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Biomarkers of Glioblastoma Multiforme: current update

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Abstract: Glioblastoma multiforme (G.B.M.) represents one of the commonest intracranial tumor associated with very poor prognosis. Despite recent advances in genomics and microneurosurgical techniques, chemotherapy regimens, radiation technology but despite of these mortality and morbidity still remains unacceptable very high. Various markers are utilized to stratify into different category in a desperate attempt to find out suitable therapeutic regimen to promote improved neurological outcome. Authors briefly reviews various biomarkers and utility in management of GBM
Key words: Glioblastoma Multiforme, prognostic factor, biomarkers, outcome, management

Introduction

Glioblastoma multiforme originates from astrocytes.[1-5] The different types are markers are expressed differently in different types and molecular subtypes of GBM.[6-14] However, with the emergence of new molecular biomarkers and its regulation such as epidermal growth factor receptor vIII, O^6-methylguanine-DNA methyltransferase, Isocitrate dehydrogenase mutation.[1-6] Further, glioblastoma specific microRNAs like miR-10b and miR-21 is labelled as promising prognostic values.

As GBM represent highly malignant potential is associated with widespread genetic alterations and protein expression, which is utilize to categorize into various types and may have prognostic significance.

Various m**olecular biomarkers of Glioblastoma multiforme includes:**

1. O^6-methylguanine-DNA methyltransferase (MGMT): It is located on the chromosome number 10q26, the MGMT gene encodes proteins, which are consumed in DNA repair. The methylation of this gene increases the efficacy of an alkylating agent like temozolamide after chemoradiotherapy.

2. Epidermal growth factor receptor (EGFR): Amplification of Epidermal growth factor receptor and the genetic rearrangement of EGFR (EGFRvIII) are considered as

common hallmarks of GBM. GBM has highly proliferative nature controlled by the presence of key growth factors and receptors; it can activate pathways essential for GBM tumor cells to proliferate and its activation causes decreased integrity of G1 to S checkpoint in the cell cycle, leading to excessive proliferation. Often presenting itself in patients with amplified wild-type EGFR, patients with EGFRvIII mutation have significantly lower survival as compared to those without the mutation (1.4 years).[2]

3. Platelet-derived growth factor alpha receptor: It represents a receptor for specific growth factors whose over expression would lead to abnormal and uncontrolled cellular growth. In, GBM may have either A or B types.[3]

4. Isocitrate dehydrogenase: is a protein enzyme coded by genes in chromosome number 2, whose primary function is catalyze the oxidative decarboxylation process within the Krebs cycle.[3]

5. Tumor protein 53: It codes for a widely known tumor suppressor protein, p53. It serves various roles in suppressing tumorigenesis. It is observed at a much higher rate in secondary GBM (90%) compared to cases in primary GBM (30%), and may even remain absent in few primary GBM.[4, 5]

II. MICRORNA as biomarkers (MiRNA): These short RNA non-coding molecules which are often correlated with progression and proliferation of GBM cells. The micron plays a major role in the development and progression of tumor based on its pathway modulatory abilities in oncogenic and tumor suppressor genes. The utilization of miRNA as molecular biomarkers is being reported to yield >90% specificity in detection of GBM itself MiRNA is thought to be an useful biomarker in oncology for cancer detection due to its less-invasive approach, mainly from samples collected from various body fluid and it also allows patient stratification over the usual prognostications.[6,7]

1. miR-21: It is expressed in GBM as well as malignancy of ovary, cervix and lungs. Modulatory ability of miR-21 lead to affect tumor suppressor genes such as PTEN, RECK, FasL and PDCD4.[8,9] It is up regulated in GBM source sample is CSF, blood and urine. It is considered as prognostic marker

2. miR-10b: It is considered as prognostic and predictive marker of GBM. Source sample is CSF, blood and urine. It is considered as prognostic marker

3. miR-15b: These are is down regulated in GBM, and also represents as one of the prognostic and predictive marker.

4. miR-137: these are usually down regulated in GBM and presents another predictive and prognostic GBM marker.[10, 11]

The molecular biomarkers and micro RNA biomarker were originally were designed and routinely utilized as drug targets to develop recent updared therapies. Authors strongly hope biomarker development and advances in therapy in near future may protect humanity against atrocities of the GBM.[12-14]

Conclusion

The aggressiveness nurture of GBM, dictate the urgent need of development of biomarkers for accurate and early diagnosis and to precisely categorization for

responsiveness to various therapeutic chemotherapy and other supportive regimen. The molecular biomarkers and micro RNA biomarker were utilized as drug targets to develop therapies. Authors strongly hope biomarker development and advances in therapy in near future may protect humanity against atrocities of the GBM.

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