

FIG. 1

(A)

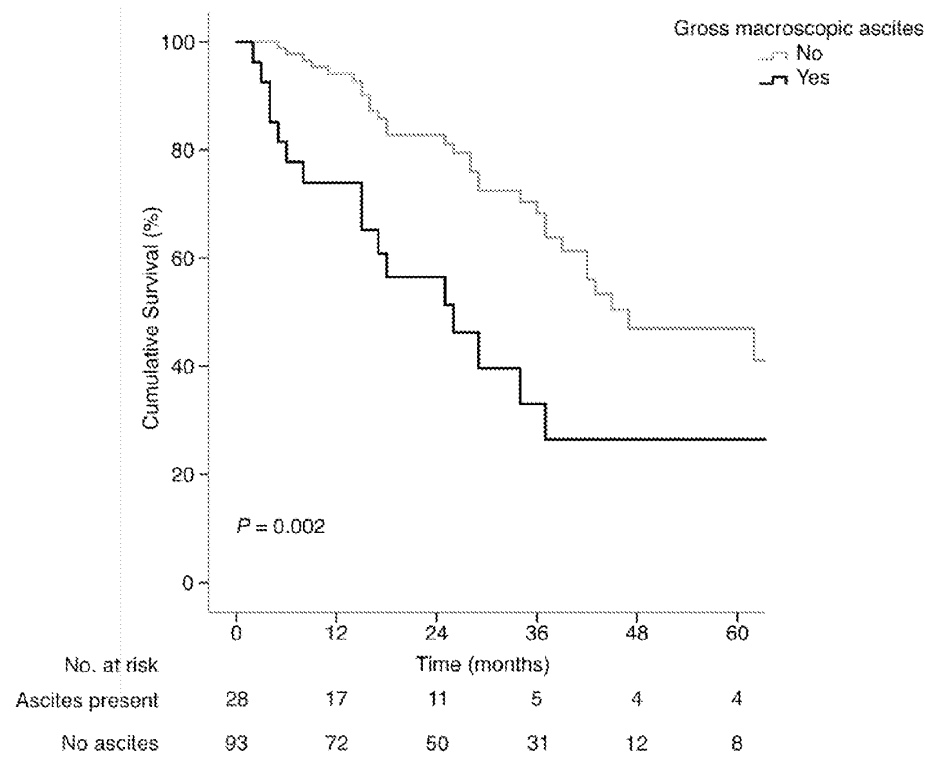


FIG. 1 continued

(B)

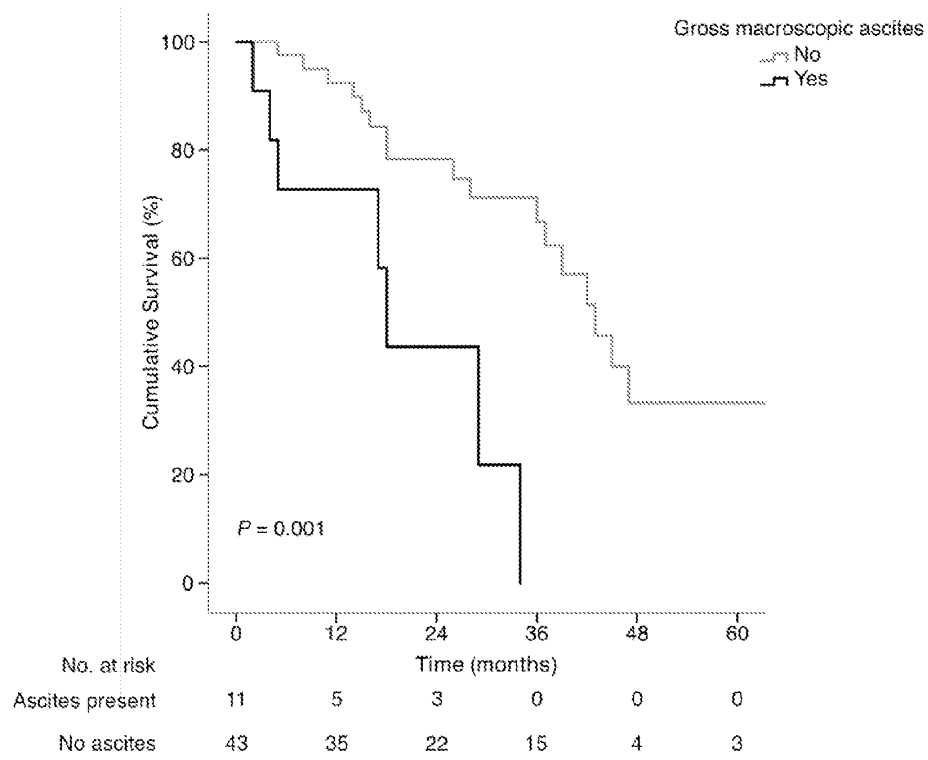


FIG. 1 continued

(C)

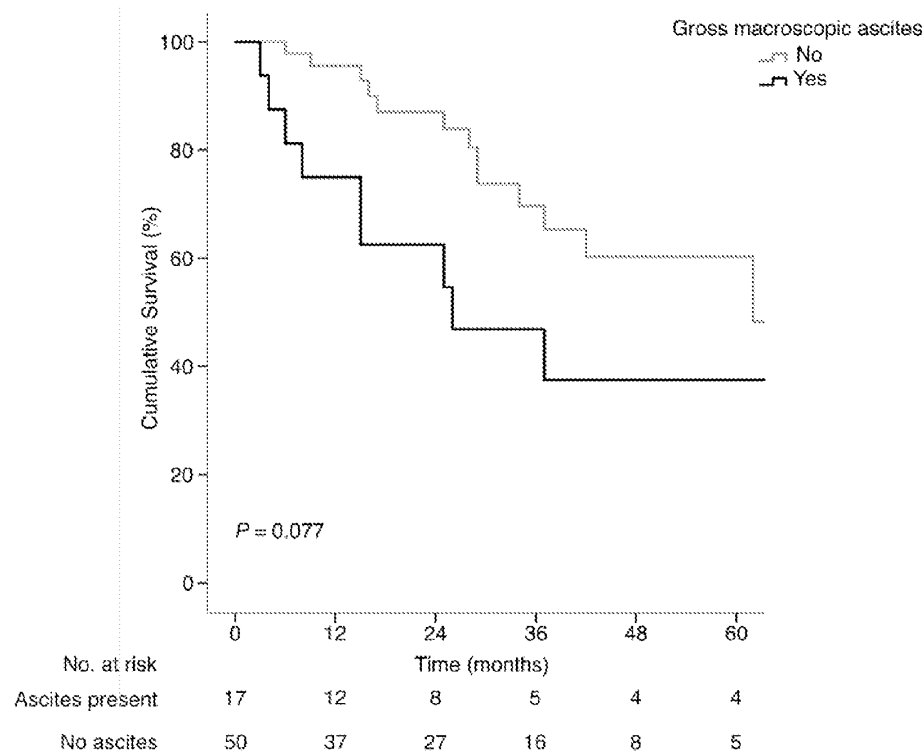
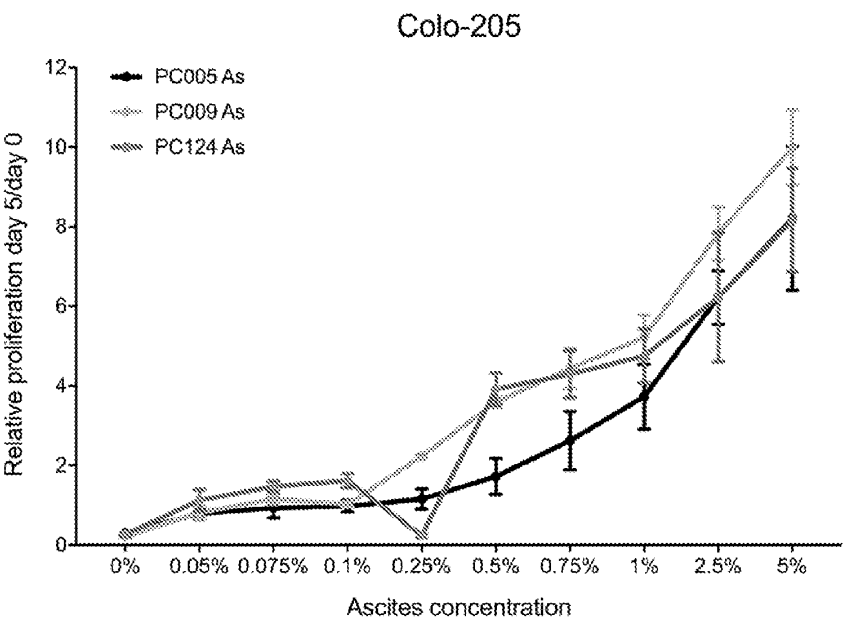
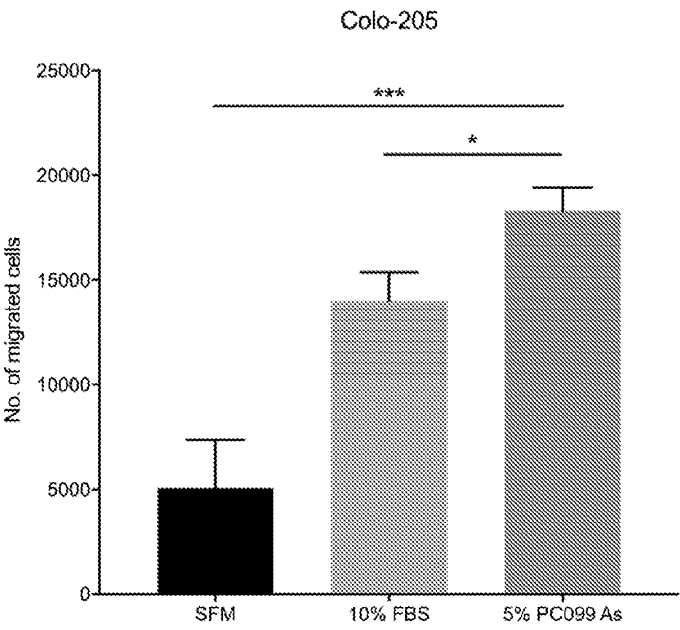


FIG. 2

(A)



(B)



