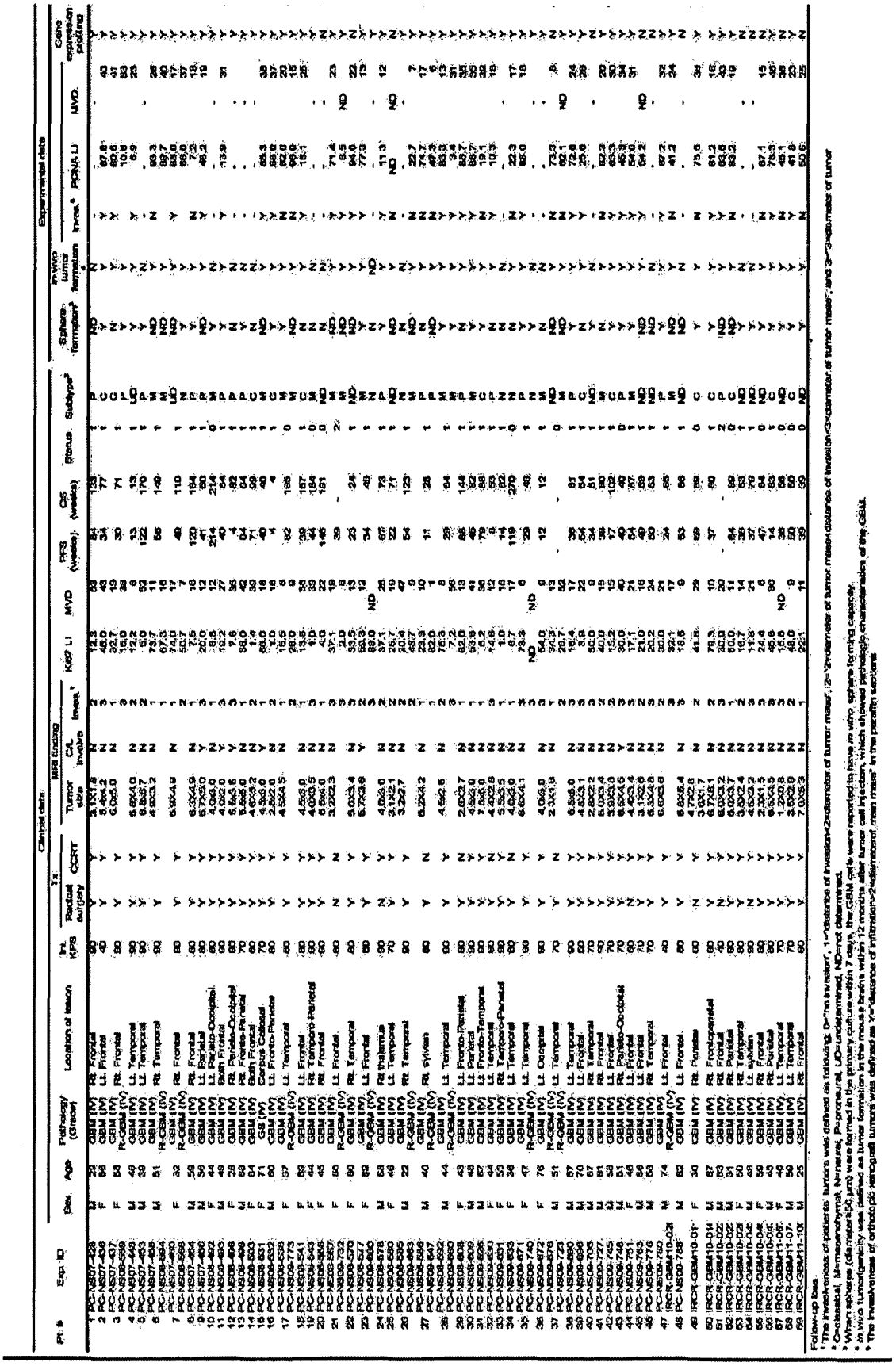
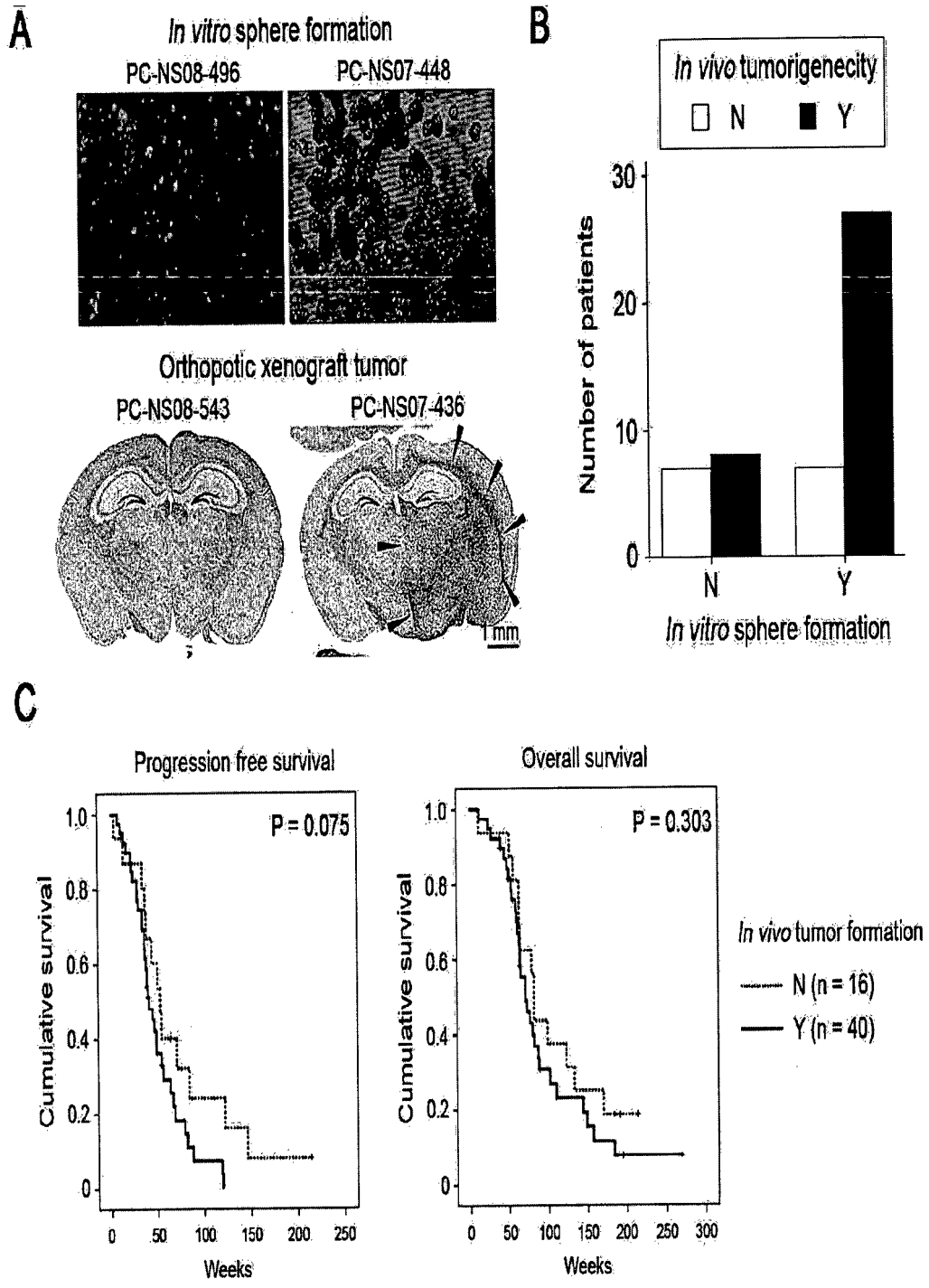
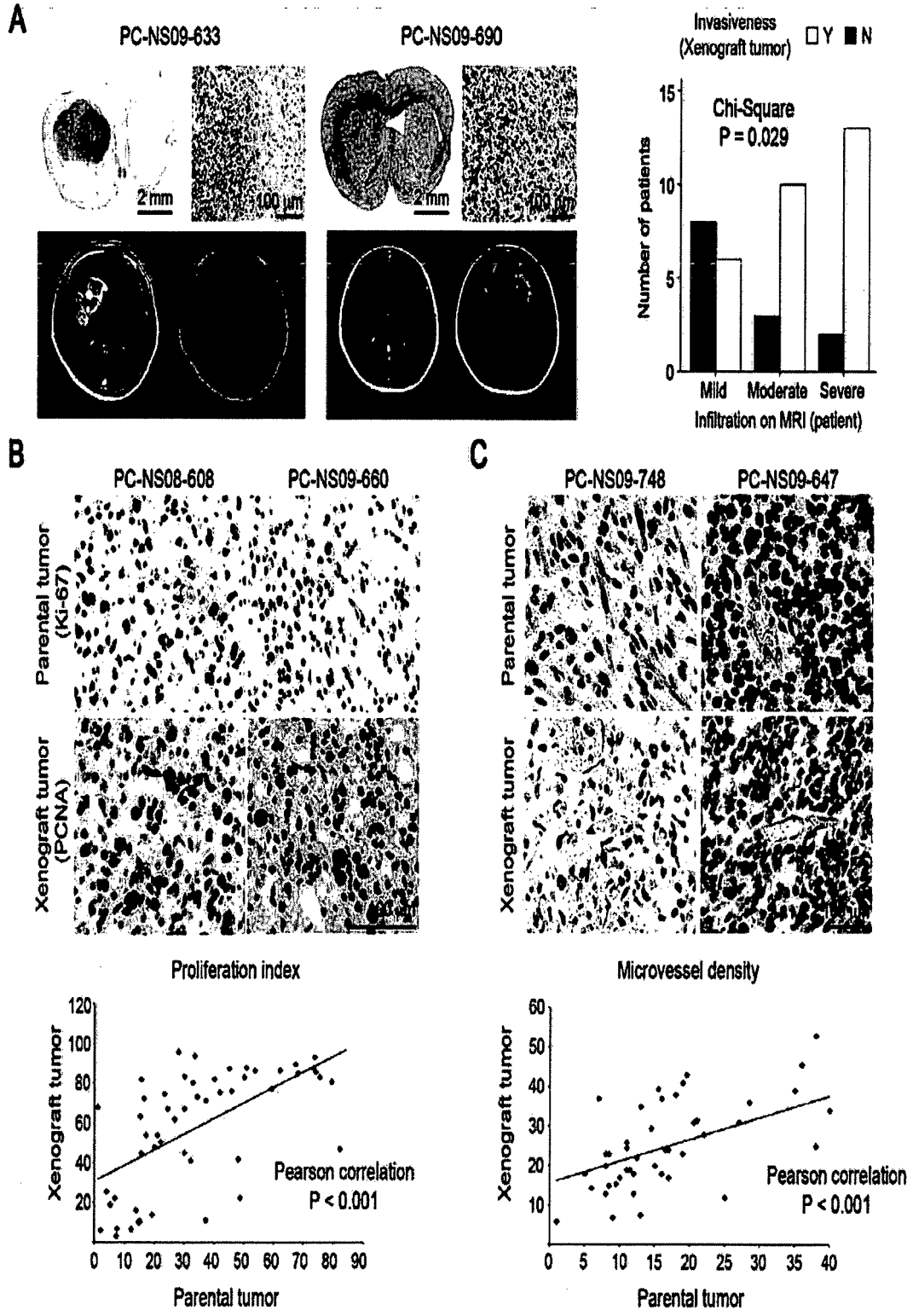
[Fig. 1]



