Supplemental Information

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Figure S1. Related to Figure 2. Compositional analysis of GBM cell-surface proteins.

Figure S2 Related to Figure 3. Statistical modeling of GBMSig classifier.

Figure S3. Related to Figure 5. Statistical assessment and power analysis of ELISA data.

Figure S4. Related to Figure 5. Longitudinal tracking of GBMSig proteins.

Figure S5. Related to Figure 6. TGFβ responsiveness among GBMSig proteins.

Table S1. Related to Figure 2. Total proteins identified from cell surface proteomics study. Details of proteins indentified from cell-surface proteomics study. All three replicate analyses of each cell line/primary (source) cells are presented as run1-3.

Table S2. Related to Figure 3. ROC analysis of GBMSig for REMBRANDT and TCGA tissue transcriptome arrays. Details of significance level P (area=0.5) for AUC of each GBMSig gene is described. Source of transcript expression was obtained from REMBRANDT or TCGA.

Table S3. Related to Figure 4 and Figure 6. SRM transition list.
Details of Q1/Q3 SRM transition list used in the study are presented.

Table S4. Related to Figure 4. SRM Analysis of GBM tissue specimens.
Quantitative expressions of GBMSig proteins in GBM tissues are presented.

Table S5. Related to Figure 4. GBM subtyping through qPCR analysis.
Transcript expression of 33 candidate genes described by Phillips *et al.*, 2006 for four GBM tissues were used for subtyping

Table S6. Related to Figure 4. SRM Analysis of GBM plasmas.
Details of GBMSig expression detected in the plasma of four GBM patients are presented.

Table S7. Related to Figure 5 and Figure S3. Training and validations sets of ELISA Data.
Changes in the level of four GBMSig proteins between GBM and healthy controls were investigated using commercial ELISA kits. Both training (21 GBM and 21 controls) and independent validation (21 GBM and 21 controls) sets contain age and gender matched specimens. GBM plasmas were collected preoperatively from two different clinical centers. Healthy controls were collected from two different sources. All specimens were collected retrospectively.

Table S8. Related to Figure 5 and Figure S4. ELISA data- Longitudinal. Changes in the level of four GBMSig proteins were investigated by commercial ELISA kits before and after tumor resection for prospectively collected blood plasma from 10 patients.

Table S9. Related to Figure 6. GBMSig summary. Details of GBMSig detected in various biospecimens and their roles in other human diseases.

Table S10. Related to Figure 6 and Figure S5. SRM analysis of TGFβ/inhibitor treatment.
Deatails of GBMSig expression upon TGFβ/inhibitor treatment was investigated by SRM mass spectrometry.

Data S1. Related to Figure 5 and Table S7. Python codes for LDA were written to interact and analyze ELISA data presented in table S7.

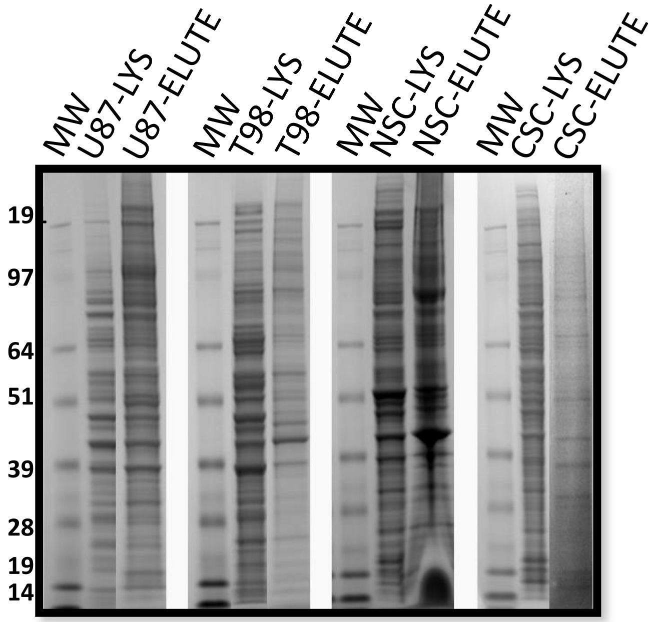
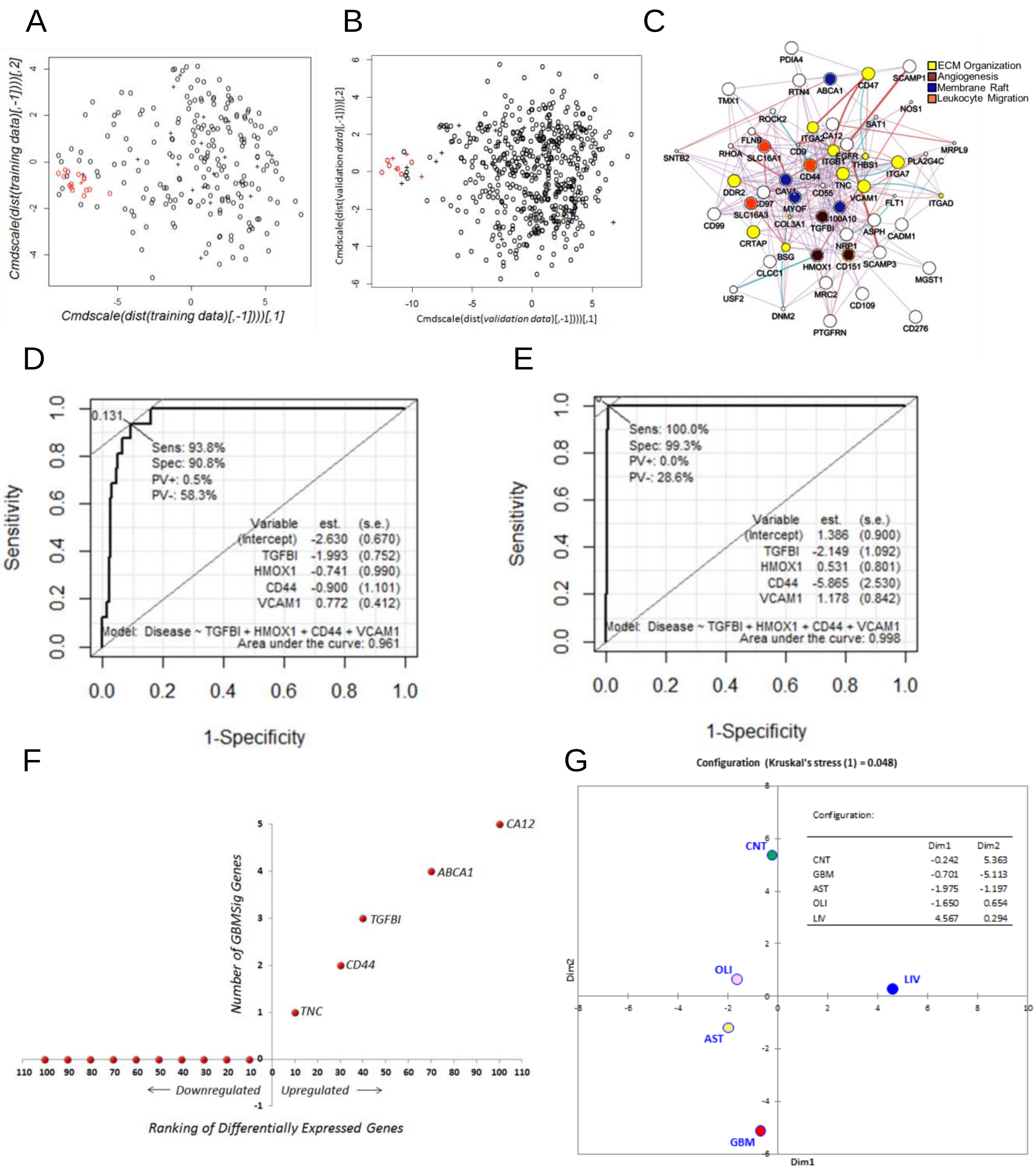


Figure S1. Related to Figure 2. Compositional analysis of GBM cell-surface proteins. Gel-separated affinity purified cell-surface proteins from various GBM cell lines revealed distinct membrane composition.