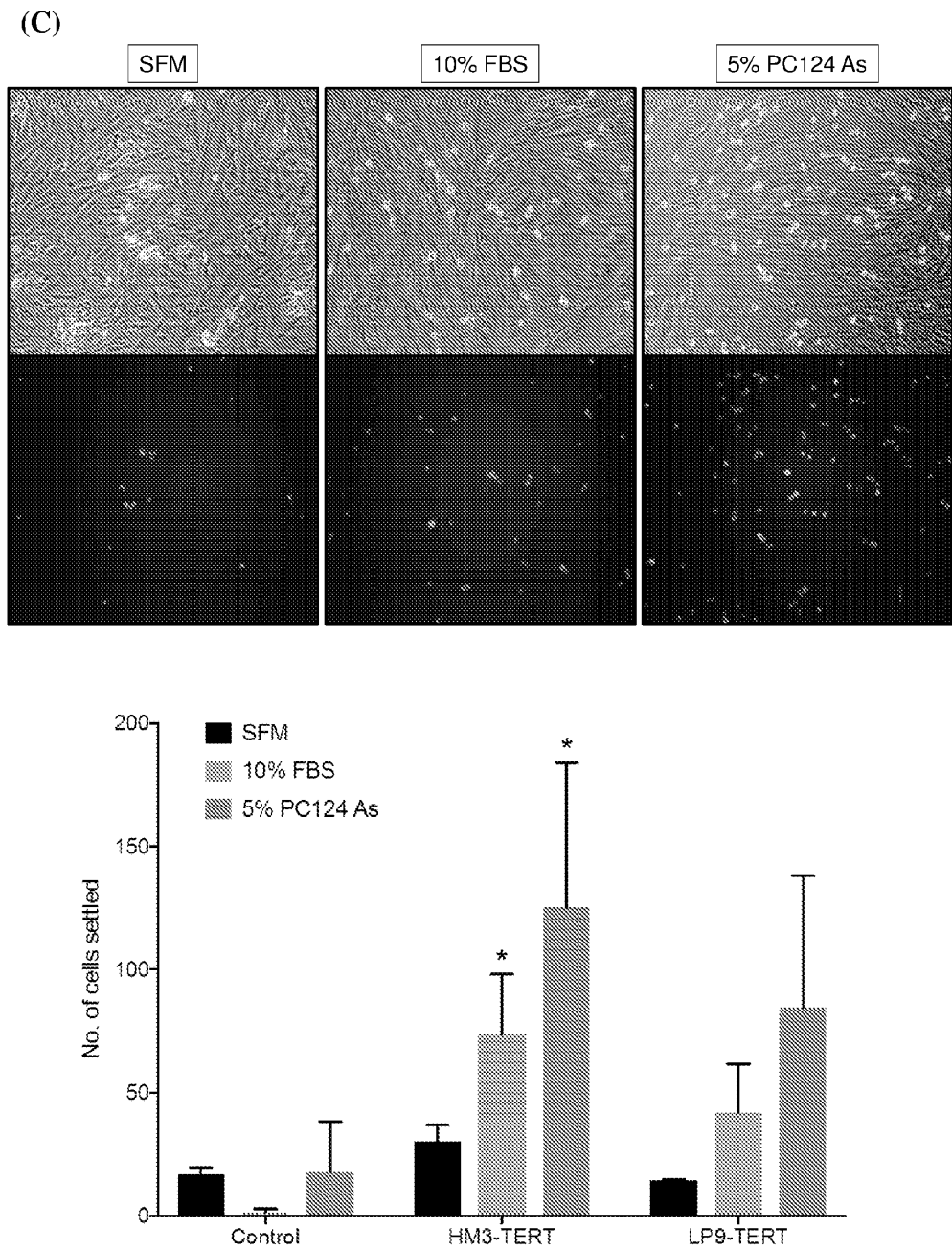


FIG. 3

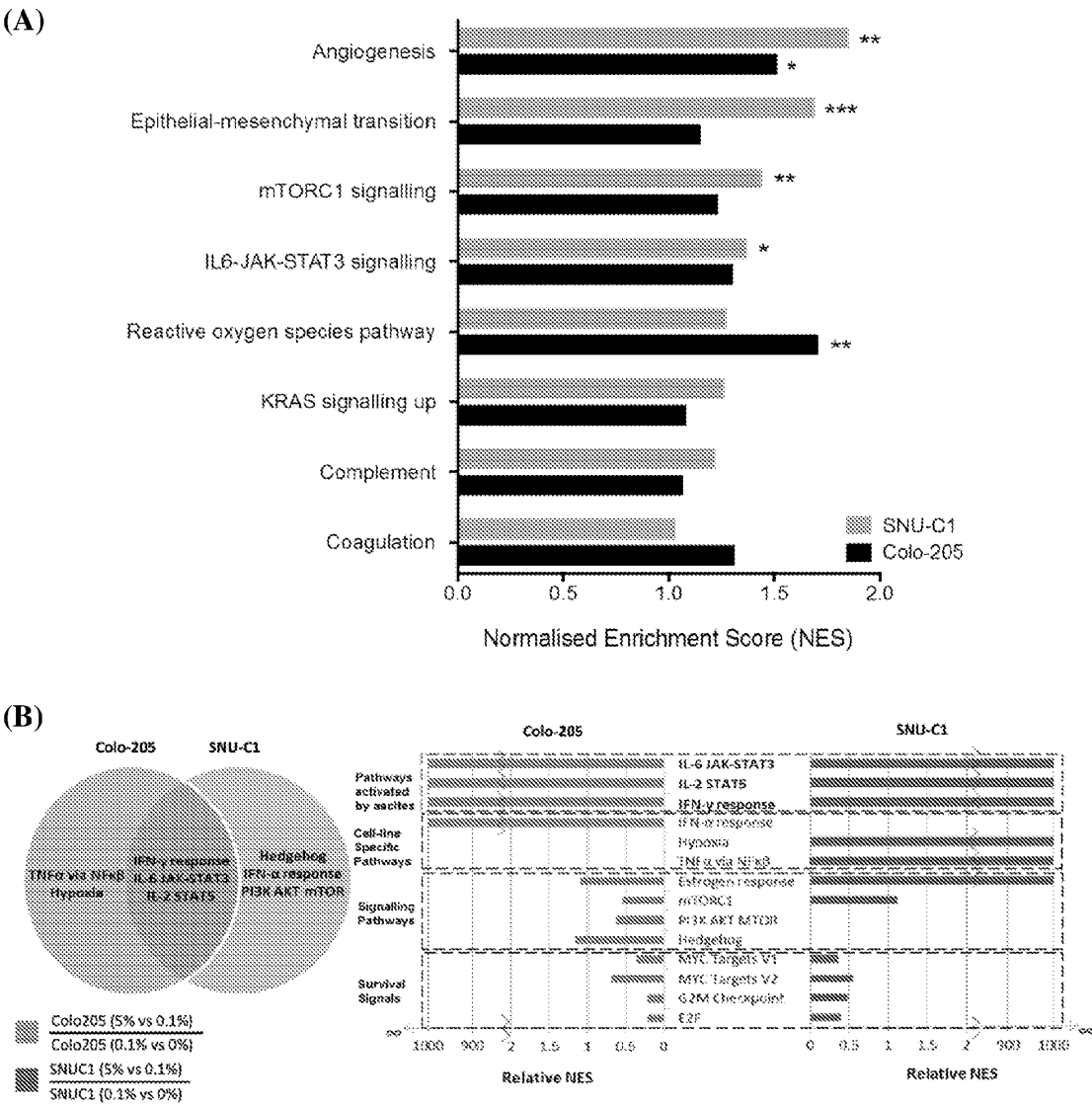


FIG. 4

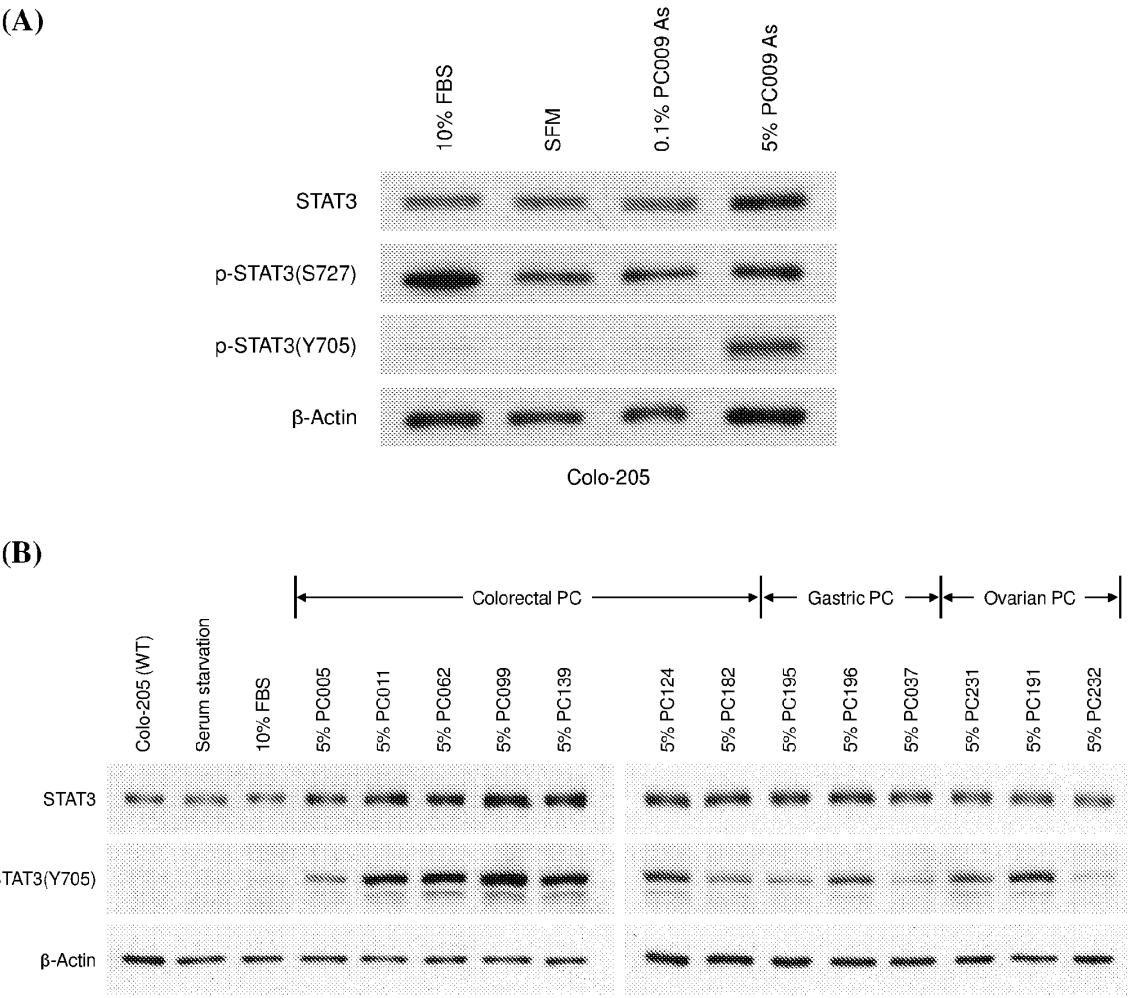


FIG. 5

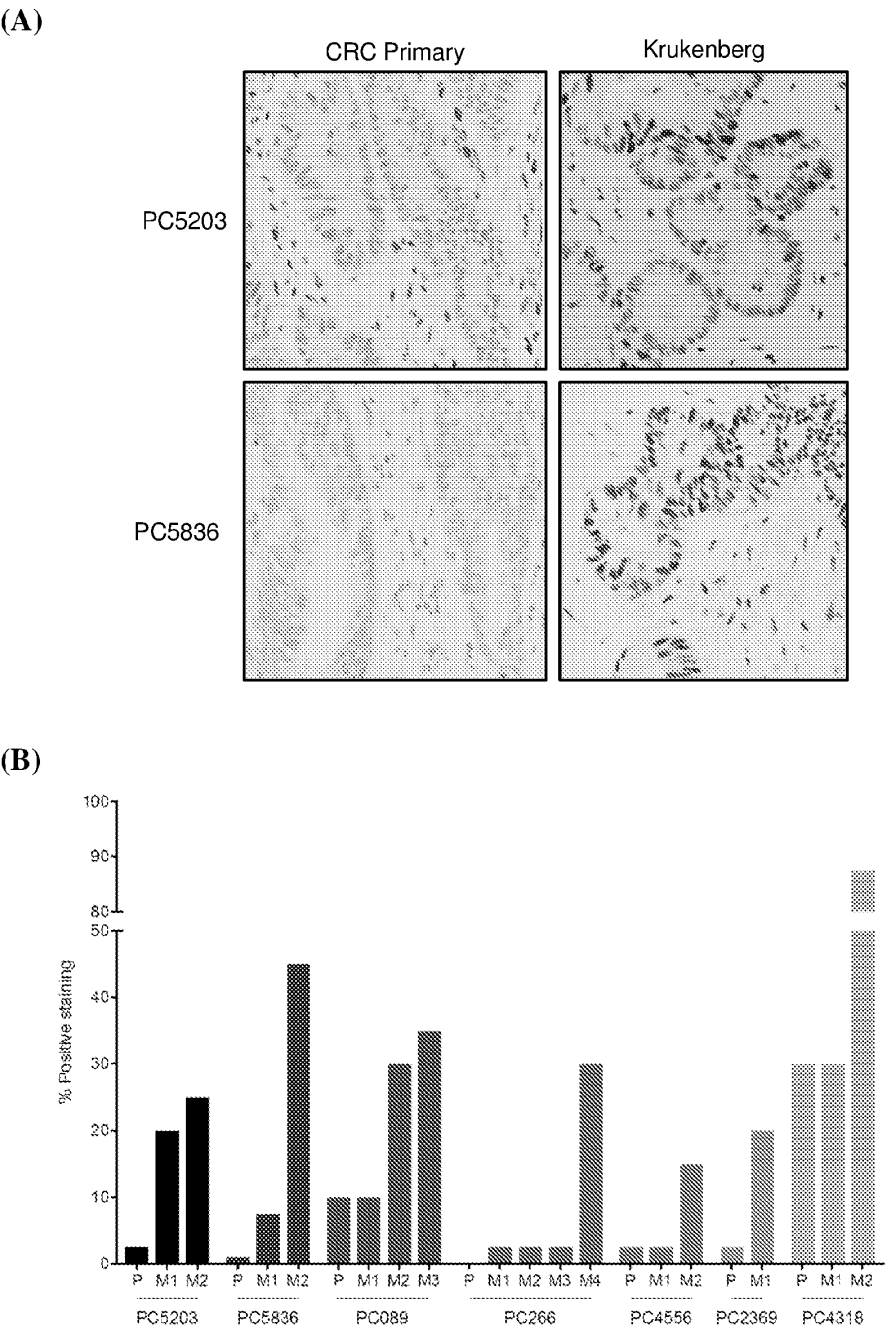