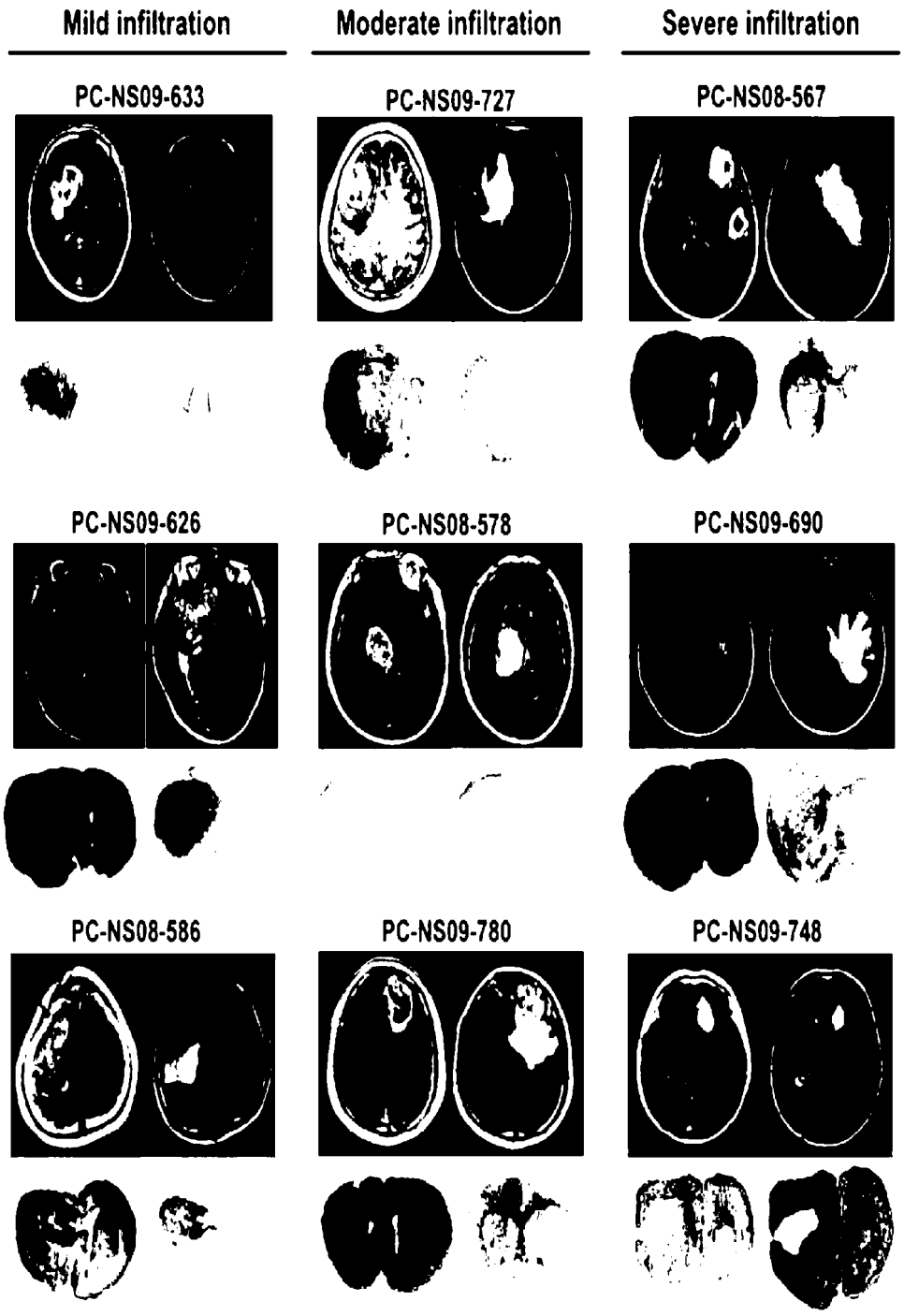
[Fig. 2]


