

Altered transcriptional regulatory proteins in glioblastoma and YBX1 as a potential regulator of tumor invasion

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SUPPLEMENTARY FILE LEGENDS

Supplementary Table S1:

Number of stromal/immune cell signature proteins present in the proteomics datasets. The stromal and immune cell signatures determined through the application of the ESTIMATE tool to TCGA gene expression data for GBM and other cancers, were taken from the study of *Yoshihara, et al., 2013* (Ref. 11). We used the same set of pooled clinical specimens of different grades of gliomas to isolate membrane and nuclear sub-cellular fractions and profiled proteins in those fractions by mass spectrometry [membrane proteins (Ref. 7-9) or nuclear proteins (present study)]. The membrane and nuclear proteins identified by us from different grades of glioma specimens were separately compared for their overlap with the stromal/immune cell signature genes. A comparison was carried out between these overlapping proteins identified in each grade and the total proteins identified in the respective grades. The comparison was done at protein level, the peptide level as well as at the level of peptide mass spectral signals for the peptides (PSMs). The numbers in the Table correspond to total proteins identified in a sample, total number of peptides for all proteins identified and total number of mass spectrum matches/signals (PSMs) identified for all peptides of all proteins. The numbers given for the nuclear protein dataset for different grades are identical because all those samples were run in one multiplexed mass spectrometry run and the protein identifications are applicable to each of the grades (see Materials and Method section).

Supplementary Table S2:

Non-redundant list of differentially expressed proteins (DEPs) identified in different grades of astrocytomas. The list contains a total of 244 non-redundant DEPs derived from 162 DEPs identified from Grade II, 131 DEPs from Grade III and 147 DEPs from Grade IV GBM. Majority of them (n=207) were identified with ≥ 2 unique peptides and ≥ 1.5 fold change. The number of peptide/PSMs information, molecular function, biological process and cellular localization for each of the proteins identified are shown. The grade-wise quantitation details of DEPs in each grade (Gr II, III and IV) is shown in **Supplementary Tables S3, S4 and S5**,

respectively. Data on mRNA level expression from literature (as mentioned in the Results section) is shown in Columns I, M and Q and supports many protein members being concordant in their expression with corresponding mRNAs. DEPs with transcription regulatory function have been marked in column V.

Supplementary Table S3:

Differentially expressed proteins in Grade II astrocytoma. A total of 162 nuclear proteins (≥ 1.5 fold change) were identified after applying quality control filters as detailed in Methods section. The Table describes the total number of proteins and peptides identified in replicate mass spectrometry runs along with their quantity values.

Supplementary Table S4:

Differentially expressed proteins in Grade III astrocytoma. A total of 131 nuclear proteins (≥ 1.5 fold change) were identified after applying quality control filters as detailed in Methods section. The Table describes the total number of proteins and peptides identified in replicate mass spectrometry runs along with their quantity values.

Supplementary Table S5:

Differentially expressed proteins in Grade IV astrocytoma (GBM). A total of 147 nuclear proteins (≥ 1.5 fold change) were identified after applying quality control filters as detailed in Methods section. The Table describes the total number of proteins and peptides identified in replicate mass spectrometry runs along with their quantity values.

Supplementary Table S6:

Ingenuity Pathway Analysis of the non-redundant list of differentially expressed nuclear proteins (n=244) identified in different grades of astrocytomas. The proteins associated with major canonical pathways (A), molecular and cellular functions (B) and networks and processes (C), are listed with their p-value. The Table shows only top 5 canonical pathways, molecular and cellular functions, and networks.

In (C), proteins present in the dataset mapping to respective networks are shown in bold.

Supplementary Table S7:

Top 5 significant Networks and processes identified in nuclear protein analysis of different grades of astrocytoma when analyzed separately using Ingenuity Pathway Analysis.

Supplementary Table S8:

Proteins identified to be differentially expressed in all the grades studied - Grade II, III and IV. A total of 53 proteins identified were found common to all the grades. This protein subset has been derived from **Supplementary Table S2**.

Supplementary Table S9:

Immunohistochemistry on tissue microarray for six differentially expressed proteins, NUCKS1, SMARCA5, PARP1, PTBP1, HMGB2, and NFIB, identified by quantitative mass spectrometric analysis. Immunohistochemistry was performed using commercially available tissue microarrays (US BioMax) consisting of 4 control subjects, 13 diffuse astrocytomas (Grade II), 11 anaplastic astrocytomas (Grade III), and 27 glioblastoma (Grade IV) patients samples. Scoring criteria used were based on both staining intensities and distributions. Scores 0, +1, +2 and +3 indicate negative, low, medium and strong staining, respectively. The distribution of staining of cancer cells was scored as 0 (less than 5% of cells staining), 1+ (5–30% of cell staining), 2+ (31–60% of cells staining) and 3+ (greater than 60% of cells staining). TMA slides were evaluated independently by two neuropathologists.

Supplementary Table S10:

List of 61 concordant mRNA and protein target entities present in the transcription interaction network and their microRNA regulators. The miRNA interaction were identified, as per pipeline shown in **Figure 5A** and described in the Methods, for mRNA and protein entities present in the transcription network as shown in **Figure 4**. Each of the miRNA-target interaction was supported by at least one PubMed ID.

Supplementary Table S11:

Immunohistochemistry on tissue microarrays of GBM for YBX1 and its interacting proteins, EGFR, MAPK1, CD44, TNC, MMP13 and SOX2 identified by protein-protein network analysis. Immunohistochemistry was performed using in-house prepared tissue microarrays consisting of 4 control subjects and 18 glioblastoma (Grade IV) patient samples. Scoring criteria used were based on both staining intensities and distributions. TMA slides were evaluated independently by two neuropathologists. The distribution of staining of cancer cells was scored as 0 (less than 5% of cells staining), 1+ (5–30% of cell staining), 2+ (31–60% of cells staining) and 3+ (greater than 60% of cells staining). Scores 0, +1, +2 and +3 indicate negative, low, medium and strong staining respectively.

Supplementary Table S12:

List of selected differentially expressed transcription regulatory proteins identified in the study and their role in tumorigenesis.

Gupta et al., 2019. Altered transcriptional regulatory proteins in glioblastoma and YBX1 as a potential regulator of tumor invasion

Supplementary Table 1: Number of stromal/immune cell signature proteins present in the proteomics datasets. The stromal and immune cell signatures determined through the application of the ESTIMATE tool to TCGA gene expression data for GBM and other cancers, were taken from the study of *Yoshihara, et al., 2013* (Ref. 11). We used the same set of pooled clinical specimens of different grades of gliomas to isolate membrane and nuclear sub-cellular fractions and profiled proteins in those fractions by mass spectrometry [membrane proteins (Ref. 7-9) or nuclear proteins (present study)]. The membrane and nuclear proteins identified by us from different grades of glioma specimens were separately compared for their overlap with the stromal/immune cell signature genes. A comparison was carried out between these overlapping proteins identified in each grade and the total proteins identified in the respective grades. The comparison was done at protein level, the peptide level as well as at the level of peptide mass spectral signals for the peptides (PSMs). The numbers in the Table correspond to total proteins identified in a sample, total number of peptides for all proteins identified and total number of mass spectrum matches/signals (PSMs) identified for all peptides of all proteins. The numbers given for the nuclear protein dataset for different grades are identical because all those samples were run in one multiplexed mass spectrometry run and the protein identifications are applicable to each of the grades (see Materials and Method section).

