Supplemental Figures and Tables:

Supplemental Fig. 1 DKFZ-EP1NS form tumors *in vivo* in a niche-dependent manner
a Subcutaneously injected DKFZ-EP1NS cells form tumors with a histology (right panel) reminiscent of the histology of the subcutaneous metastasis of the patient (left panel), recapitulating the tumor in a niche-dependent manner (original magnification: 100x). Of note, the subcutaneous tumors in mice display a clear cell-phenotype, as did the patient´s subcutaneous metastasis. **b** Intraperitoneally injected DKFZ-EP1NS cells in matrigel form tumors with compact small round cells, with no morphological correlate in the patient (original magnification: 100x).

Supplemental Fig. 2 Immunohistochemical staining for epithelial membrane antigen (EMA), smooth muscle actin (SMA) and vimentin. EMA, SMA and vimentin stain positive and xenografts stain comparable to the patient´s tumor. Black and white arrows indicate the typical granular staining pattern for EMA, insets show enlarged areas of the original image. Note the pattern for SMA, where an increase in positivity from patient´s primary tumor to second recurrence can be seen, with the staining intensity of the mouse 1° and 2° xenografts most closely resembling the second recurrence (original magnification : EMA: 400x, SMA and vimentin: 200x). rec: recurrence; 1°: mouse primary xenograft; 2°: mouse secondary xenograft; met: metastasis; s.c.: subcutaneous.

Supplemental Fig. 3 Immunohistochemical staining for CD99, cytokeratin, S100 and synaptophysin. Both the patient´s tumor, recurrences and metastasis as well as the mouse 1°, 2° orthotopic and subcutaneous xenograft stain negative for CD99, cytokeratin, S100 and synaptophysin (original magnification : 200x). All stainings were tested on positive controls. rec: recurrence; 1°: mouse primary xenograft; 2°: mouse secondary xenograft; met: metastasis; s.c.: subcutaneous.

Supplemental Fig. 4 DKFZ-EP1NS cells retain typical aberrations and belong to cytogenetic group 3 and molecular subgroup C
a Exemplary data of FISH analysis of late passage (passage 30) DKFZ-EP1NS cells cultured *in vitro*. The left panel depicts changes at chromosome 1p, as shown by loss of one signal for 1p telomere (1pTEL, green) and for 1p36 (red), while retaining the normal two signals for 1q (1q25, aqua). The right panel depicts the monosomy of chromosome 9 (9p11-q11, green, one signal only) and homozygous loss of 9p21 (orange, no signal), the locus of *CDKN2A*. P30: passage 30.

b Assessment of gene expression in DKFZ-EP1NS at different passages (P14-P23) indicative of molecular subgroup identity, as measured by quantitative real-time RT-PCR, relative to normal total brain control. Only genes from subgroup C are all consistently overexpressed, grouping DKFZ-EP1NS cells into subgroup C.

Supplemental Fig. 5 A high common proportion of upregulated genes reveals similarity of NSC and DKFZ-EP1NS cells.
a Correspondence at the top (CAT)-plots reveal a high degree of common proportion of upregulated clones in neural stem cells (NSC) and DKFZ-EP1NS (EP1NS), and to a lesser degree of downregulated genes in NSC and EP1NS. **b** CAT-plots show a high common proportion of up- and downregulated clones in orthotopic and subcutaneous models, and lesser common proportion in xenografts and EP1NS. sc: subcutaneous; ot: orthotopic; primary: primary tumors.

Supplemental Table 1 Characteristics of patients included in the gene expression profiling. PFS: progression free survival; OS: overall survival.

Supplemental Table 2 Antibodies used in this study

Supplemental Table 3 Primers used in this study. F: forward primer; R: reverse primer.

Supplemental Table 4 Calculation of half maximal effective concentration (EC50), published maximal peak plasma concentrations (max PPC), calculation of EC50/max PPC ratios; HDACi: histone deacetylase inhibitor; VPA: valproic acid; VCR: vincristine; CDDP: cisplatin; TMZ: temozolomide.