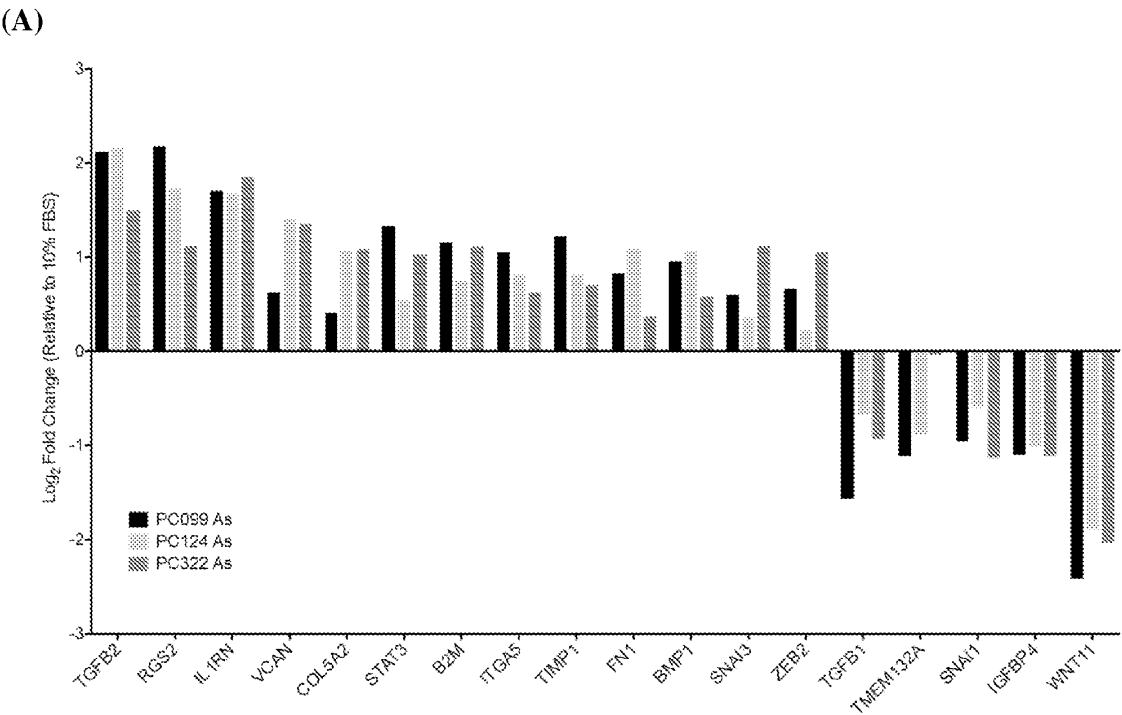
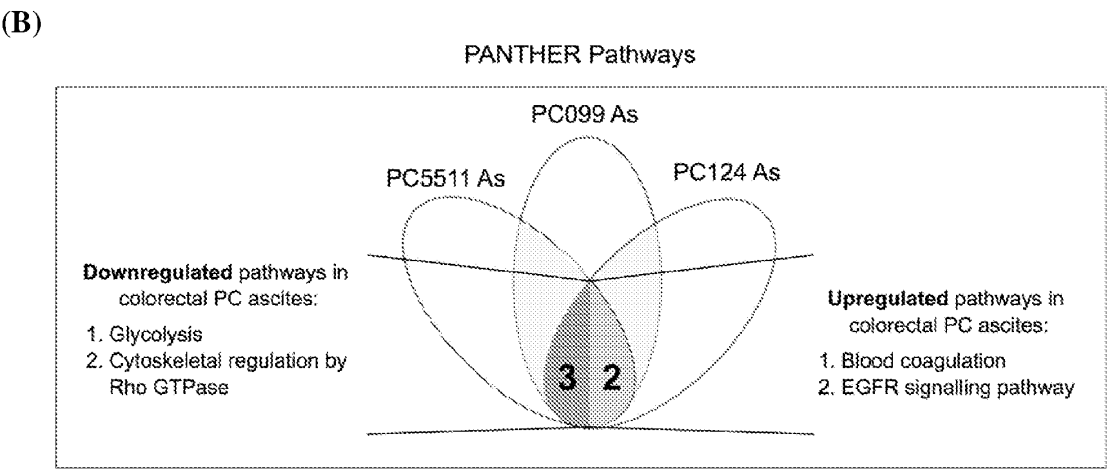
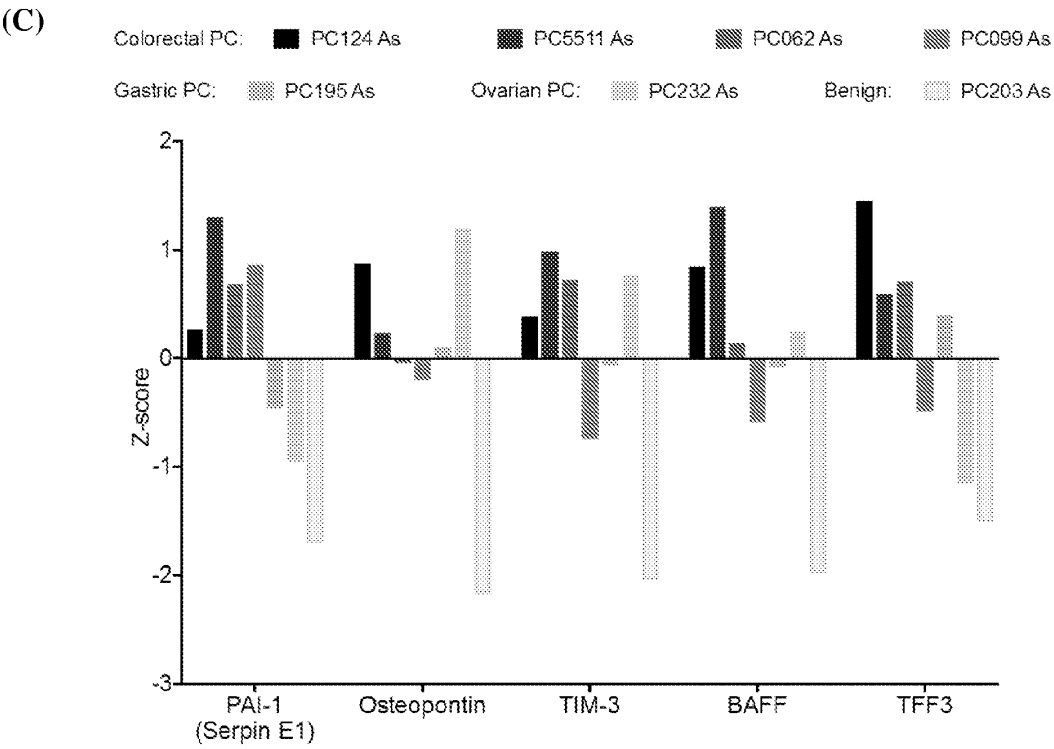
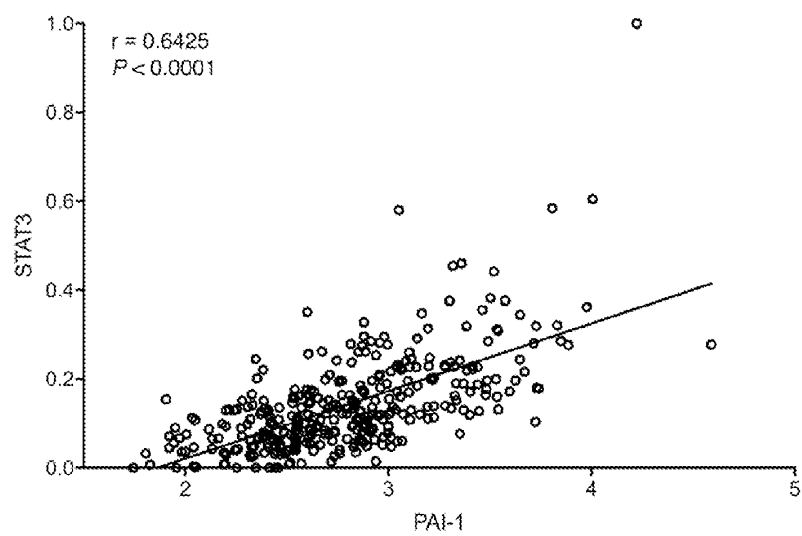


