Supplement to : de Tayrac, M., et al. A Four-Gene Signature Associated with Clinical Outcome in High-Grade Gliomas

Figure S1. Individual study analyses and combined-analysis overlap.

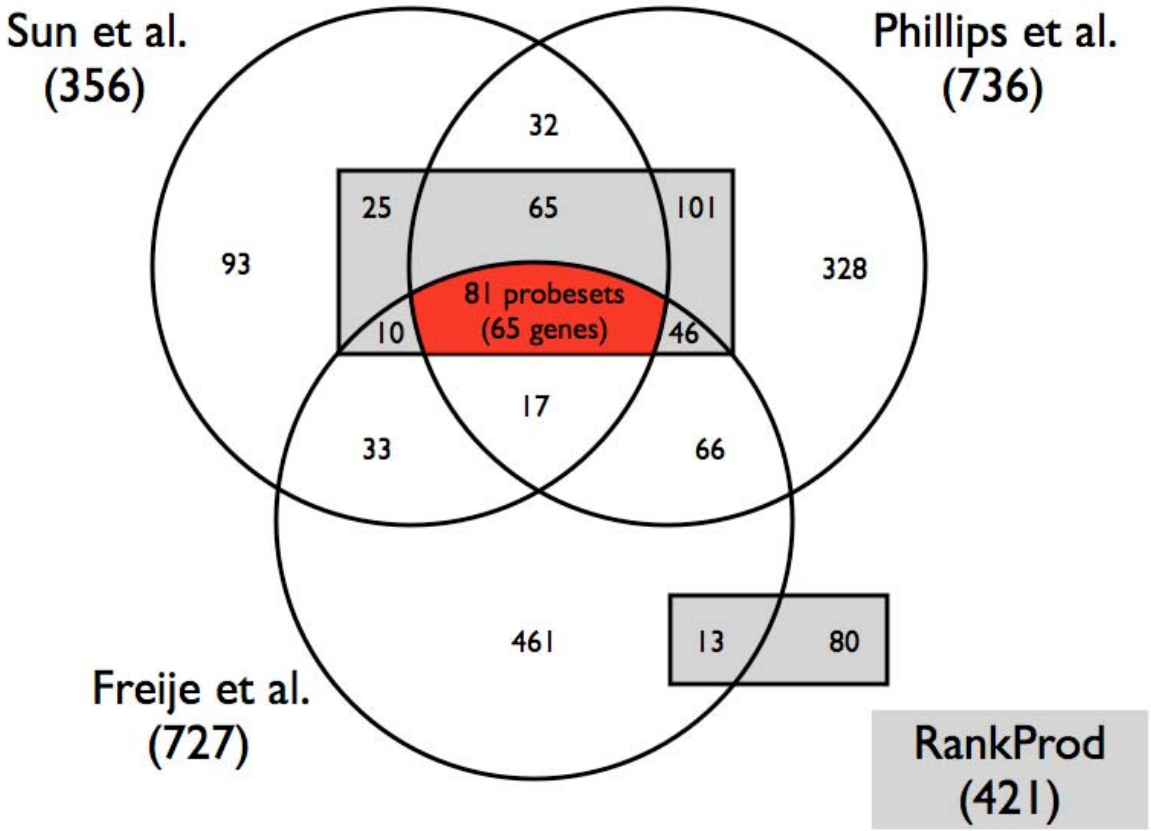


Figure S2. Unsupervised PCA of the 65 grading genes, with integration of biological knowledge

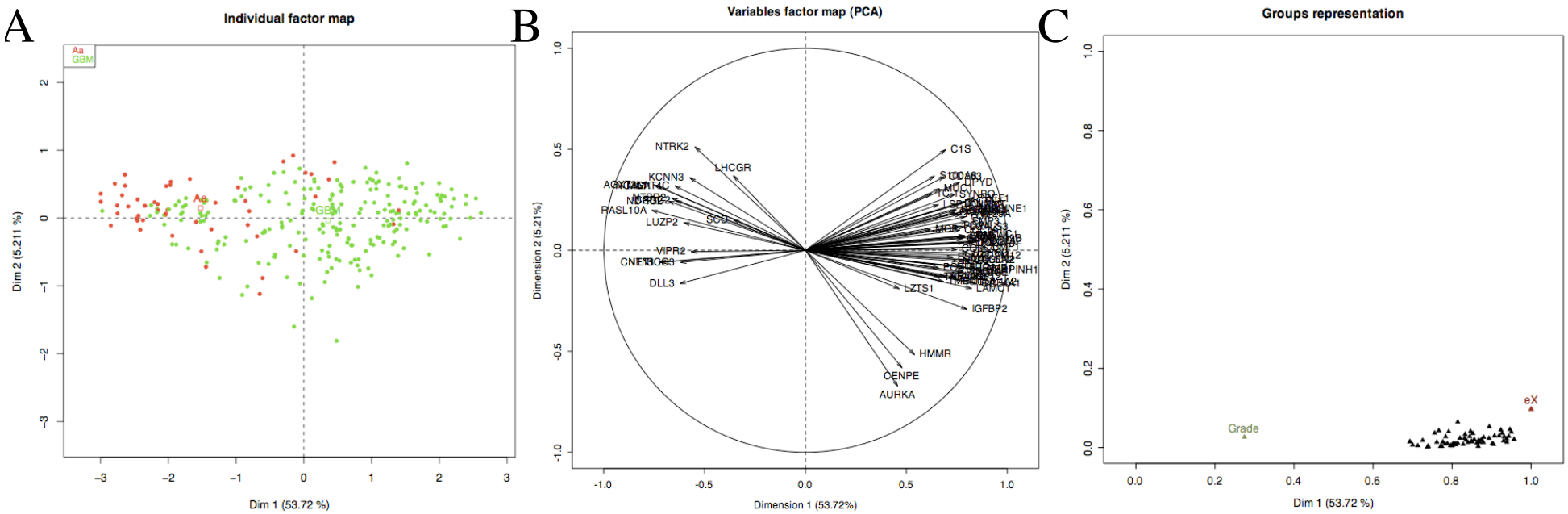


Figure S3. Grading Genes Annotation (Angiogenesis)

