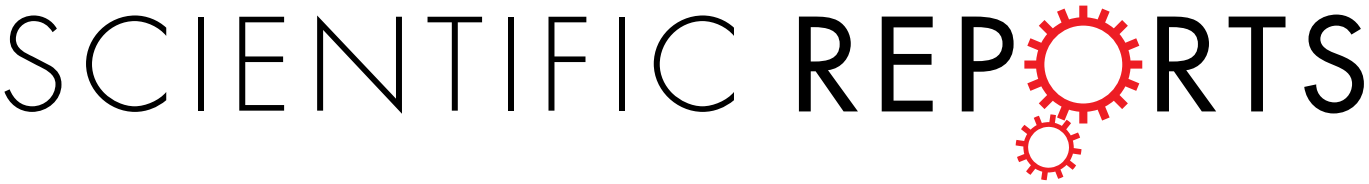

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Microsomal membrane proteome of low grade diffuse astrocytomas: Differentially expressed proteins and candidate surveillance biomarkers

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Diffuse astrocytoma (DA; WHO grade II) is a low-grade, primary brain neoplasm with high potential of recurrence as higher grade malignant form. We have analyzed differentially expressed membrane proteins from these tumors, using high-resolution mass spectrometry. A total of 2803 proteins were identified, 340 of them differentially expressed with minimum of 2 fold change and based on $\geq$2 unique peptides. Bioinformatics analysis of this dataset also revealed important molecular networks and pathways relevant to tumorigenesis, mTOR signaling pathway being a major pathway identified. Comparison of 340 differentially expressed proteins with the transcript data from Grade II diffuse astrocytomas reported earlier, revealed about 190 of the proteins correlate in their trends in expression. Considering progressive and recurrent nature of these tumors, we have mapped the differentially expressed proteins for their secretory potential, integrated the resulting list with similar list of proteins from anaplastic astrocytoma (WHO Grade III) tumors and provide a panel of proteins along with their proteotypic peptides, as a resource that would be useful for investigation as circulatory plasma markers for post-treatment surveillance of DA patients.

Diffuse astrocytoma (WHO grade II) is low-grade primary brain tumor of astrocytes. It is characterized by slow growth with low probability of infiltration into neighboring brain tissue. Though relatively rare[1], it represents 10% of all astrocytic brain tumors with the mean survival time of 6–8 years[2–4]. It typically affects young adults, the standard method for diagnosis is based on histology and treatment includes surgery followed by radiotherapy. The tumors have an inherent potential of progression to malignant anaplastic astrocytoma (WHO Grade III) or secondary glioblastoma (GBM) over time[5]. The most common genetic alteration in diffuse astrocytoma is mutations of the TP53 and IDH1/2 genes in 32% cases, 1p/19q loss and IDH1/2 mutation in 37% cases and only IDH1/2 mutation in 17% cases[6]. Promoter hypermethylation of the DNA repair gene O-6-methylguanine-DNAmethyltransferase (MGMT) and the protocadherin-gamma subfamily A11 (PCDH-gamma-A11) are some of the epigenetic alterations[7,8] reported for these tumors. Several differential gene expression studies have been carried out to understand pathogenesis or to distinguish primary and recurrent grade II tumors or to differentiate them from higher grade tumors[9–11]. Malzkorn *et al.* studied profiling of 157

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