A
In vitro sphere formation
PC-NS08-496
PC-NS07-448
Orthopotic xenograft tumor
PC-NS08-543
PC-NS07-436
1 mm
B
In vivo tumorigenecity
N
Y
Number of patients
30
20
10
0
N
Y
In vitro sphere formation
C
Progression free survival
P = 0.075
Cumulative survival
1.0
0.8
0.6
0.4
0.2
0
0 50 100 150 200 250
Weeks
Overall survival
P = 0.303
Cumulative survival
1.0
0.8
0.6
0.4
0.2
0
0 50 100 150 200 250 300
Weeks
In vivo tumor formation
N (n = 16)
Y (n = 40)

[Fig. 3]


A
PC-NS09-633
PC-NS09-690
2mm
100 μm
Invasiveness (Xenograft tumor) Y N
Chi-Square P = 0.029
Number of patients
Mild Moderate Severe
Infiltration on MRI (patient)
B
PC-NS08-608
PC-NS09-660
Parental tumor (Ki-67)
Xenograft tumor (PCNA)
Proliferation index
Xenograft tumor
Pearson correlation P < 0.001
Parental tumor
C
PC-NS09-748
PC-NS09-647
Parental tumor
Xenograft tumor
Microvessel density
Xenograft tumor
Pearson correlation P < 0.001
Parental tumor

[Fig. 4]


Mild infiltration
Moderate infiltration
Severe infiltration
PC-NS09-633
PC-NS09-727
PC-NS08-567
PC-NS09-626
PC-NS08-578
PC-NS09-690
PC-NS08-586
PC-NS09-780
PC-NS09-748

[Fig. 5]