D)

Variable	est.	(s.e.)
(Intercept)	-2.630	(0.670)
TGFBI	-1.993	(0.752)
HMOX1	-0.741	(0.990)
CD44	-0.900	(1.101)
VCAM1	0.772	(0.412)

E)

Variable	est.	(s.e.)
(Intercept)	1.386	(0.900)
TGFBI	-2.149	(1.092)
HMOX1	0.531	(0.801)
CD44	-5.865	(2.530)
VCAM1	1.178	(0.842)

G) Configuration:

	Dim1	Dim2
CNT	-0.242	5.363
GBM	-0.701	-5.113
AST	-1.975	-1.197
OLI	-1.650	0.654
LIV	4.567	0.294

Figure S2 Related to Figure 3. SVM modeling of transcriptome datasets in A) REMBRANDT (GBM=228, non-tumor control=16) and B) TCGA (GBM=547, non-tumor control=10) are presented here. Control samples are labeled in red, GBM samples are labeled in black, and support vectors are represented by '+'. ; C) GBMSig network is derived using web-based geneMANIA (www.genemania.org). A subset of GBMSig network with *$p<0.001$* is represented in color. This network analysis could not detect the TGFβ responsiveness among GBMSig proteins unlike what we demonstrated using experimental approaches described herein. D) ROC analyses of four GBMSig proteins CD44, TGFBI (BIGH3), HMOX1, and VCAM1 in REMBRANDT (GBM=228, non-tumor control=16) and E) TCGA (GBM=547, non-tumor control=10) datasets revealed mean AUC of 0.961 and 0.998 respectively. This observation highlights the characteristic of a robust subset of GBMSig in accurately identifying GBM. F) Top 200 gene expression in TCGA does not include all GBMSig genes, highlighting the requirements for a systems strategy in integrating proteomics and transcriptomic data that either dataset alone cannot generate. G) Shown here is the multidimensional scaling (MDS) analysis (XLSTAT) that can clearly separate GBM from healthy controls (CNT) and non-GBM diseases based on 33 GBMSig genes. CNT, AST, OLI datasets were obtained from REMBTANDT and the liver cancer transcriptome data was obtained from NCBI GEO GSE6222 dataset.

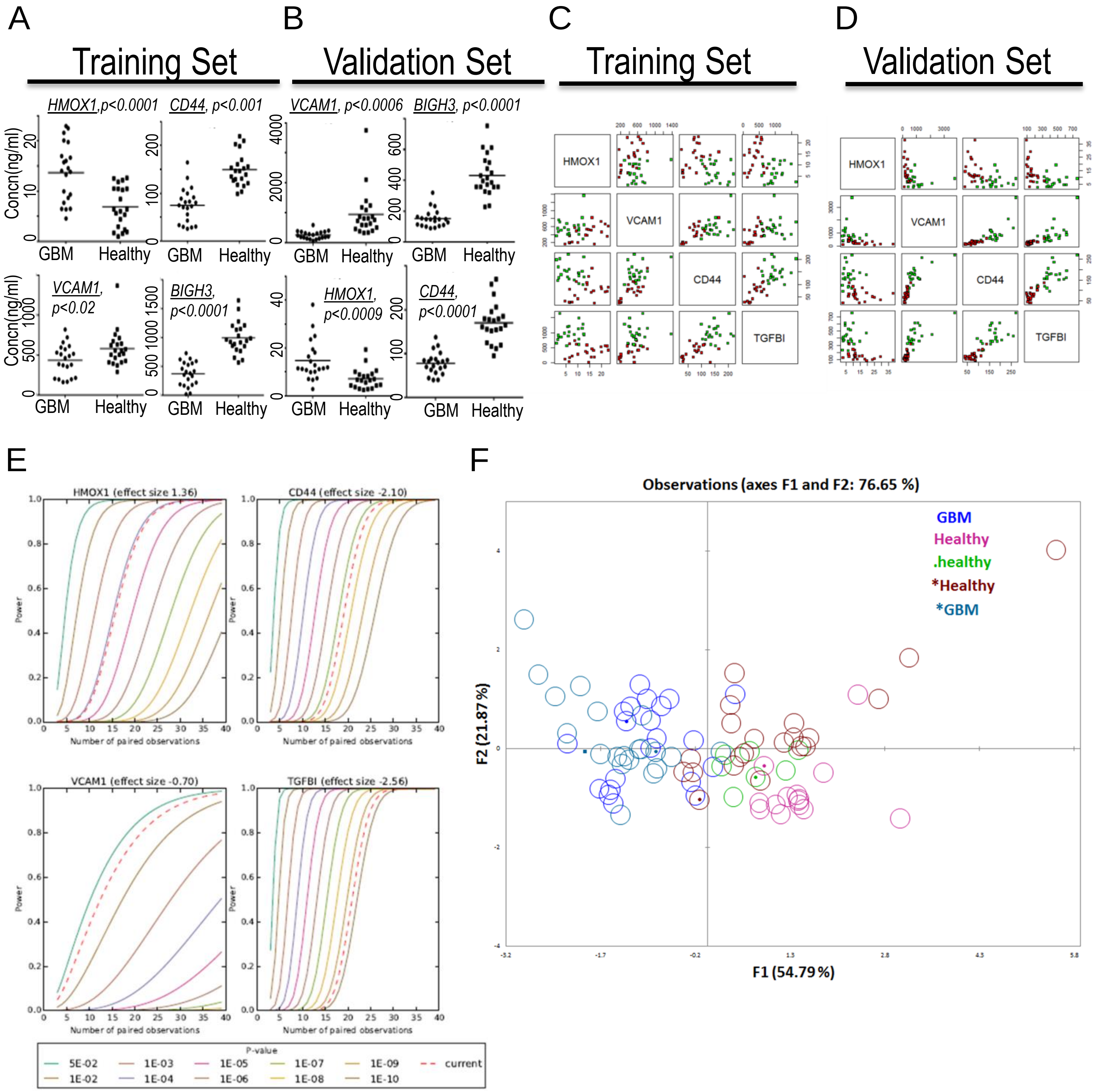


Figure S3. Related to Figure 5. ELISA analysis of four GBMSig exhibited significant differences (*p values are two tailed and welch corrected*) between GBM and healthy controls for both A) training set (GBM=21, healthy=21) and B) validation set (GBM=21, healthy=21). Scatter plots of ELISA data from C) training set (GBM=21 and healthy=21) and B) validation set (GBM=21 and Healthy=21). E) Power analysis of ELISA results for four GBMSig proteins HMOX1, CD44, VCAM1, and TGFBI (BIGH3) highlight good agreement between effect size (>|0.6|) and the sampling method (power>0.8) with indicated levels of *p* values mentioned. F) PCA analysis of ELISA data for all plasma specimens. ELISA results of 84 plasmas [2x(GBM=21, healthy=21)] for CD44, HMOX1, TGFBI (BIGH3), and VCAM1 were evaluated by PCA (XLSTAT). Individual source of samples is highlighted by unique colors.

