MUNI

COMMENTARY TO HABILITATION THESIS[1]

Although the current WHO classification of some brain tumors, especially gliomas, already considers not only histopathological features but also their molecular characteristics, it still does not allow sufficient sensitivity for determining the prognosis of the disease or prediction of therapeutic response to conventional therapy. In other diagnoses, molecular features have not yet been reflected at all. Although meningiomas WHO II, for example, show very uncertain biological behavior, which cannot be estimated based on standard histopathology. In the context of the current trend of personalized and precision medicine, the lack of sufficiently sensitive and at the same time robust prognostic and predictive biomarkers is one of the reasons for the slow inclusion of targeted drugs in the therapeutic standards for brain malignancies.

In addition, due to the heterogeneity of some brain tumors and their location, the correct diagnosis determination is often limited. Biomarkers circulating in the peripheral blood or, better yet, in the cerebrospinal fluid because of the blood-brain barrier, could be useful diagnostic tools. Cerebrospinal fluid is a body fluid that washes all the structures of the central nervous system and is a reservoir of both waste products and molecules mediating intercellular communication; therefore, it appears to be a suitable source of brain tumors biomarkers, including small non-coding RNAs. Small non-coding RNAs have all the properties to be considered as suitable candidate molecules in this regard. They are not only involved in the control of key cellular processes, and their specific expression profiles have already been associated with most cancers, but they are also highly stable molecules both in body fluids and under normal laboratory conditions. Besides, these molecules are relatively easily regulatable in the tumor and, thus, represent promising therapeutic targets. We have confirmed many of these facts in glioblastoma and other brain tumors and presented the observed results in many scholarly publications in the last ten years; these works are commented in this habilitation thesis. Ten years of research in this field also represents a period during which the knowledge about the importance of small non-coding RNAs in cancer in general has increased exponentially. It has reached a level where efforts to introduce these molecules into routine diagnostic and oncological practice are the next logical step to make the disease management more effective and to prolong the overall survival of cancer patients.

[1][2] Užitný vzor: **Šána J**, Slabý O, Kopková A, Fadrus P. Diagnostická sada pro neinvazivní diagnostiku mozkových nádorů. Úřad průmyslového vlastnictví, Česká republika, Číslo dokumentu 33 336, zapsáno 31.10.2019

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	50	80	20

[1] The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.
[2] Bibliographic record of a published scientific result, which is part of the habilitation thesis.

[2] Sana J, Faltejskova P, Svoboda M, Slaby O. Novel classes of non-coding RNAs and cancer. J Transl Med 2012, 10 103.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	20	80	0

[3] Lakomy R, Fadrus P, Slampa P, Svoboda T, Kren L, Lzicarova E, Belanova R, Sikova I, Poprach A, Schneiderova M, Prochazkova M, **Sana J**, Slaby O, Smrcka M, Vyzula R, Svoboda M. Výsledky multimodální léčby glioblastoma multiforme: Konsekutivní série 86 pacientů diagnostikovaných v letech 2003–2009 [Multimodal treatment of glioblastoma multiforme: results of 86 consecutive patients diagnosed in period 2003-2009]. Klin Onkol 2011, 24 (2) 112-120.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	5	20	0

[4] Lakomy R, Kazda T, Selingerova I, Poprach A, Pospisil P, Belanova R, Fadrus P, Vybihal V, Smrcka M, Jancalek R, Hynkova L, Muckova K, Hendrych M, **Sana J**, Slaby O, Slampa P. Real-World Evidence in Glioblastoma: Stupp's Regimen After a Decade. Front Oncol 2020, 10 840.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	5	15	0

[5] Lakomy R, Kazda T, Selingerova I, Poprach A, Pospisil P, Belanova R, Fadrus P, Smrcka M, Vybihal V, Jancalek R, Kiss I, Muckova K, Hendrych M, Knight A, **Sana J**, Slampa P, Slaby O. Pre-Radiotherapy Progression after Surgery of Newly Diagnosed Glioblastoma: Corroboration of New Prognostic Variable. Diagnostics (Basel) 2020, 10 (9).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	5	15	0