A

Locus	Chromosome location	PC-NS07-448		PC-NS07-464		PC-NS08-559		PC-NS09-626	
		Parental	Xenograft	Parental	Xenograft	Parental	Xenograft	Parental	Xenograft
CSF1PO	5q33.3-34	11 12	11 12	9 12	9 12	12 13	12 13	11 13	11 13
D13S317	13q22-31	8	8	8 10	8 10	12	12	8 11	8 11
D16S539	16q24-qter	9 13	9 13	11 13	11 13	9 13	9 13	11	11
D18S51	18q21.3	16	16	14 16	14 16	13 18	13 18	14 17	14 17
D19S433	19q12-13.1	13 13.2	13 13.2	13 14	13 14	13 14	13 14	13 14	13 14
D21S11	21q11.2-q21	30 33.2	30 33.2	29 32.2	29 32.2	30 32	30 32	29	29
D2S1338	2q35-37.1	19 25	19 25	17 23	17 23	19 25	19 25	23 25	23 25
D3S1358	3p	16 17	16	15	15	14 18	14 18	16 17	16 17
D5S818	5q21-31	9 11	9 11	11 13	11 13	11	11	10 11	10 11
D7S820	7q11.21-22	10	10	8 11	8 11	10	10	8 10	8 10
D8S1179	8	10	10	10 16	10 16	13 16	13 16	16	16
FGA	4q28	19 24	19 24	21 23	21 23	20 22	20 22	24	24
TH01	11p15.5	6 9	6 9	7	7	9	9	9.3 9.3	9.3 9.3
TPOX	2p23-2per	8 11	8 11	9 11	9 11	11	11	8 9	8 9
vWA	12p12-pter	14 17	14 17	16 19	16 19	17 18	17 18	17 18	17 18
X	X:p22.1-22.3 Y:p11.2	XY	XY	XY	XY	X	X	XY	XY

C

Sample ID		TP53 exon5	TP53 exon6	TP53 exon7	TP53 exon8	IDH1
PC-NS07-448	Parental tumor	wt	wt	wt	wt	wt
	Xenograft tumor	wt	wt	wt	wt	wt
PC-NS07-464	Parental tumor	wt	wt	wt	wt	wt
	Xenograft tumor	wt	wt	wt	wt	wt
PC-NS08-559	Parental tumor	wt	wt	R248Q	wt	wt
	Xenograft tumor	wt	wt	R248Q	wt	wt
PC-NS08-608	Parental tumor	wt	Y220C	wt	wt	R132H
	Xenograft tumor	wt	Y220C	wt	wt	R132H
PC-NS09-626	Parental tumor	wt	wt	wt	wt	wt
	Xenograft tumor	wt	wt	wt	wt	wt
PC-NS09-630	Parental tumor	R175H	wt	wt	wt	R132H
	Xenograft tumor	R175H	wt	wt	wt	R132H
PC-NS09-633	Parental tumor	wt	wt	wt	wt	wt
	Xenograft tumor	wt	wt	wt	wt	wt
PC-NS09-690	Parental tumor	H179Y	wt	wt	wt	wt
	Xenograft tumor	H179Y	wt	wt	wt	wt
PC-NS09-748	Parental tumor	wt	wt	wt	wt	wt
	Xenograft tumor	wt	wt	wt	wt	wt

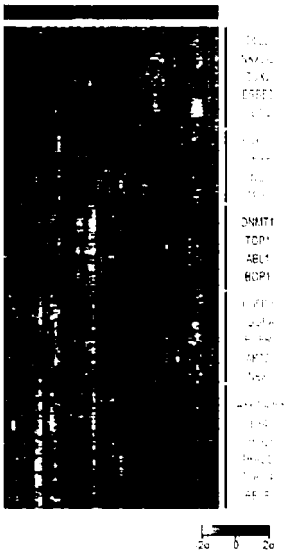
B

PC-NS08-559
Parental tumor

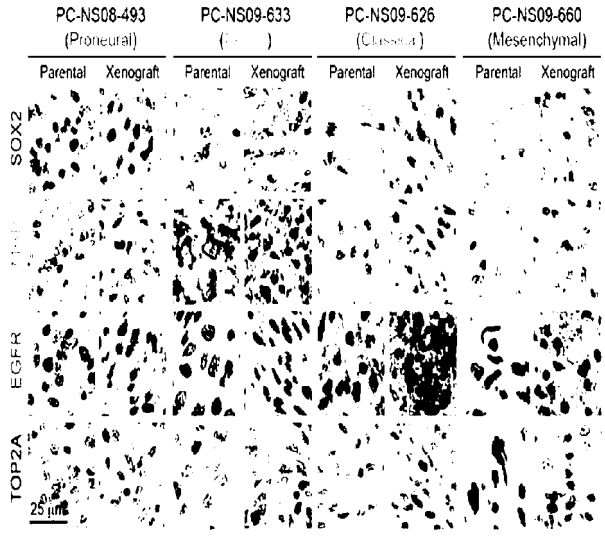
Xenograft tumor

		PC-NS07-448		PC-NS08-559		PC-NS09-626	
		Parental	Xenograft	Parental	Xenograft	Parental	Xenograft
Amp	EGFR						
	CDK2						
	PDGFRA						
	MDM2						
	MDM4						
	MET						
	CDK6						
	PIK3CA						
	AKT3						
Del	CDKN2A/B						
	PTEN						
	CDKN2C						
	RB1						
	PARK2						
	NF1						