Protein Level			
Specimen - dataset	Total proteins	Stromal Cell Signature proteins	Immune Cell Signature proteins
GBM - Nuclear	743	1	3
GrIII - Nuclear			
GrII - Nuclear			
GBM - Membrane	1834	12	16
GrIII - Membrane	2642	9	19
GrII - Membrane	2803	6	17
Peptide Level			
Specimen - dataset	Total peptides	Stromal Cell Signature peptides	Immune Cell Signature peptides
GBM - Nuclear	2409	1	4
GrIII - Nuclear			
GrII - Nuclear			
GBM - Membrane	7596	34	84
GrIII - Membrane	9393	20	45
GrII - Membrane	9352	20	48
PSM Level			
Specimen - dataset	Total PSMs	Stromal Cell Signature PSMs	Immune Cell Signature PSMs
GBM - Nuclear	5623	19	5
GrIII - Nuclear			
GrII - Nuclear			
GBM - Membrane	21408	44	213
GrIII - Membrane	22991	31	69
GrII - Membrane	23688	35	105

344925834	NP_001230710.1	FAM213A	84293	redox-regulatory protein FAM213A isoform 2 precursor						4	8	2.140							oxidation-reduction process	antioxidant activity	Cytoplasm		
12056465	NP_001427.2	FBL	2091	rRNA 2'-O-methyltransferase fibrillarin	9	16	1.638				6	11	1.662	1.78				Ribonucleoprotein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Ribonucleoprotein	Nucleolus	+	
283135173	NP_001164406.1	FUS	2521	RNA-binding protein FUS isoform 3							3	5	1.486	1.60				RNA binding protein	RNA localization	Nucleocytoplasmic transporter activity	Nucleus	+	
378404908	NP_001243728.1	GAPDH	2597	glyceraldehyde-3-phosphate dehydrogenase isoform 2	2	4	2.460			2	4	1.875						Enzyme: Dehydrogenase	Metabolism,Energy pathways	Catalytic activity	Cytoplasm		
9506713	NP_061856.1	GAR1	54433	H1ACA ribonucleoprotein complex subunit 1						3	6	1.616	1.49					Enzyme: Reductase	Regulation of nucleobase, nucleoside and nucleic acid metabolism	Ribonucleoprotein	Nucleolus	+	
4503979	NP_002046.1	GFAP	2670	glial fibrillary acidic protein isoform 1	17	25	3.054	4.91	16	23	2.078	5.25	14	21	1.940	1.40		Structural protein	Cell growth and/or maintenance	Structural molecule activity	Cytoplasm		
4885281	NP_005282.1	GLUD1	2746	glutamate dehydrogenase 1, mitochondrial precursor	4	5	2.417											Enzyme: Dehydrogenase	Metabolism,Energy pathways	Catalytic activity	Mitochondrion		
40556376	NP_115958.2	GLYR1	84656	putative oxidoreductase GLYR1						2	3	1.507						Enzyme: Dehydrogenase	Metabolism,Energy pathways	Catalytic activity	Nucleus		
10567816	NP_066268.1	GNAO1	2775	guanine nucleotide-binding protein G(o) subunit alpha isoform a	3	3	1.563	0.46					4	5	0.626	0.16		G protein	Cell communication,Signal transduction	GTPase activity	Membrane		
54114974	NP_444292.1	GNG2	54331	guanine nucleotide-binding protein G12(G13)/G12(G13) subunit gamma-2 precursor									2	3	0.425	0.40		G protein	Cell communication,Signal transduction	GTPase activity	Membrane		
387598076	NP_001248376.1	GPM6A	2823	neuronal membrane glycoprotein M6-a isoform 2	3	3	1.759	0.77					2	2	0.484	0.45		Integral membrane protein	Neurogenesis	Ion channel activity	Membrane		
4885371	NP_005309.1	H1FO	3005	histone H1.0	4	30	1.713			5	35	2.249						DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
5174449	NP_006017.1	H1FX	8971	histone H1x	4	13	1.653			4	17	2.438		4	16	1.889	1.55		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
4504253	NP_002096.1	H2AFX	3014	histone H2AX	2	2	0.431											DNA binding protein	DNA repair	DNA binding	Nucleus	+	
20336748	NP_613075.1	H2AFY	9555	core histone macro-H2A.1 isoform 1									7	11	3.786	1.49		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
4504255	NP_002097.1	H2AFZ	3015	histone H2AZ	2	6	1.998			2	5	1.561		2	6	2.701	1.64		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
117168248	NP_057479.2	HACD3	51495	very-long-chain (3R)-hydroxyl-CoA dehydratase 3	2	2	2.053											-	-	-	Endoplasmic reticulum		
4504347	NP_000549.1	HBA1	3039	hemoglobin subunit alpha	3	14	2.181	1.65										Transport/cargo protein	Transport	Transporter activity	Cytoplasm		
4504349	NP_000509.1	HB	3043	hemoglobin subunit beta	11	39	2.147	1.53										Transport/cargo protein	Transport	Transporter activity	Extracellular		
4885373	NP_005316.1	HIST1H1A	3024	histone H1.1						3	4	3.136						DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
4885381	NP_005313.1	HIST1H1B	3009	histone H1.5	7	27	2.815	0.73	8	27	2.788		7	18	4.726	13.30		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
4885375	NP_005310.1	HIST1H1C	3006	histone H1.2	3	9	3.478	1.44	3	10	4.044	2.06	3	10	3.483	2.65		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
4885377	NP_005311.1	HIST1H1D	3007	histone H1.3	1	2	2.183			2	4	4.208		2	4	7.321	3.60		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
4885379	NP_005312.1	HIST1H1E	3008	histone H1.4						2	7	2.002	1.81	2	8	1.811	1.89		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
10800144	NP_066544.1	HIST1H2AJ	8331	histone cluster 1, H2aj	1	6	3.829			1	5	2.115		1	7	4.403	1.38		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
10800140	NP_066406.1	HIST1H2BB	3018	histone H2B type 1-B	2	3	3.463			2	3	1.755		2	3	2.666	2.59		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
10800138	NP_066407.1	HIST1H2BD	3017	histone H2B type 1-D	2	5	2.654			1	4	1.553		2	5	2.499	1.39		DNA binding protein	Chromosome organization and biogenesis (sensu Eukarya)	DNA binding	Nucleus	+
4504313	NP_003535.1	HIST1H4B	8366	histone H4	6	19	3.717			6	25	2.142	1.33	6	27	3.327	3.79		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+
751368126	NP_001291434.1	HMG20A	10363	high mobility group protein 20A isoform a	2	2	0.404			2	2	0.546						Transcription regulatory protein	Regulation of nucleobase, nucleoside and nucleic acid metabolism	Transcription regulator activity	Nucleus	+	
22208967	NP_665906.1	HMG1A	3159	high mobility group protein 1/HMG-Y isoform a						3	13	2.201						DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
4504425	NP_002119.1	HMG1B	3146	high mobility group protein B1	5	16	3.679	1.41	5	16	2.634	1.52	5	16	3.346	1.56		DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleus	+	
194688133	NP_001124160.1	HMG1C	3148	high mobility group protein B2	5	8	1.959	1.64	5	7	2.729	2.35	5	7	3.890	3.31		Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	+	
48255833	NP_004956.5	HMG1N	3150	non-histone chromosomal protein HMG-14									4	9	1.940	1.48		Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	+	
10635240	NP_006344.1	HMG1D	10473	high mobility group nucleosome-binding domain-containing protein 4						1	2	1.757	1.28					Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	+	
5803036	NP_006796.1	HNRNPA0	10949	heterogeneous nuclear ribonucleoprotein A0	4	7	0.549						4	7	0.209	1.39		Ribonucleoprotein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding	Nucleus	+	
4504445	NP_002127.1	HNRNPA1	3178	heterogeneous nuclear ribonucleoprotein A1 isoform a	7	16	0.287						7	16	0.165	1.52		RNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding	Nucleus	+	
14043072	NP_112533.1	HNRNPA2B1	3181	heterogeneous nuclear ribonucleoproteins A2/B1 isoform B1	14	36	0.226			11	28	0.649	1.37	12	29	0.173	1.39		RNA binding protein, Ribonucleoprotein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding, Transcription factor binding	Nucleus	+
34740329	NP_919223.1	HNRNPA3	220988	heterogeneous nuclear ribonucleoprotein A3	10	29	0.278			10	31	0.613		10	26	0.148			Ribonucleoprotein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding	Nucleus	+
5595921	NP_004490.2	HNRNPAB	3182	heterogeneous nuclear ribonucleoprotein A/B isoform b	4	11	0.353						3	9	0.146	2.03		Ribonucleoprotein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	MRNA binding	Nucleolus	+	
117190174	NP_004491.2	HNRNPC	3183	heterogeneous nuclear ribonucleoproteins C1/C2 isoform b	12	35	0.452	1.30					13	40	0.383	2.98		RNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding	Nucleus	+	

