

Supplementary Materials: *CHI3L1*, *NTRK2*, *1p/19q* and *IDH* Status Predicts Prognosis in Glioma

Elise Deluche, Barbara Bessette, Stephanie Durand, François Caire, Valérie Rigau, Sandrine Robert, Alain Chaunavel, Lionel Forestier, François Labrousse, Marie-Odile Jauberteau, Karine Durand and Fabrice Lalloué

Table S1. Clinical and histological characteristics of the French cohort according to molecular group.

Characteristics	Total	Group A	Group B	<i>p</i> -Value
<i>N</i>	64	31	33	
Age, years				
Median	47.5	55.0	40.0	0.0024
Range	22–81	26–81	22–80	
Sex				
Female/male	26/38	12/19	14/19	0.7
Surgical approach, <i>n</i> (%)				
Complete resection	29 (45)	11 (35)	18(54)	0.12
Subtotal resection	35 (55)	20 (65)	15(46)	
Histology, <i>n</i> (%)				
Astrocytoma (II/III/IV)	7/17/21	4/4/17	8/13/4	0.0002
Oligodendroglioma (II/III)	7/8	2/6	5/2	
<i>IDH</i> mutant/ <i>IDH</i> wild-type	36/28	14/17	22/11	0.04
1p19q codeletion: yes/no	14/50	6/25	8/25	0.6
Localization, <i>n</i> (%)				
Frontal	30 (46)	15 (48)	15 (45)	
Temporal	19 (30)	7 (23)	12 (37)	0.2
Parietal	11 (18)	8 (25)	3 (9)	
Occipital	4 (6)	1 (4)	3 (9)	
Radiotherapy in first line, <i>n</i> (%)	44 (69)	25 (80)	19 (63)	0.04
Chemotherapy in first line, <i>n</i> (%)	35 (54)	20 (64)	15 (51)	0.1

p-value was calculated for all patients in the histology and localization groups by chi-square test.

Table S2. Clinical and histological characteristics of the TCGA cohort.

Characteristics	Total	Group A	Group B	<i>p</i> -Value
Number	671	283	388	
Age, years				
Median	46.0	58.0	38.0	<0.001
Range	18–89	21–89	18–87	
Histology				
Astrocytomas (II/III/IV)	144/186/157	22/90/154	122/96/3	<0.001
Oligodendrogliomas (II/III)	105/79	7/10	98/69	
<i>IDH</i> mutant/ <i>IDH</i> wild-type	421/250	53/230	368/20	<0.001
1p19q codeletion: yes/no	181/491	18/265	163/225	<0.001

Table S3. Univariate and Multivariate Cox Proportional-Hazards Models for gliomas in TCGA cohort.

Characteristics	No. of Patients	Overall survival			
		Univariate		Multivariate	
		HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>
Age at diagnosis	671	1.067 (1.05–1.07)	<0.0001	1.033 (1.02–1.04)	<0.0001
Histologic type					
Astrocytoma	487	Reference	<0.0001	Reference	
Oligodendroglioma	184	0.075 (0.0001–0.14)		0.775 (0.37–1.59)	0.489
Grade					
II	249	Reference		Reference	
III	265	3.185 (2.16–4.69)	<0.0001	1.93 (1.28–2.91)	0.002
IV	157	19.313 (13.01–28.67)	<0.0001	3.65 (2.17–6.14)	<0.0001
Molecular group					
Poor prognosis group	235	29.129 (12.80–66.26)	<0.0001	7.55 (2.69–21.20)	0.0001
Intermediate group	355	3.347 (1.455–7.702)	0.004	2.69 (1.07–6.77)	0.035
Good prognosis group	81	Reference		Reference	

Table S4. Custom-made human-specific TaqMan® micro-fluidic cards containing panels of 96 gene expression assays.

