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Coronin 1C and miR-128A as Potential Diagnostic Biomarkers for Glioblastoma Multiform

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Abstract : Glioblastoma multiform (GBM) is a heterogenous primary brain tumour that kills most affected patients. To the authors best knowledge, despite all research efforts there is no early diagnostic biomarker for GBM. MicroRNAs (miRNAs) are short non-coding RNA molecules which are deregulated in many cancers. The aim of this research was to determine miRNAs with a diagnostic impact and to potentially identify promising therapeutic targets for glioblastoma multiform. In silico analysis was performed to identify deregulated miRNAs with diagnostic relevance for glioblastoma. The expression profiles of the chosen miRNAs were then validated in vitro in the human glioblastoma cell lines A172 and U-87MG. Briefly, RNA extraction was carried out using the Trizol method, whilst miRNA extraction was performed using the mirVANA miRNA isolation kit. Quantitative Real-Time Polymerase Chain Reaction was performed to verify their expression. The presence of five target proteins within the A172 cell line was evaluated by Western blotting. The expression of the CORO1C protein within 32 GBM cases was examined via immunohistochemistry. The miRNAs identified in silico included miR-21-5p, miR-34a and miR-128a. These miRNAs were shown to target deregulated GBM genes, such as CDK6, E2F3, BMI1, JAG1, and CORO1C. miR-34a and miR-128a showed low expression profiles in comparison to a control miR-RNU-44 in both GBM cell lines suggesting tumour suppressor properties. Opposing, miR-21-5p demonstrated greater expression indicating that it could potentially function as an oncomiR. Western blotting revealed expression of all five proteins within the A172 cell line. In silico analysis also suggested that CORO1C is a target of miR-128a and miR-34a. Immunohistochemistry demonstrated that 75% of the GBM cases showed moderate to high expression of CORO1C protein. Greater understanding of the deregulated expression of miR-128a and the upregulation of CORO1C in GBM could potentially lead to the identification of a promising diagnostic biomarker signature for glioblastomas.

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