FIG. 6

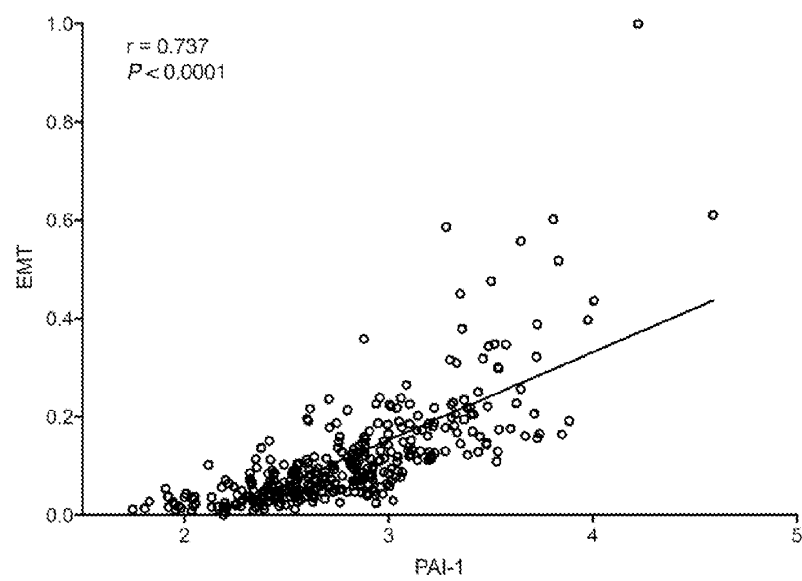




(A)



(B)



(C)

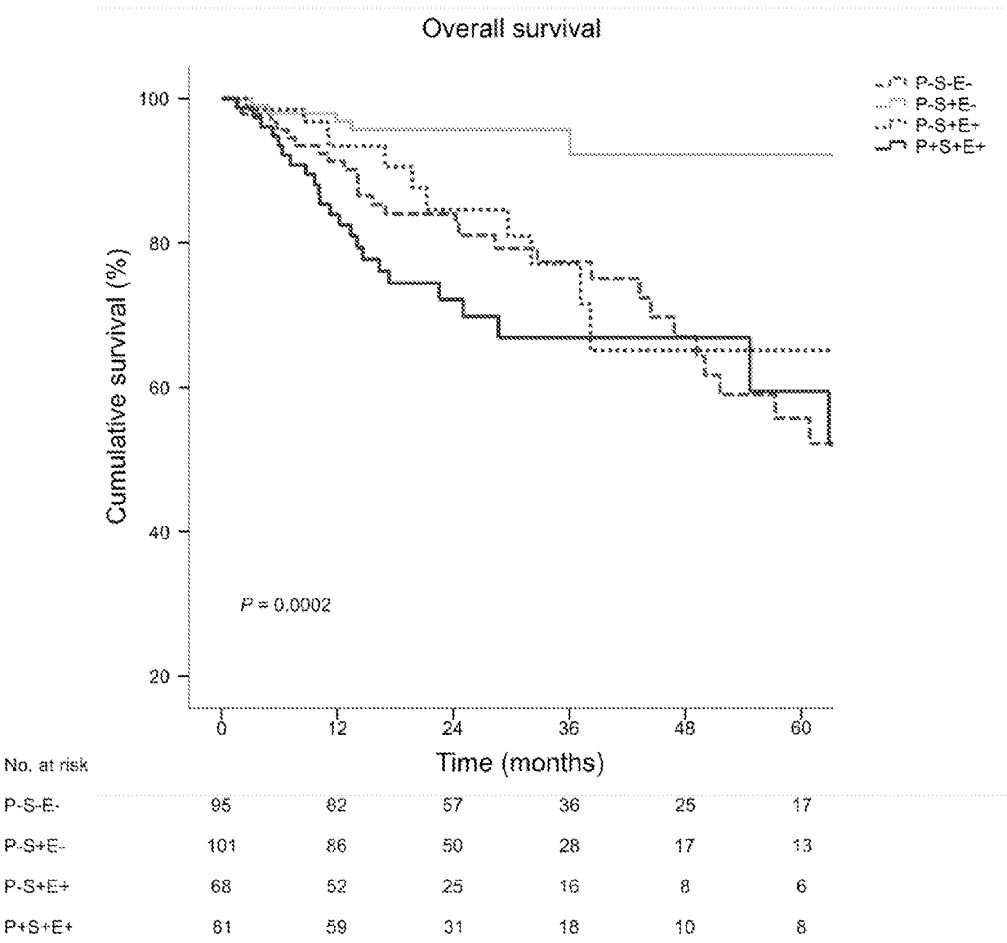
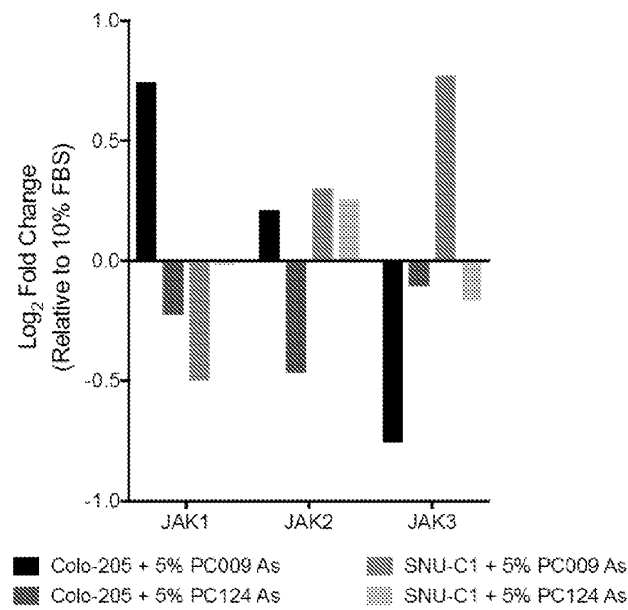


FIG. 8

(A)



(B)