supplemental figure 1

Suppl Fig 1

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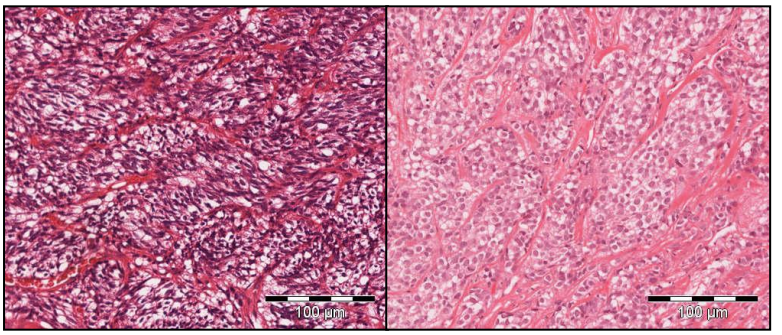
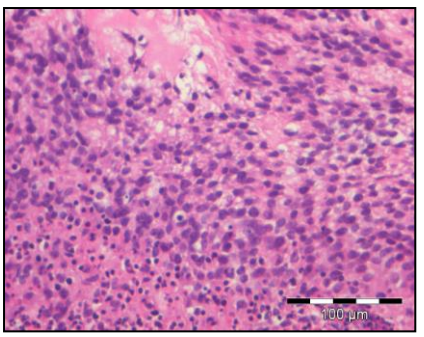
a



patient subcutaneous mouse subcutaneous

b



mouse intraperitoneal

supplemental figure 2

Suppl Fig 2

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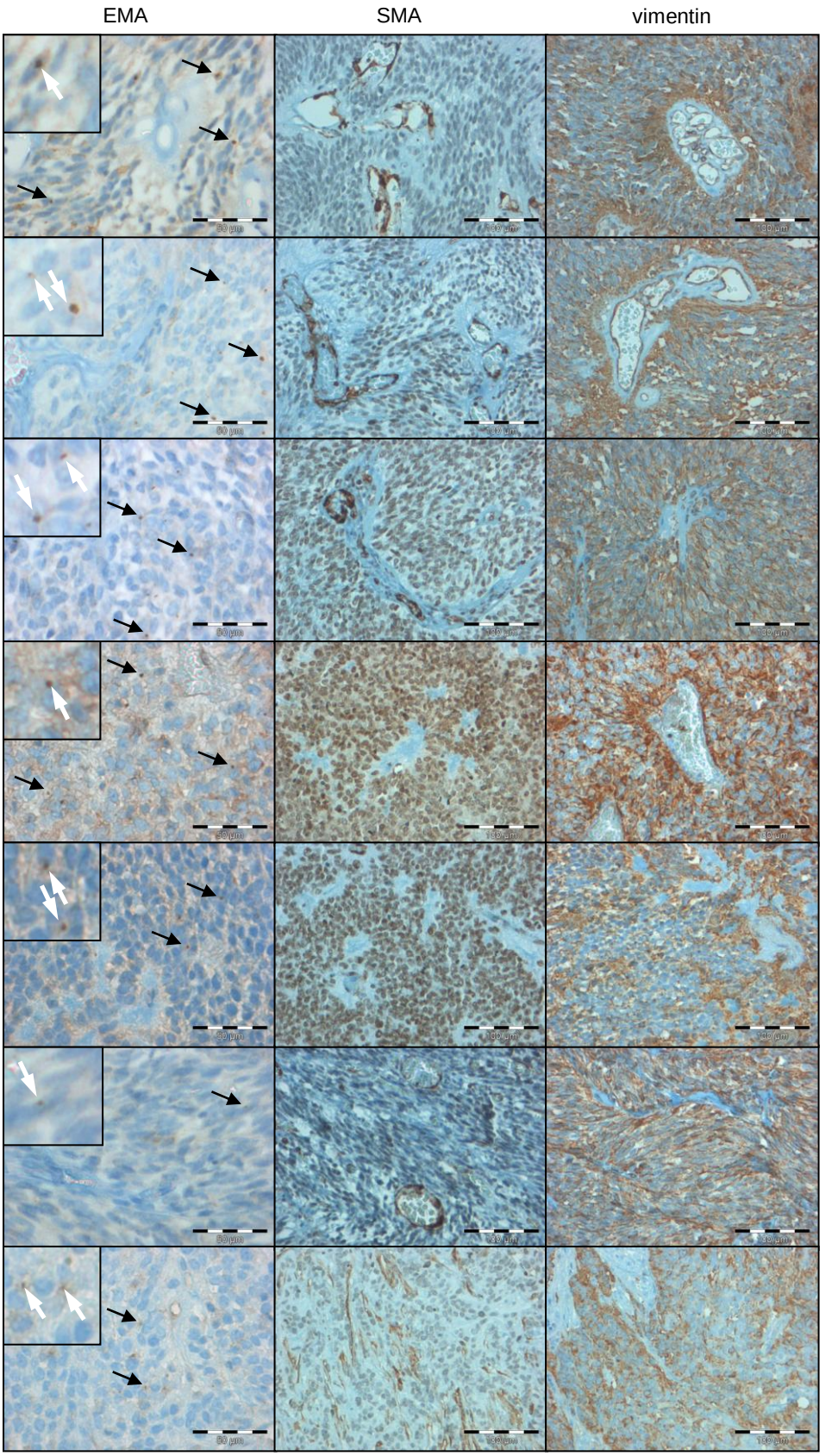