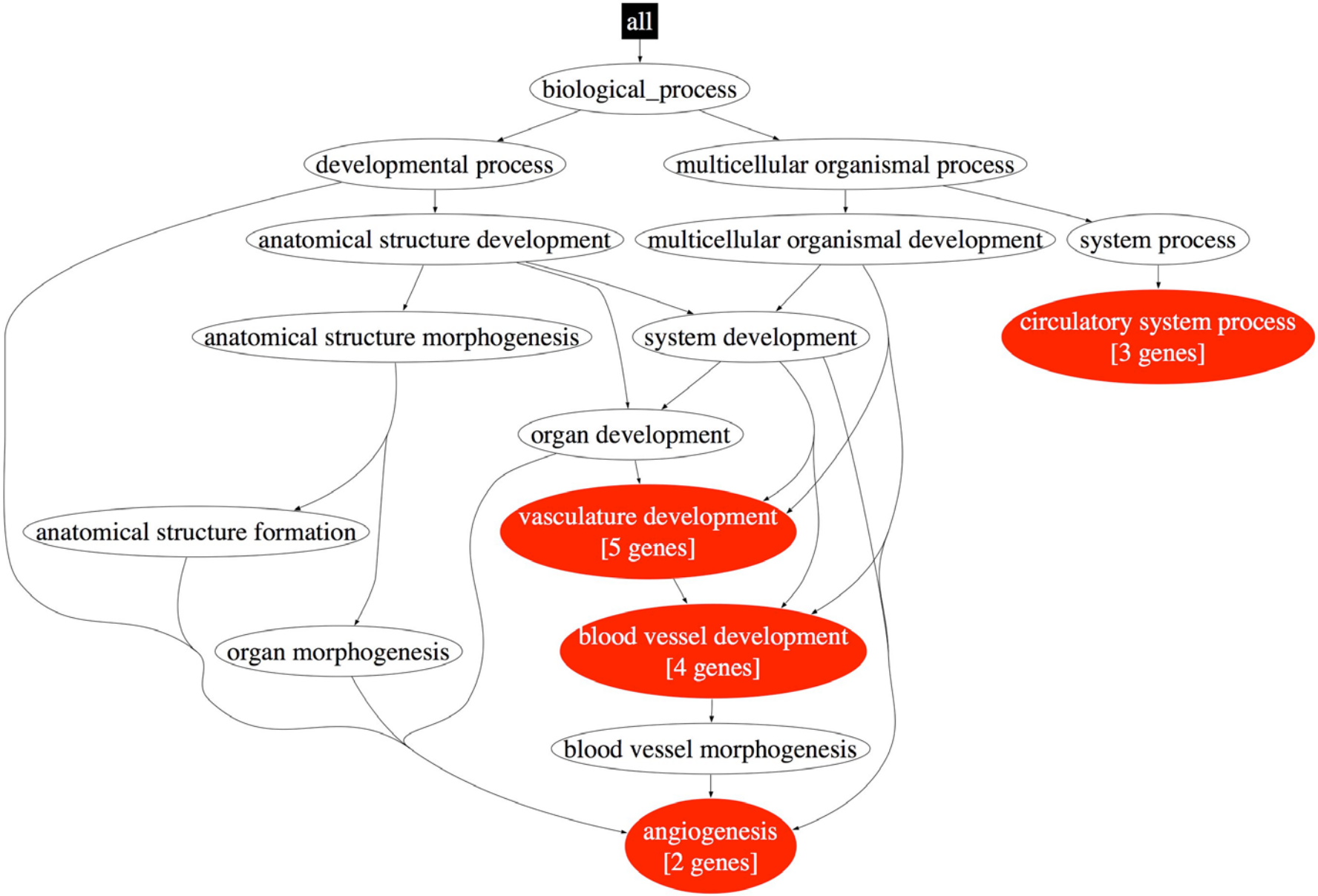


Figure S4. Grading Genes Annotation (Morphogenesis)

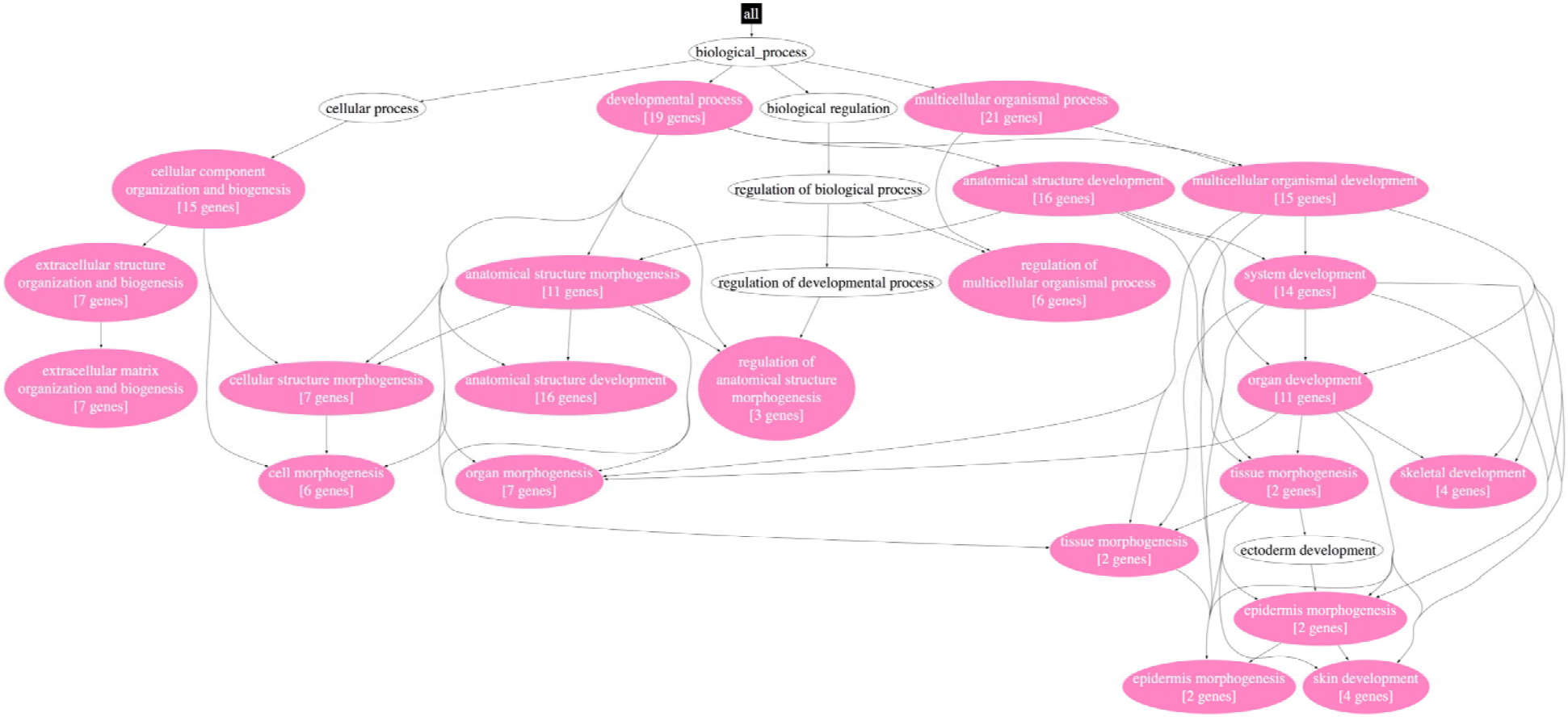


Figure S5. Grading Genes Annotation (Invasion)