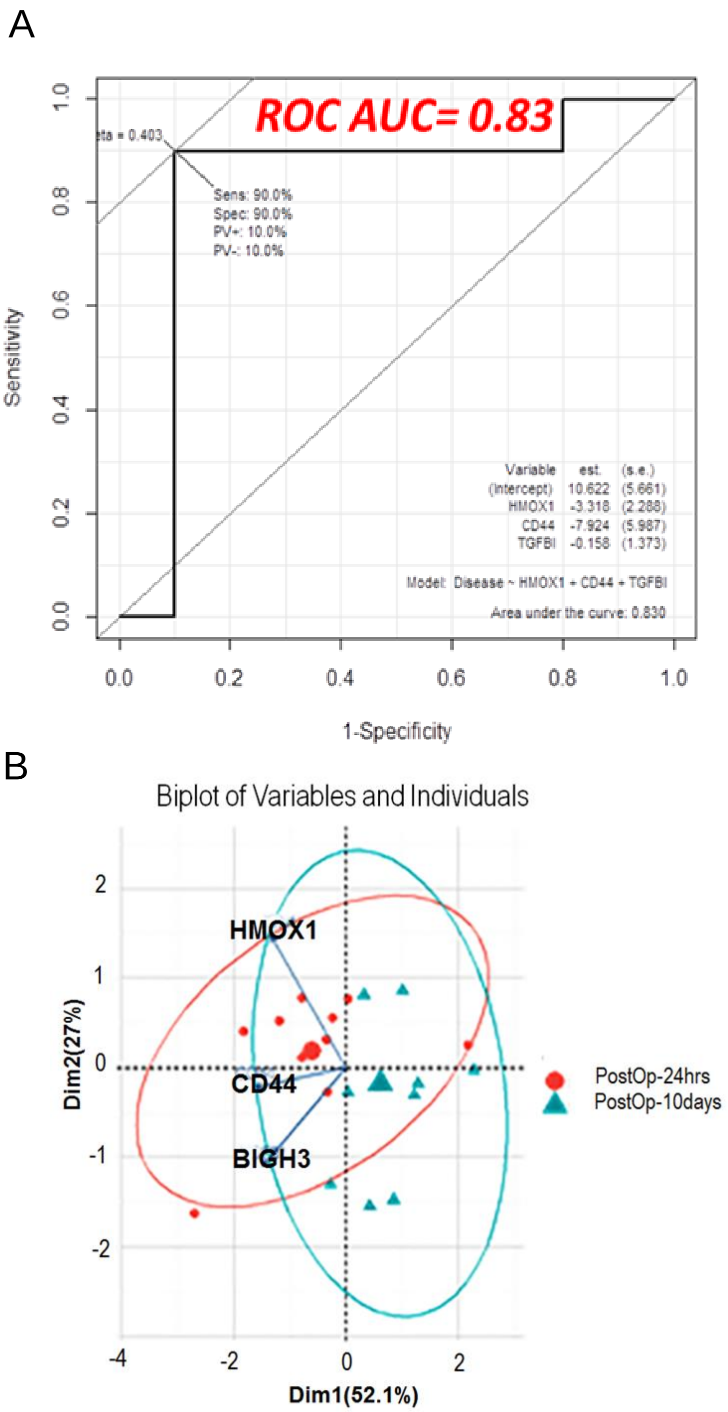


Figure S4. Related to Figure 5. Longitudinal assessment of ten GBM plasmas at preoperative and postoperative stages of 24hrs, 48hrs, and 10days(~) were performed through ELISA assays for HMOX1, CD44, BIGH3, and VCAM1. Based on the plasma concentrations of HMOX1, CD44, and BIGH3 within ten days of tumor resection for the patients tested, we observed an ROC AUC of 0.83 (A) in separating distinct treatment-associated changes longitudinally. PCA (B) analysis also revealed robust separation of early postoperative (24hrs) and late postoperative (~10days) conditions. Together, the results may reflect treatment (resection) associated-changes as demonstrated through GBMSig expression. Elliposoidal boundaries represent 95% confidence interval for each group.

