sclerosis; inherited or perinatal disorders like spinocerebellar ataxia-1 and down syndrome; psychiatric disorders like mood disorders and schizophrenia; and bowel inflammation. Increasing or giving the protein frequently makes the condition worse, whereas deactivating or removing it frequently makes it better. Various results imply that S100β may be a viable therapeutic target for various disorders, which regardless of where they originate, have similar characteristics associated with neuroinflammation [14].

Conclusion

The intricate roles of glia markers within the central nervous system serve as essential keys in delineating and understanding the diverse functions and origins of glial cells. These markers, such as GFAP, OLIG2, Iba1, and S100β, play pivotal roles in identifying specific glial subtypes and investigating their involvement in various neurological conditions. From acting as diagnostic indicators in traumatic brain injury and CNS tumors to their correlation with inflammatory responses and neurodegenerative diseases, these markers hold immense potential in both clinical diagnostics and therapeutic approaches.

Their distinct functions elucidate the complexities of glial cells' contributions to brain health and pathology, marking a promising avenue for further research and potential therapeutic interventions across a spectrum of neurological disorders.

References

1. Huang H, He W, Tang T, Qiu M (2023) Immunological Markers for Central Nervous System Glia. Neurosci Bul 39(3): 379-392.
2. Roots BI (1981) Comparative studies on glial markers. J Exp Biol 95: 167-180.
3. Raff MC, Fields KL, Hakomori SI, Mirsky R, Pruss RM, et al. (1979) Cell-type-specific markers for distinguishing and studying neurons and the major classes of glial cells in culture. Brain Res 174(2): 283-308.
4. Zwirner J, Lier J, Franke H, Niels Hammer, Jakob Matschke, et al. (2021) GFAP positivity in neurons following traumatic brain injuries. Int J Legal Med 135(6): 2323-2333.
5. Nunes IJG, Recamonde-Mendoza M, Feltes BC (2021) Gene Expression Analysis Platform (GEAP): A highly customizable, fast, versatile and ready-to-use microarray analysis platform. Genet Mol Biol 45(1): e20210077.
6. Wegener A, Deboux C, Bachelin C, Magali Frah, Christophe Kerninon, et al. (2015) Gain of Olig2 function in oligodendrocyte progenitors promotes remyelination. Brain 138(Pt 1): 120-135.
7. Matsumura N, Yokoo H, Mao Y, Yin W, Nakazato Y (2013) Olig2-positive cells in glioneuronal tumors show both glial and neuronal characters: the implication of a common progenitor cell? Neuropathology 33(3): 246-255.
8. Ligon KL, Fancy SP, Franklin RJ, Rowitch DH (2006) Olig gene function in CNS development and disease. Glia 54(1): 1-10.
9. Zhang X, Wang LP, Ziober A, Zhang PJ, Bagg A (2021) Ionized Calcium Binding Adaptor Molecule 1 (IBA1). Am J Clin Pathol 156(1): 86-99.
10. Ohsawa K, Imai Y, Sasaki Y, Kohsaka S (2004) Microglia/macrophage-specific protein Iba1 binds to fimbrin and enhances its actin-bundling activity. J Neurochem 88(4): 844-856.
11. Ryczko D, Hanini Daoud M, Condamine S, Benjamin J B Bréant, Maxime Fougère, et al. (2021) S100β-mediated astroglial control of firing and input processing in layer 5 pyramidal neurons of the mouse visual cortex. J Physiol 599(2): 677-707.
12. Egea-Guerrero JJ, Revuelto-Rey J, Murillo-Cabezas F, M A Muñoz-Sánchez, A Vilches-Arenas, et al. (2012) Accuracy of the S100β protein as a marker of brain damage in traumatic brain injury. Brain Inj 26(1): 76-82.
13. Maksimovich N Ye, Bon EI, Portonenko AM (2023) Cell Death. Morpho-functional Features Biomed J Sci & Tech Res 48(5): 40181-40187.
14. Maksimovich N Ye, Bon E I, and Kohan N V (2023) Mediators of the Nervous System Kinds Characteristic. 48(4): 39975-39984.

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