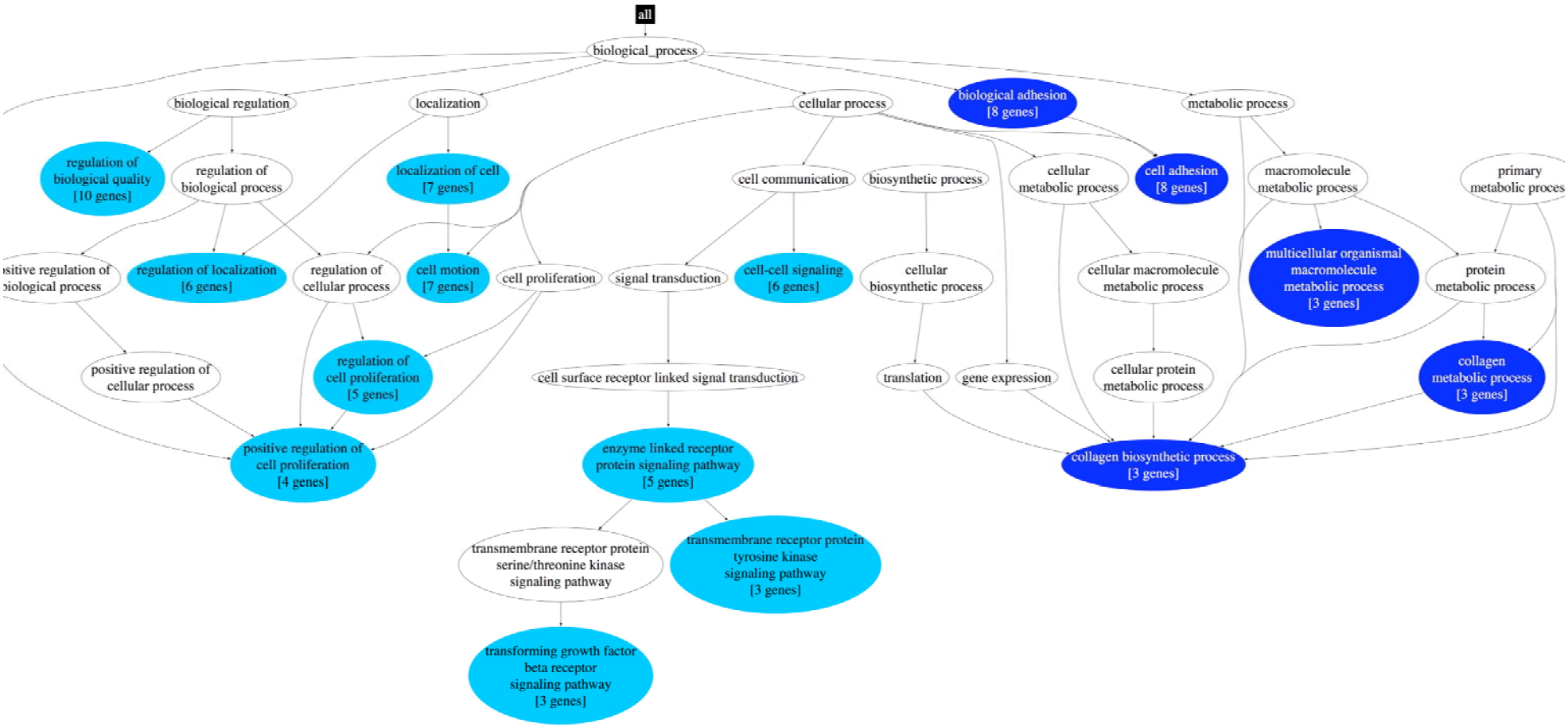


Figure S6. Grading Genes Annotation (Stress)

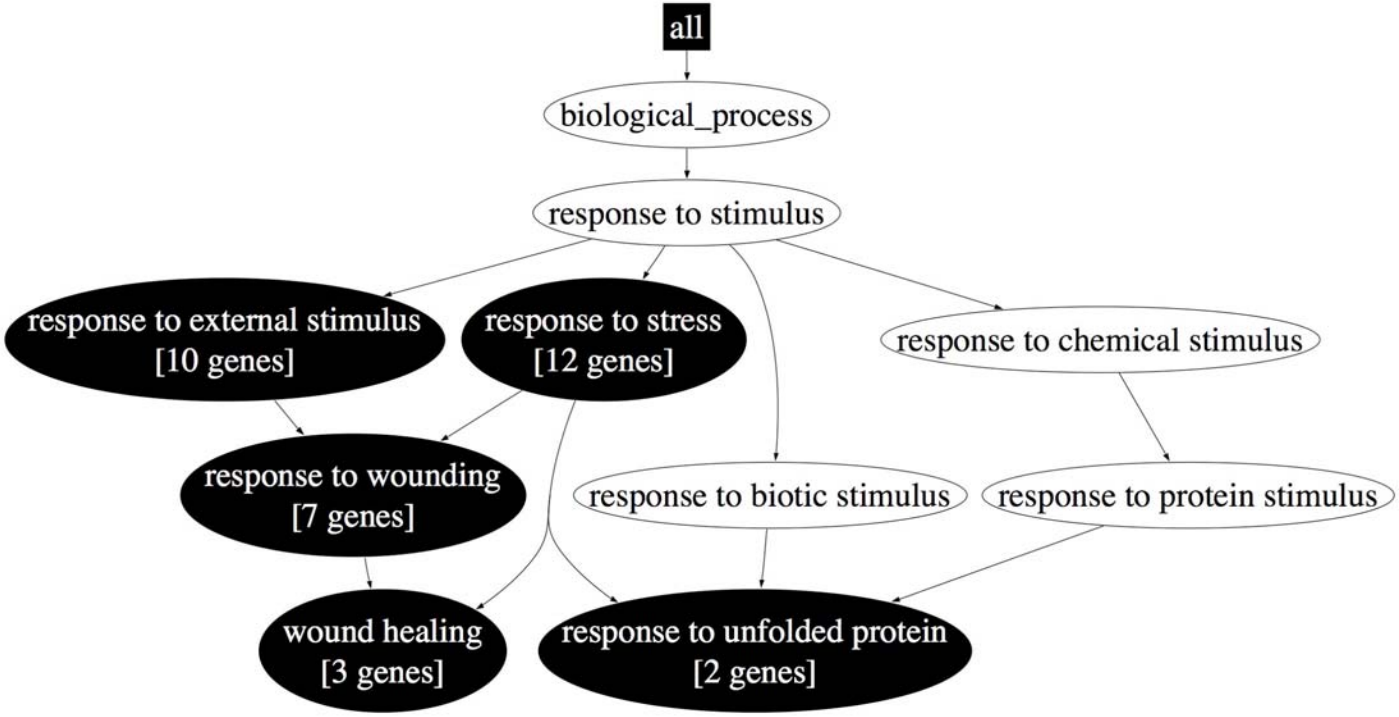


Figure S7. RT-qPCR Validation of Nine Genes Strongly Associated with Grading

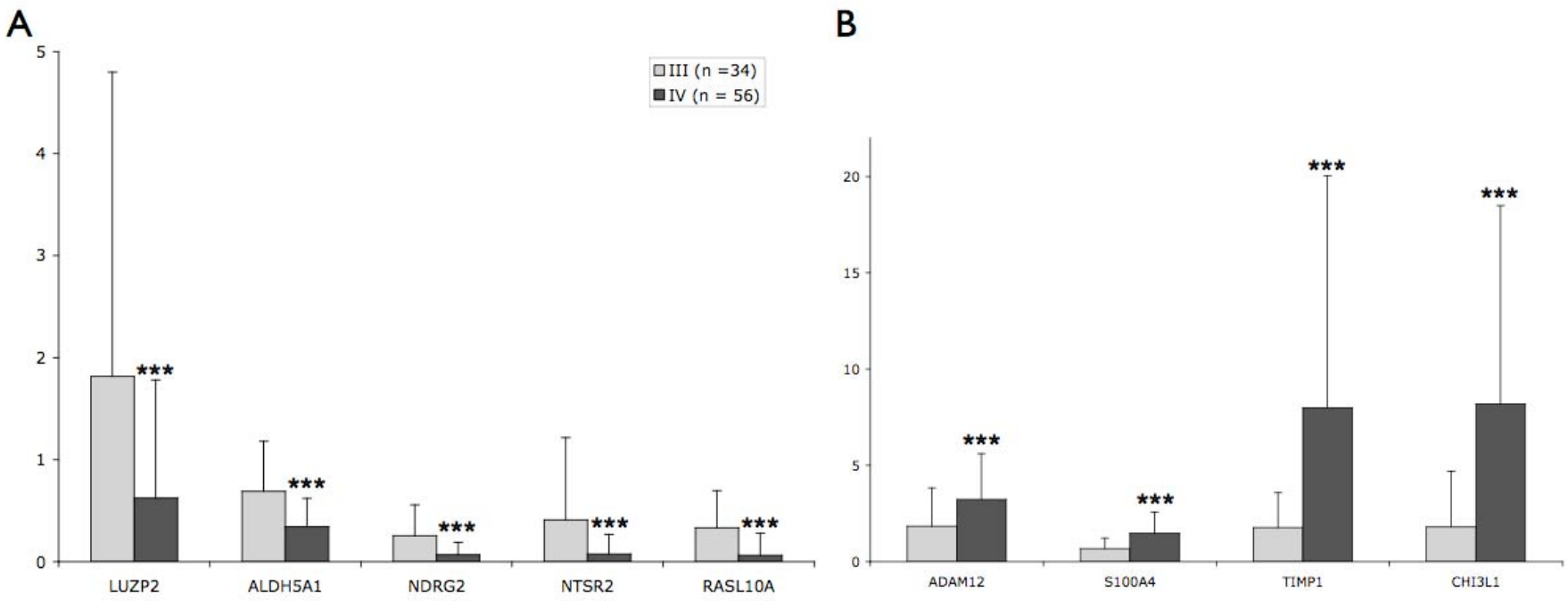


Figure S8. Univariate Analysis of Expression of 40 Genes with Overall Survival as a Dependent Variable