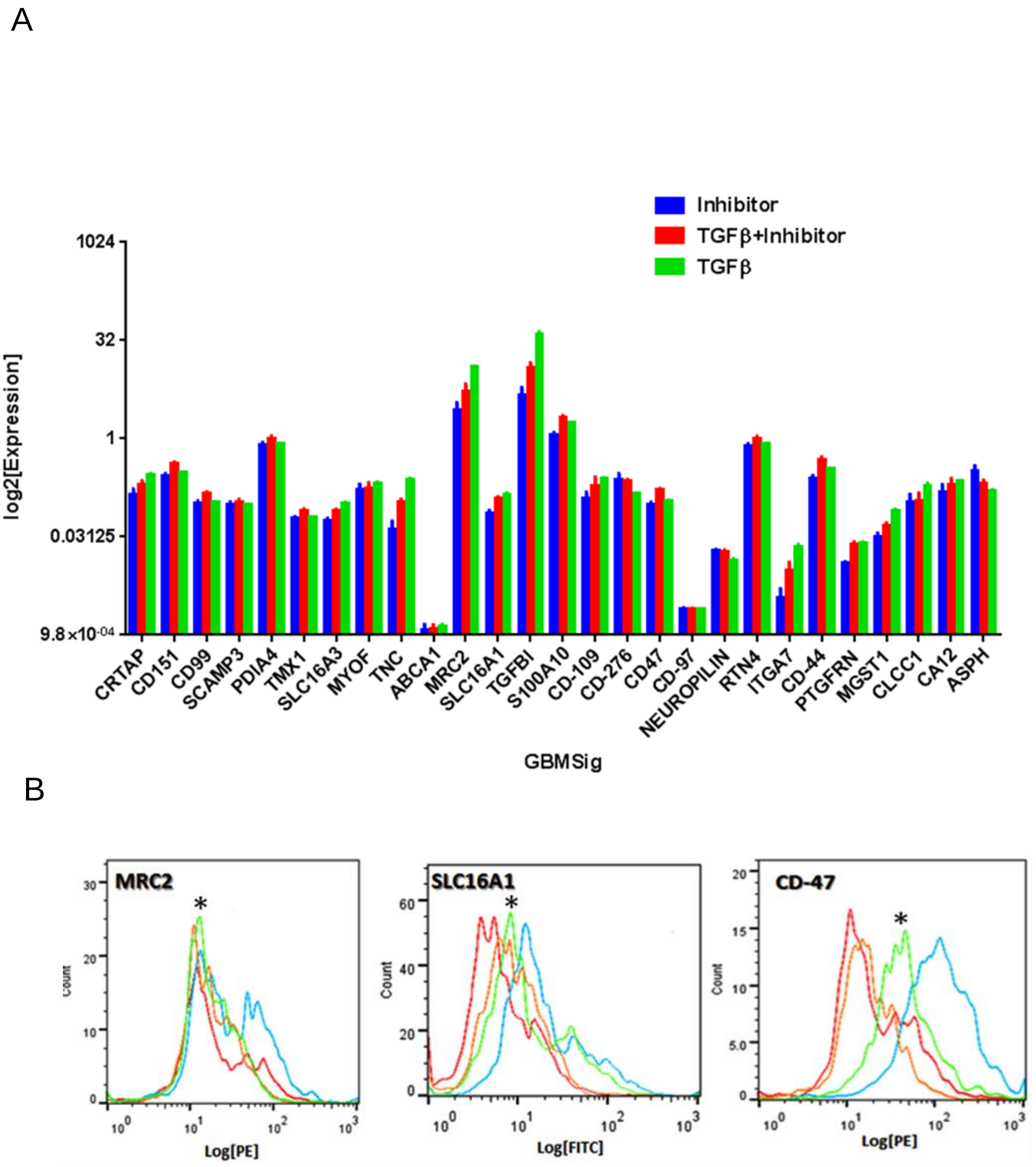


Figure S5. Related to Figure 6. TGFβ/Inhibitor responsiveness among GBMSig. A) Parental U87MG cell lines were treated with TGFβ or its inhibitor and the changes in expression of GBMSig were evaluated by SRM analysis. Changes in GBMSig expression are presented as log2 ratio of $\frac{TGF\beta\ treatment}{Inhibitor\ treatment}$. A subset of a GBMSig is observed to be responsive towards TGFβ treatment, highlighting the association of these GBMSig proteins with previously undescribed TGFβ signaling network. B) Flow cytometry analysis (histogram) of GBMSig expressions on the cell surface following siRNA mediated inhibition. Individual siRNA targeted inhibition of GBMSig proteins are in green color and marked '*'; non-targeting pool of siRNAs (control) are in cyan color, isotypes are in red/orange color.

Table S1. Related to Figure 2. Proteins identified from cell surface proteomics study.
Details of proteins identified from cell-surface proteomics study. All three replicate analyses of each cell line/primary (source) cells are presented as run1-3.

Table S2. Related to Figure 3. ROC analysis of GBMSig for REMBRANDT and TCGA tissue transcriptome arrays. Details of significance level P (area=0.5) for AUC of earh GBMSig gene is decribed. Source of transcript expression was obtained from REMBRANDT or TCGA.

Gene Symbol	Specificity	Sensitivity	Significance level P (Area=0.5)	AUC	SE	Source	Type
CRTAP	100	90.8	0.0001	0.962	0.012	REMBRANDT	Training
CAV1	93.7	89.5	0.0001	0.933	0.017	REMBRANDT	Training
SLC16A3	100	73.7	0.0001	0.894	0.023	REMBRANDT	Training
CA12	100	85.5	0.0001	0.942	0.015	REMBRANDT	Training
CD151	100	93.9	0.0001	0.974	0.009	REMBRANDT	Training
VCAM1	93.7	66.7	0.0001	0.823	0.033	REMBRANDT	Training
PTGFRN	100	81.1	0.0001	0.87	0.022	REMBRANDT	Training
CD99	100	91.2	0.0001	0.977	0.009	REMBRANDT	Training
S100A10	100	92.1	0.0001	0.95	0.013	REMBRANDT	Training
BIGH3(TGFBI)	93.7	92.1	0.0001	0.954	0.014	REMBRANDT	Training
HMOX1	87.5	93.9	0.0001	0.928	0.02	REMBRANDT	Training
SLC16A1	81.2	91.2	0.0001	0.929	0.028	REMBRANDT	Training
SCAMP3	81.2	78.5	0.0001	0.829	0.043	REMBRANDT	Training
PDIA4	100	82.9	0.0001	0.952	0.016	REMBRANDT	Training
TMX1	100	81.1	0.0001	0.904	0.02	REMBRANDT	Training
CADM1	100	37.3	0.016	0.618	0.049	REMBRANDT	Training
MRC2	100	87.3	0.0001	0.963	0.012	REMBRANDT	Training
MGST1	100	53.5	0.0001	0.685	0.033	REMBRANDT	Training
CLCC1	81.2	75	0.0001	0.787	0.048	REMBRANDT	Training
MYOF	100	82.9	0.0001	0.936	0.017	REMBRANDT	Training
ITGA7	100	93	0.0001	0.966	0.011	REMBRANDT	Training
DDR2	100	81.1	0.0001	0.897	0.022	REMBRANDT	Training
TNC	100	92.1	0.0001	0.955	0.013	REMBRANDT	Training
ABCA1	100	90.8	0.0001	0.973	0.009	REMBRANDT	Training
EGFR	87.5	70.6	0.0001	0.838	0.039	REMBRANDT	Training
ASPH	87.5	70.6	0.0001	0.864	0.027	REMBRANDT	Training
CD109	100	70.6	0.0001	0.849	0.027	REMBRANDT	Training
CD276	93.7	90.4	0.0001	0.95	0.015	REMBRANDT	Training
RTN4	100	88.6	0.0001	0.963	0.012	REMBRANDT	Training
NRP1	100	80.3	0.0001	0.916	0.019	REMBRANDT	Training
CD97	93.7	82	0.0001	0.907	0.024	REMBRANDT	Training
CD47	87.5	43.4	0.07	0.595	0.053	REMBRANDT	Training
CD44	100	89.9	0.0001	0.968	0.011	REMBRANDT	Training
ABCA1	100	95.1	0.0001	0.976	0.007	TCGA	Validation
CA12	100	89.9	0.0001	0.948	0.011	TCGA	Validation
CADM1	100	39.9	0.004	0.632	0.04	TCGA	Validation
CAV1	100	96.7	0.0001	0.974	0.006	TCGA	Validation
CD151	100	87.6	0.0001	0.954	0.014	TCGA	Validation
CD44	100	98.2	0.0001	0.994	0.003	TCGA	Validation
CLCC1	100	89.2	0.0001	0.972	0.01	TCGA	Validation

CRTAP	100	90.9	0.0001	0.969	0.01	TCGA	Validation
DDR2	100	74.2	0.0001	0.87	0.02	TCGA	Validation
EGFR	100	74.8	0.0001	0.888	0.02	TCGA	Validation
ITGA7	100	82.4	0.0001	0.862	0.01	TCGA	Validation
MRC2	100	86.8	0.0001	0.931	0.01	TCGA	Validation
MYOF	100	90.1	0.0001	0.956	0.01	TCGA	Validation
NRP1	100	84.8	0.0001	0.947	0.01	TCGA	Validation
PDIA4	100	98.9	0.0001	0.999	0.001	TCGA	Validation
RTN4	100	89.6	0.0001	0.916	0.01	TCGA	Validation
S100A10	100	87.9	0.0001	0.924	0.01	TCGA	Validation
SCAMP3	100	80.8	0.0001	0.925	0.01	TCGA	Validation
SLC16A1	100	97.8	0.0001	0.984	0.005	TCGA	Validation
SLC16A3	100	72	0.0001	0.848	0.027	TCGA	Validation
BIGH3(TGFBI)	100	97.4	0.0001	0.988	0.004	TCGA	Validation
TMX1	100	99	0.0001	0.997	0.002	TCGA	Validation
TNC	100	97.4	0.0001	0.988	0.004	TCGA	Validation
ASPH	90	70.4	0.0001	0.776	0.04	TCGA	Validation
CD47	90	79.5	0.0001	0.84	0.04	TCGA	Validation
HMOX1	90	89.4	0.0001	0.949	0.03	TCGA	Validation
VCAM1	90	81.9	0.0001	0.894	0.03	TCGA	Validation

Table S3. Related to Figure 4 and Figure 6. SRM transition list.
Details of Q1/Q3 SRM transition list used in the study are presented.