[6] Lakomy R, **Sana J**, Hankeova S, Fadrus P, Kren L, Lzicarova E, Svoboda M, Dolezelova H, Smrcka M, Vyzula R, Michalek J, Hajduch M, Slaby O. MiR-195, miR-196b, miR-181c, miR-21 expression levels and O-6-methylguanine-DNA methyltransferase methylation status are associated with clinical outcome in glioblastoma patients. Cancer Sci 2011, 102 (12) 2186-2190.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
80	10	80	0

[7] Sana J, Radova L, Lakomy R, Kren L, Fadrus P, Smrcka M, Besse A, Nekvindova J, Hermanova M, Jancalek R, Svoboda M, Hajduch M, Slampa P, Vyzula R, Slaby O. Risk Score based on microRNA expression signature is independent prognostic classifier of glioblastoma patients. Carcinogenesis 2014, 35 (12) 2756-2762.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
80	10	90	0

[8] Kazda T, Lakomý R, Pospíšil P, Hynková L, **Šána J**, Fadrus P, Jančálek R, Bartoš R, Belanová R, Slabý O, Šlampa P. Diagnostika, operační a systémová terapie metastáz solidních nádorů. Onkologie 2019, 13 (3) 123-128.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	5	10	0

[9] Sana J, Hajduch M, Michalek J, Vyzula R, Slaby O. MicroRNAs and glioblastoma: roles in core signalling pathways and potential clinical implications. J Cell Mol Med 2011, 15 (8) 1636-1644.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	0	90	0

[10] Kopkova A, **Sana J**, Fadrus P, Slaby O. Cerebrospinal fluid microRNAs as diagnostic biomarkers in brain tumors. Clin Chem Lab Med 2018, 56 (6) 869-879.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	70	50	30

[11] Kopkova A, **Sana J**, Fadrus P, Machackova T, Vecera M, Vybihal V, Juracek J, Vychytilova-Faltejskova P, Smrcka M, Slaby O. MicroRNA isolation and quantification in cerebrospinal fluid: A comparative methodical study. PLoS One 2018, 13 (12) e0208580.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	70	50	30

[12] Kopkova A, **Sana J**, Machackova T, Vecera M, Radova L, Trachtova K, Vybihal V, Smrcka M, Kazda T, Slaby O, Fadrus P. Cerebrospinal Fluid MicroRNA Signatures as Diagnostic Biomarkers in Brain Tumors. Cancers (Basel) 2019, 11 (10).

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	70	50	30

[13] Besse A, **Sana J**, Fadrus P, Slaby O. MicroRNAs involved in chemo- and radioresistance of high-grade gliomas. Tumour Biol 2013, 34 (4) 1969-1978.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	70	10	30

[14] Besse A, **Sana J**, Lakomy R, Kren L, Fadrus P, Smrcka M, Hermanova M, Jancalek R, Reguli S, Lipina R, Svoboda M, Slampa P, Slaby O. MiR-338-5p sensitizes glioblastoma cells to radiation through regulation of genes involved in DNA damage response. Tumour Biol 2016, 37 (6) 7719-7727.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	70	10	30

[15] Ondracek J, Fadrus P, **Sana J**, Besse A, Loja T, Vecera M, Radova L, Smrcka M, Slampa P, Slaby O. Global MicroRNA Expression Profiling Identifies Unique MicroRNA Pattern of Radioresistant Glioblastoma Cells. Anticancer Res 2017, 37 (3) 1099-1104.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	70	20	30

[16] Kleinova R, Slaby O, **Sana J**. Význam mikroRNA u glioblastomových kmenových buněk [The Relevance of MicroRNAs in Glioblastoma Stem Cells]. Klin Onkol 2015, 28 (5) 338-344.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
not applicable	70	20	30

[17] Sana J, Busek P, Fadrus P, Besse A, Radova L, Vecera M, Reguli S, Stollinova Sromova L, Hilser M, Lipina R, Lakomy R, Kren L, Smrcka M, Sedo A, Slaby O. Identification of microRNAs differentially expressed in glioblastoma stem-like cells and their association with patient survival. Sci Rep 2018, 8 (1) 2836.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	50	70	30

V Brně 29.3.2021