Editorial

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miRNA Signature for Glioblastoma Subtyping

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Editorial

Glioblastoma (GBM) is the most malignant IV grade [according to The World Health Organization (WHO)] primary central nervous system tumour with a particularly poor outcome. Median survival without treatment is approximately a year, with radiotherapy and chemotherapy 5-year survival rates are 60% to 80% [1]. Glioblastomas are characterized by high heterogeneity, differentiated and undifferentiated cells with many genetic aberrations. Until now GBM treatment is not personalized and all patients are treated according to common criteria with standard methods: surgical intervention, radiotherapy and chemotherapy with temozolomide (TMZ) [1,2]. Meanwhile, the creation of the genetic profile of gliomas, using genetic, epigenetic and transcriptional methods of analysis, could help more objectively and accurately assess the histopathological diagnosis, also to determine the type of tumour or response to treatment because prognosis of a treatment can vary in different subtypes of tumour [3,4]. Therefore, miRNR profile based GBM classification is a helpful tool for predicting the disease and for choosing more effective treatment to increase patient survival. Taken together, the above considerations were the motivation for the editorial article “miRNA signature for glioblastoma subtyping” and we believe that this article can provide the interesting points of view for the researchers interested in this topic.

More recently, in 2010 an American scientist Verhaak with colleagues published the article in which they classified GBM into four molecular subtypes according to 840 gene expression profiles: Neural (N) that was typified by the expression of neuron markers (NEFL, GABRA1, SYT1 and SLC12A5), Proneural (PN) – alterations of PDGFRA and point mutations in Isocitrate Dehydrogenase 1 (IDH1), Mesenchymal (MES) – lower NF1 expression levels, and classical (CL) - high level of EGFR amplification [3]. In other studies, all these glioblastoma subtypes were associated with patient survival and response to therapy [3,5,6]. For example, Le Mercier with co-authors used immunohistochemical analysis and classified 100 GBM samples into two subtypes: CL subtype, characterized by EGFR-positive and PDGFRA-negative staining, and PN - characterized by PDGFRA–positive staining. They showed that a significantly longer survival was associated with the PN subtype (10.5 months) compared to CL subtype (5 months, p=0.047). Moreover, authors showed that these two GBM subtypes exhibit different response to radiotherapy and chemotherapy with TMZ. Radiotherapy alone did not improve patient survival while TMZ with radiotherapy significantly improved patient survival with classical GBM subtype (p=0.15 and 0.002, respectively). On the contrary, in proneural subtype, radiotherapy alone statistically improved patient survival while TMZ with radiotherapy exhibited no significant effect (p=0.0014 and 0.51, respectively) [5]. Also, Sandmann et al. revealed the bevacizumab effect on overall survival (OS) for patients with different GBM subtypes. They showed that bevacizumab statistically improved OS for patients with PN IDH1 wild-type tumours (4.3 months, p= 0.002) [6].

In last decade, some studies have revealed the specific effects of miRNA in cancer molecular biology. Micro-RNA is a small single stranded non-coding RNA molecule (containing about 22 nucleotides) that plays an important role in regulation of various cellular processes including carcinogenesis (oncogenic or tumour suppressor function) [7]. Also, with the deepening of the research, there are many studies where miRNA-based diagnosis can be applied to determine the origin of cancer tissue [8], progression of the disease, resistance to therapy or to monitor the therapeutic effect [9] and to classify tumours into subtypes [10]. For example, Li with co-authors used The Cancer Genome Atlas (TCGA) Research Network database and tried to identify significant miRNAs that were associated with patient clinical outcomes in each GBM subtype: PN G-CIMP, PN non-G-CIMP, CL, MES and N [11]. According to 470 miRNA expression profiles that were associated with patient clinical data in 448 primary GBMs, authors revealed that in CL subtype (n=120) the expression of five identified miRNRs: miR-26a, miR-767-3p, miR-153, miR-31 and miR-222 were associated with an increased risk of shorter survival. In N subtype (n=73) with shorter survival was associated miR-222, in PN G-CIMP (n=29): miR- 582, in PN non-G-CIMP (n=85): miR-335, miR-34a, miR-581, miR-21 and in MES (n=141): miR-373, miR-296, miR-191 and miR-602 [11]. Taken together, miRNA-based diagnosis is a useful molecular tool that could help to detect clinically meaningful information from patient samples. Moreover, disease-associated miRNAs are also detectable in blood, both in the cellular fraction and in serum, and the expression profile of these miRNAs could be used as a novel non-invasive biomarker for diagnosis of cancer and for the most effective treatment [12].

In conclusion, treatment methods for patients with GBMs are not adjusted to glioblastoma subtypes yet. However,

studies showed that since miRNAs expression in GBMs is often altered compared to healthy cells, they are particularly suitable for GBM subtyping and could be used to determine the effectiveness of treatment. Moreover, miRNAs circulate in the blood, making it possible to use less invasive methods for diagnosis and prognosis of GBMs. Lastly, miRNR is a sufficiently stable marker.

Conflict of Interest

The researchers were conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions

All authors listed, have made intellectual contribution to the work and approved it for publication.

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