Table S4. Related to Figure 4. SRM Analysis of GBM tissue specimens. Quantitative expression of GBMSig proteins in GBM tissues are presented.

		NT-1*		**NT-2***		**GBM-1**		**GBM-2**		**GBM-3**		**GBM-4**	
Gene Symbol	**Peptide Sequence**	Quant	%CV	Quant	%CV	Quant	%CV	Quant	%CV	Quant	%CV	Quant	%CV
PTGFRN	ALSADQGSYR	-1.086	3.076	0.402	47.844	0.001	40.387	0.826	10.812	-1.29	8.366	1.146	28.419
**SLC16A1	DLHDANTDLIGR	-0.984	9.233	-0.973	17.238	0.313	10.548	1.545	5.321	-0.495	6.853	0.595	9.001
SCAMP3	FAAGVFSNPAVR	-0.705	3.715	-0.338	5.106	2.014	4.614	-0.224	4.046	-0.406	3.737	-0.341	8.895
CD-44	FAGVFHVEK	-1.053	4.571	-1.104	6.79	1.455	3.57	0.111	2.371	-0.133	5.204	0.724	0.258
SLC16A3	GGAVVDEGPTGVK	-0.947	3.296	-0.655	37.274	1.625	12.507	0.045	10.626	-0.752	19.918	0.684	4.41
HMOX1	GLAFFTFPNIASATK	-0.602	7.214	-1.192	11.052	0.226	8.659	1.495	6.926	-0.645	14.314	0.717	2.223
**RTN4	GPLPAAPPVAPER	-0.809	0.694	-0.929	3.075	0.775	2.919	1.574	0.919	-0.636	3.398	0.026	2.273
**PDIA4	IDATSASVLASR	-0.881	20.108	-0.972	6.313	1.121	3.402	1.346	3.955	-0.415	8.962	-0.199	5.119
CLCC1	LLLVNPIWLVPPTK	-0.677	8.147	-0.503	5.199	1.616	2.634	0.841	3.224	-0.918	10.466	-0.359	3.451
CD99	NANAEPAVQR	-0.518	23.522	-0.71	14.23	1.772	8.455	0.511	9.681	-0.894	13.512	-0.161	59.04
**S100A10	NQKDPLAVDK	-0.876	30.191	-0.957	43.558	0.599	14.819	1.487	6.64	-0.725	4.673	0.471	64.05
EGFR	NYDLSFLK	-0.393	13.779	-0.401	29.583	-0.398	17.371	-0.41	19.706	2.041	9.554	-0.439	31.962
CD-47	STVPTDFSSAK	0.373	3.661	1.211	0.993	-0.879	3.707	-1.153	2.094	0.996	3.492	-0.548	1.977
**MRC2	TPLWIGLAGEEGSR	-1.124	20.531	-0.912	58.351	1.151	11.776	0.964	4.18	-0.607	7.691	0.529	8.308
SLC16A1	TSIDVAGKPNEVTK	-1.022	16.895	-0.913	32.4	0.647	11.185	1.371	3.329	-0.683	12.055	0.6	7.838
**CD151	TVVALCGQR	-1.042	18.211	-0.664	6.014	0.841	7.288	1.541	2.551	-0.622	6.342	-0.054	16.308
**TNC	VDNLLVSDATPDGFR	-1.033	11.654	-0.898	2.775	0.271	6.727	-0.296	3.691	0.252	3.962	1.703	3.973
**TMX1	VDVTEQPGLSGR	-0.948	13.354	-1.171	14.286	0.792	5.024	1.369	3.79	-0.36	2.436	0.317	3.915
MGST1	VFANPEDCVAFGK	-0.464	12.278	-0.434	19.214	2.03	6.365	-0.274	4.99	-0.297	3.787	-0.56	29.865
CD-97	VFQGQGLSTR	-0.343	10.762	1.651	11.565	0.56	11.068	-0.549	6.963	-0.08	12.081	-1.239	14.438
**HMOX1	VQDSAPVETPR	-0.689	2.351	-1.172	25.403	0.281	7.604	1.061	6.706	-0.693	15.061	1.211	4.166
TGFBI	LTLLAPLNSVFK	-0.644	22.066	-0.661	16.465	-0.271	11.728	1.965	9.762	-0.458	31.1	0.068	24.666
vcam1	QSTQTLYVNVAPR	-0.3	51.265	-1.146	43.889	0.012	18.428	1.845	4	-0.436	21.115	0.025	23.591

*N.B. Data presentenced here are normalized to standard score; *NT= Non Tumor; **p<0.05*

Table S5. Related to Figure 4. GBM subtyping through qPCR analysis. Transcript expression of 33 candidate genes described by Phillips *et al.*, 2006 for four GBM tissues were used for subtyping.

Gene Symbol	**GBM-3**	**GBM-1**	**GBM-2**	**GBM-4**
ANGPTL4	0.429974	0.60744	0.824421	-0.65713
CHI3L1	-0.35738	1.273979	0.586551	-1.08236
COL4A1	0.573346	-0.81739	-1.3296	-1.68486
COL4A2	0.465508	-0.48244	-1.56547	-1.50989
FOSL2	-1.05975	-1.21989	-0.54294	1.156786
MYL9	-1.38236	0.855816	-1.48956	-0.1333
LIF	0.320224	-0.29687	0.420016	-1.84979
PDLIM4	-1.88806	1.154762	-2.55367	0.530769
PDPN	0.300351	0.071721	-0.49754	-1.18398
PLA2G5	0.73888	0.734418	0.409405	1.048274
SERPINE1	0.284661	1.061193	1.001113	-1.31462
SPOCD1	-0.10865	0.828137	0.852429	-1.26794
TAGLN	-1.1416	-0.6268	-1.29981	-0.69518
TIMP1	-0.17403	1.453403	0.924835	-0.92329
CENPK	0.336664	0.113303	-2.64994	-1.32445
DTL	0.687576	-0.00869	-2.06114	-1.49195
E2F7	0.677845	0.841358	-0.11044	-2.01339
HMMR	0.570898	1.076727	-2.6867	-1.52911
IQGAP3	0.475118	0.566497	-2.31515	-0.92048
ATP6V1G2	-0.48441	-1.19221	-2.41009	2.150858
CSDC2	-0.75705	-1.13477	-2.69911	1.461367
DLL3	0.559942	-0.89695	-3.19712	0.93178
FERMT1	-0.34544	-0.56393	-1.48605	0.763864
GABBR1	-0.2335	-0.83881	-2.18127	2.032776
GALNT13	-1.22221	-0.47749	-2.82567	1.092921
KLRC3	-2.18812	-1.49119	-2.28498	0.939863
NCAM1	0.112807	-1.39244	-3.61889	1.385489
NDRG2	0.529651	-1.86671	-1.90595	1.704755
RASL10A	-0.16439	-2.10212	-1.38395	1.700626
SCG3	-0.65182	-2.19039	-3.06252	1.475903
SNAP91	0.806224	-1.20199	-1.98318	1.662239
SOX8	-1.16984	-1.81015	-2.56564	1.039618
SRRM2	-0.42324	-0.8466	-2.85981	0.738262

Table S6. Related to Figure 4. SRM Analysis of GBM plasma. Details of GBMSig expression detected in the plasma of four GBM patients are presented.