Function	Gene Name	Gene Symbol	GenBank No.	Human Assay ID	Function	Gene Name	Gene Symbol	GenBank No.	Human Assay ID
Receptors	EGFRa	EGFR	NM_005228	Hs01076078_m1	Neurotrophin pathways	NTRK1	NTRK1	NM_001007792.1	Hs01021011_m1
	EGFRb	EGFRb	NM_201282	A189KGC		NTRK2	NTRK2	NM_001007097.1	Hs00178811_m1
	EGFRc	EGFRc	NM_201283	A1AAZL5		NTRK2	NTRK2 T1 (NTRK2 bis)	NM_001007097.1	Hs01093110_m1
	EGFRD	EGFRD	NM_201284	A1BJXSD		NTRK2	NTRK2 FL (NTRK2 variant)	NM_006180.3	Hs01093096_m1
	EGFRvIII	EGFRvIII	custom-designed	A1CSVYL		NTRK3	NTRK3	NM_001007156.2	Hs00176797_m1
	ERB-2	ERRB2	NM_004448	Hs01001580_m1		P75	P75	NM_002507.3	Hs00609977_m1
	ERB-3	ERRB3	NM_001982	Hs00951464_m1		SORTILIN 1	SORT1	NM_001205228.1	Hs00361760_m1
	ERB-3	sERRB3	NM_001005915.1	Hs00176538_m1		NEUROTENSIN	NTS	NM_006183.4	Hs00175048_m1
	ERB-4	ERB4	NM_005235	Hs00955525_m1		NEUROTENSIN RECEPTOR 1	NTSR1	NM_002531.2	Hs00901551_m1
	MET	MET	NM_000245	Hs01565584_m1		NEUROTENSIN RECEPTOR 2	NTSR2	NM_012344.3	Hs00892563_m1
Ligands	EGF	EGF	NM_001963	Hs01099999_m1	Hypoxia	HIF-a	HIF-a	NM_001243084.1	Hs00153153_m1
	TGF-a	TGF-a	NM_003236	Hs00608187_m1		HIF-b	HIF-b	NM_001197325.1	Hs01121918_m1
	AMPHIREGULIN	AREG	NM_001657	Hs00950669_m1		VEGF-A	VEGF-A	NM_001025366.2	Hs00900055_m1
	EPIREGULIN	EREG	NM_001432	Hs00914313_m1		VEGF-2	KDR	NM_001243733.1	Hs00173634_m1
	BETACELLULIN	BTC	NM_001729	Hs01101204_m1		VEGF-3	FLT4	NM_005429.2	Hs00153458_m1
	HEPARIN-BINDING GROWTH FACTOR	HB-EGF	NM_001945	Hs00181813_m1		VEGF-D	VEGF-D	NM_004469.4	Hs01128657_m1
	NEUREGULIN 1	NRG1-1	NM_001160001.1....	Hs00247620_m1		VEGFR-I	VEGFR-I	NM_001159920.1	Hs01052961_m1
		NRG1-2	NM_001160002.1	Hs01108479_m1		VEGFR-II	VEGFR-II	NM_002253.2	Hs00911700_m1
		NRG1-3	NM_013959.3	Hs01103792_m1		VEGFR-III	VEGFR-III	NM_002020.4	Hs01047677_m1
	NEUREGULIN 2	NRG2	NM_001184935.1	Hs00171706_m1		LC3	LC3	NM_032514.3	Hs01076567_g1
	NEUREGULIN 3	NRG3	NM_001165972.1	Hs01377907_m1	BNIP3	BNIP3	NM_004052.2	Hs00969291_m1	
	NEUREGULIN 4	NGR4	NM_138573.3	Hs00945535_m1	BECLIN	BECLIN	NM_003766.3	Hs00186838_m1	
	TOMOREGULIN	TMEFF- 1	NM_003692.4	Hs00902905_m1	PINK1	PINK1	NM_032409.2	Hs00260868_m1	
	TOMOREGULIN (ERB4)	TMEFF- 2	NM_016192.2	Hs01086906_m1	PARKIN	PARK2	NM_004562.2	Hs01038325_m1	
	KRAS	KRAS	NM_033360.2	Hs00364284_g1	NIX	NIX	NM_004331.2	Hs01087963-m1	
	NRAS	NRAS	NM_002524.4	Hs00180035_m1	ATG5	ATG5	NM_004849.2	Hs00169468_m1	
Intracellular signaling	BRAF	BRAF	NM_004333.4	Hs00269944_m1	P62	P62	NM_001142298.1	Hs01061917_g1	
	PIK3CA	PIK3CA	NM_006218.2	Hs00907957_m1	Glycosylation	CHI3L1	CHI3L1	NM_001276.2	Hs00609691_m1