supplemental figure 3

Suppl. Fig. 3

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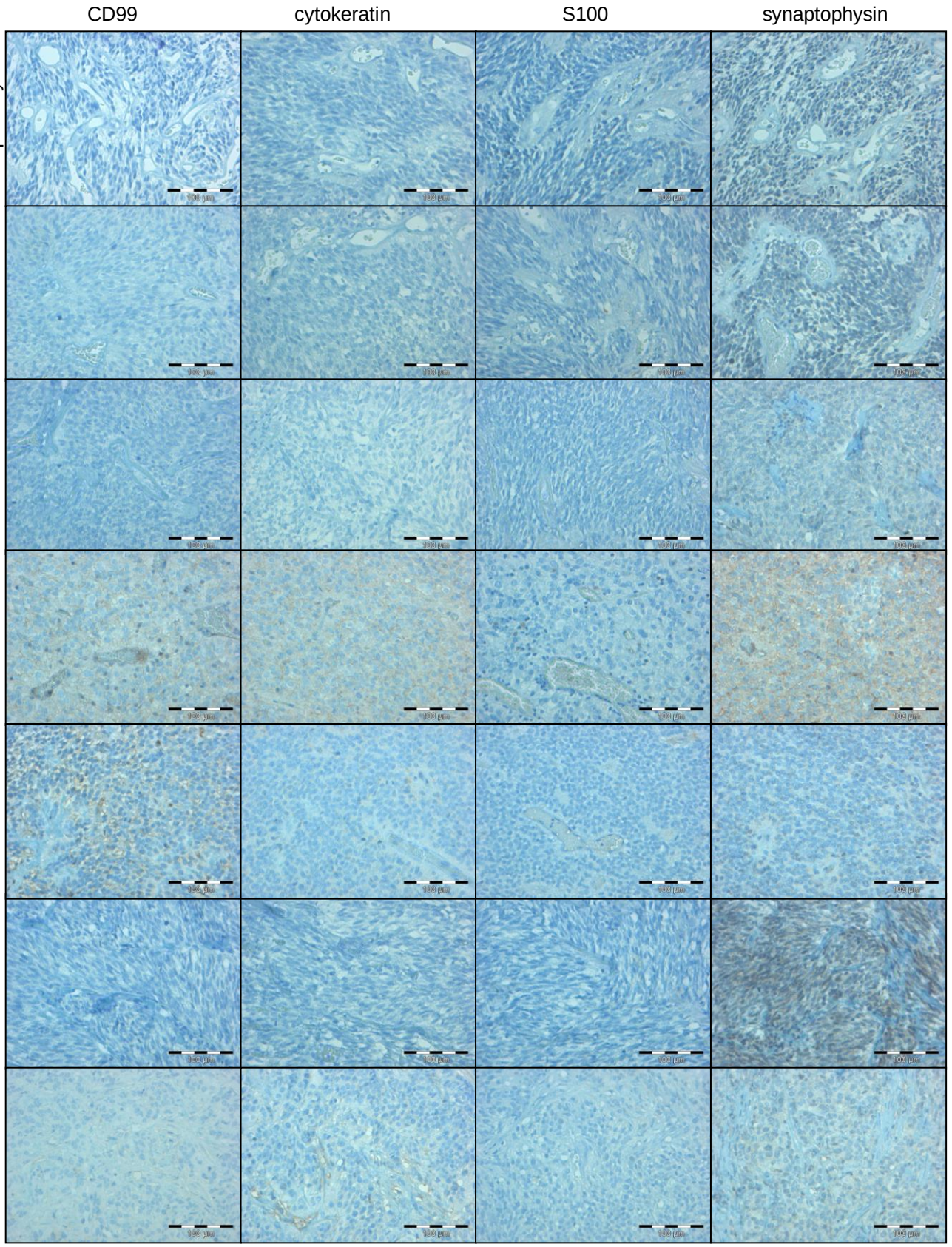