		GBM-1		**GBM-2**		**GBM-3**		**GBM-4**	
Gene Symbol	**Peptide Sequence**	Quant	%CV	Quant	%CV	Quant	%CV	Quant	%CV
CADM1	SDDSVIQLLNPNR	-1.356	15.715	0.84	4.297	-0.144	29.544	0.66	11.427
CD44	FAGVFHVEK	-0.684	7.535	-0.004	3.561	-0.727	4.582	1.415	3.459
CD47	STVPTDFSSAK	-1.245	14.761	0.817	7.113	0.802	19.864	-0.375	17.698
DDR2	QVLDGNSNPYDIFLK	-1.266	63.59	-0.328	32.78	0.701	4.645	0.894	29.197
HMOX1	GLAFFTFPNIASATK	-0.247	23.129	0.275	26.907	1.182	13.38	-1.211	61.288
HMOX1	VQDSAPVETPR	-0.936	48.917	1.376	31.744	-0.479	47.444	0.04	41.723
MRC2	TLGDQLSLLLGAR	0.041	32.15	1.374	19.869	-0.475	71.225	-0.94	52.967
MYOF	IYPLPDDPSVPAPPR	-0.55	20.223	-0.653	5.587	-0.279	15.666	1.481	12.968
NRP1-1	FVTAVGTQGAISK	0.388	3.367	-0.187	9.854	-1.283	12.335	1.081	18.299
NRP1-2	IAPPPVVSSGPFLFIK	1.473	11.839	-0.434	3.139	-0.747	19.91	-0.292	16.304
PDIA4	GESDPAYQQYQDAANNLR	-1.098	51.626	0.715	17.857	-0.586	34.033	0.969	9.324
PDIA4	IDATSASVLASR	-0.679	25.539	-0.654	49.177	1.448	19.208	-0.115	6.897
RTN4	GPLPAAPPVAPER	-0.91	7.873	1.377	9.362	0.055	28.934	-0.521	5.413
SCAMP3	FAAGVFSNPAVR	-1.392	2.066	0.923	1.108	0.46	0.949	0.009	81.408
TGFBI-1	LTLLAPLNSVFK	-0.02	47.802	0.911	1.376	0.497	4.523	-1.387	40.232
TGFBI-2	SDVSTAIDLFR	0.468	2.165	-0.209	8.733	1.034	4.278	-1.292	3.092
TNC	VDNLLVSDATPDGFR	1.446	2.343	-0.742	30.038	-0.586	64.885	-0.118	3.146
VCAM1-1	VPSVYPLDR	-0.869	15.746	1.218	0	-0.766	0	0.418	16.667
N.B. Data presentenced here are normalized to standard score									

Table S7. Related to Figure 5 and Figure S3. Training and validations sets of ELISA Data. Changes in the level of four GBMSig proteins between GBM and healthy controls were investigated by commercial ELISA kits. Both training (21 GBM and 21 controls) and independent validation (21 GBM and 21 controls) sets contain age and gender matched specimens. GBM plasmas were collected preoperatively from two different clinical centeers. Healthy controls were collected from two different sources. All specimens were collected retrospectively.

Sample	**Age**	**Gender**	VCAM1		BIGH3(TGFBI)		HMOX1		CD44		Type
			Replicate-1	Replicate-2	Replicate-1	Replicate-2	Replicate-1	Replicate-2	Replicate-1	Replicate-2	
GBM-S1	17	F	558.38	464.33	197.87	184.74	16.41	15.15	67.44	70.85	Training
GBM-S2	17	M	459.88	468.77	293.82	418.35	20.37	19.89	71.41	94.02	Training
GBM-S3	18	F	201.16	193.34	161.58	175.39	6.7	6.25	29.54	27.79	Training
GBM-S4	37	F	233.7	198.29	226.24	217.56	7.69	7.72	26.96	33.04	Training
GBM-S5	46	M	552.59	641.98	421.83	396.27	16.53	16.85	62.08	87.91	Training
GBM-S6	47	M	389.87	358.68	608.75	664.8	6.36	6.62	74.37	88.51	Training
GBM-S7	47	F	407.98	573.2	594.09	653.21	9.32	9.37	108.75	115.03	Training
GBM-S8	50	F	354.47	407.22	342.93	326.78	14.6	13.5	101.34	98.11	Training
GBM-S9	50	F	333.72	443.53	404.46	362.2	13.67	12.89	73.82	86.99	Training
GBM-S10	52	F	636.99	686.61	634	496.09	23.55	19.76	70.45	71.57	Training
GBM-S11	52	F	746.63	896.76	431.46	492.47	16.12	16	161.31	167.89	Training
GBM-S12	54	F	362.12	353.32	535.36	576.24	22.42	22.69	71.49	74.37	Training
GBM-S13	55	M	494.94	571.39	595.04	590.32	14.17	13.56	104.56	109.18	Training
GBM-S14	55	F	452.83	581.49	21.56	23.81	14.5	14.66	133.03	131.53	Training
GBM-S15	56	M	206.9	190.04	46.54	24.04	6.65	6.13	31.15	29.74	Training
GBM-S16	60	M	159.11	176.75	132.73	118.8	5.23	3.89	31.55	35.58	Training
GBM-S17	61	M	206.9	204.45	269.14	294.22	9.64	10.31	44.32	41.74	Training
GBM-S18	64	M	671.78	773.81	491.57	566.42	20.12	19.49	94.69	88.44	Training
GBM-S19	64	M	143.37	185.07	222.46	142.54	18.46	15.56	23.03	28.93	Training
GBM-S20	66	M	527.15	620.94	713.08	748.67	9.94	7.42	57.1	54.87	Training
GBM-S21	69	F	530.79	698.6	500.62	339.19	24.87	21.11	94.32	83.15	Training
Healthy-F	25	F	554.04	695.78	1167.14	717.51	8.52	8.38	122.76	113.11	Training
Healthy-E	26	F	536.98	580.77	800.25	784.14	11.24	9.83	105.21	102	Training
Healthy-6	27	F	711.26	641.26	613.98	524.79	6.09	4.53	165.83	138.59	Training
Healthy-8	27	F	787.35	731.25	939.04	766.11	2.14	1.65	130.5	123.32	Training
Healthy-B	30	F	496.04	515.1	571.09	647.92	11.12	9.85	129.81	140.54	Training
Healthy-9	31	F	446.51	564.17	774.11	945.32	3.71	2.17	129.47	149.07	Training
Healthy-C	35	M	772.41	872.82	1176.49	1119.54	11.91	11.83	143.09	163.19	Training
Healthy-2	37	M	522.04	587.97	650.32	886.02	1.44	1.67	108.32	122.27	Training
Healthy-A	40	F	269.26	311.64	1245.78	1312	12.77	11.65	92.59	105.5	Training
Healthy-D	41	M	601.97	686.97	833.71	1019.32	13.51	11.79	126.85	134.32	Training
Healthy-5	44	M	376.97	368.98	607.33	698.86	1.1	0.82	184.28	212.37	Training
Healthy-G	48	F	638.77	630.93	1057.33	1216.29	11.77	8.76	144.62	148.74	Training
Healthy-11	48	M	425.24	397.05	1400.72	1589.07	11.14	9.81	135.41	158.65	Training