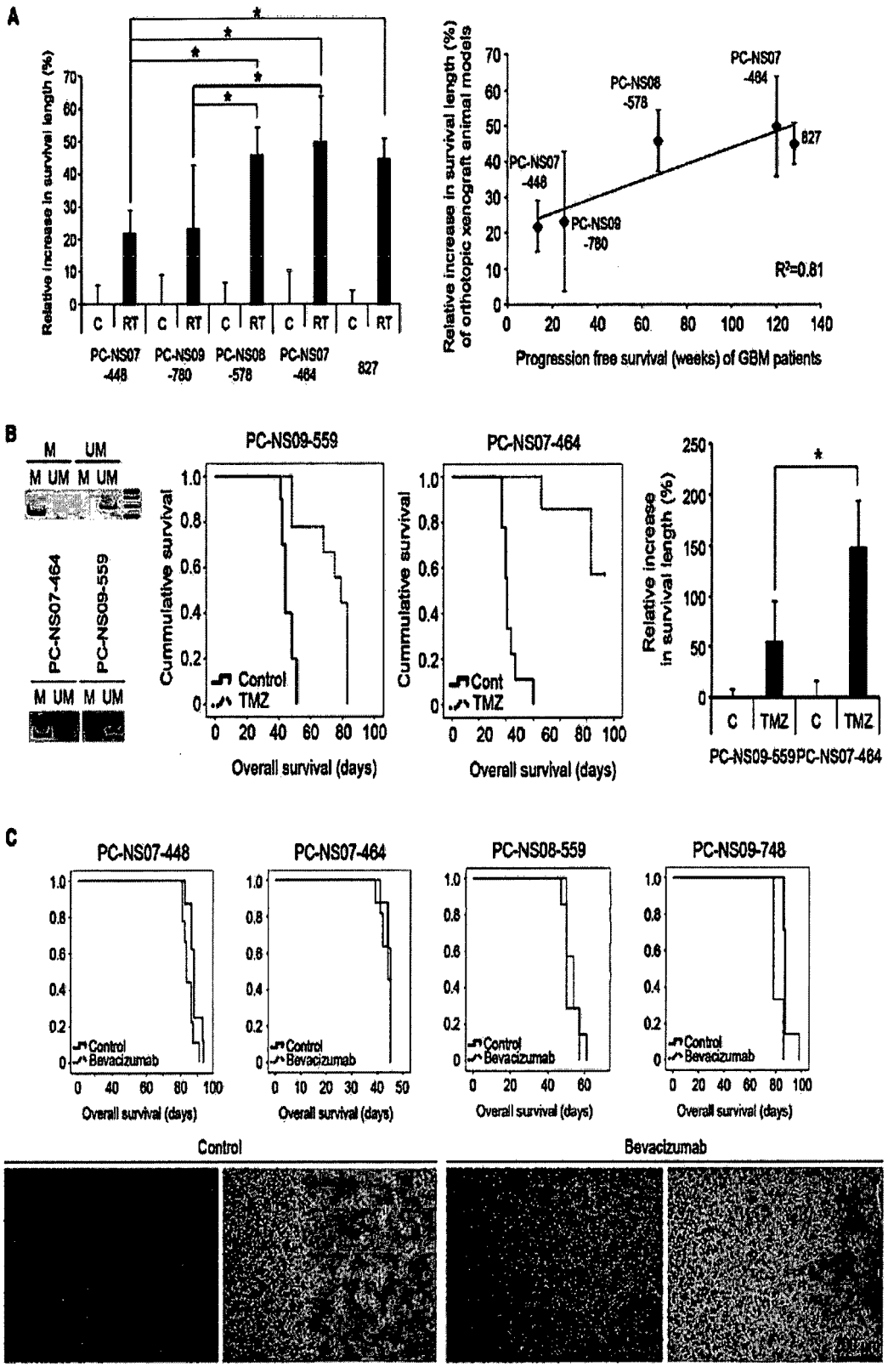
D



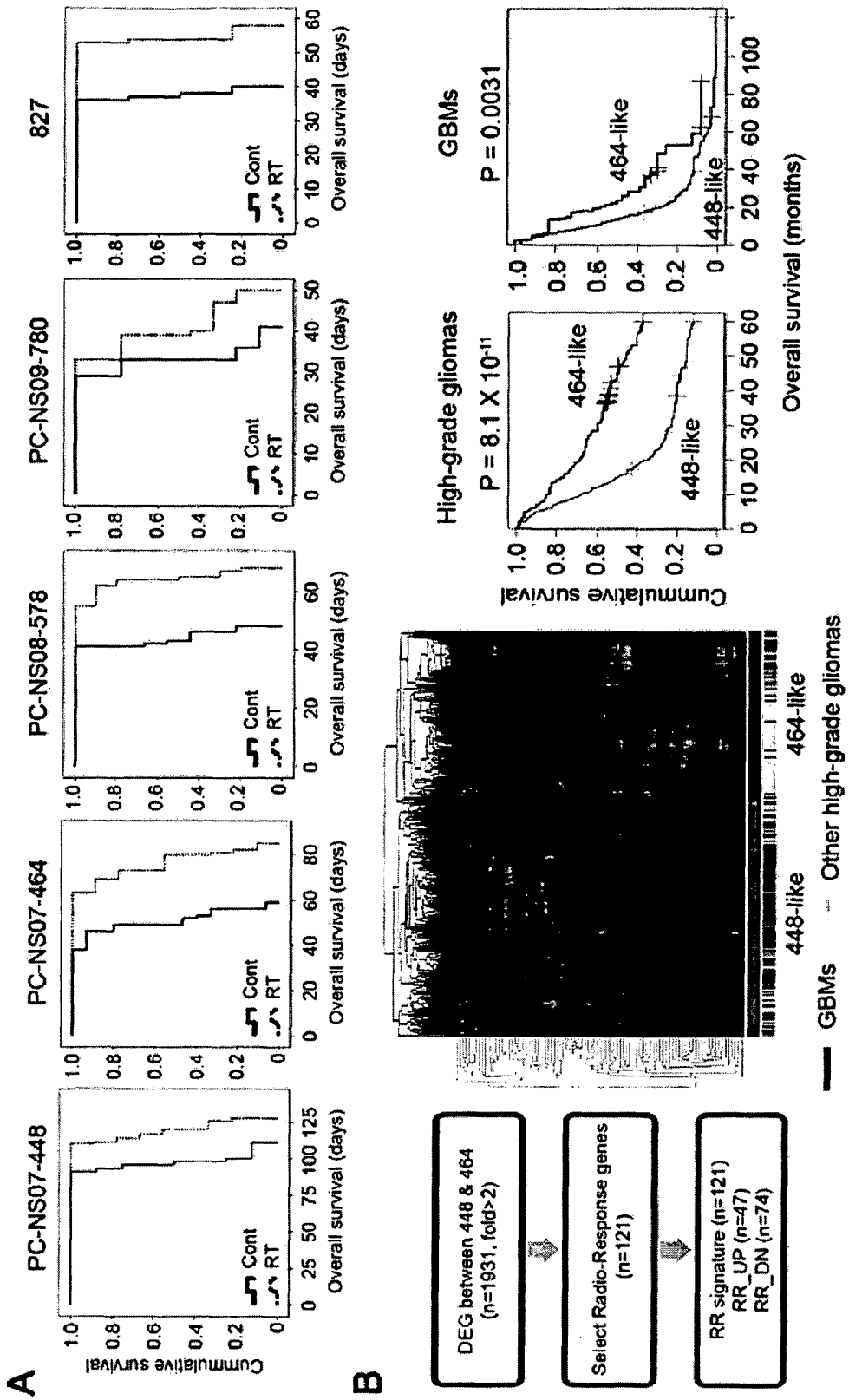
E



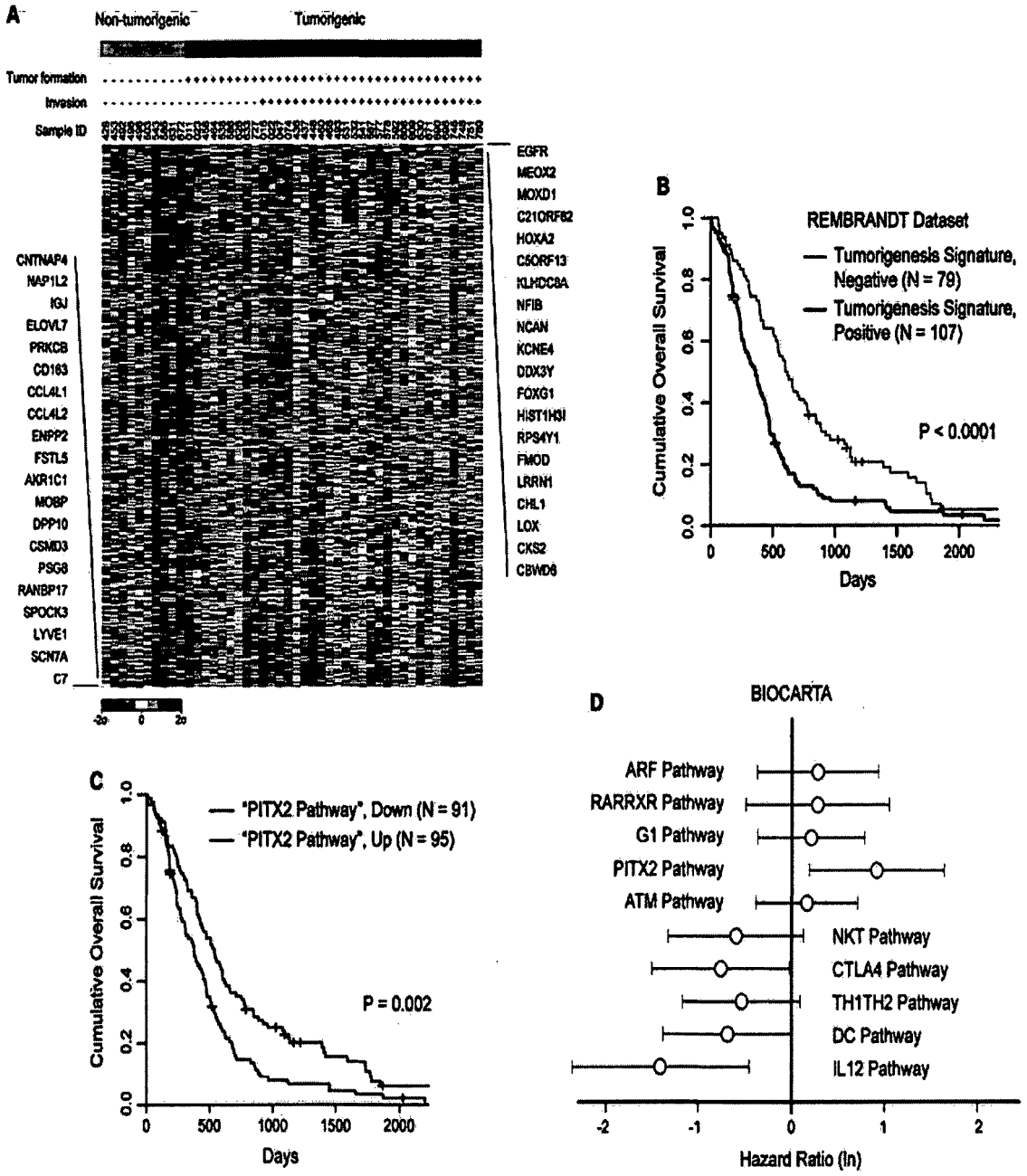
[Fig. 6]


A
Relative increase in survival length (%)
C RT C RT C RT C RT C RT
PC-NS07 -448
PC-NS09 -780
PC-NS08 -578
PC-NS07 -464
827
Relative increase in survival length (%) of orthotopic xenograft animal models
PC-NS07 -464
PC-NS08 -578
827
PC-NS07 -448
PC-NS09 -780
R²=0.81
Progression free survival (weeks) of GBM patients
B
M UM M UM
PC-NS07-464
PC-NS09-559
M UM M UM
PC-NS09-559
Cummulative survival
Control
TMZ
Overall survival (days)
PC-NS07-464
Cummulative survival
Cont
TMZ
Overall survival (days)
Relative increase in survival length (%)
C TMZ C TMZ
PC-NS09-559 PC-NS07-464
C
PC-NS07-448
PC-NS07-464
PC-NS08-559
PC-NS09-748
Control
Bevacizumab
Overall survival (days)
Control
Bevacizumab