supplemental figure 4

Suppl. Fig. 4

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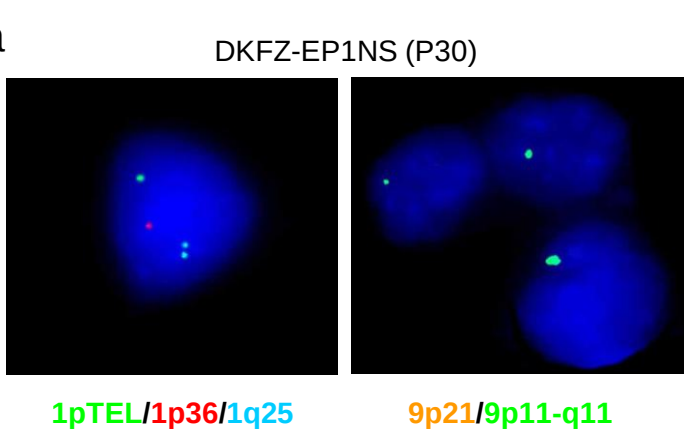
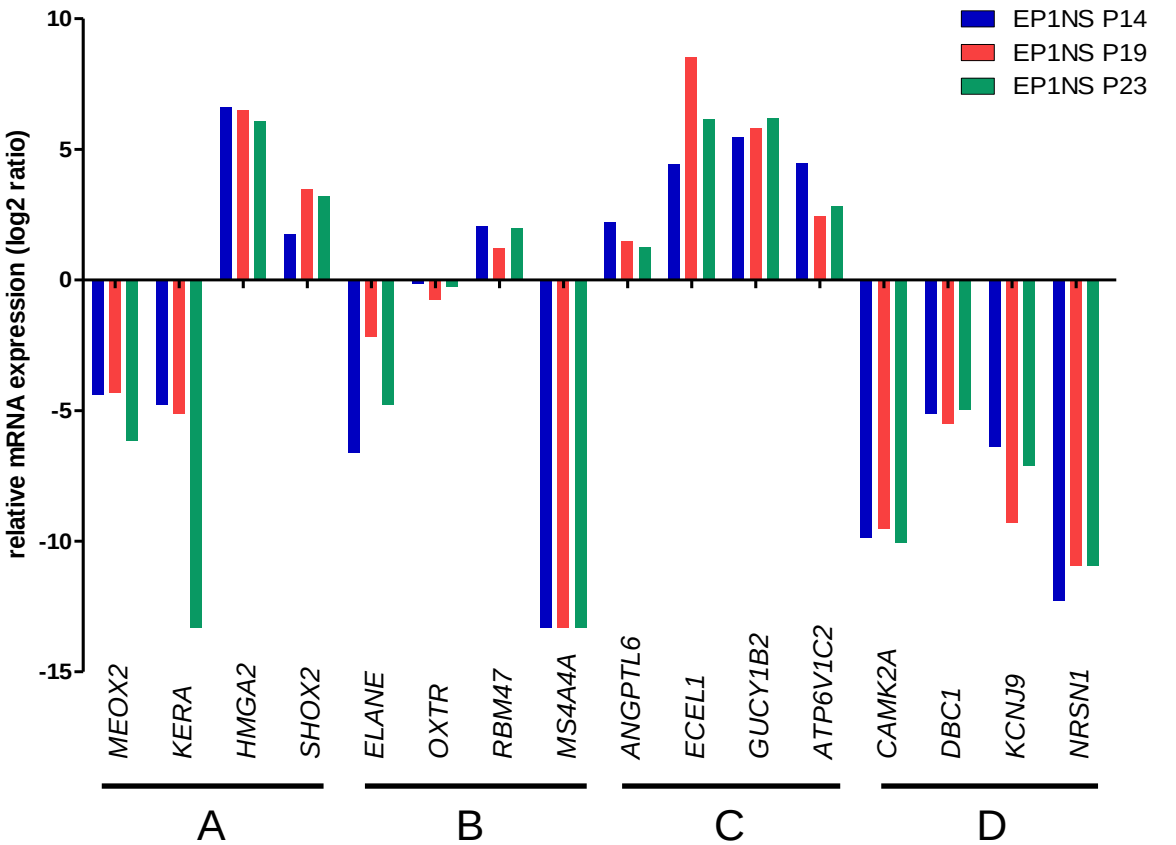
a



