MEMBRANE-BOUND COMPLEMENT REGULATORY PROTEINS MAY PROVIDE PROGNOSTIC AND PREDICTIVE SIGNIFICANCE IN GLIOBLASTOMA

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Abstract: Brain cancers make up approximately 1.4% of all cancer cases and 2.6% of all cancer deaths in the United States and among these cancers, Gliobastoma multiforme (GBM) is the fastest growing, most aggressive. Ranked fourth among cancer deaths in the middle-aged man, GBM is extremely lethal and treatment is often difficult. In fact, patients with GBM usually have a poor prognosis with survival rates lower than 15 months following diagnosis. GBM are highly malignant and can spread rapidly and invade nearby normal brain tissue, making treatment difficult. Currently, there are no effective long-term, highly effective treatments for this disease. Although standard treatment of GBM has been segmentectomy of the tumor combined with chemotherapy and/or radiation, the mean survival still remains low. The poor efficacy of these treatments and poor survival rates have evoked the interest in the identification of molecular targets against glioblastoma. Membrane-bound complement regulatory proteins (MCRPs) are present on the cell surface of many cancer cells, to restrict the activity of the complement system, thereby preventing complement attack on host tissues. CD46, CD55, and CD59 MCRPs are expressed on cells throughout the body that are exposed to complement to protect them from autologous attack. The functional role of CD55 and CD46 MCRPS in glioblastoma has not been fully investigated. Therefore, we hypothesize that siRNA-mediated silencing of complement membrane regulatory proteins CD55, CD46, and CD59 will inhibit proliferation, angiogenesis, adhesion, and migration in glioblastoma cells. We have carried out pre-validation of these novel set of biomarkers for the assessing the malignant potential of glioblastoma lesions and for early detection. It is hoped that more molecular targeted, immunotherapy- specific, and more effective strategies against GBM can arise from this work.

Key words: Glioblastoma, MCRPs, siRNA, immunotherapy

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