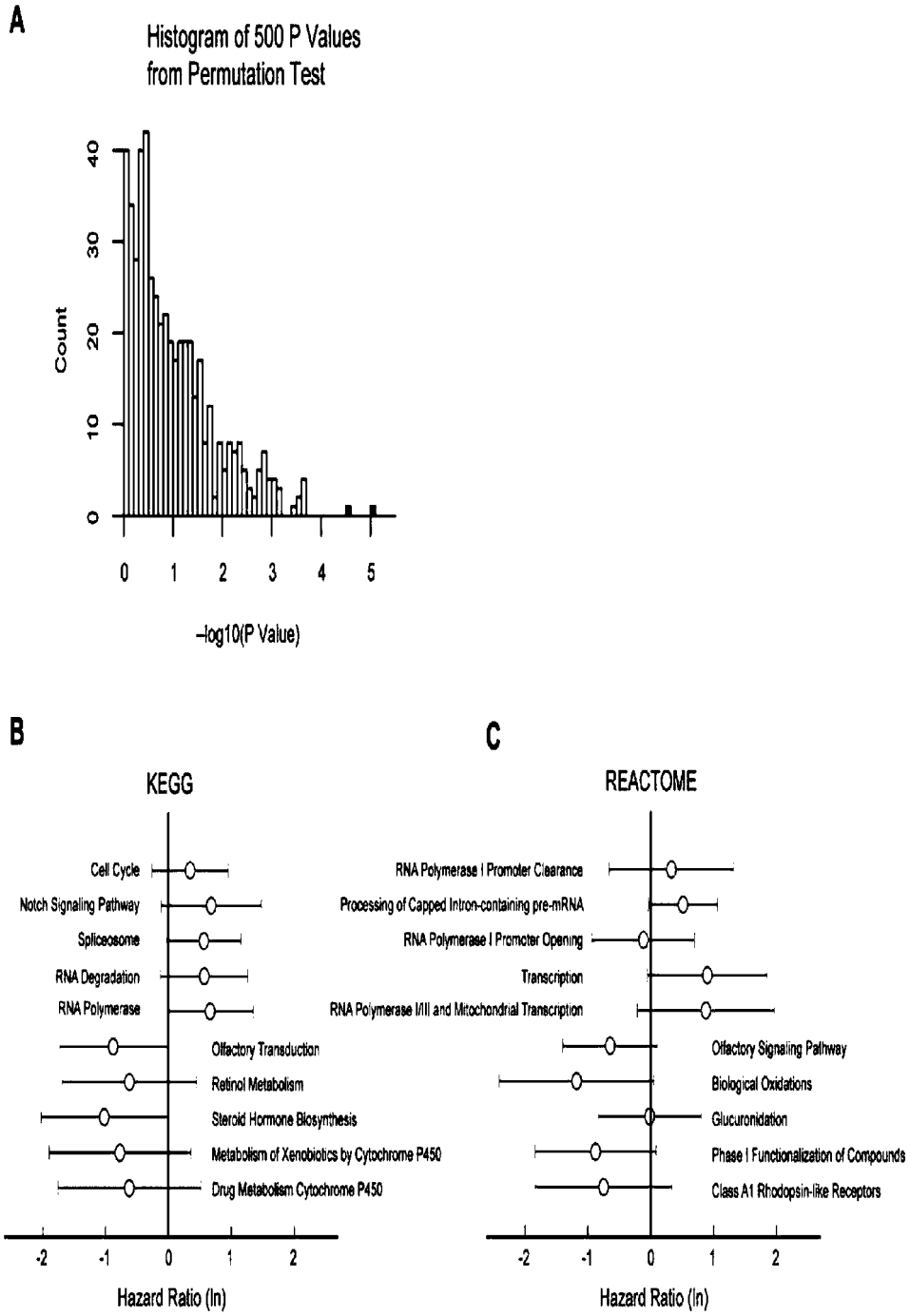
[Fig. 7]


A
PC-NS07-448
PC-NS07-464
PC-NS08-578
PC-NS09-780
827
Cummulative survival
Cont
RT
Overall survival (days)
B
DEG between 448 & 464 (n=1931, fold>2)
Select Radio-Response genes (n=121)
RR signature (n=121)
RR_UP (n=47)
RR_DN (n=74)
448-like
464-like
GBMs
Other high-grade gliomas
High-grade gliomas
P = 8.1 X 10-11
GBMs
P = 0.0031
Overall survival (months)