	AKT1	AKT1	NM_004562.2	Hs00178289_m1		KLRC3	KLRC3	NM_002261.2	Hs00749702_s1
	AKT2	AKT2	NM_013987.2	Hs01086102_m1		ST3GAL5	ST3GAL5	NM_001042437.1	Hs00187405_m1
	AKT3	AKT3	NM_013988.2	Hs00987350_m1		ATHL1	ATHL1	NM_025092.4	Hs00228253_m1
	CDC42	CDC42	NM_001791	Hs00918044_g1		ST8SIA1	ST8SIA1	NM_003034.3	Hs00268157_m1
	RHOA	RHOA	NM_001664	Hs00357608_m1		PRUNE2/KIAA0367	PRUNE2/KIAA0367	NM_015225.2	Hs00322421_m1
	RAC1	RAC-1	NM_018890	Hs01588892_g1		GLT25D2	GLT25D2	NM_015101.2	Hs00362851_m1
	INTERNEXIN-A	INA	NM_032727.3	Hs00190771		GAA	GAA	NM_000152.3	Hs00164635_m1
	IDH1	IDH1	NM_005896.2	Hs01855675_s1		CD133	CD133	NM_001145847.1	Hs01009250_m1
	IDH2	IDH2	NM_002168.2	Hs00158033_m1		38261	38261	NM_001173531.1	Hs04260367_gH
	GFAP	GFAP	NM_001131019.2	Hs00909233_m1	Stem cell markers	SOX-2	SOX-2	NM_003106.3	Hs01053049_s1
	NESTINE	NESTINE	NM_006617.1	Hs04187831_g1		CXR4	CXCR4	NM_001008540.1	Hs00607978_s1
	OLIG2	OLIG2	NM_005806.3	Hs00300164_s1		SSEA1	SSEA1	NM_002033.3	Hs01106466_s1
	NEUROFILAMENT	NEFL	NM_006158	Hs00196245_m1		NANOG	NANOG	NM_024865.2	Hs04260366_g1
	SYNAPTOPHYSIN	SYP	NM_003179.2	Hs00300531_m1					
Glioma markers	CD34	CD34	NM_001025109.1 NM_001773.2	Hs00990732_m1	Housekeeping genes	HPRT	HPRT	NM_000194.2	Hs02800695_m1
	P53	P53	NM_000546.5	Hs01034249_m1		18S	18S	NR_003286.2	Hs03928985_g1
	NOTCH2	NOTCH2	NM_001200001.1 NM_024408.3	Hs01050702_m1		BETA 2-MICROGLOBULIN	B2M	NM_004048.2	Hs00984230_m1
	BDNF	BDNF	NM_001143809.1	Hs03805848_m1		GAPDH	GAPDH	NM_001256799.1	Hs02758991_g1
	NERVE GROWTH FACTOR	NGF	NM_002506.2	Hs01113193_m1					
	NT3	NT3	NM_001102654.1	Hs00267375_s1					
	NTF4	NT4	NM_006179.4	Hs01921834_s1					