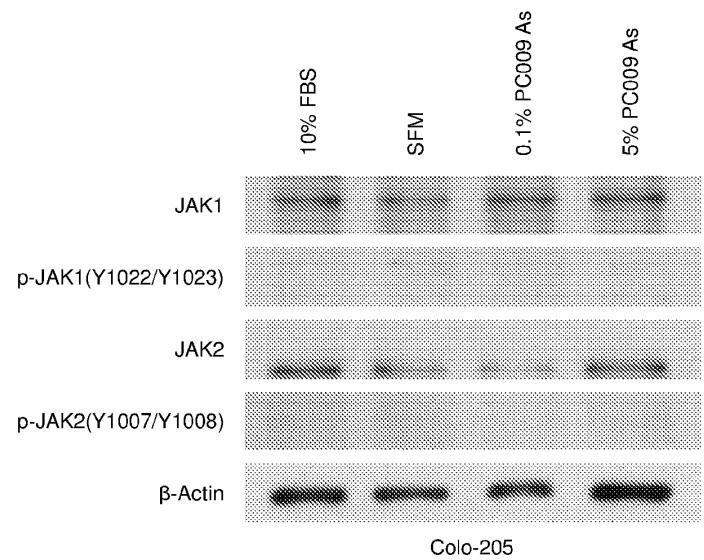


FIG. 9

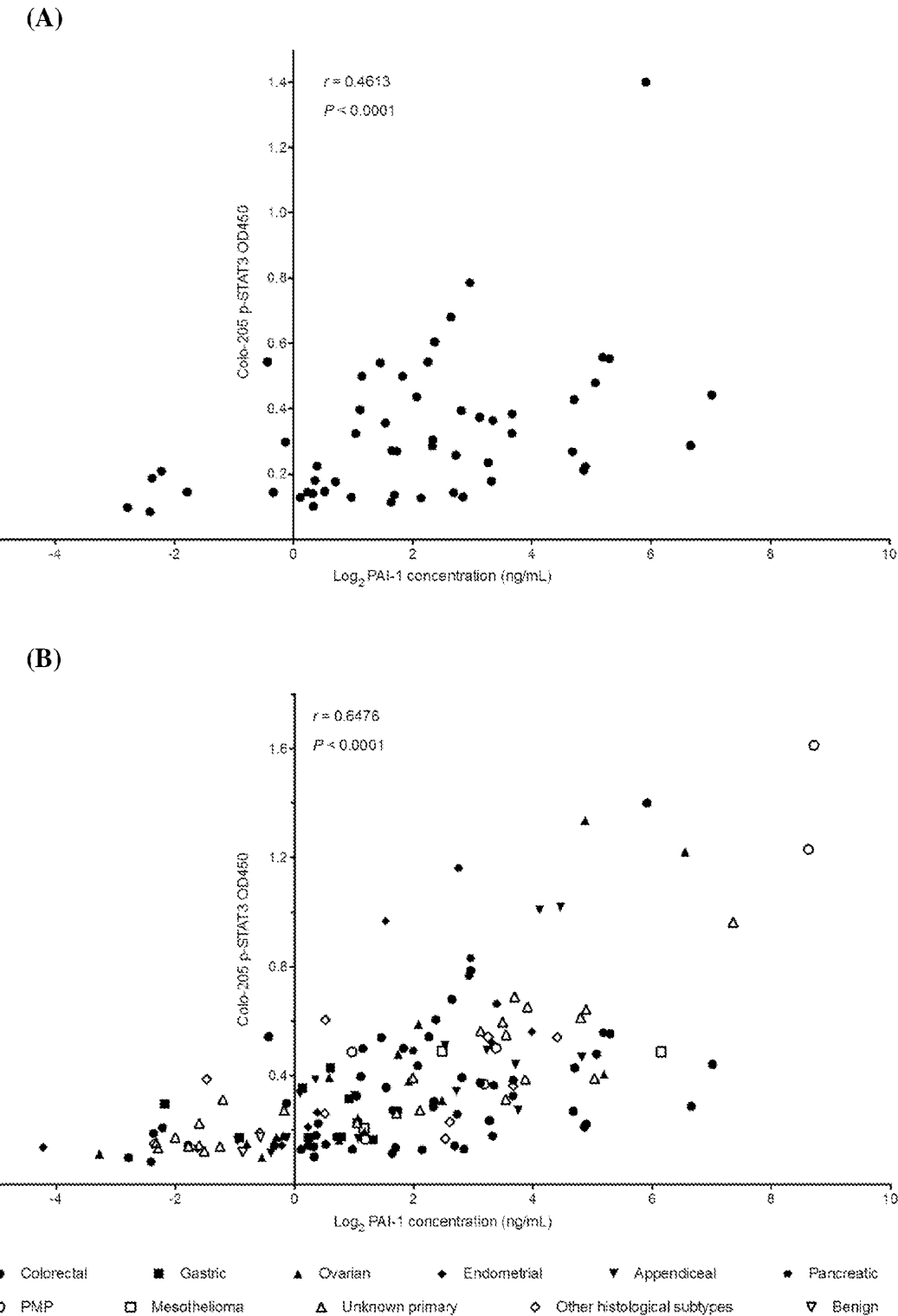
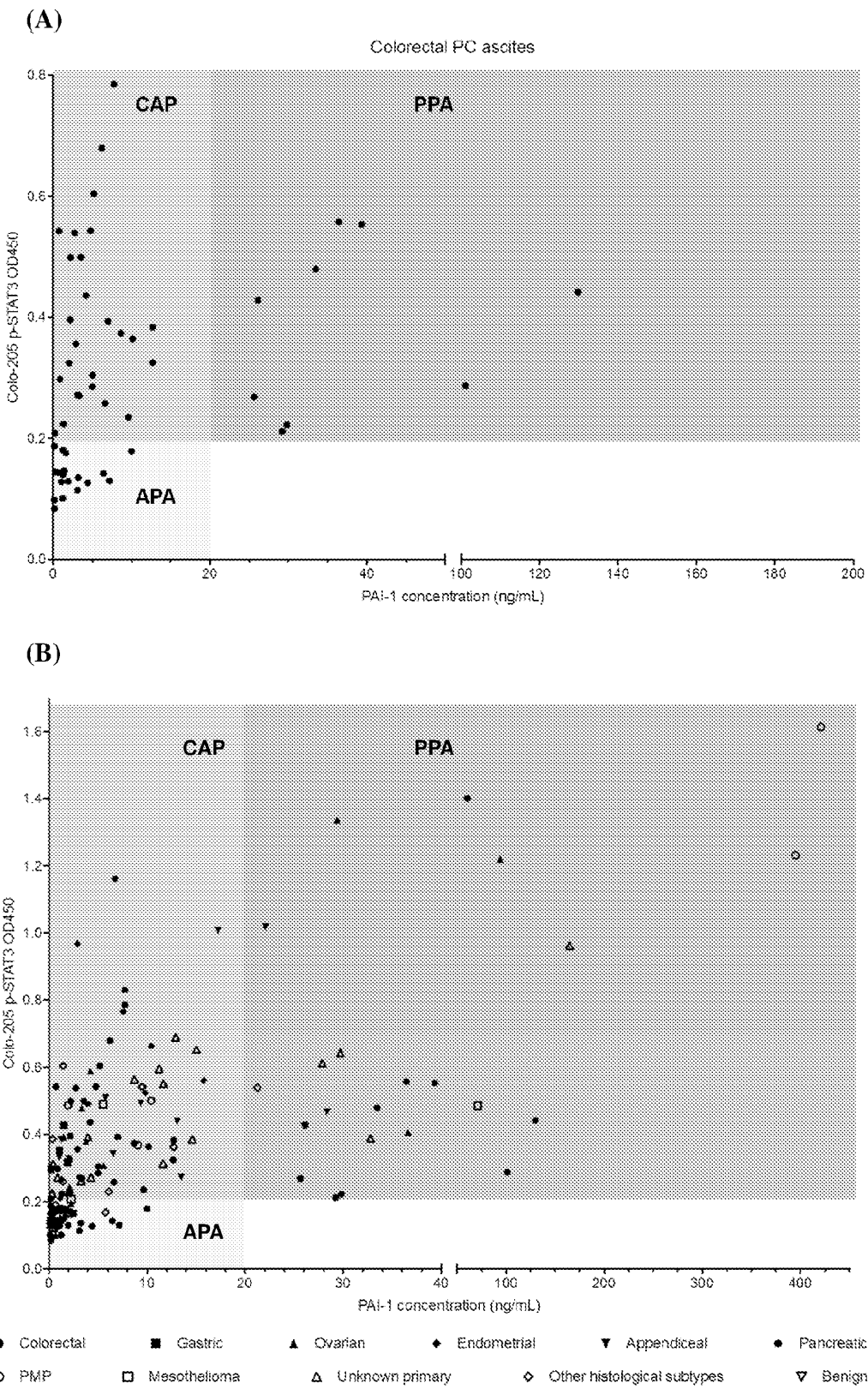


FIG. 10



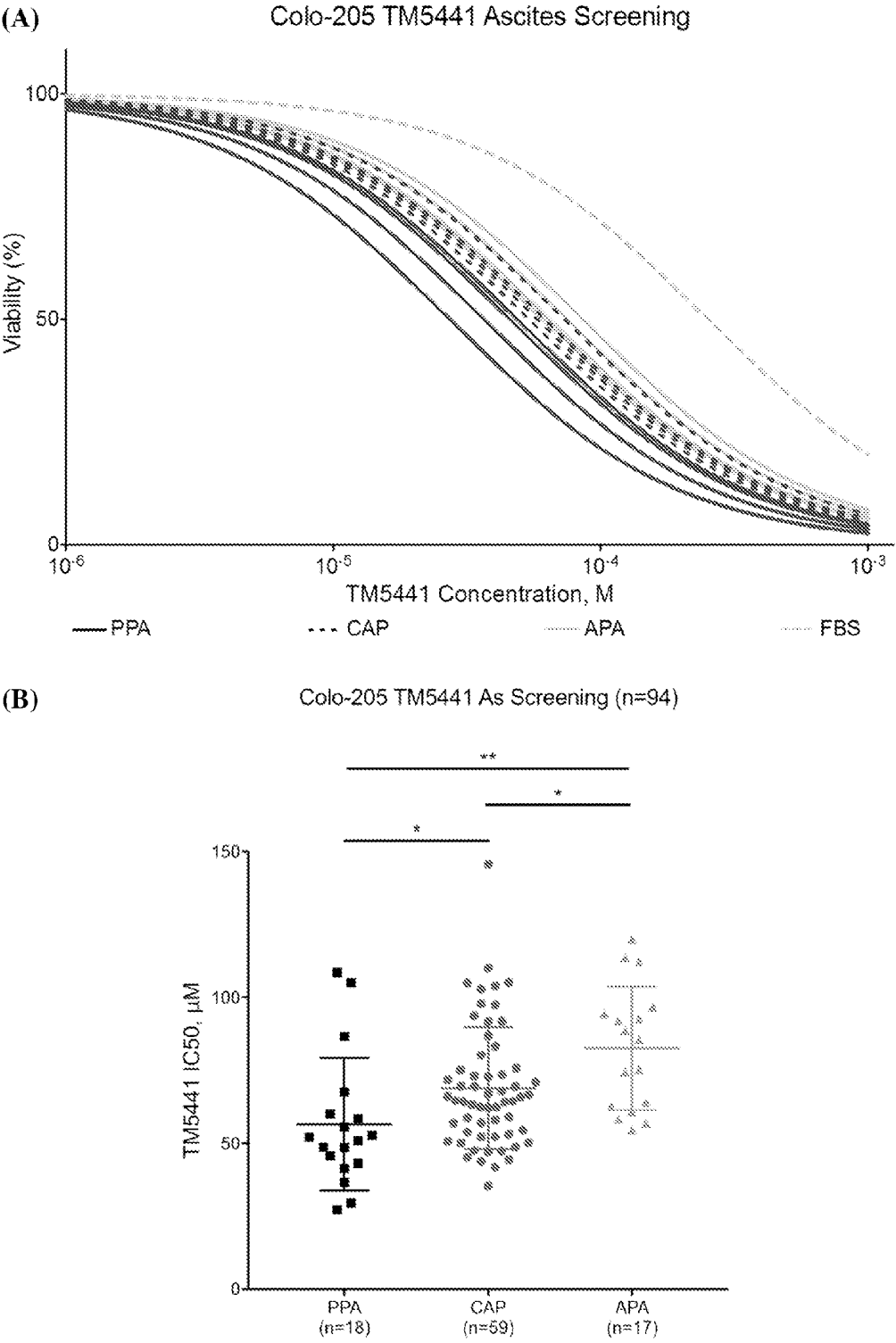
(C)

	PAI-1 concentration (ng/mL)	p-STAT3 (Y705) OD450
Alternative pathways activation (APA)	< 20	< 0.2
Co-activators predominant (CAP)	< 20	≥ 0.2
PAI-1 paracrine addiction (PPA)	≥ 20	≥ 0.2

(D)

Histology of PC subtypes	No. of samples
Colorectal	55
Gastric	9
Ovarian	17
Endometrial	7
Appendiceal	17
Pancreatic	5
Pseudomyxoma peritonei (PMP)	6
Mesothelioma	3
Unknown primary	25
Other PC histologies	
Lung	2
Breast	2
Primary peritoneal cancer	2
Gastric and ovarian (synchronous)	1
Small bowel	1
Urothelial	1
Palate	1
Benign	
Benign serous cystadenofibroma	1
Mucinous cyst adenoma	1
Total	156