b



supplemental figure 5

Suppl. Fig. 5

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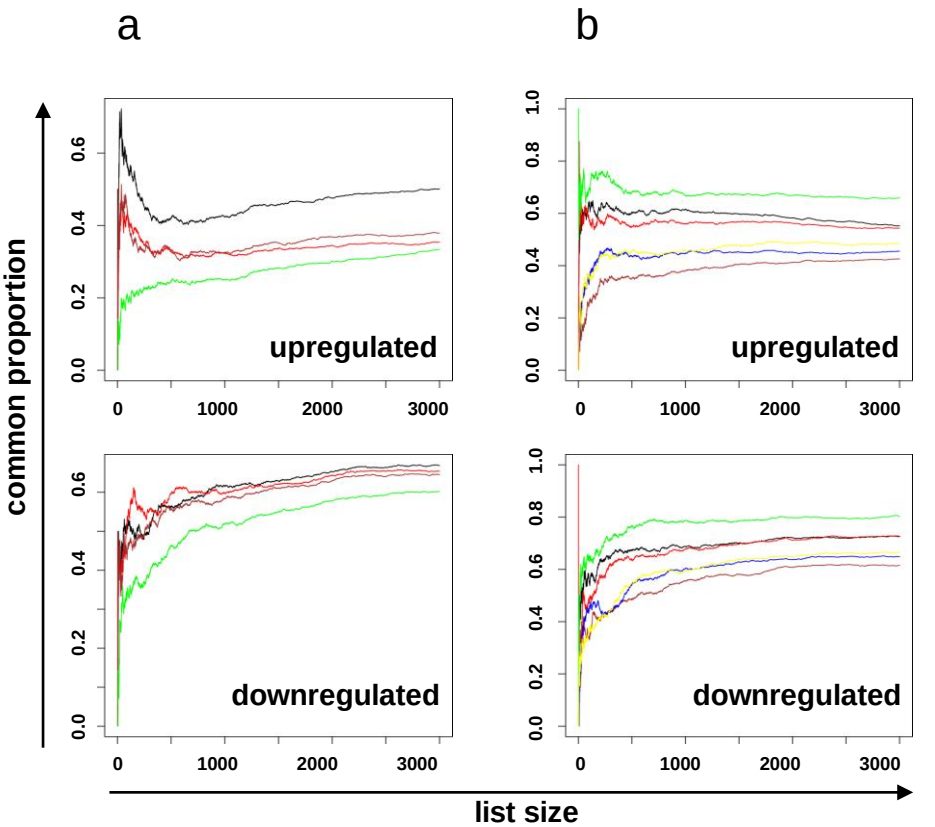

NSC vs. EP1NS
NSC vs. sc
NSC vs. ot
NSC vs. primary
sc vs. ot
EP1NS vs. sc
EP1NS vs. ot
ot vs. primary
sc vs. primary
EP1NS vs. primary

Supplemental table 1
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Supplemental Table 1

Characteristics of patients included in the gene expression profiling

Total number of patients = 7

ID	*age (years)*	*gender*	*location*	*WHO grade*	*recurrence*	*PFS (months)*	*death*	*OS (months)*	*metastases*
Primary1	12	female	supratentorial	III	yes	72	yes	98	no
Primary2	4	female	supratentorial	III	yes	12	yes	76	yes
Primary3	10	male	supratentorial	III	yes	24	yes	57	yes
Primary4	9	male	supratentorial	III	yes	26	yes	51	yes
Primary5	9	male	supratentorial	III	yes	31	yes	60	yes
Primary6	5	female	supratentorial	III	yes	8	yes	53	yes
Primary7	20	female	supratentorial	III	yes	28	yes	52	yes

Supplemental table 2
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Supplemental Table 2

Antibodies used in this study

antigen	*application*	*company*	*cat.no.*
CD15	flow cytometry	BD Pharmingen	551376
CD44	flow cytometry	BD Pharmingen	555478
CD133	flow cytometry	Miltenyi Biotec	130-092-334
CD271	flow cytometry	Miltenyi Biotec	130-091-884
CXCR4	flow cytometry	RD Systems	FAB173A
Nestin	flow cytometry	Millipore	AB5922
Ki67/MiB1	IHC	Thermo Scientific	RM-9106-S
GFAP	IHC	Dako	Z0334
Nestin	IHC	Millipore	AB5326
CD99	IHC	Thermo Scientific	MS-294-P
Cytokeratin AE	IHC	DCS	CI702R06
EMA	IHC	Neo Markers	MS-348-P
S100	IHC	Dako	Z0311
SMA	IHC	Dako	M0851
Synaptophysin	IHC	Dako	M0776
Vimentin	IHC	Dako	M0725
acetylated Histone 4	western blot	Upstate	06-866
beta-Actin	western blot	Sigma-Aldrich	A5441
GFAP	western blot	Millipore	MAB3402
NEFM	western blot	Upstate	05-744