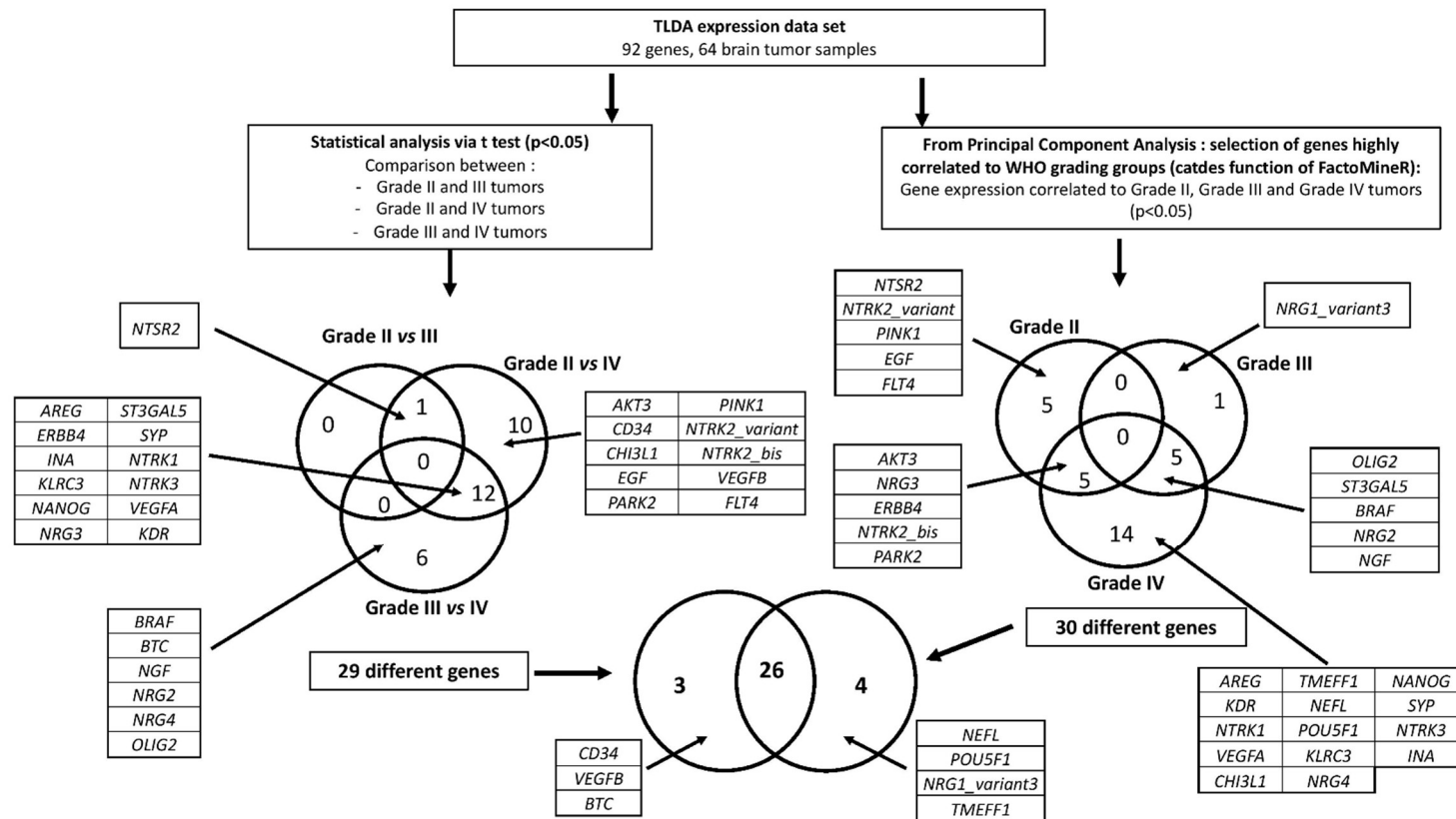


Figure 1. Venn diagram of gene selection in the studied cohort. Intersections between sets indicate the numbers of shared genes, whereas numbers of specific genes are shown in set-specific areas. A total of 92 genes were analyzed from 64 tumor samples, and 26 genes were selected from the cross-section of two statistical methods (*t*-test and principal component analysis).