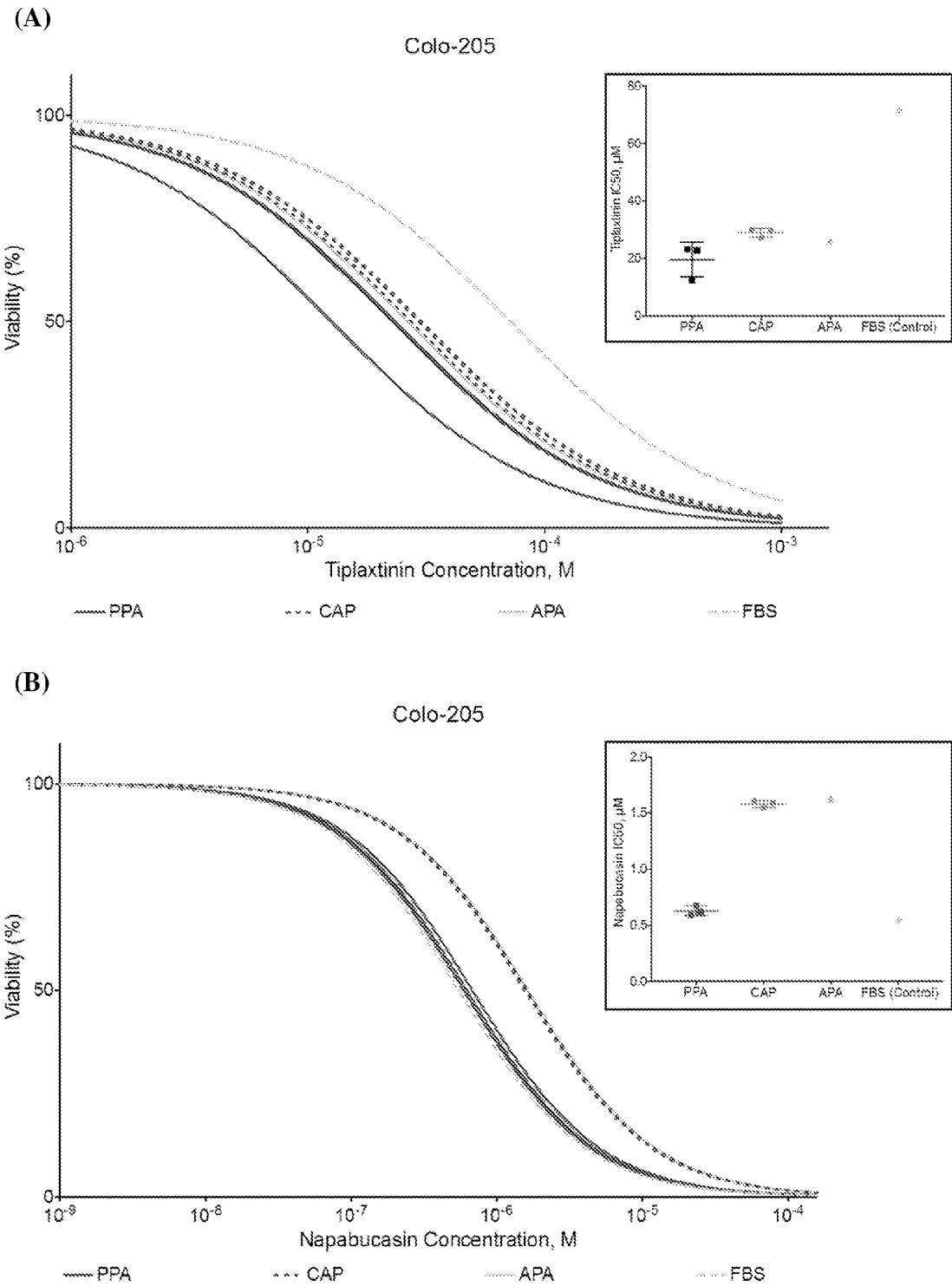
FIG. 11



(C)

Histology of PC subtypes	No. of samples
Colorectal	32
Gastric	5
Ovarian	11
Endometrial	5
Appendiceal	12
Pancreatic	3
Pseudomyxoma peritonei (PMP)	4
Mesothelioma	3
Unknown primary	11
Other PC histologies	
Lung	1
Breast	2
Primary peritoneal cancer	1
Gastric and ovarian (synchronous)	1
Small bowel	1
Urothelial	1
Palate	1
Total	94

FIG. 12



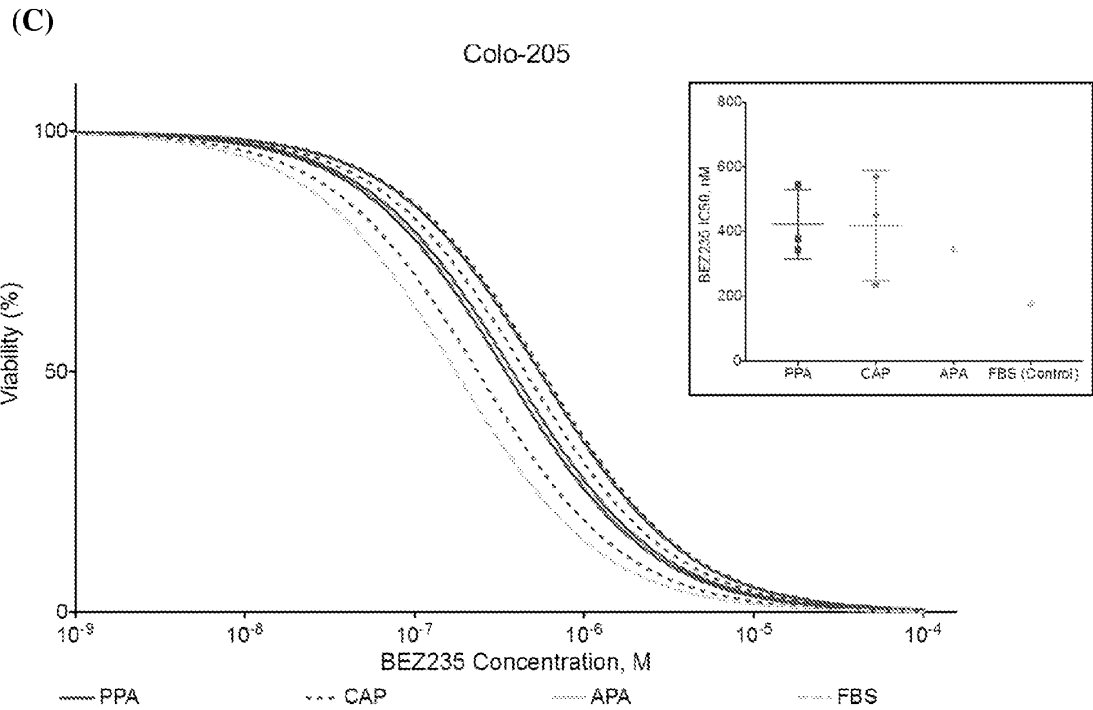
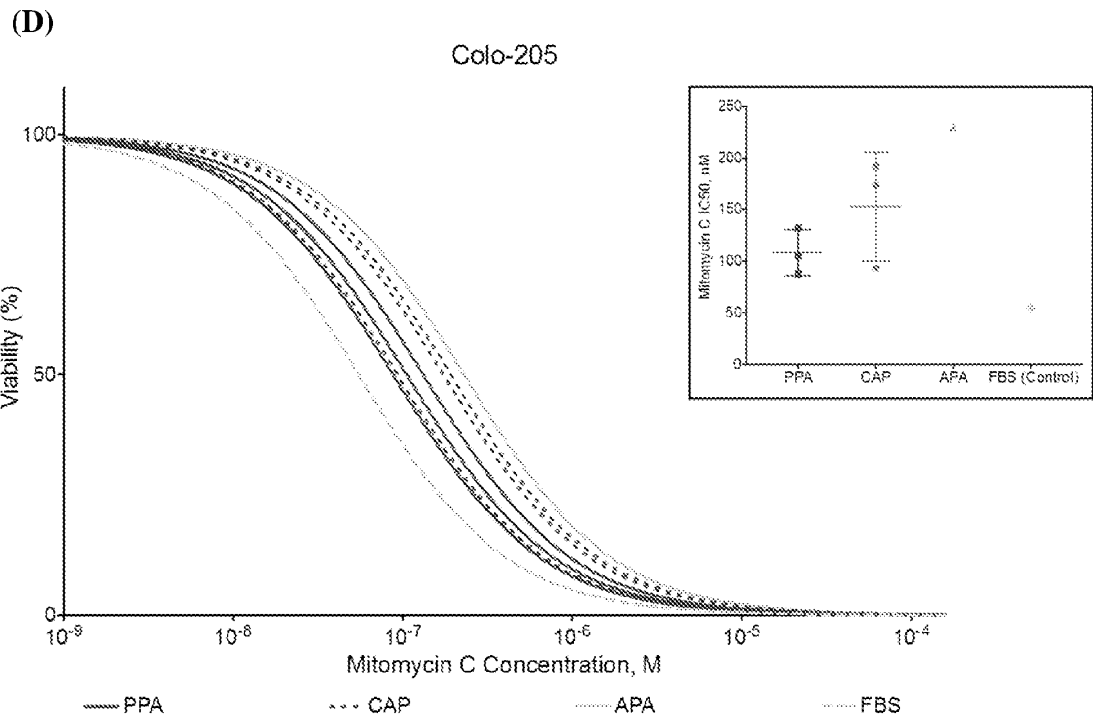
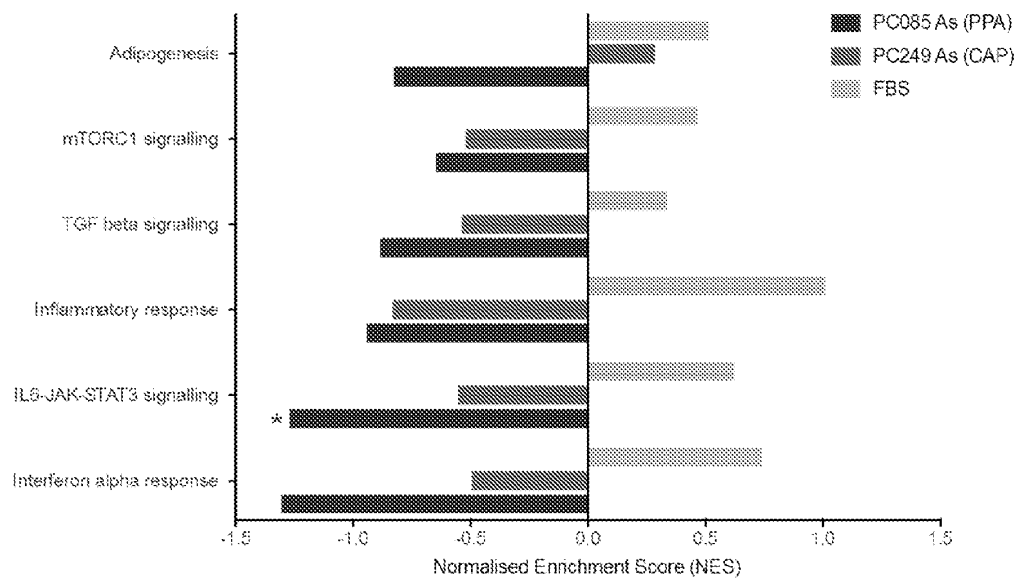
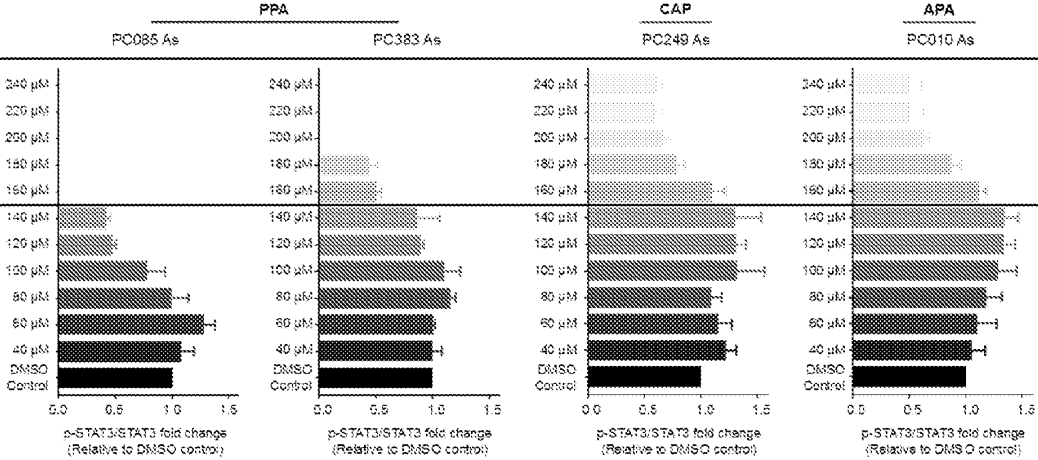