5032179	NP_005753.1	TRIM28	10155	transcription intermediary factor 1-beta						3	3	0.523	1.28				Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	*				
733606247	NP_001290046.1	TUBA1C	84790	tubulin alpha-1C chain isoform b									4	7	0.556	6.50	Cytoskeletal protein	Cell growth and/or maintenance	Structural constituent of cytoskeleton	Cytoplasm					
28788768	NP_821080.1	TUBB2B	347733	tubulin beta-2B chain						2	5	0.537	1.47	2	4	0.404	1.74	Cytoskeletal protein	Cell growth and/or maintenance	Structural constituent of cytoskeleton	Cytoplasm				
60279268	NP_001012496.1	UZAF2	11338	splicing factor UZAF 65 kDa subunit isoform b										3	6	1.662	1.41	RNA binding protein	RNA metabolism	Spliceosomal catalysis	Nucleus	*			
122937227	NP_001073884.1	UZSURP	23350	U2 snRNP-associated SURP motif-containing protein	2	2	1.489	1.88										RNA binding protein	RNA processing	RNA-binding	Nucleus	*			
601984520	NP_066289.3	UBC	7316	polyubiquitin-C	1	2	2.545											Ubiquitin proteasome system protein	protein metabolism	Ubiquitin-specific protease activity	Cytoplasm				
4759302	NP_004729.1	VAPB	9217	vesicle-associated membrane protein-associated protein B/C isoform 1	2	3	0.657	1.57	2	3	0.442	1.56	1	2	0.505	0.68		Membrane transport protein	transport	Auxiliary transport protein activity	Membrane				
6005942	NP_009057.1	VCP	7415	transitional endoplasmic reticulum ATPase	2	2	0.657											ATPase	Metabolism,Energy pathways	ATPase activity	Nucleolus				
4507879	NP_003365.1	VDAC1	7416	voltage-dependent anion-selective channel protein 1	1	2	1.851		2	3	0.626							Voltage-gated channel	Transport	Voltage-gated ion channel activity	Mitochondrion				
62414289	NP_003371.2	VIM	7431	vimentin	9	14	2.007	2.40						9	14	3.373	5.10		Cytoskeletal protein	Cell growth and/or maintenance	Structural constituent of cytoskeleton	Cytoplasm			
63025214	NP_001017980.1	VMA21	203547	vacuolar ATPase assembly integral membrane protein VMA21					1	2	0.558			1	2	0.549	1.33		Unclassified	vacuolar proton-transporting V-type ATPase complex assembly	Molecular function unknown	Cytoplasm			
7706501	NP_057396.1	WBP11	51729	WW domain-binding protein 11					1	2	1.952								RNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	RNA binding	Nucleus	*		
10863945	NP_066964.1	XRCC5	7520	X-ray repair cross-complementing protein 5	4	7	0.661	1.72											DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA repair protein	Nucleus	*		
34101286	NP_057191.2	ZFR	51663	zinc finger RNA-binding protein	3	3	0.401						4	4	0.671	1.43	4	4	0.552	0.74	Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	*
33946297	NP_892021.1	ZNF326	284695	DBIRD complex subunit ZNF326 isoform 1	2	3	0.512							2	3	0.438			DNA binding protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	DNA binding	Nucleolus	*		
404501455	NP_001258218.1	ZNF512	84450	zinc finger protein 512 isoform d	5	6	1.634						5	7	1.570				Transcription regulatory protein	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	Transcription regulator activity	Nucleus	*		

Supplementary Table S2: Differentially expressed proteins in Grade 4 astrocytoma. A list of 102 unique proteins (at 5% FDR) were identified after applying quality control (see also Methods in Methods section). The table displays the total number of proteins identified in individual experiments along with their quality scores.

Protein Accession	RefSeq ID	Gene Symbol	Gene ID	Protein Name	Coverage	DP Proteins	DP Unique Peptides	DP FDRs	151514	151514 Count	151514 Variability	Maximum Score	# AA	MW (kDa)	Exp. ID	151514	116	115	Peptides Matched	KCov	Probability	# of Sequences	Ion Ratio	Charge	m/z [D]	MW [D]	AM [D]	RT [min]	Final Score	Lab. Score	MS Order	Exp. Number	Section File
G00207	NP_001045.1	SLB	313	serpin family B member 1	23.32	1	10	1	1	10	1.00	7.31	28	45.4	34.0	63	2		1000	0.00	0.00	1	0.00	2.56	528.230	150.022	0.50	45.50	4550	4550	1452	14	010018_0001_0001_0001_0001
G00207	NP_001045.1	SLB	313	serpin family B member 1	23.32	1	10	1	1	10	1.00	7.31	28	45.4	34.0	63	2		1000	0.00	0.00	1	0.00	2.56	528.230	150.022	0.50	45.50	4550	4550	1452	14	010018_0001_0001_0001_0001_0001
G00207	NP_001045.1	SLB	313	serpin family B member 1	23.32	1	10	1	1	10	1.00	7.31	28	45.4	34.0	63	2		1000	0.00	0.00	1	0.00	2.56	528.230	150.022	0.50	45.50	4550	4550	1452	14	010018_0001_0001_0001_0001_0001
G00207	NP_001045.1	SLB	313	serpin family B member 1	23.32	1	10	1	1	10	1.00	7.31	28	45.4	34.0	63	2		1000	0.00	0.00	1	0.00	2.56	528.230	150.022	0.50	45.50	4550	4550	1452	14	010018_0001_0001_0001_0001_0001
G00207	NP_001045.1	SLB	313	serpin family B member 1	23.32	1	10	1	1	10	1.00	7.31	28	45.4	34.0	63	2		1000	0.00	0.00	1	0.00	2.56	528.230	150.022	0.50	45.50	4550	4550	1452	14	010018_0001_0001_0001_0001_0001

Product Code	Product Name	Brand	Category	Material	Dimensions	Weight	Price	Availability	Supplier	Supplier Address	Supplier Phone	Supplier Email	Supplier Website
8077950	HP OFFICEJET PLUS	HP	Printer	HP OfficeJet Plus	425 x 344 x 132	2.1	187.00	In Stock	HP Inc.	151 Street, Fort Collins, CO 80504	970.221.4000	hp.support@hp.com	hp.com
8077950	HP OFFICEJET PLUS	HP	Printer	HP OfficeJet Plus	425 x 344 x 132	2.1	187.00	In Stock	HP Inc.	151 Street, Fort Collins, CO 80504	970.221.4000	hp.support@hp.com	hp.com
8077950	HP OFFICEJET PLUS	HP	Printer	HP OfficeJet Plus	425 x 344 x 132	2.1	187.00	In Stock	HP Inc.	151 Street, Fort Collins, CO 80504	970.221.4000	hp.support@hp.com	hp.com
8077950	HP OFFICEJET PLUS	HP	Printer	HP OfficeJet Plus	425 x 344 x 132	2.1	187.00	In Stock	HP Inc.	151 Street, Fort Collins, CO 80504	970.221.4000	hp.support@hp.com	hp.com
8077950	HP OFFICEJET PLUS	HP	Printer	HP OfficeJet Plus	425 x 344 x 132	2.1	187.00	In Stock	HP Inc.	151 Street, Fort Collins, CO 80504	970.221.4000	hp.support@hp.com	hp.com

ID	Code	Category	Name	Species	Status	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...	Value	Unit	...					
46981	NP_00074.1	NP22	HL68	RNA essential protein 12 (Homo sapiens)	NCBI:NM_001019	10.18	1	0.9113	14.2	4.38	124	14.8	9.10		
46982	NP_00074.1	NP22	HL68	RNA essential protein 12 (Homo sapiens)	NCBI:NM_001019	10.18	1	0.9113	14.2	4.38	124	14.8	9.10

Supplementary Table S6: Ingenuity Pathway Analysis of the non-redundant list of differentially expressed nuclear proteins (n=244) identified in different grades of astrocytomas.

The proteins associated with major canonical pathways (A), molecular and cellular functions (B) and networks and processes (C), are listed with their p-value. The Table shows only top 5 canonical pathways, molecular and cellular functions, and networks. In (C), proteins present in the dataset mapping to respective networks are shown in bold.

A. Canonical pathways

Pathway	Molecules	-log (P-value)	Ratio
Granzyme A Signaling	HIST1H1A, HIST1H1B, HIST1H1C, HIST1H1E, H1FX, HIST1H1D, HMGB2, H1F0	1.48E-11	4.71E-01
Granzyme B Signaling	PRKDC, NUMA1, LMNB2, LMNB1, PARP1	1.32E-06	3.12E-01
EIF2 Signaling	RPS19, RPL22, RPLP2, RPS25, RPS3, PPP1CA, RPL7A, RPL18, RPL31, RPS14	8.07E-05	5.81E-02
DNA Double-Strand Break Repair by Non-Homologous End Joining	PRKDC, XRCC5, PARP1	6.92E-04	2.14E-01
Telomere Extension by Telomerase	HNRNPA1, HNRNPA2B1, XRCC5	8.56E-04	2E-01

