Small footprint, giant steps – non-coding RNAs in glioblastoma progression

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According to Paget's „seed and soil hypothesis" from year 1889 „metastasis is not due to chance events, but rather that some tumor cells (the "seed") grew preferentially in the microenvironment of select organs (the "soil") and that metastases resulted only when the appropriate seed was implanted in its suitable soil". Extracellular matrix (ECM) that comprises tumor stroma is in this context tumor "soil" which provides vital cues that control cell phenotype and enable the tumor to thrive. Moreover, emerging evidence reveals the importance of the ECM in permitting colonization of secondary tumor sites by creating a specific environmental niche tailored to enhance metastatic cell survival.
Invasion of glioblastoma (GBM) cells involves detachment, migration and invasion processes and is regulated by the complex and multi-step mechanisms requiring cell-cell and cell-ECM interactions. In gliomas, many ECM components are upregulated within both tumor stroma and at advancing edge of tumor. Since the transition from a proliferative epithelial to an invasive mesenchymal phenotype is likely dependent on the microenvironment, changes in ECM components are supposed to modulate invasion of brain tumor, although specific interactions and detailed mechanisms remain elusive. Detachment and migration facilitate invasion of individual tumor cells into surrounding brain tissues even after surgical resection leading to the failure of current therapeutic approaches.
Given the growing evidence of certain small and long-ncRNAs (lncRNAs) as potential regulators of cell fate and insights into their molecular mechanisms which facilitate regulatory functions, broad studies are required to comprehensively understand the mechanisms by which aberrant RNAs contribute to the development and progression of cancer. Nowadays, circRNAs are becoming a new research hotspot in the field of RNA and could be broadly involved in biological processes.
In our studies, we show the involvement of miR-218 and circRNA CLIP2 (circCLIP2) in ECM rearrangement. Performed analyses revealed that miR-218 and circCLIP2 have an impact on the migration and adhesion processes and regulate the gene expression of many factors involved in GBM progression.

Funding: The work was supported by the Polish National Science Center 2017/25/B/NZ3/02173 and 2017/26/E/NZ3/01004 grants.