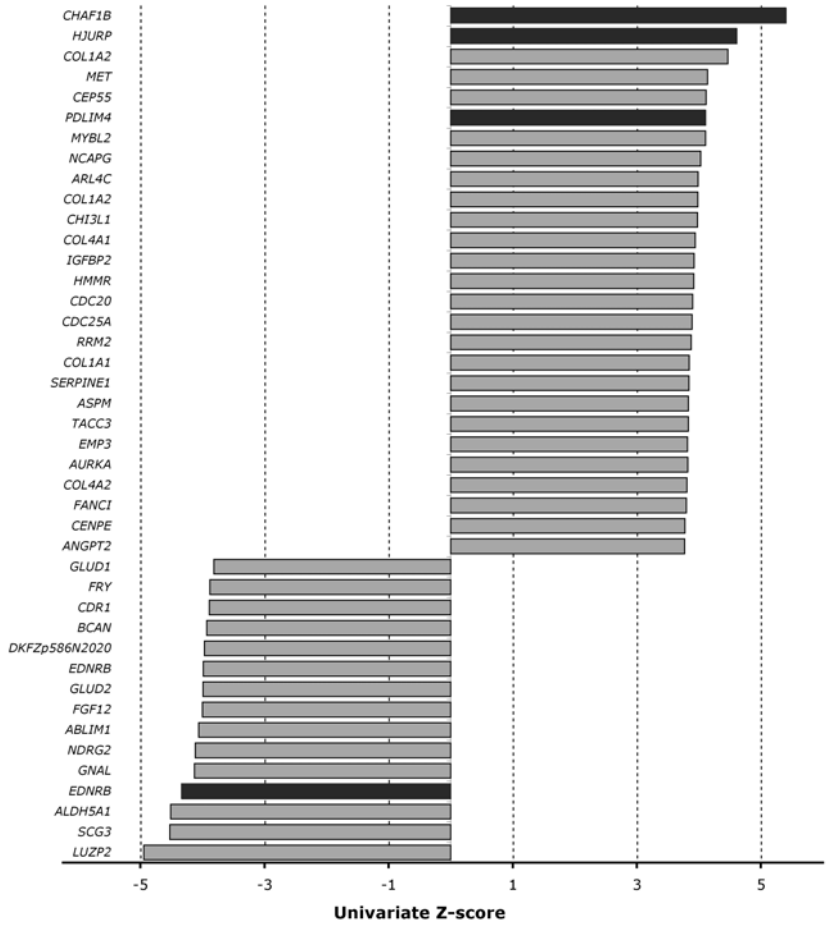
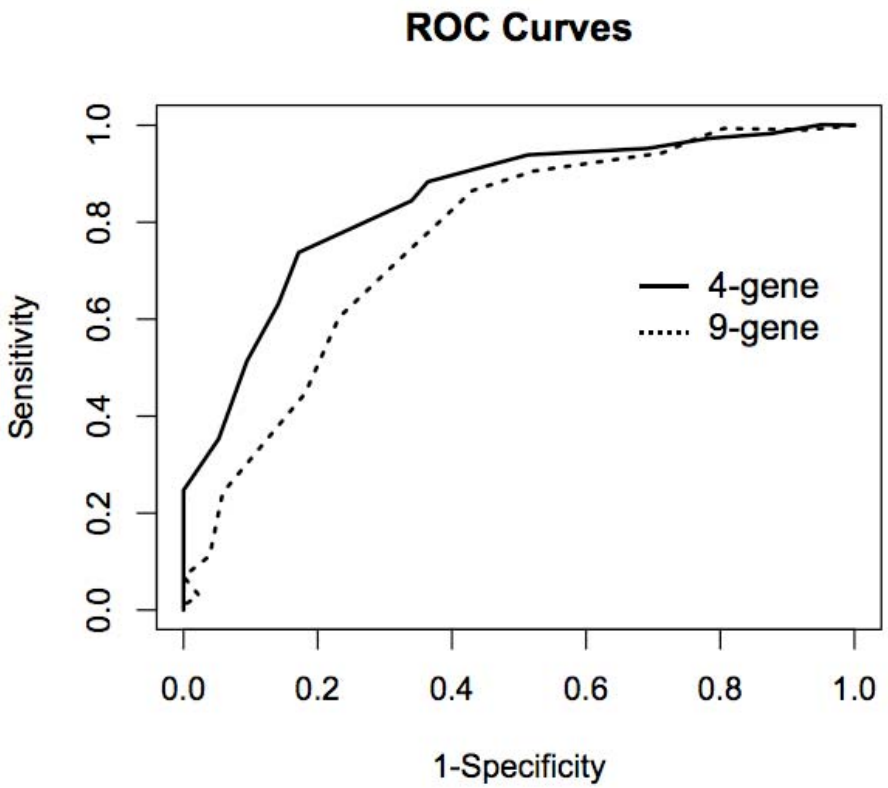


Figure S9. ROC curves for the 4-genes and 9-genes model comparison



Supplemental Figure Legends

Figure S1. Individual study analyses and combined-analysis overlap.
Venn Diagram of the four gene selections resulting from the combined analysis (rank product) and from the three individual study analyses (Student t-test). GEO data sets: GSE4412 (Freije et al., 2004), GSE4271 (Phillips et al., 2006) and GDS1962 (Sun et al.,2006). Red: consensus gene selection of 81 probesets (65 genes). See also Figures S1, S2, S3, S4, S5 and S6 and Tables S1, S2 and S3.

Figure S2. Unsupervised PCA of the 65 grading genes, with integration of biological knowledge
To determine whether the different types of tumors could be molecularly distinguished, we used a method of data reduction called principal component analysis (PCA) in which the high dimensionality of the data was reduced to two viewable dimensions representing linear combinations of variables (genes) that account for most of the variance in the original data set.
(A) PCA Individual Factor Map: Grade III tumors (red) and grade IV tumors (green) are separated along the first principal component (PC1).
(B) PCA Correlation Circle, see also Table S2.
(C) PCA Groups representation, see also Table S3 and Figures S2, S3, S4 and S5.

Figure S3. Grading Genes Annotation (Angiogenesis)
Directed Acyclic Graph for Enriched Gene Ontology 'Angiogenesis' Biological Processes associated with the Grading-genes in PCA.

Figure S4. Grading Genes Annotation (Morphogenesis)
Directed Acyclic Graph for Enriched Gene Ontology 'Morphogenesis' Biological Processes associated with the Grading-genes in PCA.

Figure S5. Grading Genes Annotation (Invasion)
Directed Acyclic Graph for Enriched Gene Ontology 'Invasion' Biological Processes associated with the Grading-genes in PCA.

Figure S6. Grading Genes Annotation (Stress)
Directed Acyclic Graph for Enriched Gene Ontology 'Stress' Biological Processes associated with the Grading-genes in PCA.

Figure S7. RT-qPCR Validation of Nine Genes Strongly Associated with Grading
Panel A and Panel B show mRNA expression changes in a subset of 90 patients with malignant gliomas (34 grade III gliomas and 56 glioblastomas): genes under-expressed (Panel A) and over-expressed (Panel B) in glioblastomas, genes from the 4-gene signature (Panel C). ***$P < 0.001$. Three genes (LUZP2, TIMP1, and CHI3L1) display a high-inter-individual expression variability (standard deviation ≥ 3). This was already reported in glioblastomas for CHI3L1 and TIMP1 (Tanwar MK, Gilbert MR, Holland EC, et al. Gene expression microarray analysis reveals YKL-40 to be a potential serum marker for malignant character in human glioma. Cancer Res. 62(15):4364-8, 2002).