B. Molecular and cellular functions

Category	p-value	Molecules
RNA Post-Transcriptional Modification	6.57E-35-1.26E-03	HNRNPL, DDX21, SRSF9, PRPF8, HNRNPA2B1, SFPQ, ELAVL4, DDX17, HNRNPK, ELAVL1, TRA2A, SRSF1, DDX5, THRAP3, U2AF2, RBMX, NOLC1, HNRNPC, CDC5L, FBL, HNRNPA0, RPS19, SNRPA, SON, HNRNPU, KHDRBS1, RBM5, PPIG, DKC1, SYNCRIP, HNRNPD, SNW1, ADAR, HBB, HNRNPM, PTBP1, ALB, ZNF326, FUS, SNRPC, HNRNPA1, CIRBP, SRSF7, PABPN1, RBM8A, SNRNP70, SRSF5, HNRNPH3
Cell Death and Survival	4.42E-12-1.29E-02	CRYAB, THOC2, MBP, TRAP1, CTSG, SFPQ, RSL1D1, HBA1/HBA2, HSPA5, CBX5, LMNB1, ELAVL1, HMGB1, SRSF1, TOP1, LTF, SMPD4, SUB1, VAPB, PPP1CA, PGRMC1, MGST1, PELP1, SON, ATP5A1, LMNA, SNW1, ANXA2, HMGA1, SSRP1, MPO, CD9, SMARCA2, HNRNPA1, H2AFX, TMX1, HNRNPUL2, RTN4, GAPDH, GPM6A, VDAC1, PML,

		MTDH, XRCC5, RBBP4, HIST1H1C, APOE, DEK, NFIX, PRDX5, PRPF8, SNRPE, PPIA, ILF2, TMEM214, DDX17, CD74, HNRNPK, TOP2B, ANXA1, ANXA5, VCP, HNRNPC, NCL, PCBP2, RPS3, BCAP31, DHX9, PRKDC, RPS19, HNRNPU, KHDRBS1, RBM5, TRIM28, GLUD1, HSPD1, MSI2, PSIP1, HBB, PARP1, PLG, ENO1, ALB, APOA1, NFIB, TP53BP1, CYB5A
Cellular Growth and Proliferation	9.35E-12-1.29E-02	HP1BP3, ILF3, PLP1, MBP, CTSG, TRAP1, SFPQ, RSL1D1, HSPA5, LMNB1, ELAVL1, HMGB1, SRSF1, TOP1, DDX5, THRAP3, LTF, PPP1CA, HNRNPA0, SON, PELP1, NUMA1, ATP5A1, DKC1, LMNA, ANXA2, SNW1, HMGA1, ADAR, PTBP1, HNRNPAB, ATP5B, CD9, FUS, SMARCA2, HNRNPA1, RTN4, HIST1H1D, GAPDH, RPS25, VDAC1, PML, ACTG1, XRCC5, RBBP4, PBRM1, DDX21, APOE, PRPF8, TPR, HNRNPA2B1, ILF2, PPIA, HMGB2, CD74, DDX17, H2AFZ, HNRNPK, TOP2B, TRA2A, HNRNPR, ANXA1, HNRNPC, BCAP31, NCL, PURA, RPS19, HNRNPU, KHDRBS1, RBM5, TRIM28, HNRNPD, HSPD1, HNRNPM, PARP1, HIST1H1B, PLG, ENO1, ANXA6, APOA1, H2AFY, CIRBP, NOP2, PSAP, TP53BP1, NFIB, UBC, RPS14
Gene Expression	5.23E-10-1.29E-02	HP1BP3, ILF3, SFPQ, CBX5, ELAVL1, HMGB1, DDX5, TOP1, LTF, THRAP3, SUB1, NOLC1, ALYREF, PELP1, GNG2, SMARCA5, SYNCRIP, LMNA, SNW1, HMGA1, ADAR, SSRP1, MPO, TFAM, BASP1, CD9, SMARCA2, HNRNPA1, BUD31, PABPN1, GAPDH, PML, MTDH, XRCC5, DEK, DDX21, APOE, NFIX, PPIB, PRPF8, TPR, HNRNPA2B1, ILF2, HMGB2, DDX17, RPL7A, H2AFZ, HNRNPK, RBMX, RPS3, PURA, HNRNPC, DHX9, PRKDC, RBM5, MECP2, TRIM28, PSIP1, HBB, PARP1, PLG, HIST1H1B, ENO1, ALB, SNRPC, CIRBP, H2AFY, TP53BP1, NFIB, RPS14
Cellular Development	1.08E-08-1.29E-02	ILF3, MBP, CTSG, SFPQ, RSL1D1, HSPA5, LMNB1, ELAVL1, HMGB1, TOP1, DDX5, LTF, HIST1H4B, ALYREF, FBL, SON, PELP1, NUMA1, SMARCA5, SYNCRIP, ANXA2, SNW1, HMGA1, PTBP1, ATP5B, FUS, CD9, SMARCA2, HNRNPA1, HIST1H1D, GAPDH, FAM213A, GPM6A, RPS25, PML, XRCC5, DEK, DDX21, APOE, PRPF8, HNRNPA2B1, HMGB2, DDX17, CD74, H2AFZ, HNRNPK, TRA2A, RBMX, ANXA1, HSPE1, HNRNPC, NCL, PURA, DHX9, RPS19, HNRNPU, RBM5, TRIM28, HSPD1, PARP1, PLG, ENO1, ALB, ANXA6, APOA1, H2AFY, CIRBP, NFIB, RPS14

C. Networks and processes

Top Functions	Molecules in Network	Score	Focus Molecules
Gene Expression, Cell Death and Survival, Embryonic	ANXA1, CD74, CDC5L, ELAVL1, GSK3, H2AFX, HIST1H1C, HMGA1, HNRNPD, IFN Beta, ILF2, ILF3, LTF, MECP2, MEK, MPO, MSI2, MTDH, NCL, NFIX, NFkB (complex), PI3K (family), PRKDC, Rnr, RPA, RPS14, SNW1, SSRP1, TFAM, THRAP3, TOP1,	43	28

Development	TOP2B, TP53BP1, U2AF2, XRCC5		
RNA Post-Transcriptional Modification, Infectious Diseases, Cellular Development	ANXA2, ANXA5, ANXA6, Cyclin A, Cyclin E, DDX21, DHX9, ERK1/2, FBL, HBB, HNRNPAB, HNRNPC, HNRNPL, HNRNPR, HNRNPU, HSPA5, JINK1/2, KHDRBS1, KHDRBS2, KHDRBS3, MAP2K1/2,p85 (pik3r), PELP1, PLG, PPIA, PPIB, Ras, RSL1D1, SFPQ, SNRNP70, SRSF1, SRSF5, SYNCRIP, TUBA1C, VDAC1	43	28
RNA Post-Transcriptional Modification, Cell Death and Survival, Neurological Disease	Actin, ALYREF, BAZ1B, DDX5, DDX17, ENO1, FUS, GAPDH, Histone h3, Histone h4, HMGB1, HMGB2, HNRNPA1, HNRNPDL, HNRNPH3, HNRNPK, Hsp90, HSPD1, MATR3, MYEF2, MYL12A, NUMA1, P38 MAPK, PCBP1, RBBP4, RBMX, RNA polymerase II, RPS3, SMARCA5, SNRPD3, SRSF9, THOC2, TRAP1, VEGF, ZNF326	43	28
RNA Post-Transcriptional Modification, Molecular Transport, RNA Trafficking	APP, ATXN2, CASC3, CSNK2A1, DDX6, Dynamin, Eif4g, G3BP1, GRB2, HNRNPA2B1, MAGOH, MBP, NME1, NOP58, NTRK3, PABPC1, PABPC4, PABPN1, PAPOLG, PPIA, PPIG, RBM8A, RPL18, RPL36, RPL7A, RPS19, RTN4, SNRPA, STRAP, STXBP1, SUB1, SYNCRIP, SYT1, TPI1, UPF3B	17	15
Dermatological Diseases and Conditions, Developmental Disorder, Hereditary Disorder	ADD2, AGTR1, ARID2, CARD16, CARD17, CASP1, CHD4, CNTN1, DKC1, FBP1, GARI, GPM6A, GSTT2/GSTT2B, Histone h3, HMBOX1, HMGNI,HSPA6, MAFF, NCEH1, NFIB, NHP2, NOP10, PBRM1, PSG5, PTBP2, RGS10, RPL22, SBDS, SMARCA4, SRRM2, TERC, UBC, UBE2H, USP24, WDR1	17	15

Supplementary Table S7: Top 5 significant Networks and processes identified in nuclear protein analysis of different grades of astrocytoma when analyzed separately using Ingenuity Pathway Analysis.