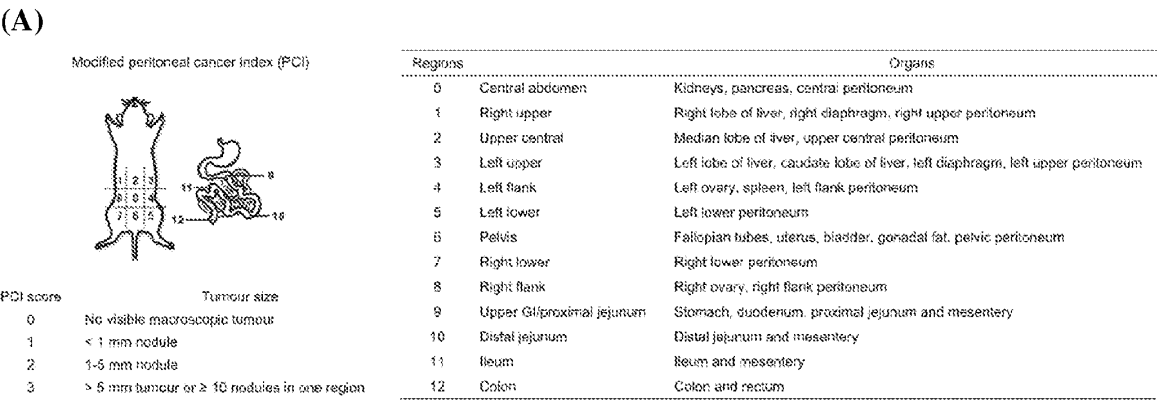
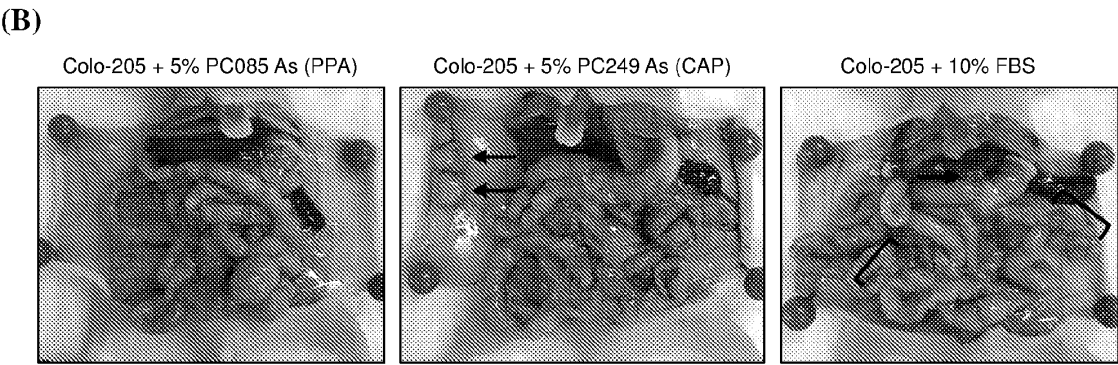
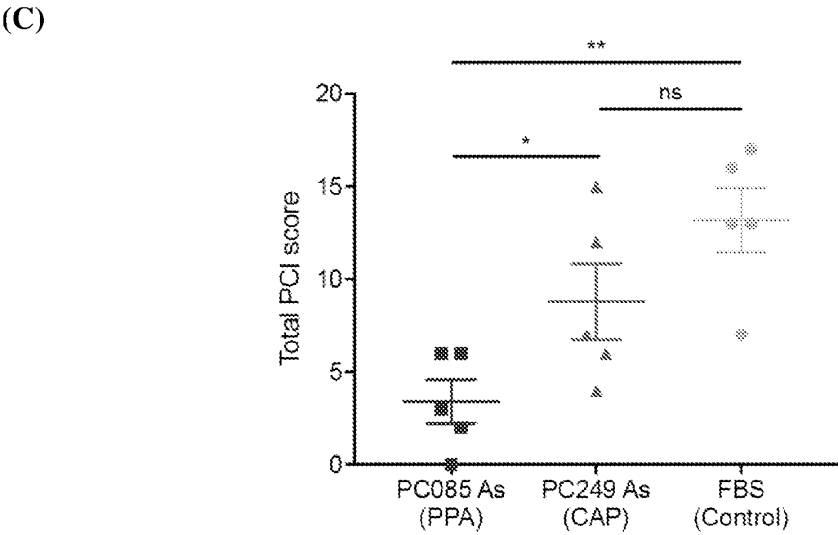
FIG. 13

(A)



(B)





PCT/SG2020/050177

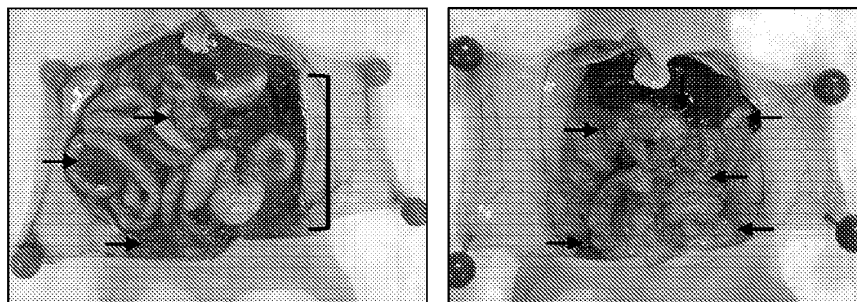
Figure 2 is a dot plot with error bars showing the Total PCI Score for four groups. The Y-axis is labeled 'Total PCI Score' and ranges from 0 to 30. The X-axis labels are '1% DMSO', '1 mM TM5441', '2 mM TM5441', and '2 mM TM5441'. The first three groups are grouped under 'i.p.' (intraperitoneal), and the last group is under 'oral'. Statistical significance is indicated by asterisks: * for p < 0.05 and **** for p < 0.0001. 'ns' indicates non-significant.

Group	Treatment	Total PCI Score (Mean ± SEM)
i.p.	1% DMSO	23.5 ± 2.5
i.p.	1 mM TM5441	17.5 ± 2.5
i.p.	2 mM TM5441	1.0 ± 0.5
oral	2 mM TM5441	21.0 ± 2.5

(A)

PC383 PDADX

PC249 PDADX



(B)