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Supplemental Table 3

Primers used in this study

Primer	*Gene*	*for/rev/mix*	*company*	*cat.no.*	*sequence*
PGK1	*PGK1*	mix	Qiagen	QT00013776	n/a
SDHA	*SDHA*	mix	Qiagen	QT01668919	n/a
NES	*NES*	mix	Qiagen	QT00235781	n/a
MSI1	*MSI1*	mix	Qiagen	QT00025389	n/a
DCX	*DCX*	mix	Qiagen	QT00008540	n/a
NEFM	*NEFM*	mix	Qiagen	QT00073885	n/a
TUBB3_F	*TUBB3*	for	Thermo Scientific	n/a	AGCAAGAACAGCAGCTACTTCGT
TUBB3_R	*TUBB3*	rev	Thermo Scientific	n/a	GATGAAGGTGGAGGACATCTTGA
MAP2	*MAP2*	mix	Qiagen	QT00057358	n/a
GFAP	*GFAP*	mix	Qiagen	QT00081151	n/a
MOG	*MOG*	mix	Qiagen	QT00023954	n/a
WDR16_F	*WDR16*	for	Thermo Scientific	n/a	GCACCGATGGGACTTGTATC
WDR16_R	*WDR16*	rev	Thermo Scientific	n/a	TATCGACCCAGACAGGGAAC
FABP7	*FABP7*	mix	Qiagen	QT00007322	n/a
MEOX2	*MEOX2*	mix	Qiagen	QT00236852	n/a
KERA	*KERA*	mix	Qiagen	QT00021280	n/a
HMGA2	*HMGA2*	mix	Qiagen	QT01157674	n/a
ELANE	*ELANE*	mix	Qiagen	QT00017010	n/a
OXTR	*OXTR*	mix	Qiagen	QT00001715	n/a
RBM47	*RBM47*	mix	Qiagen	QT00082670	n/a
ANGPTL6	*ANGPTL6*	mix	Qiagen	QT01027075	n/a
ECEL1	*ECEL1*	mix	Qiagen	QT01012830	n/a
GUCY1B2	*GUCY1B2*	mix	Qiagen	QT00063574	n/a
CAMK2A	*CAMK2A*	mix	Qiagen	QT00024010	n/a
DBC1	*DBC1*	mix	Qiagen	QT00093058	n/a
KCNJ9	*KCNJ9*	mix	Qiagen	QT00011935	n/a

Supplemental table 4

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Supplemental Table 4

Calculation of EC50, peak plasma concentrations and ratios

Type	*Drug*	*EC50 (M)*	*95% CI of EC50 (M)*	*max PPC (M)*	*EC50/max PPC*	*reference for PPC*
HDACi	**VPA**	1.68E-03	0.888E-03 - 3.166E-03	3.41E-04	***4.92***	Voso MT, Clin Cancer Res. (2009) Aug 1;15(15):5002-7
	Entinostat	1.20E-06	9.663E-07 - 1.496E-06	3.90E-07	***3.08***	Kummar S, Clin Cancer Res. (2007) Sep 15;13(18 Pt 1):5411-7
	Vorinostat	7.76E-07	5.681E-07 - 1.060E-06	4.49E-06	***0.17***	Fakih MG, Clin cancer Res (2010) 16: 3786-3794
	Panobinostat	2.90E-09	1.04E-09 - 8.09E-09	4.09E-08	***0.07***	Rathkopf D, Cancer Chemother Pharmacol (2010) 66:181–189
chemotherapeutic	**VCR**	6.23E-06	7.517E-07 - 5.155E-05	5.30E-08	***117.51***	Corona G, Rapid Commun Mass Spectrom. (2008) 22(4):519-25
	CDDP	9.38E-03	1.702E-03 - 51.75E-03	4.98E-05	***188.43***	van Hennik MB, Cancer Res. (1987) Dec 1;47(23):6297-301
	TMZ	7.67E-02	n/d	7.21E-05	***1064.43***	Ostermann S, Clin Cancer Res (2004) 10: 3728–3736