Astrocytoma Grade	Networks and processes
Diffuse astrocytoma (Grade II)	<ol style="list-style-type: none"> 1. RNA Post-Transcriptional Modification, DNA Replication, Recombination, and Repair, Gene Expression 2. Cell Death and Survival, Cellular Growth and Proliferation, DNA Replication, Recombination, and Repair 3. Gene Expression, Cell Death and Survival, Embryonic

	<p>Development</p> <ol style="list-style-type: none"> 4. RNA Post-Transcriptional Modification, Cellular Movement, Hematological Disease 5. Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry
<p>Anaplastic astrocytoma (Grade III)</p>	<ol style="list-style-type: none"> 1. Cell Death and Survival, Cell Morphology, Cellular Assembly and Organization 2. Dermatological Diseases and Conditions, Developmental Disorder, Hereditary Disorder 3. DNA Replication, Recombination, and Repair, Cell Death and Survival, Nervous System Development and Function 4. Cell Cycle, Cellular Development, Connective Tissue Development and Function 5. Embryonic Development, Organ Development, Organ Morphology
<p>Glioblastoma multiforme (Grade IV)</p>	<ol style="list-style-type: none"> 1. RNA Post-Transcriptional Modification, Cell Death and Survival, Cell-To-Cell Signaling and Interaction 2. RNA Post-Transcriptional Modification, Cell Cycle, DNA Replication, Recombination, and Repair 3. Organismal Survival, Nervous System Development and Function, Cellular Development 4. RNA Post-Transcriptional Modification, DNA Replication, Recombination, and Repair, Gene Expression 5. Cell Cycle, Cell Morphology, Cellular Function and Maintenance

Supplementary Table S8: Proteins identified to be differentially expressed in all the grades studied - Grade II, III and IV. A total of 53 proteins identified were found common to all the grades. This protein subset has been derived from **Supplementary Table S2**.

Accession	NP accession	Gene Symbol	Gene id	Protein name	Grade II protein fold change [115/114]	Grade III protein fold change [116/114]	Grade IV protein fold change [117/114]	Molecular class
14043072	NP_112533.1	HNRNPA2B1	3181	heterogeneous nuclear ribonucleoproteins A2/B1 isoform B1	0.226	0.649	0.173	RNA binding protein,Ribonucleoprotein
109240550	NP_001035879.1	PSPC1	55269	paraspeckle component 1	0.261	0.315	0.423	RNA binding protein
34740329	NP_919223.1	HNRNPA3	220988	heterogeneous nuclear ribonucleoprotein A3	0.278	0.613	0.148	Ribonucleoprotein
5730027	NP_006550.1	KHDRBS1	10657	KH domain-containing, RNA-binding, signal transduction-associated protein 1 isoform 1	0.282	0.468	0.277	RNA binding protein
189217895	NP_689901.2	KHDRBS2	202559	KH domain-containing, RNA-binding, signal transduction-associated protein 2	0.282	0.294	0.185	RNA binding protein
5730073	NP_006549.1	KHDRBS3	10656	KH domain-containing, RNA-binding, signal transduction-associated protein 3	0.316	0.657	0.200	RNA binding protein
13676857	NP_068814.2	HSPA2	3306	heat shock-related 70 kDa protein 2	0.322	0.341	0.449	Heat shock protein
5032007	NP_005850.1	PURA	5813	transcriptional activator protein Pur-alpha	0.331	0.594	0.147	Transcription factor
667743700	NP_001288139.1	MYEF2	50804	myelin expression factor 2 isoform b	0.345	0.589	0.303	Transcription regulatory protein
160707950	NP_001104262.1	MECP2	4204	methyl-CpG-binding protein 2 isoform 2	0.359	0.608	0.456	DNA binding protein
68509932	NP_001020263.1	MBP	4155	myelin basic protein isoform 4	0.373	0.404	0.400	Structural protein
664806003	NP_001287744.1	CIRBP	1153	cold-inducible RNA-binding protein isoform 2	0.381	0.434	0.157	RNA binding protein
56118234	NP_859067.2	CENPV	201161	centromere protein V	0.397	0.597	0.582	DNA binding protein
62750354	NP_954659.1	MATR3	9782	matrin-3 isoform a	0.400	0.644	0.375	RNA binding protein
34101286	NP_057191.2	ZFR	51663	zinc finger RNA-binding protein	0.401	0.671	0.592	Transcription regulatory protein
38201710	NP_006377.2	DDX17	10521	probable ATP-dependent RNA helicase DDX17 isoform 1	0.417	0.567	0.535	ATPase,RNA helicase
221316767	NP_001138246.1	ELAVL4	1996	ELAV-like protein 4 isoform 2	0.427	0.450	0.418	RNA binding protein
70167113	NP_001020278.1	ADAR	103	double-stranded RNA-specific adenosine deaminase isoform d	0.448	0.560	0.509	Enzyme: Deaminase
4758138	NP_004387.1	DDX5	1655	probable ATP-dependent RNA helicase DDX5	0.450	0.597	0.552	RNA binding protein
25952118	NP_741960.1	CAMK2A	815	calcium/calmodulin-dependent protein kinase type II subunit alpha isoform 2	0.459	0.357	0.294	Serine/threonine kinase
8923900	NP_061156.1	CMAS	55907	N-acylneuraminate cytidyltransferase	0.481	0.647	0.535	Enzyme: Ligase
109689718	NP_001035937.1	ABHD12	26090	monoacylglycerol lipase ABHD12 isoform a	0.486	0.622	0.654	Integral membrane protein
4758876	NP_004634.1	PABPN1	8106	polyadenylate-binding protein 2	0.488	0.617	0.567	RNA binding protein
68051721	NP_065843.3	NCEH1	57552	neutral cholesterol ester hydrolase 1 isoform b	0.500	0.528	0.590	Unclassified
66346730	NP_001015001.1	CKMT1A	548596	creatine kinase U-type, mitochondrial precursor	0.503	0.444	0.458	Enzyme: Phosphotransferase
157412270	NP_112480.2	HNRNPM	4670	heterogeneous nuclear ribonucleoprotein M isoform b	0.504	0.548	0.674	Ribonucleoprotein
19923653	NP_150091.2	PSIP1	11168	PC4 and SFRS1-interacting protein isoform 2	0.524	0.559	0.594	Transcription regulatory protein
49355765	NP_115657.2	ELAVL3	1995	ELAV-like protein 3 isoform 2	0.581	0.630	0.127	RNA binding protein
4506671	NP_000995.1	RPLP2	6181	60S acidic ribosomal protein P2	0.633	0.673	0.575	Ribosomal subunit
223555917	NP_848927.2	MTDH	92140	protein LYRIC	0.651	0.646	0.645	Unclassified
4759302	NP_004729.1	VAPB	9217	vesicle-associated membrane protein-associated protein B/C isoform 1	0.657	0.442	0.505	Membrane transport protein
5174449	NP_006017.1	H1FX	8971	histone H1x	1.653	2.438	1.889	DNA binding protein
5031877	NP_005564.1	LMNB1	4001	lamin-B1 isoform 1	1.846	1.943	3.019	Structural protein
21536286	NP_001814.2	CKB	1152	creatine kinase B-type	1.867	1.610	0.665	Enzyme: Phosphotransferase
4503183	NP_001905.1	CYB5A	1528	cytochrome b5 isoform 2	1.899	1.887	1.871	Enzyme: Oxidoreductase
194688133	NP_001124160.1	HMGB2	3148	high mobility group protein B2	1.959	2.729	3.890	Transcription regulatory protein
4504255	NP_002097.1	H2AFZ	3015	histone H2A.Z	1.998	1.561	2.701	DNA binding protein
4885377	NP_005311.1	HIST1H1D	3007	histone H1.3	2.183	4.208	7.321	DNA binding protein
217330646	NP_006704.3	SUB1	10923	activated RNA polymerase II transcriptional coactivator p15	2.200	1.505	1.642	Transcription factor
302129652	NP_001180473.1	ANXA6	309	annexin A6 isoform 2	2.613	1.828	2.405	Calcium binding protein
10800138	NP_066407.1	HIST1H2BD	3017	histone H2B type 1-D	2.654	1.553	2.499	DNA binding protein
402534522	NP_001257973.1	NFIX	4784	nuclear factor 1 X-type isoform 3	2.655	1.906	1.590	Transcription factor
4502107	NP_001145.1	ANXA5	308	annexin A5	2.695	2.263	2.963	Calcium binding protein
4885381	NP_005313.1	HIST1H1B	3009	histone H1.5	2.815	2.788	4.726	DNA binding protein
151101292	NP_110382.3	TMX1	81542	thioredoxin-related transmembrane protein 1 precursor	2.917	2.209	1.511	Enzyme: Oxidoreductase
4503979	NP_002046.1	GFAP	2670	glial fibrillary acidic protein isoform 1	3.054	2.076	1.940	Structural protein
4502027	NP_000468.1	ALB	213	serum albumin preproprotein	3.103	1.887	2.684	Transport/cargo protein
66529396	NP_001018171.1	PON2	5445	serum paraoxonase/arylesterase 2 isoform 2	3.150	4.699	2.579	Enzyme: Esterase
10800140	NP_066406.1	HIST1H2BB	3018	histone H2B type 1-B	3.463	1.755	2.666	DNA binding protein
4885375	NP_005310.1	HIST1H1C	3006	histone H1.2	3.478	4.044	3.483	DNA binding protein
4504425	NP_002119.1	HMGB1	3146	high mobility group protein B1	3.679	2.634	3.346	DNA binding protein
4504313	NP_003535.1	HIST1H4B	8366	histone H4	3.717	2.142	3.327	DNA binding protein
10800144	NP_066544.1	HIST1H2AJ	8331	histone cluster 1, H2aj	3.829	2.115	4.403	DNA binding protein