Figure S8. Univariate Analysis of Expression of 40 Genes with Overall Survival as a Dependent Variable

The genes are ranked on the basis of their predictive power (univariate z score), with a negative score associated with longer overall survival and a positive score associated with shorter overall survival.

Figure S9. ROC curves for the 4-gene and the 9-gene models comparison

We compared the four-gene panel with the MD Anderson group nine-gene predictor (Colman et al., 2009). Both models are highly significant (P=1e-08 and P=3e-05, respectively). The discrimination of the four-gene model is significantly higher than the discrimination of the nine-gene model (C statistic, 0.80 [95% CI, 0.72-0.86] vs. 0.76 [95% CI, 0.64-0.81], P<0.001, respectively).

Table S1. Inter-Study Common Gene Set (65 consensus grading-genes).
Corrected P-value (P) and ratio (R) for each study are provided

Gene Symbol	Gene Title	GSE4290		GSE4271		GSE4412	
		P	R	P	R	P	R
ACTN1	actinin, alpha 1	0.001	2.70	0.044	2.20	0.003	3.90
ADAM12	ADAM metallopeptidase domain 12 (meltrin alpha)	0.000	3.61	0.001	3.23	0.047	3.94
ADM	adrenomedullin	0.004	3.45	0.000	3.81	0.002	5.04
AGXT2L1	alanine-glyoxylate aminotransferase 2-like 1	0.002	0.20	0.001	0.24	0.017	0.16
ANGPT2	angiopoietin 2	0.023	2.48	0.000	3.77	0.000	8.22
ARL4C	ADP-ribosylation factor-like 4C	0.002	2.06	0.000	3.46	0.002	3.68
BCL3	B-cell CLL/lymphoma 3	0.006	2.18	0.003	2.64	0.013	4.04
C8orf4	chromosome 8 open reading frame 4	0.008	2.77	0.037	2.34	0.016	4.21
CD163	CD163 molecule	0.004	3.47	0.027	2.22	0.005	5.68
CENPE	centromere protein E, 312kDa	0.016	2.48	0.004	2.69	0.036	3.53
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	0.008	4.63	0.001	9.40	0.000	40.49
CNTN1	contactin 1	0.005	0.37	0.000	0.34	0.007	0.29
COL1A1	collagen, type I, alpha 1	0.005	5.46	0.000	4.22	0.021	9.28
COL1A2	collagen, type I, alpha 2	0.007	2.90	0.000	3.97	0.008	6.32
COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)	0.006	4.19	0.001	3.00	0.021	5.70
COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)	0.005	5.08	0.000	5.97	0.013	7.67
COL4A1	collagen, type IV, alpha 1	0.002	3.66	0.000	3.98	0.002	5.64
COL4A2	collagen, type IV, alpha 2	0.002	3.20	0.000	2.79	0.001	4.96
COL5A1	collagen, type V, alpha 1	0.029	2.34	0.012	2.74	0.020	7.19
COL6A2	collagen, type VI, alpha 2	0.020	3.55	0.004	4.04	0.023	6.41
COL6A3	collagen, type VI, alpha 3	0.011	4.00	0.004	2.95	0.041	6.66
CSDC2	cold shock domain containing C2, RNA binding	0.006	0.28	0.000	0.23	0.039	0.29
DLL3	delta-like 3 (Drosophila)	0.008	0.38	0.013	0.36	0.023	0.22
EMP3	epithelial membrane protein 3	0.002	3.75	0.003	2.84	0.011	4.53
ESM1	endothelial cell-specific molecule 1	0.019	2.16	0.000	2.78	0.001	4.66
GDF15	growth differentiation factor 15	0.014	2.48	0.015	2.45	0.013	4.26
HMMR	hyaluronan-mediated motility receptor (RHAMM)	0.030	2.08	0.000	4.00	0.003	5.78
HSPA6	heat shock 70kDa protein 6 (HSP70B')	0.022	2.33	0.011	2.22	0.002	8.53
HSPG2	heparan sulfate proteoglycan 2	0.005	3.61	0.000	5.20	0.012	6.67
IGFBP2	insulin-like growth factor binding protein 2, 36kDa	0.003	5.27	0.000	5.02	0.006	7.35
KCNN3	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 3	0.016	0.44	0.001	0.26	0.017	0.24

LAMB1	laminin, beta 1	0.001	2.89	0.001	2.82	0.020	3.39
LOX	lysyl oxidase	0.004	3.56	0.001	3.83	0.037	4.35
LOX	lysyl oxidase	0.004	4.19	0.000	6.43	0.047	3.92
LSP1	lymphocyte-specific protein 1	0.030	2.17	0.011	2.37	0.001	8.54
LUM	lumican	0.015	3.39	0.000	5.80	0.009	16.81
LUZP2	leucine zipper protein 2	0.010	0.48	0.000	0.28	0.002	0.15
LZTS1	leucine zipper, putative tumor suppressor 1	0.026	2.21	0.007	2.38	0.023	3.75
MGAT4C	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme C (putative)	0.014	0.36	0.012	0.45	0.003	0.32
MUC1	mucin 1, cell surface associated	0.045	2.39	0.020	2.67	0.015	4.14
NCAM1	neural cell adhesion molecule 1	0.008	0.50	0.000	0.38	0.020	0.39
NDRG2	NDRG family member 2	0.005	0.45	0.000	0.22	0.016	0.23
NET1	neuroepithelial cell transforming gene 1	0.011	0.45	0.001	0.29	0.004	0.19
NNMT	nicotinamide N-methyltransferase	0.004	4.22	0.000	4.97	0.006	6.20
NRP1	neuropilin 1	0.004	4.04	0.024	2.29	0.042	4.13
NTRK2	neurotrophic tyrosine kinase, receptor, type 2	0.025	0.46	0.006	0.37	0.029	0.31
NTSR2	neurotensin receptor 2	0.000	0.08	0.003	0.18	0.042	0.11
PCOLCE	procollagen C-endopeptidase enhancer	0.005	3.37	0.000	3.11	0.013	4.48
PDPN	podoplanin	0.013	4.30	0.006	4.49	0.010	13.64
PLP2	proteolipid protein 2 (colonic epithelium-enriched)	0.002	3.10	0.002	2.50	0.041	3.85
POSTN	periostin, osteoblast specific factor	0.014	4.48	0.027	2.91	0.050	6.51
PTX3	pentraxin-related gene, rapidly induced by IL-1 beta	0.005	4.10	0.000	5.34	0.037	5.21
RASL10A	RAS-like, family 10, member A	0.006	0.44	0.000	0.30	0.006	0.34
S100A4	S100 calcium binding protein A4	0.010	2.72	0.001	3.05	0.002	8.52
S100A8	S100 calcium binding protein A8	0.050	2.35	0.014	2.65	0.016	4.50
SCD	stearoyl-CoA desaturase (delta-9-desaturase)	0.025	0.45	0.000	0.25	0.007	0.16
SCG3	secretogranin III	0.005	0.43	0.018	0.37	0.010	0.18
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	0.004	3.26	0.002	3.31	0.006	6.81
SERPINH1	serpin peptidase inhibitor, clade H (heat shock protein 47), member 1, (collagen binding protein 1)	0.001	7.68	0.000	6.75	0.031	9.50
STC1	stanniocalcin 1	0.004	4.39	0.000	5.76	0.010	4.84
TAGLN2	transgelin 2	0.015	2.38	0.001	2.98	0.004	4.89
TIMP1	TIMP metallopeptidase inhibitor 1	0.004	3.39	0.007	2.48	0.012	5.21
TNFAIP6	tumor necrosis factor, alpha-induced protein 6	0.008	2.30	0.001	3.18	0.028	3.15
VEGFA	vascular endothelial growth factor A	0.007	2.93	0.000	2.83	0.018	3.14
VIPR2	vasoactive intestinal peptide receptor 2	0.023	0.34	0.007	0.40	0.049	0.24

Table S2. PC1 variable coordinates for the 65 grading-genes.