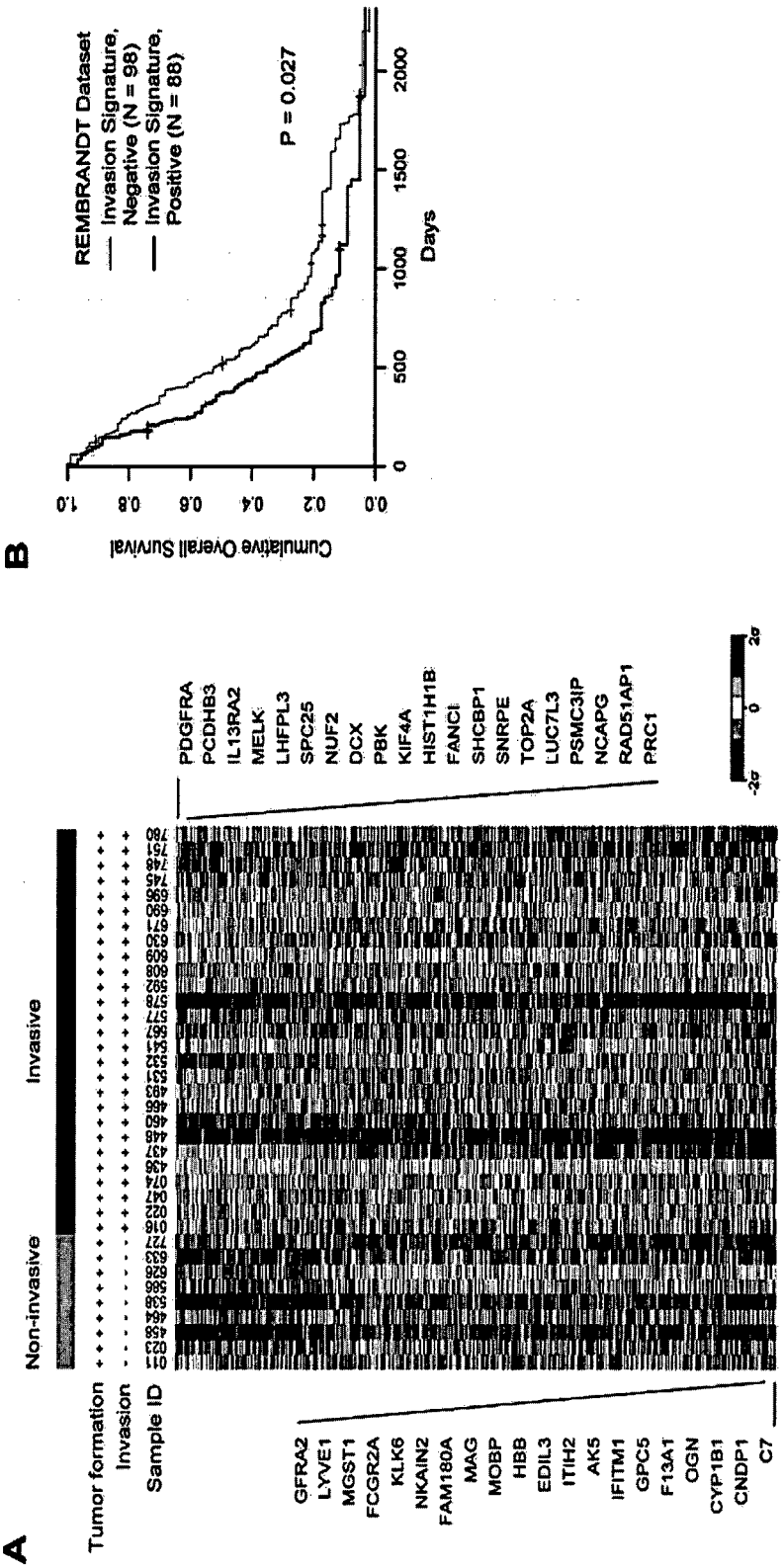
[Fig. 8]


A
Non-tumorigenic
Tumorigenic
Tumor formation
Invasion
Sample ID
CNTNAP4
NAP1L2
IGJ
ELOVL7
PRKCB
CD163
CCL4L1
CCL4L2
ENPP2
FSTL5
AKR1C1
MOBP
DPP10
CSMD3
PSG8
RANBP17
SPOCK3
LYVE1
SCN7A
C7
EGFR
MEOX2
MOXD1
C21ORF62
HOXA2
C5ORF13
KLHDC8A
NFIB
NCAN
KCNE4
DDX3Y
FOXG1
HIST1H3I
RPS4Y1
FMOD
LRRN1
CHL1
LOX
CKS2
CBWD6
B
REMBRANDT Dataset
Tumorigenesis Signature, Negative (N = 79)
Tumorigenesis Signature, Positive (N = 107)
P < 0.0001
Cumulative Overall Survival
Days
C
"PITX2 Pathway", Down (N = 91)
"PITX2 Pathway", Up (N = 95)
P = 0.002
Cumulative Overall Survival
Days
D
BIOCARTA
ARF Pathway
RARRXR Pathway
G1 Pathway
PITX2 Pathway
ATM Pathway
NKT Pathway
CTLA4 Pathway
TH1TH2 Pathway
DC Pathway
IL12 Pathway
Hazard Ratio (ln)

[Fig. 9]


A
Histogram of 500 P Values
from Permutation Test
Count
0
10
20
30
40
0
1
2
3
4
5
-log10(P Value)
B
KEGG
Cell Cycle
Notch Signaling Pathway
Spliceosome
RNA Degradation
RNA Polymerase
Olfactory Transduction
Retinol Metabolism
Steroid Hormone Biosynthesis
Metabolism of Xenobiotics by Cytochrome P450
Drug Metabolism Cytochrome P450
-2
-1
0
1
2
Hazard Ratio (ln)
C
REACTOME
RNA Polymerase I Promoter Clearance
Processing of Capped Intron-containing pre-mRNA
RNA Polymerase I Promoter Opening
Transcription
RNA Polymerase I/II and Mitochondrial Transcription
Olfactory Signaling Pathway
Biological Oxidations
Glucuronidation
Phase I Functionalization of Compounds
Class A1 Rhodopsin-like Receptors
-2
-1
0
1
2
Hazard Ratio (ln)

[Fig. 10]


B
Cumulative Overall Survival
0.0
0.2
0.4
0.6
0.8
1.0
0
500
1000
1500
2000
Days
P = 0.027
REMBRANDT Dataset
Invasion Signature, Negative (N = 98)
Invasion Signature, Positive (N = 88)
A
Non-invasive
Invasive
Tumor formation
Invasion
Sample ID
PDGFRA
PCDHB3
IL13RA2
MELK
LHFPL3
SPC25
NUF2
DCX
PBK
KIF4A
HIST1H1B
FANCI
SHCBP1
SNRPE
TOP2A
LUC7L3
PSMC3IP
NCAPG
RAD51AP1
PRC1
GFRA2
LYVE1
MGST1
FCGR2A
KLK6
NKAIN2
FAM180A
MAG
MOBP
HBB
EDIL3
ITIH2
AK5
IFITM1
GPC5
F13A1
OGN
CYP1B1
CNDP1
C7