Supplementary Table S9: Immunohistochemistry on tissue microarray for six differentially expressed proteins, NUCKS1, SMARCA5, PARP1, PTBP1, HMGB2, and NFIB, identified by quantitative mass spectrometric analysis. Immunohistochemistry was performed using commercially available tissue microarrays (US BioMax) consisting of 4 control subjects, 13 diffuse astrocytomas (Grade II), 11 anaplastic astrocytomas (Grade III), and 27 glioblastoma (Grade IV) patients samples. Scoring criteria used were based on both staining intensities and distributions. Scores 0, +1, +2 and +3 indicate negative, low, medium and strong staining, respectively. The distribution of staining of cancer cells was scored as 0 (less than 5% of cells staining), 1+ (5–30% of cell staining), 2+ (31–60% of cells staining) and 3+ (greater than 60% of cells staining). TMA slides were evaluated independently by two neuropathologists.

Sl. No	Proteins	Mass spectrometry analysis	Samples (n) used for IHC	IHC scores (Staining intensity)			
				0	1+	2+	3+
1	NUCKS1	Grade II (Up)	Grade II (13)	0	0	0	13
		Grade III (Up)	Grade III (11)	0	0	0	11
		Grade IV (Up)	Grade IV (27)	0	1	0	26
		-	Control (4)	1	2	1	0
2	SMARCA5	Grade II No change	Grade II (13)	0	1	0	12
		Grade III No change	Grade III (11)	0	0	0	11
		Grade IV (Up)	Grade IV (27)	0	1	0	26
		-	Control (4)	2	1	1	0
3	PARP1	Grade II (Up)	Grade II (13)	0	1	0	12
		Grade III (Up)	Grade III (11)	0	2	0	9
		Grade IV No change	Grade IV (27)	1	6	1	19
		-	Control (4)	0	2	1	1
4	PTBP1	Grade II (Up)	Grade II (13)	1	3	0	9
		Grade III (Up)	Grade III (11)	0	0	0	11
		Grade IV No change	Grade IV (27)	2	6	5	14
		-	Control (4)	3	1	0	0
5	HMGB2	Grade II (Up)	Grade II (13)	0	1	1	11
		Grade III (Up)	Grade III (11)	0	2	3	6
		Grade IV (Up)	Grade IV (27)	0	9	4	14
		-	Control (4)	2	1	1	0
6	NFIB	Grade II (Up)	Grade II (13)	4	4	1	4
		Grade III (Up)	Grade III (11)	5	2	3	1
		Grade IV (Up)	Grade IV (27)	11	5	2	9
		-	Control (4)	4	0	0	0

Supplementary Table S10: List of 61 concordant mRNA and protein target entities present in the transcription interaction network and their microRNA regulators. The miRNA interaction were identified, as per pipeline shown in **Figure 5A** and described in the Methods, for mRNA and protein entities present in the transcription network as shown in **Figure 4**. Each of the miRNA-target interaction was supported by at least one PubMed ID.

Gene Symbol	Protein Fold change in our study	Transcript Fold change in GBM TCGA data	MicroRNA interactor	MIMATid	MicroRNA Fold change in GBM data from TCGA
ADAR	0.51	0.77	hsa-miR-106a-5p	MIMAT0000103	2.12
			hsa-miR-106b-5p	MIMAT0000680	2.58
			hsa-miR-130b-3p	MIMAT0000691	2.29
			hsa-miR-17-5p	MIMAT0000070	1.99
			hsa-miR-20a-5p	MIMAT0000075	2.23
			hsa-miR-20b-5p	MIMAT0001413	1.59
			hsa-miR-27a-3p	MIMAT0000084	3.40
			hsa-miR-93-5p	MIMAT0000093	2.25
BAZ1B	1.82	2.27	hsa-let-7e-5p	MIMAT0000066	0.59
BUD31	2.02	1.57	hsa-miR-218-5p	MIMAT0000275	0.12
BZW1	1.55	1.36	hsa-let-7d-5p	MIMAT0000065	0.72
			hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-let-7g-5p	MIMAT0000414	0.58
			hsa-miR-101-3p	MIMAT0000099	0.45
			hsa-miR-136-5p	MIMAT0000448	0.21
			hsa-miR-144-3p	MIMAT0000436	0.78
			hsa-miR-323a-3p	MIMAT0000755	0.42
			hsa-miR-376c-3p	MIMAT0000720	0.79
			hsa-miR-582-5p	MIMAT0003247	0.63
hsa-miR-98-5p	MIMAT0000096	0.75			
CBX5	1.51	1.78	hsa-let-7d-5p	MIMAT0000065	0.72
			hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-let-7g-5p	MIMAT0000414	0.58
			hsa-miR-1-3p	MIMAT0000416	0.79
			hsa-miR-98-5p	MIMAT0000096	0.75
CENPV	0.58	0.56	hsa-let-7b-5p	MIMAT0000063	1.16
			hsa-miR-28-5p	MIMAT0000085	1.19
DDX17	0.53	0.69	hsa-let-7b-5p	MIMAT0000063	1.16
			hsa-miR-106b-5p	MIMAT0000680	2.58
			hsa-miR-142-3p	MIMAT0000434	1.54
			hsa-miR-155-5p	MIMAT0000646	2.52
			hsa-miR-92a-3p	MIMAT0000092	2.69
DDX27	1.73	1.35	hsa-miR-23b-3p	MIMAT0000418	0.62
			hsa-let-7g-5p	MIMAT0000414	0.58

EEF1A1	1.95	1.40	hsa-miR-125a-5p	MIMAT0000443	0.85
			hsa-miR-185-5p	MIMAT0000455	0.79
			hsa-miR-221-3p	MIMAT0000278	0.58
			hsa-miR-23b-3p	MIMAT0000418	0.62
			hsa-miR-30e-5p	MIMAT0000692	0.69
ELAVL2	0.44	0.37	hsa-miR-340-3p	MIMAT0000750	0.61
			hsa-miR-106a-5p	MIMAT0000103	2.12
			hsa-miR-106b-5p	MIMAT0000680	2.58
			hsa-miR-17-5p	MIMAT0000070	1.99
			hsa-miR-20a-5p	MIMAT0000075	2.23
			hsa-miR-20b-5p	MIMAT0001413	1.59
			hsa-miR-26b-5p	MIMAT0000083	1.35
			hsa-miR-373-5p	MIMAT0000725	1.46
			hsa-miR-500a-3p	MIMAT0002871	1.21
			hsa-miR-93-5p	MIMAT0000093	2.25
ELAVL3	0.13	0.28	hsa-miR-26b-5p	MIMAT0000083	1.35
			hsa-miR-296-5p	MIMAT0000690	1.99
ELAVL4	0.42	0.15	hsa-miR-21-5p	MIMAT0000076	15.50
			hsa-miR-373-5p	MIMAT0000725	1.46
			hsa-miR-526b-5p	MIMAT0002835	1.30
FBL	1.66	1.78	hsa-miR-324-5p	MIMAT0000761	0.58
FUS	1.49	1.60	hsa-miR-221-3p	MIMAT0000278	0.58
			hsa-miR-331-3p	MIMAT0000760	0.54
H1FX	1.89	1.55	hsa-miR-1-3p	MIMAT0000416	0.79
H2AFY	3.79	1.49	hsa-miR-148b-3p	MIMAT0000759	0.82
H2AFZ	2.70	1.84	hsa-miR-148b-3p	MIMAT0000759	0.82
HIST1H1B	4.73	13.30	hsa-miR-1-3p	MIMAT0000416	0.79
HIST1H1C	3.48	2.65	hsa-miR-27b-3p	MIMAT0000419	0.56
			hsa-miR-98-5p	MIMAT0000096	0.75
HIST1H1E	1.81	1.89	hsa-miR-331-3p	MIMAT0000760	0.54
HIST1H2BD	2.50	1.39	hsa-let-7d-5p	MIMAT0000065	0.72
			hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-let-7g-5p	MIMAT0000414	0.58
			hsa-miR-490-3p	MIMAT0002806	0.72
			hsa-miR-98-5p	MIMAT0000096	0.75
HIST1H3F	7.32	4.79	hsa-miR-299-5p	MIMAT0002890	0.57
HMGB1	3.35	1.56	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-let-7g-5p	MIMAT0000414	0.58
			hsa-miR-129-5p	MIMAT0000242	0.14
			hsa-miR-148b-3p	MIMAT0000759	0.82
			hsa-miR-218-5p	MIMAT0000275	0.12
			hsa-miR-22-3p	MIMAT0000077	0.70
HMGB2	3.89	3.31	hsa-miR-139-5p	MIMAT0000250	0.08
			hsa-miR-218-5p	MIMAT0000275	0.12
			hsa-miR-23b-3p	MIMAT0000418	0.62
			hsa-miR-329-3p	MIMAT0001629	0.55
			hsa-miR-33a-5p	MIMAT0000091	0.34
			hsa-miR-381-3p	MIMAT0000736	0.50
			hsa-miR-582-5p	MIMAT0003247	0.63
HMGN1	1.94	1.48	hsa-miR-27b-3p	MIMAT0000419	0.56
			hsa-miR-495-3p	MIMAT0002817	0.73
			hsa-miR-101-3p	MIMAT0000099	0.45
			hsa-miR-144-3p	MIMAT0000436	0.78