The genes with positive coordinates are over-expressed in glioblastoma and genes with negative coordinates are under-expressed in gliomas of grade III. See details on PCA in Supplemental Experimental Procedures.

Probe	Gene Symbol	Gene Name	PC1
201666_at	*TIMP1*	TIMP METALLOPEPTIDASE INHIBITOR 1	0,89
208659_at	*CLIC1*	CHLORIDE INTRACELLULAR CHANNEL 1	0,88
211980_at	*COL4A1*	COLLAGEN, TYPE IV, ALPHA 1	0,88
207714_s_at	*SERPINH1*	SERPIN PEPTIDASE INHIBITOR, CLADE H (HEAT SHOCK PROTEIN 47), MEMBER 1, (COLLAGEN BINDING PROTEIN 1)	0,87
202404_s_at	*COL1A2*	COLLAGEN, TYPE I, ALPHA 2	0,86
201505_at	*LAMB1*	LAMININ, BETA 1	0,85
206157_at	*PTX3*	PENTRAXIN-RELATED GENE, RAPIDLY INDUCED BY IL-1 BETA	0,84
202403_s_at	*COL1A2*	COLLAGEN, TYPE I, ALPHA 2	0,84
202952_s_at	*ADAM12*	ADAM METALLOPEPTIDASE DOMAIN 12 (MELTRIN ALPHA)	0,84
215076_s_at	*COL3A1*	COLLAGEN, TYPE III, ALPHA 1 (EHLERS-DANLOS SYNDROME TYPE IV, AUTOSOMAL DOMINANT)	0,84
211161_s_at	*COL3A1*	COLLAGEN, TYPE III, ALPHA 1 (EHLERS-DANLOS SYNDROME TYPE IV, AUTOSOMAL DOMINANT)	0,84
212464_s_at	*FN1*	FIBRONECTIN 1	0,84
211964_at	*COL4A2*	COLLAGEN, TYPE IV, ALPHA 2	0,84
217739_s_at	*PBEF1*	PRE-B-CELL COLONY ENHANCING FACTOR 1	0,83
202627_s_at	*SERPINE1*	SERPIN PEPTIDASE INHIBITOR, CLADE E (NEXIN, PLASMINOGEN ACTIVATOR INHIBITOR TYPE 1), MEMBER 1	0,83
211719_x_at	*FN1*	FIBRONECTIN 1	0,83
200770_s_at	*LAMC1*	LAMININ, GAMMA 1 (FORMERLY LAMB2)	0,82
211981_at	*COL4A1*	COLLAGEN, TYPE IV, ALPHA 1	0,82
202238_s_at	*NNMT*	NICOTINAMIDE N-METHYLTRANSFERASE	0,82
201655_s_at	*HSPG2*	HEPARAN SULFATE PROTEOGLYCAN 2 (PERLECAN)	0,81
202237_at	*NNMT*	NICOTINAMIDE N-METHYLTRANSFERASE	0,81
221729_at	*COL5A2*	COLLAGEN, TYPE V, ALPHA 2	0,81
201852_x_at	*COL3A1*	COLLAGEN, TYPE III, ALPHA 1 (EHLERS-DANLOS SYNDROME TYPE IV, AUTOSOMAL DOMINANT)	0,81
200916_at	*TAGLN2*	TRANSGELIN 2	0,81
209395_at	*CHI3L1*	CHITINASE 3-LIKE 1 (CARTILAGE GLYCOPROTEIN-39)	0,81
215446_s_at	*LOX*	LYSYL OXIDASE	0,80
211651_s_at	*LAMB1*	LAMININ, BETA 1	0,80
202718_at	*IGFBP2*	INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 2, 36KDA	0,80

204597_x_at	*STC1*	STANNIOCALCIN 1	0,80
202628_s_at	*SERPINE1*	SERPIN PEPTIDASE INHIBITOR, CLADE E (NEXIN, PLASMINOGEN ACTIVATOR INHIBITOR TYPE 1), MEMBER 1	0,80
201744_s_at	*LUM*	LUMICAN	0,80
203729_at	*EMP3*	EPITHELIAL MEMBRANE PROTEIN 3	0,79
210512_s_at	*VEGF*	VASCULAR ENDOTHELIAL GROWTH FACTOR	0,79
202912_at	*ADM*	ADRENOMEDULLIN	0,79
209396_s_at	*CHI3L1*	CHITINASE 3-LIKE 1 (CARTILAGE GLYCOPROTEIN-39)	0,79
203186_s_at	*S100A4*	S100 CALCIUM BINDING PROTEIN A4 (CALCIUM PROTEIN, CALVASCULIN, METASTASIN, MURINE PLACENTAL HOMOLOG)	0,78
201136_at	*PLP2*	PROTEOLIPID PROTEIN 2 (COLONIC EPITHELIUM-ENRICHED)	0,78
208949_s_at	*LGALS3/GALIG*	GALECTIN-3 INTERNAL GENE / LECTIN, GALACTOSIDE-BINDING, SOLUBLE, 3 (GALECTIN 3)	0,78
217967_s_at	*C1ORF24*	NIBAN PROTEIN	0,78
202310_s_at	*COL1A1*	COLLAGEN, TYPE I, ALPHA 1	0,78
208636_at	*ACTN1*	ACTININ, ALPHA 1	0,78
203325_s_at	*COL5A1*	COLLAGEN, TYPE V, ALPHA 1	0,77
218802_at	*FLJ20647*	HYPOTHETICAL PROTEIN FLJ20647	0,77
202465_at	*PCOLCE*	PROCOLLAGEN C-ENDOPEPTIDASE ENHANCER	0,77
204298_s_at	*LOX*	LYSYL OXIDASE	0,77
211527_x_at	*VEGF*	VASCULAR ENDOTHELIAL GROWTH FACTOR	0,76
212489_at	*COL5A1*	COLLAGEN, TYPE V, ALPHA 1	0,76
205572_at	*ANGPT2*	ANGIOPOIETIN 2	0,76
204646_at	*DPYD*	DIHYDROPYRIMIDINE DEHYDROGENASE	0,76
212171_x_at	*VEGF*	VASCULAR ENDOTHELIAL GROWTH FACTOR	0,76
204908_s_at	*BCL3*	B-CELL CLL/LYMPHOMA 3	0,76
210510_s_at	*NRP1*	NEUROPILIN 1	0,76
221898_at	*PDPN*	PODOPLANIN	0,75
209156_s_at	*COL6A2*	COLLAGEN, TYPE VI, ALPHA 2	0,75
201438_at	*COL6A3*	COLLAGEN, TYPE VI, ALPHA 3	0,75
213418_at	*HSPA6*	HEAT SHOCK 70KDA PROTEIN 6 (HSP70B')	0,74
204879_at	*PDPN*	PODOPLANIN	0,74
202796_at	*SYNPO*	SYNAPTOPODIN	0,74
208394_x_at	*ESM1*	ENDOTHELIAL CELL-SPECIFIC MOLECULE 1	0,74
211160_x_at	*ACTN1*	ACTININ, ALPHA 1	0,74
221577_x_at	*GDF15*	GROWTH DIFFERENTIATION FACTOR 15	0,72

217966_s_at *C1ORF24*	NIBAN PROTEIN	0,71
211148_s_at *ANGPT2*	ANGIOPOIETIN 2	0,71
206850_at *RRP22*	RAS-RELATED ON CHROMOSOME 22	-0,75
221008_s_at *AGXT2L1*	ALANINE-GLYOXYLATE AMINOTRANSFERASE 2-LIKE 1	-0,74
217359_s_at *NCAM1*	NEURAL CELL ADHESION MOLECULE 1	-0,72
201830_s_at *NET1*	NEUROEPITHELIAL CELL TRANSFORMING GENE 1	-0,72
211203_s_at *CNTN1*	CONTACTIN 1	-0,71

Table S3. Enriched Gene Ontology Biological Processes associated with the 65 grading-genes.