Healthy-12	48	M	744.18	684.85	1610.92	1676.26	2.44	2.2	208.75	196.74	Training
Healthy-14	52	F	576.8	459.88	828.11	947.42	6.04	5.97	232.48	206.15	Training
Healthy-3	53	M	473.58	463.22	876.74	957.39	1.82	1.55	175.79	163.97	Training
Healthy-4	53	M	436.08	387.22	1200.78	1209.64	5.4	5.84	138.39	120.32	Training
Healthy-15	55	F	1533.43	1207.48	965.28	966.86	13.23	11.84	193.54	226.23	Training
Healthy-10	56	M	366.32	424.87	1195.25	1228.51	7.35	5.4	152.77	168.53	Training
Healthy-13	58	M	435.71	420	1125.54	937.47	7.07	5.72	131.05	111.05	Training
Healthy-1	63	M	612.36	538.07	778.12	1189.73	4.08	4.73	148.55	163.51	Training
Cont-1	48	F	333.25	437.1	461.02	331.84	3.1	2.51	104.09	86.13	Validation
Cont-2	72	F	764.15	869.08	608.57	446.55	7.13	6.36	182.39	176.23	Validation
Cont-3	52	F	2138.86	2070.82	356.83	543.08	5.93	5.27	240.46	231.56	Validation
Cont-4	54	F	1585.53	1209.7	489.43	372.49	4.72	4.53	263.13	253.74	Validation
Cont-5	56	F	3984.53	3510.81	660.42	846.46	9.86	8.52	274.17	265.12	Validation
Cont-6	45	F	1245.49	1240.69	484.89	677.13	4.63	3.99	156.83	152.02	Validation
Cont-7	58	F	1147.75	1032.49	555.63	668.06	4.55	4.24	161.52	160.88	Validation
Cont-8	57	M	1186.14	1184.75	363.38	353.56	2.94	2.93	162.34	151.65	Validation
Cont-9	61	M	938.81	796.96	644.65	586.13	10.36	9.8	199.2	192.69	Validation
Cont-10	56	M	605.23	588.38	511.68	521.12	8.18	8.1	154.26	150.12	Validation
Cont-11	56	M	386.63	298	413.98	242.81	7.46	6.57	120.66	118.69	Validation
Cont-12	49	M	441.69	366.51	555.63	275.25	3.5	2.62	183.55	176.06	Validation
Cont-13	60	M	903.76	722.17	428.52	316.77	3.93	3.33	206.22	206.17	Validation
Cont-14	54	M	512.55	505.51	407.78	307.45	6.88	6.17	166.01	163.6	Validation
Cont-15	59	M	627.76	563.71	432.16	282.46	15.9	13.71	189.68	180.9	Validation
Cont-16	76	M	624.44	663.19	486.76	286.79	8.67	7.91	183.18	172.45	Validation
Cont-17	61	M	515.19	403.65	437.65	277.41	9.7	8.05	115.64	107.63	Validation
Cont-18	43	F	800.84	726.16	269.51	201.18	2.37	2.59	125.67	123.61	Validation
Cont-19	54	F	695.68	772	392.88	249.85	9.28	11.89	156.41	154.98	Validation
Cont-20	58	M	951.4	782.17	521.93	430.6	18.13	20.6	180.9	168.94	Validation
Cont-21	54	M	356.82	305.14	259.53	197.35	6.28	6.6	119.94	112.77	Validation
GBM-CP-1	68	M	288.75	337.21	240.7	225.15	10.07	12.3	103.52	100.38	Validation
GBM-CP-2	55	M	438.94	376.13	233.02	130.93	6.81	6.56	73.57	70.54	Validation
GBM-CP-3	71	M	324.29	253.02	290.18	200.05	8.82	10.98	115.34	121.82	Validation
GBM-CP-4	68	F	623.61	563.71	362.87	277.41	6.65	8.02	135.91	139.39	Validation
GBM-CP-5	45	F	215.8	173.11	161.98	164.16	9.88	11.63	71.31	70.43	Validation
GBM-CP-6	64	M	312.23	329.27	135.95	137.84	10.92	11.55	89.83	87.53	Validation
GBM-CP-7	57	F	382.82	351.94	206.16	178.18	11.29	11.73	83.17	81.62	Validation
GBM-CP-8	59	F	388.53	349.99	152.07	155.93	14.58	18.33	113.07	113.15	Validation

GBM-CP-9	61	F	137.48	146.3	148.01	144.82	26.26	32.18	54.27	52.92	Validation
GBM-CP-10	49	M	283.58	244.41	145.45	149.93	10.33	12.66	63.35	62.99	Validation
GBM-CP-11	39	F	387.58	394.22	184.16	111.63	6.88	7.2	86.22	82.88	Validation
GBM-CP-12	68	F	214.68	169.53	131.56	89.44	12.54	13.08	60.07	53.6	Validation
GBM-CP-13	49	F	142.54	68.29	146.09	110.42	2.31	3.37	42.23	38.36	Validation
GBM-CP-14	76	M	405.53	285.65	117.73	90.41	22.38	24.86	72.07	68.21	Validation
GBM-CP-15	64	M	209.05	145.05	196.45	117.93	11.13	12.7	84.42	80.24	Validation
GBM-CP-16	69	M	258.36	232.43	107.81	92.95	9.57	10.63	86.41	73.46	Validation
GBM-CP-17	70	M	50.59	83.31	141.22	87.51	23.58	26.47	70.65	63.47	Validation
GBM-CP-18	64	M	234.62	183.75	101.81	77.58	17.36	21.51	94.83	80.43	Validation
GBM-CP-19	51	F	224.71	132.37	189.28	108.41	13.44	15.45	42.4	38.53	Validation
GBM-CP-20	60	M	111.33	123.29	119.98	94.51	16.71	19.52	47.21	41.74	Validation
GBM-CP-21	84	F	189.58	97.6	104.8	80.8	33.69	42.57	89.47	81.42	Validation

N.B. Values are in ng/ml; training and validation samples were run on different plates as the number of plasma specimens (84 plasmas x 2= 168) could not be accommodated for data acquisition in a single 96 well plate. However, each training and validation set was independent having own healthy controls and GBM plasmas. Data were normalized to z-score prior to modeling using LDA.

Table S8. Related to Figure 5 and Figure S4. ELISA data- Longitudinal. Changes in the level of four GBMSig proteins were investigated by commercial ELISA kits before and after tumor resection for prospectively collected blood plasmas from 10 patients.

Table S9. Related to Figure 6. GBMSig summary. Details of GBMSig detected in various biospecimens and their roles in other human diseases.