HNRNPAB	2.03	2.03	hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-504-5p	MIMAT0002875	0.68
			hsa-miR-625-5p	MIMAT0003294	0.81
HNRNPC	1.46	2.98	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-miR-342-3p	MIMAT0000753	0.45
			hsa-miR-485-3p	MIMAT0002176	0.67
HNRNPD	1.49	1.59	hsa-miR-1-3p	MIMAT0000416	0.79
			hsa-miR-221-3p	MIMAT0000278	0.58
			hsa-miR-222-3p	MIMAT0000279	0.43
HNRNPM	1.49	1.72	hsa-miR-191-5p	MIMAT0000440	0.82
			hsa-miR-29a-3p	MIMAT0000086	0.57
			hsa-miR-331-3p	MIMAT0000760	0.54
HNRNPR	1.65	1.61	hsa-miR-203a-3p	MIMAT0000264	0.80
			hsa-miR-409-3p	MIMAT0001639	0.73
KHDRBS3	0.20	0.67	hsa-miR-192-5p	MIMAT0000222	1.15
KHSRP	2.15	1.36	hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-185-5p	MIMAT0000455	0.79
			hsa-miR-221-3p	MIMAT0000278	0.58
			hsa-miR-27b-3p	MIMAT0000419	0.56
			hsa-miR-410-3p	MIMAT0002171	0.22
LMNB1	3.02	3.58	hsa-miR-1-3p	MIMAT0000416	0.79
			hsa-miR-101-3p	MIMAT0000099	0.45
			hsa-miR-124-3p	MIMAT0000422	0.03
			hsa-miR-128-3p	MIMAT0000424	0.22
			hsa-miR-154-5p	MIMAT0000452	0.69
			hsa-miR-218-5p	MIMAT0000275	0.12
			hsa-miR-23b-3p	MIMAT0000418	0.62
MATR3	0.38	0.73	hsa-miR-125b-5p	MIMAT0000423	1.34
			hsa-miR-155-5p	MIMAT0000646	2.52
			hsa-miR-18a-5p	MIMAT0000072	1.28
			hsa-miR-24-3p	MIMAT0000080	1.50
			hsa-miR-26b-5p	MIMAT0000083	1.35
			hsa-miR-615-3p	MIMAT0003283	1.26
			hsa-miR-106a-5p	MIMAT0000103	2.12
MECP2	0.46	0.77	hsa-miR-106b-5p	MIMAT0000680	2.58
			hsa-miR-155-5p	MIMAT0000646	2.52
			hsa-miR-17-5p	MIMAT0000070	1.99
			hsa-miR-195-5p	MIMAT0000461	1.50
			hsa-miR-199a-3p	MIMAT0000232	1.27
			hsa-miR-19a-3p	MIMAT0000073	1.61
			hsa-miR-19b-3p	MIMAT0000074	2.02
			hsa-miR-20a-5p	MIMAT0000075	2.23
			hsa-miR-20b-5p	MIMAT0001413	1.59
			hsa-miR-527	MIMAT0002862	1.43
			hsa-miR-92a-3p	MIMAT0000092	2.69
			hsa-miR-93-5p	MIMAT0000093	2.25
			NFIB	1.41	1.42
hsa-miR-301a-3p	MIMAT0000688	0.83			
hsa-miR-331-3p	MIMAT0000760	0.54			

			hsa-miR-379-5p	MIMAT0000733	0.29
			hsa-miR-491-5p	MIMAT0002807	0.30
NFIX	1.59	1.56	hsa-miR-124-3p	MIMAT0000422	0.03
			hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-324-5p	MIMAT0000761	0.58
NHP2	1.51	1.30	hsa-miR-218-5p	MIMAT0000275	0.12
NOLC1	0.58	0.71	hsa-let-7b-5p	MIMAT0000063	1.16
			hsa-miR-155-5p	MIMAT0000646	2.52
			hsa-miR-195-5p	MIMAT0000461	1.50
			hsa-miR-27a-3p	MIMAT0000084	3.40
			hsa-miR-324-3p	MIMAT0000762	1.79
			hsa-miR-513a-5p	MIMAT0002877	1.65
			hsa-miR-615-3p	MIMAT0003283	1.26
NT5E	1.79	1.54	hsa-miR-1-3p	MIMAT0000416	0.79
			hsa-miR-124-3p	MIMAT0000422	0.03
PARP1	1.93	1.54	hsa-miR-128-3p	MIMAT0000424	0.22
			hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-301a-3p	MIMAT0000688	0.83
			hsa-miR-31-5p	MIMAT0000089	0.81
			hsa-miR-379-5p	MIMAT0000733	0.29
			hsa-miR-7-5p	MIMAT0000252	0.11
PBRM1	1.94	1.59	hsa-miR-181c-5p	MIMAT0000258	0.73
			hsa-miR-30e-5p	MIMAT0000692	0.69
PRKDC	1.95	1.34	hsa-miR-218-5p	MIMAT0000275	0.12
PSIP1	0.59	0.57	hsa-miR-155-5p	MIMAT0000646	2.52
			hsa-miR-193b-3p	MIMAT0002819	1.67
PURA	0.15	0.62	hsa-miR-106b-5p	MIMAT0000680	2.58
			hsa-miR-15a-5p	MIMAT0000068	1.54
			hsa-miR-15b-5p	MIMAT0000417	3.33
			hsa-miR-16-5p	MIMAT0000069	2.29
			hsa-miR-192-5p	MIMAT0000222	1.15
			hsa-miR-195-5p	MIMAT0000461	1.50
			hsa-miR-20a-5p	MIMAT0000075	2.23
			hsa-miR-21-5p	MIMAT0000076	15.50
			hsa-miR-34b-5p	MIMAT0000685	1.30
hsa-miR-93-5p	MIMAT0000093	2.25			
RBBP4	1.57	2.01	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-miR-128-3p	MIMAT0000424	0.22
			hsa-miR-129-5p	MIMAT0000242	0.14
			hsa-miR-324-5p	MIMAT0000761	0.58
			hsa-miR-342-3p	MIMAT0000753	0.45
RBM8A	2.24	1.81	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-miR-136-5p	MIMAT0000448	0.21
			hsa-miR-144-3p	MIMAT0000436	0.78
			hsa-miR-148b-3p	MIMAT0000759	0.82
RPS15	1.49	1.27	hsa-miR-124-3p	MIMAT0000422	0.03
RPS27	1.77	1.32	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-miR-143-3p	MIMAT0000435	0.58
			hsa-miR-331-3p	MIMAT0000760	0.54