Association with

Morphogenesis
Angiogenesis
Invasion (Adhesion, Proliferation)
Stress

GO ID	Term	P-value - enrichment	Nb_genes	PC1
GO:0065008	**regulation of biological quality**	1,97E-02	10	0,96
GO:0048731	**system development**	3,10E-04	14	0,95
GO:0048856	**anatomical structure development**	5,42E-04	16	0,95
GO:0016043	**cellular component organization**	7,75E-03	15	0,94
GO:0009605	**response to external stimulus**	1,55E-04	10	0,94
GO:0006950	**response to stress**	2,05E-02	12	0,94
GO:0022610	**biological adhesion**	8,52E-04	8	0,93
GO:0048513	**organ development**	2,77E-04	11	0,93
GO:0009653	**anatomical structure morphogenesis**	1,03E-04	11	0,93
GO:0032501	**multicellular organismal process**	7,73E-04	21	0,92
GO:0000902	**cell morphogenesis**	2,44E-03	6	0,92
GO:0006928	**cell motion**	1,03E-03	7	0,91
GO:0043062	**extracellular structure organization**	5,19E-08	7	0,90
GO:0032879	**regulation of localization**	5,87E-03	6	0,90
GO:0032989	**cellular structure morphogenesis**	2,44E-03	7	0,89
GO:0051239	**regulation of multicellular organismal process**	3,74E-02	6	0,89
GO:0042127	**regulation of cell proliferation**	2,44E-02	5	0,88
GO:0032502	**developmental process**	4,95E-03	19	0,88
GO:0007267	**cell-cell signaling**	2,97E-02	6	0,87
GO:0008544	**epidermis development**	7,78E-04	4	0,87
GO:0051674	**localization of cell**	1,04E-03	7	0,87
GO:0048646	**anatomical structure formation**	8,18E-03	3	0,87
GO:0032964	**collagen biosynthetic process**	5,35E-06	3	0,87
GO:0007169	**transmembrane receptor protein tyrosine kinase signaling pathway**	4,06E-02	3	0,86
GO:0009887	**organ morphogenesis**	4,22E-05	7	0,86

GO:0003013	**circulatory system process**	4,25E-02	3	0,85
GO:0009611	**response to wounding**	6,79E-04	7	0,85
GO:0009888	**tissue development**	2,19E-02	4	0,85
GO:0001525	**angiogenesis**	1,35E-02	2	0,85
GO:0001568	**blood vessel development**	2,78E-04	4	0,84
GO:0001944	**vasculature development**	2,14E-06	5	0,84
GO:0007155	**cell adhesion**	8,52E-04	8	0,84
GO:0001501	**skeletal system development**	2,77E-03	4	0,83
GO:0044259	**multicellular organismal macromolecule metabolic process**	6,65E-05	3	0,83
GO:0048729	**tissue morphogenesis**	4,13E-02	2	0,83
GO:0032963	**collagen metabolic process**	4,95E-05	3	0,82
GO:0042060	**wound healing**	1,62E-02	3	0,81
GO:0008284	**positive regulation of cell proliferation**	6,45E-03	4	0,81
GO:0030198	**extracellular matrix organization**	1,76E-10	7	0,81
GO:0007275	**multicellular organismal development**	1,50E-03	15	0,81
GO:0007167	**enzyme linked receptor protein signaling pathway**	7,67E-03	5	0,80
GO:0006986	**response to unfolded protein**	2,25E-02	2	0,80
GO:0007179	**transforming growth factor beta receptor signaling pathway**	8,79E-03	3	0,80
GO:0048730	**epidermis morphogenesis**	4,91E-03	2	0,80
GO:0043588	**skin development**	7,62E-08	4	0,80
GO:0022603	**regulation of anatomical structure morphogenesis**	3,70E-02	3	0,79
GO:0030199	collagen fibril organization	2,28E-09	5	0,79
GO:0044236	multicellular organismal metabolic process	1,11E-04	3	0,78
GO:0051270	regulation of cell motion	1,71E-03	4	0,78
GO:0051272	positive regulation of cell motion	1,15E-03	3	0,78
GO:0042476	odontogenesis	1,60E-05	3	0,77
GO:0031589	cell-substrate adhesion	3,88E-02	2	0,77
GO:0003018	vascular process in circulatory system	2,32E-02	2	0,77
GO:0051789	response to protein stimulus	2,38E-02	2	0,76
GO:0030335	positive regulation of cell migration	1,41E-02	2	0,76
GO:0007398	ectoderm development	1,30E-03	4	0,74
GO:0043589	skin morphogenesis	1,29E-05	2	0,74
GO:0048514	blood vessel morphogenesis	1,87E-02	2	0,74
GO:0007178	transmembrane receptor protein serine/threonine kinase signaling pathway	9,63E-03	3	0,73

GO:0008015	blood circulation	4,25E-02	3	0,71
GO:0043206	fibril organization	4,57E-04	2	0,70
GO:0007160	cell-matrix adhesion	3,40E-02	2	0,69
GO:0045765	regulation of angiogenesis	2,38E-02	2	0,69

Table S4. Differential analysis : malignant gliomas with high risk score *vs.* malignant gliomas with low risk score (Student t-test, P<0.001 with Bonferroni correction)

Only genes with a fold-change (FC) up to 2 are given

**: the gene have been implicated in glioma tumorigenicity, progression or survival

*: the gene have been implicated in different types of cancer

bold: The four genes of the pronostic classifier

Gene Symbol	Probe Set ID	Chromosomal Location	FC
CHAF1B*	204775_at	chr21q22.13	5.4
*SERPINH1***	207714_s_at	chr11q13.5	5.0
*IGFBP2***	202718_at	chr2q33-q34	4.7
*COL6A2**	209156_s_at	chr21q22.3	4.7
*SERPINE***	202628_s_at	chr7q21.3-q22	4.6
PDLIM4*	211564_s_at, 214175_x_at	chr5q31.1	4.5
*NDC80***	204162_at	chr18p11.32	4.1
*TACC3**	218308_at	chr4p16.3	4.0
*RARRES2**	209496_at	chr7q36.1	4.0
*COL1A2***	202404_s_at, 202403_s_at	chr7q22.1	4.0
*MYL9**	201058_s_at	chr20q11.23	4.0
*ASPM***	219918_s_at	chr1q31	3.8
*COL4A1***	211981_at, 211964_at	chr13q34	3.4
*FBLN1**	201787_at	chr22q13.31	3.4
*CDC45L**	204126_s_at	chr22q11.21	3.3
*COL5A1**	212489_at	chr9q34.2-q34.3	3.3
*CHAF1A**	203976_s_at	chr19p13.3	3.3
*MCM5**	201755_at	chr22q13.1	3.2
HJURP*	218726_at	chr2q37.1	3.2
*CDC20***	202870_s_at	chr1p34.1	3.1
*TIMP1***	201666_at	chrXp11.3-p11.23	3.1
*NCAPG**	218663_at	chr4p15.33	3.1
*PLP2**	201136_at	chrXp11.23	3.1
*CEP55**	218542_at	chr10q23.33	3.0