Current Study						Published Reports	
Gene Symbol	**Role in TGFβ-Signaling**	**Blood**	**Tissue**	**SignalIP**	***U87MG-Secretome**	**Other Disease**	**Detectable in blood**
PDIA4	N	Y	Y	y	y	lung adenocarcinoma drug resistance (PMID:24464223)	
RTN4	N	Y	Y	n	y	neurodegenerative disease (PMID: 24218324)	
NRP1	Y	Y		y	y	melanoma (PMID: 25954957)	Y(PMID:25873749)
CD44	Y	Y	Y	y	y	epithelial ovarian cancer(PMID:26762850), thyroid carcinoma(PMID:26799258)	Y (PMID: 9316006)
TGFBI	Y	Y	Y	y	y	lattice corneal dystrophy (PMID: 23455751)	Y (PMID: 21900154)
TNC	Y	Y	Y	y	y	juvenile idiopathic arthritis (PMID:25774061)	
CD151	N				y	gastric cancer (PMID:24005419)	
CD276	Y		Y	y	y	cutaneous melanoma (PMID:23474948)	Y(PMID:25567370)
CD109	Y		Y	y	y	triple-negative-breast cancer (PMID:25149155)	Y(PMID:24667143)
S100A10	Y			y	y	irritable bowel syndrome (PMID:23595519)	Y(PMID:21687958)
PTGFRN	Y			y	y	metastatic lung cancer (PMID: 21206492)	
EGFR	N/A				y	multiple cancers	Y(PMID:17679463)
HMOX1	Y	Y	Y	n		neurodegenerative disease (PMID: 25111043)	Y(PMID:26595496)
MYOF	Y	Y	Y	n		Duchenne muscular dystrophy (PMID: 25338682)	Y(PMID: 19067001)
MRC2	Y	Y	Y	y		renal fibrosis(PMID:22095946)	
CD97	N		Y	y		arthritis (PMID: 19717518)	
CD99	N			y		CNS autoimmune disease (PMID:26773145)	
CRTAP	Y		Y	y		osteogenesis imperfecta type VII (PMID:19895918)	
CA12	Y		Y	y		cervical cancer (PMID:16416108)	Y(PMID:21367885)
SCAMP3	N	Y	Y	n	y	medullary cystic kidney disease type 1 (PMID: 16738948)	
CLCC1	Y				y	neurodegeneration (PMID:25698737)	
CD47	Y	Y	Y	y		atherosclerosis (PMID:27437576)	Y(PMID:17163870)

CADM1	N/A	Y	Y	y		cervical and endometrial cancer (PMID:25281766)	
VCAM1	N/A	Y	Y	y		acute respiratory distress syndrome (PMID: 26919714)	Y(PMID:11865089)
DDR2	N/A	Y		y		osteoporosis (PMID: 25805889)	
TMX1	N			y		melanoma (PMID: 27502484)	
ASPH	Y		Y			Traboulsi syndrome (PMID:24768550)	Y(PMID:25250314)
ITGA7	Y		Y			congenital muscle disease (PMID:10199978)	
ABCA1	Y		Y			Tangier disease (PMID: 10431238)	Y(PMID:26004638)
SLC16A1	Y					erytrhrocyte lactate transporter defect (PMID: 10590411)	
MGST1	Y					reactive intermediate induced injury (PMID:21633660)	
SLC16A3	Y					clear cell renal cell carcinoma(PMID:26384346)	
CAV1	N/A		Y			Iidiopathic pulmonary artery hypertension (PMID:26539466)	Y(PMID:26539466)

**Ghosh D., and Hood L., unpublished data*

Table S10. Related to Figure 6 and Figure S5. SRM analysis of TGFβ/inhibitor treatment. Details of GBMSig expression upon TGFβ/inhibitor treatment was investigated by SRM mass spectrometry.

		Inhibitor Treatment		Inhibitor+TGFβ Treatment		TGFβ Treatment	
Gene Symbol	**Peptide Sequence**	Quant	%CV	Quant	%CV	Quant	%CV
*CRTAP	LFGGLLR	0.141	35.199	0.198	27.315	0.283	3.739
CD151	TVVALCGQR	0.273	10.949	0.414	10.705	0.308	2.19
CD99	NANAEPAVQR	0.101	14.8	0.145	11.14	0.107	1.541
SCAMP3	FAAGVFSNPAVR	0.096	20.902	0.106	20.431	0.097	3.546
PDIA4	IDATSASVLASR	0.808	14.419	1.018	13.529	0.841	1.459
TMX1	VDVTEQPGLSGR	0.059	12.155	0.08	10.118	0.062	1.304
*SLC16A3	GGAVVDEGPTGVK	0.055	13.803	0.077	13.292	0.103	4.164
+MYOF	IYPLPDDPSVPAPPR	0.168	33.854	0.176	33.81	0.208	7.373
*TNC	VDNLLVSDATPDGFR	0.041	54.142	0.106	22.114	0.234	10.228
+ABCA1	NMLQYQLPSSLSSLAR	0.001	38.651	0.001	24.771	0.001	11.456
*MRC2	TLGDQLSLLLGAR	2.685	55.866	5.357	46.725	12.746	3.624
*SLC16A1	DLHDANTDLIGR	0.071	21.291	0.121	11.593	0.141	6.244
*TGFBI	LTLLAPLNSVFK	4.591	55.32	12.187	31.958	39.97	13.018
*S100A10	NQKDPLAVDK	1.15	13.107	2.104	12.371	1.763	1.178
*CD-109	SYSQSILLDLTDNR	0.119	44.891	0.186	66.426	0.245	5.072
±CD-276	TALQPLK	0.233	43.331	0.229	6.165	0.144	4.562
+ CD-47	STVPTDFSSAK	0.098	12.377	0.164	9.719	0.113	2.718
CD-97	VFQGQGLSTR	0.003	4	0.002	6.278	0.002	2.341
±NRP-1	FVTAVGTQGAISK	0.019	7.58	0.018	12.575	0.014	8.041
RTN4	GPLPAAPPVAPER	0.767	14.291	1.014	13.073	0.851	0.449
*ITGA7	LIPVPANSYFGFSIDSGK	0.004	63.043	0.01	54.483	0.022	14.302
+CD-44	FAGVFHVEK	0.246	19.456	0.478	16.959	0.351	0.343
*PTGFRN	VPGFADDPTELACR	0.012	8.206	0.024	10.13	0.025	4.204
*MGST1	IYHTIAYLTPLPQPNR	0.031	24.558	0.046	18.961	0.077	13.19
*CLCC1	LLLVNPIWLVPPTK	0.107	53.406	0.114	51.19	0.189	16.141
*CA12	GSLTTPPCNPTVLWTVFR	0.15	51.948	0.199	39.11	0.225	3.865
±ASPH	SSGNSSSSGSGSGSTSAGSSSPGAR	0.326	30.179	0.203	23.63	0.159	6.475

Values presented here are the ratios of GBMSig expression in TGFβ/inhibitor treatment conditions;
** At least 1.5 folds change in expression after TGFβ treatment relative to inhibitor treatment*
+ At least 1.2 folds change in expression after TGFβ treatment relative to inhibitor treatment.
± reduced expression following TGFβ treatment relative to inhibitor treatment.
Unmarked genes remained largely unchanged.