SFPQ	1.52	1.39	hsa-miR-218-5p	MIMAT0000275	0.12
			hsa-miR-26a-5p	MIMAT0000082	0.76
			hsa-miR-29b-3p	MIMAT0000100	0.26
			hsa-miR-331-3p	MIMAT0000760	0.54
			hsa-miR-383-5p	MIMAT0000738	0.49
SMARCA5	1.95	2.54	hsa-miR-101-3p	MIMAT0000099	0.45
			hsa-miR-103a-3p	MIMAT0000101	0.64
			hsa-miR-107	MIMAT0000104	0.50
SNRPD2	2.01	1.37	hsa-miR-144-3p	MIMAT0000436	0.78
			hsa-miR-149-5p	MIMAT0000450	0.31
SNRPD3	1.75	1.58	hsa-miR-124-3p	MIMAT0000422	0.03
			hsa-miR-218-5p	MIMAT0000275	0.12
			hsa-miR-330-3p	MIMAT0000751	0.35
			hsa-miR-410-3p	MIMAT0002171	0.22
			hsa-miR-490-3p	MIMAT0002806	0.72
SNRPE	1.77	1.90	hsa-miR-137	MIMAT0000429	0.09
SON	1.56	1.34	hsa-miR-103a-3p	MIMAT0000101	0.64
			hsa-miR-203a-3p	MIMAT0000264	0.80
			hsa-miR-222-3p	MIMAT0000279	0.43
SRSF1	1.87	1.46	hsa-miR-103a-3p	MIMAT0000101	0.64
			hsa-miR-107	MIMAT0000104	0.50
			hsa-miR-128-3p	MIMAT0000424	0.22
			hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-27b-3p	MIMAT0000419	0.56
			hsa-miR-377-3p	MIMAT0000730	0.29
			hsa-miR-7-5p	MIMAT0000252	0.11
SRSF9	1.72	1.40	hsa-miR-1-3p	MIMAT0000416	0.79
			hsa-miR-218-5p	MIMAT0000275	0.12
SSRP1	2.39	1.62	hsa-miR-23b-3p	MIMAT0000418	0.62
SUB1	1.64	1.55	hsa-let-7e-5p	MIMAT0000066	0.59
			hsa-miR-101-3p	MIMAT0000099	0.45
XRCC5	1.68	2.40	hsa-miR-331-3p	MIMAT0000760	0.54
			hsa-miR-7-5p	MIMAT0000252	0.11
			hsa-miR-124-3p	MIMAT0000422	0.03
YBX1	6.20	2.02	hsa-miR-137	MIMAT0000429	0.09
			hsa-miR-149-5p	MIMAT0000450	0.31
			hsa-miR-29b-3p	MIMAT0000100	0.26
			hsa-miR-379-5p	MIMAT0000733	0.29

Supplementary Table S11: Immunohistochemistry on tissue microarrays of GBM for YBX1 and its interacting proteins, EGFR, MAPK1, CD44, TNC, MMP13 and SOX2 identified by protein-protein network analysis. Immunohistochemistry was performed using in-house prepared tissue microarrays consisting of 4 control subjects and 18 glioblastoma (Grade IV) patient samples. Scoring criteria used were based on both staining intensities and distributions. TMA slides were evaluated independently by two neuropathologists. The distribution of staining of cancer cells was scored as 0 (less than 5% of cells staining), 1+ (5–30% of cell staining), 2+ (31–60% of cells staining) and 3+ (greater than 60% of cells staining). Scores 0, +1, +2 and +3 indicate negative, low, medium and strong staining respectively.

Gene Symbol	Subjects	Pathologist I				Pathologist II		FINAL SCORING	
		IHC Scoring				IHC Scoring		Negative	Positive
		0	1+	2+	3+	Negative	Positive (2+ or 3+)		
YBX1	GBM	0	0	1	17	0	18	0	18
	Controls	4	0	0	0	4	0	4	0
EGFR	GBM	1	0	8	9	1	17	1	17
	Controls	4	0	0	0	4	0	4	0
MAPK1	GBM	1	0	9	8	1	17	1	17
	Controls	1	3	0	0	4	0	4	0
CD44	GBM	1	1	6	10	2	16	2	16
	Controls	4	0	0	0	4	0	4	0
TNC	GBM	6	0	6	6	6	12	6	12
	Controls	4	0	0	0	4	0	4	0
MMP13	GBM	2	0	11	5	2	16	2	16
	Controls	4	0	0	0	4	0	4	0
SOX2	GBM	0	0	1	17	0	18	0	18
	Controls	4	0	0	0	4	0	4	0

Supplementary Table S12: List of selected differentially expressed transcription regulatory proteins identified in the study and their role in tumorigenesis.

Protein	Expression status Up / Down (Gr II, III, IV)*	Molecular function	Molecular mechanism	Role in cancer	Ref.
<i>HMGA1</i>	Up in Gr III	DNA binding protein with chromatin remodelling activity	HMGA1 expression correlates with Ki-67, MMP-9, and VEGF-A; The downstream targets include COX2 and STAT3, involved in tumor progression	regulator of cell invasion and metastasis, potential therapeutic target	[1-5]
<i>HMGB1</i>	Up in Gr II, III, IV	DNA binding protein with chromatin remodelling activity	HMGB1 promotes autophagy with low p53 expression and leads to tumor cell survival	promotes autophagy and tumor cell survival, correlated to shorter overall survival and linked to chemoresistance in GBM cells	[6-10]
<i>HMGB2</i>	Up in Gr II, III, IV	DNA binding protein with chromatin remodelling activity	HMGB2 affects cell invasion by altering expression of p53 and MMP2/ TIMP2	involved in cell invasion activity, prognostic factor and therapeutic target for GBM	[7]
<i>NUCKS1</i>	Up in Gr II, III; novel to gliomas	DNA binding protein involved in DNA damage repair	NUCKS1 repairs DNA double-strand breaks by homologous recombination	having a role in tumor progression, prognostic factor	[11, 12]
<i>SMARCA5</i>	Up in Gr IV	Helicase and ATPase activity and regulates transcription by	Knockdown of SMARCA5-arrested cell cycle. Analysis of	overexpression of SMARCA5 correlates with increased cell	[13, 14]

		altering chromatin structure	cell cycle and invasion-related molecules showed that SMARCA5 downregulated cyclin A, MMP2 expression and upregulated p21 expression	proliferation, invasion and chemo resistance in glioma, potential therapeutic target	
<i>TFAM</i>	Up in Gr II, III	Transcription factor for mitochondrial DNA replication, transcription	TFAM is involved in the activity of PI3K/Akt signaling pathway for cell proliferation. In addition, cell migration and invasion activity-related MMP2 and MMP9, is increased with overexpression of TFAM	involved in increased malignancy of glioma, promising target for therapeutics	[15, 16]
<i>NF1B</i>	Up in Gr II, III, IV	Transcription factor, promotes differentiation of astrocytes	NF1B is involved in STAT3 signaling in classical and mesenchymal GBM cells	GBM sub-type specific tumor suppressor, associated with improved survival in GBM	[17]
<i>NF1X</i>	Up in Gr II, III, IV	Transcription factor, important for activation of GFAP transcription in astrocytes	NF1X regulates the expression of GFAP, an astrocyte marker protein	implicated in glioma	[18]
<i>PURA</i>	Down in Gr II, III, IV	Transcription factor, implicated in progression of cell cycle	PURA binds to hypophosphorylated form of the retinoblastoma protein, pRb, a regulator of S-phase initiation	ectopic overexpression of PURA suppress tumor cell proliferation in GBM cells, potential use of this protein and its derivative(s) in blocking proliferation of tumor cells	[19]

<i>SON</i>	Up in Gr IV; novel to gliomas	Transcription factor, involved in mRNA splicing and having a role in mitotic spindle pole separation, chromosome alignment and microtubule dynamics	SON regulates RNA splicing for effective cell cycle progression and genome stability; Knockdown of SON leads to splicing defects in transcripts containing weak splice sites, and many genes necessary for cell-cycle progression and epigenetic modification	regulates genes involved in cell cycle progression and DNA repair, Potential therapeutic target	[20]
<i>SUB1</i>	Up in Gr II, III, IV	Transcription factor, ssDNA-binding protein involved in DNA replication, repair and heterochromatinization	SUB1 binds to promoter regions of several oncogenes such as PLK1 (Polo-like kinase 1), C-MYC, serine-threonine kinase BUB1B and regulates their expression	Elevated PC4 expression is strongly correlated with the progression of astrocytoma; Role in cell proliferation, invasion and migration; Potential prognostic marker and therapeutic target	[21-23]
<i>SSRP1</i>	Up in Gr II	Transcription factor, involved in chromatin remodeling	SSRP1 is a subunit of the FACT (Facilitates Chromatin Transcription) complex involved in chromatin remodeling	Involved in maintenance of pluripotent cell state; Role in cell proliferation, invasion and migration in GBM cells; Predictive marker for disease progression and therapeutic target	[24-26]
<i>PTBPI</i>	Up in Gr II, III	RNA-binding protein and a major repressive regulator of alternative splicing, causing exon skipping in numerous alternatively spliced pre-mRNAs	PTBPI is involved in tumorigenesis through an aberrant alternate splicing of several genes involved in cell proliferation (FGFR1, FGFR2), invasion	Role in cell proliferation and migration in glioma; Potential therapeutic target	[27-29]

			(CSRC), motility (ACTN, FBN), apoptosis (FAS, CASP2), and multi-drug resistance (ABCC1)		
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*if fold change for a grade is not shown in column 2, it implies differential expression was not observed

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