*KIF23**	204709_s_at	chr15q23	2.8
*FOXM1***	202580_x_at	chr12p13	2.8
*BIRC5***	202095_s_at, 202094_at	chr17q25	2.6
ARL4C	202208_s_at	chr2q37.1	2.6
*MDK***	209035_at	chr11p11.2	2.6
CDCA3	221436_s_at	chr12p13	2.6
TYMS	202589_at	chr18p11.32	2.5
*RRM2***	209773_s_at	chr2p25-p24	2.4
*MKI67***	212022_s_at	chr10q25-qter	2.4
CCNB2	202705_at	chr15q22.2	2.4
*MAP3K6**	219278_at	chr1p36.11	2.4
POLA2	204441_s_at	chr11q13.1	2.3
NUP210	212315_s_at	chr3p25.1	2.3
*SHMT1**	209980_s_at	chr17p11.2	2.2
*ESPL1**	204817_at	chr12q	2.2
*GTSE1**	215942_s_at, 204315_s_at, 204318_s_at	chr22q13.2-q13.3	2.2
*TAGLN2***	210978_s_at	chr1q21-q25	2.2
*NUSAP1**	218039_at	chr15q15.1	2.2
*TK1**	202338_at	chr17q23.2-q25.3	2.2
NDUFA4L2	218484_at	chr12q13.3	2.2
SLC43A3	210692_s_at	chr11q11	2.1
*CENPF**	207828_s_at	chr1q32-q41	2.1
*PPP1R15A**	202014_at	chr19q13.2	2.1
*PRC1**	218009_s_at	chr15q26.1	2.1
*CDC25C***	205167_s_at	chr5q31	2.1
*PDLIM1**	208690_s_at	chr10q22-q26.3	2.1
CCNF	204826_at	chr16p13.3	2.1
*MCM2***	202107_s_at	chr3q21	2.0
CALU	200755_s_at	chr7q32	2.0
*AURKA**	204092_s_at	chr20q13.2-q13.3	2.0
*PDLIM7**	203370_s_at	chr5q35.3	2.0
*HSPB1**	201841_s_at	chr7q11.23	2.0

*CTNND2**	209618_at	chr5p15.2	-2.0
FRY	204072_s_at	chr13q13.1	-2.1
*LRP1B***	219643_at	chr2q21.2	-2.1
*MAPT**	203928_x_at, 206401_s_at	chr17q21.1	-2.2
*ZEB1***	212758_s_at	chr10p11.2	-2.2
*CPEB3**	205773_at	chr10q23.32	-2.2
*ID4***	209292_at	chr6p22-p21	-2.2
*PLCB1***	213222_at	chr20p12	-2.2
PMP2	206826_at	chr8q21.3-q22.1	-2.4
*NDRG2***	206453_s_at	chr14q11.2	-2.4
EDNRB*	206701_x_at, 204273_at, 204271_s_at	chr13q22	-2.5
FAM13C1	214914_at	chr10q21.1	-2.8
*ALDH5A1**	203609_s_at	chr6p22.2-p22.3	-2.8
*SCG3***	219196_at	chr15q21	-3.4
*LUZP2**	215323_at	chr11p14.3	-3.9

Table S5. IDH1 mutational sequencing

Characteristic	All Patients (N=194)	Patients with Low-Risk of Death (N=47)	Patients with High-Risk of Death (N=147)
IDH1 mutation — no. (%)			
Mutated (**)	30 (16)	20 (43)	10 (7)
G395A	27 (90)	19 (95.5)	8 (80)
C394A	2 (7)	0	2 (20)
C394T	1 (3)	1 (0.5)	0
Wild-type	159 (84)	25 (57)	134 (93)
ND — no.	5	2	3
Univariate analysis	p<0.001	p=0.001	p=0.05

Supplemental Experimental Procedures

Sequences of the primers used for real-time PCR.

Gene	Ensembl Gene ID	Forward primer	Reverse primer	Amplif. efficiency
ADAM12	ENSG00000148848	5'-CTG CAT CAT GAA CGC TTC C-3'	5'-CAC ACC CCC ATT CCT TTC T-3'	1.8
ALDH5A1	ENSG00000112294	5'-CCT CTG GCA CCA GTT ATC AAG-3'	5'-CAG CTG CGT TAG CGA TTG-3'	1.9
CHAF1B	ENSG00000159259	5'-TGA CGG TGC CTC TGA CTG T-3'	5'-GGC ACC GTT CTA CTT CTT CAA-3'	1.9
CHI3L1	ENSG00000133048	5'-CCC AAC CTG AAG ACT CTC TTG T-3'	5'-TGT TGG AGG CTA TCT TGG AAA-3'	2.1
EDNRB	ENSG00000136160	5'-ATC GTC ATT GAC ATC CCT ATC A-3'	5'-GCT TAC ACA TCT CAG CTC CAA A-3'	2.2
HJURP	ENSG00000123485	5'-GCC ATC AAG CAT CAT CTC CA-3'	5'-AGA ACG TCT GGC TCC TTT GC-3'	2.1
LUZP2	ENSG00000187398	5'-CTT GAC ATC TGT TTT CCG TGA T-3'	5'-TCC AGA AGC ACT TTG TTG AGG-3'	1.9
NDRG2	ENSG00000165795	5'-GAC CTC GTT CCT CAA GAT GG-3'	5'-ACT TGA AGG CCT CGG TCA G-3'	1.9
NTSR2	ENSG00000169006	5'-GCC TGG TGA GAC ATA AAG ACG-3'	5'-TAC ATG ACC ACG ATG GCT CT-3'	1.9
PDLIM4	ENSG00000131435	5'-GCC ACG ATC ACC TCA CAC T-3'	5'-GCT GTC ATC AGG GGC ACT-3'	2.1
RASL10A	ENSG00000100276	5'-CGG ACA GTT TCG ACT ACG TG-3'	5'-GTT GCC TAC CAC GAG GAT G-3'	2.1
S100A4	ENSG00000196154	5'-GCT CAA CAA GTC AGA ACT AAA GGA G-3'	5'-GCA GCT TCA TCT GTC CTT TTC-3'	2.0
TIMP1	ENSG00000102265	5'-CTG TTG TTG CTG TGG CTG AT-3'	5'-AAC TTG GCC CTG ATG ACG-3'	1.6
HPRT1	ENSG00000165704	5'-TGA CCT TGA TTT ATT TTG CAT ACC-3'	5'-CGA GCA AGA CGT TCA GTC CT-3'	1.8
B2M	ENSG00000166710	5'-TCT GGC CTG GAG GCT ATC-3'	5'-TCA GGA AAT TTG ACT TTC CAT TC-3'	2.0

Dimensional reduction and integration of GO annotations

Principal Component Analysis (PCA) method projects the data points from the high dimension in which they are embedded into a low dimensional space, in a way that best preserves their relative distances. Euclidian distances in the space of log-transformed intensities were used. PCA was performed with the R package FactoMineR. We used a Multiple Factor Analysis (MFA) approach to map Gene Ontology terms onto the gene expression space issued from PCA.

See de Tayrac M, Lé S, Aubry M, Mosser J, Husson F. Simultaneous analysis of distinct Omics data sets with integration of biological knowledge: Multiple Factor Analysis approach. BMC Genomics 10:32, 2009.

Supplemental References

Cancéropôle Grand-Ouest Glioma Project

The Cancéropôle Grand-Ouest Glioma Project is a French project involving 7 University hospitals, 8 research laboratories (INSERM U646, INSERM UMR 601, INSERM E0211, UMR 6061 CNRS, UMR 6187, UPRES 3890, UPRES EA 2633, UPRES EA 2216, EA 3805) and 3 platforms distributed on 7 towns of the West of France (Grand Ouest). It is dedicated to the translational research and the development of new therapeutic approaches of glioblastoma.