H&E

CK20

CK7

CDX2

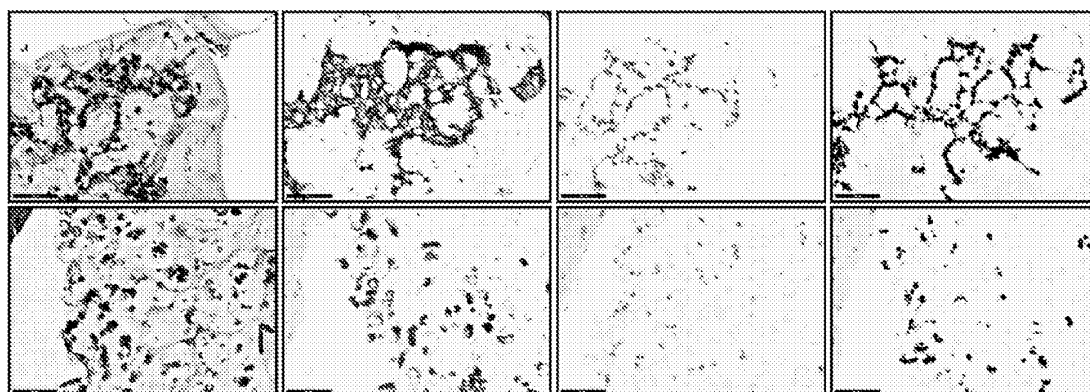
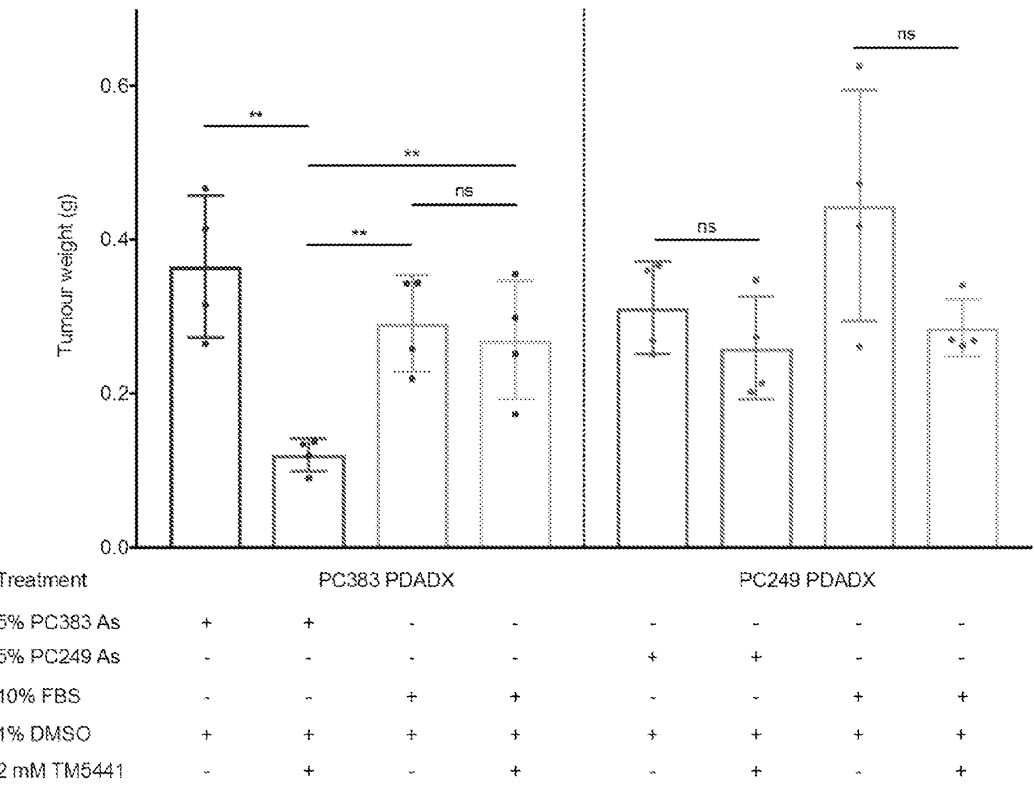
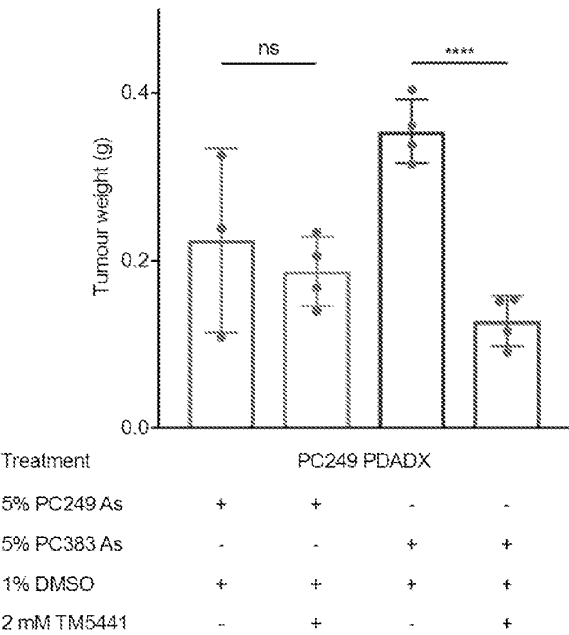
PC383
PDADXPC249
PDADX

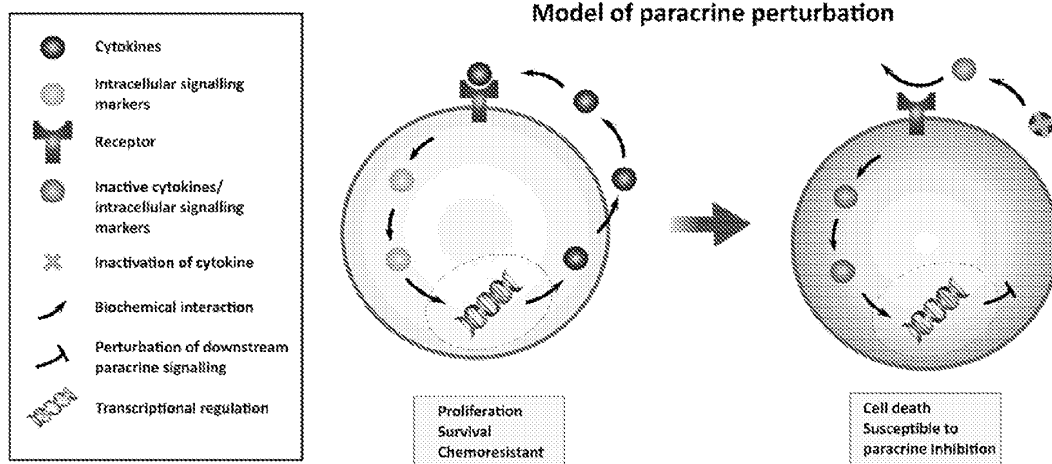
FIG. 17

(A)

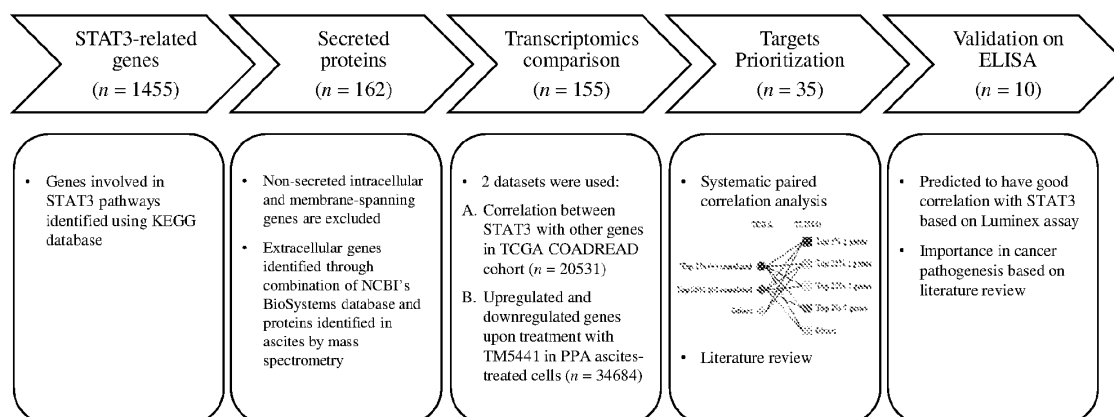


(B)





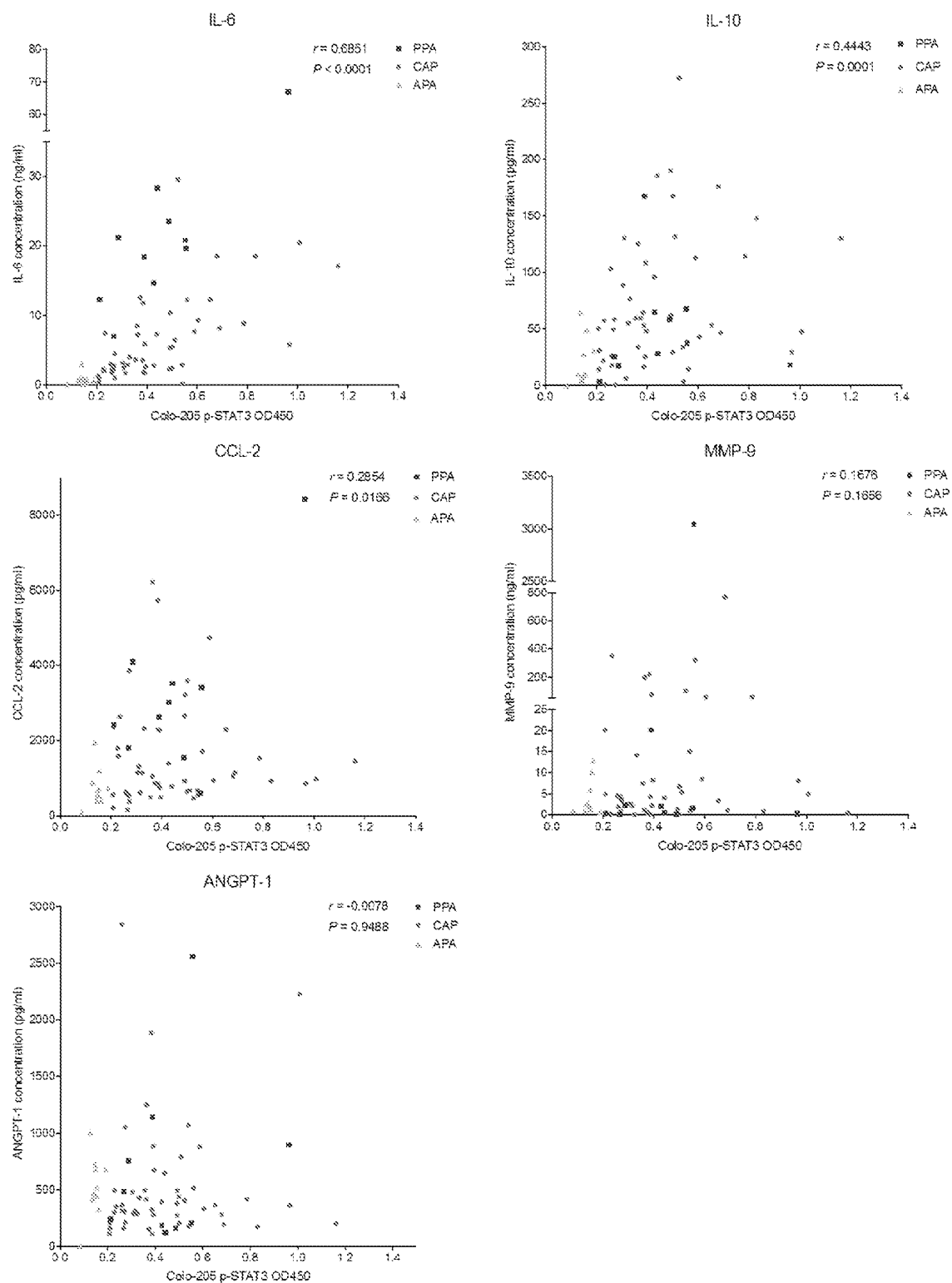
(A)



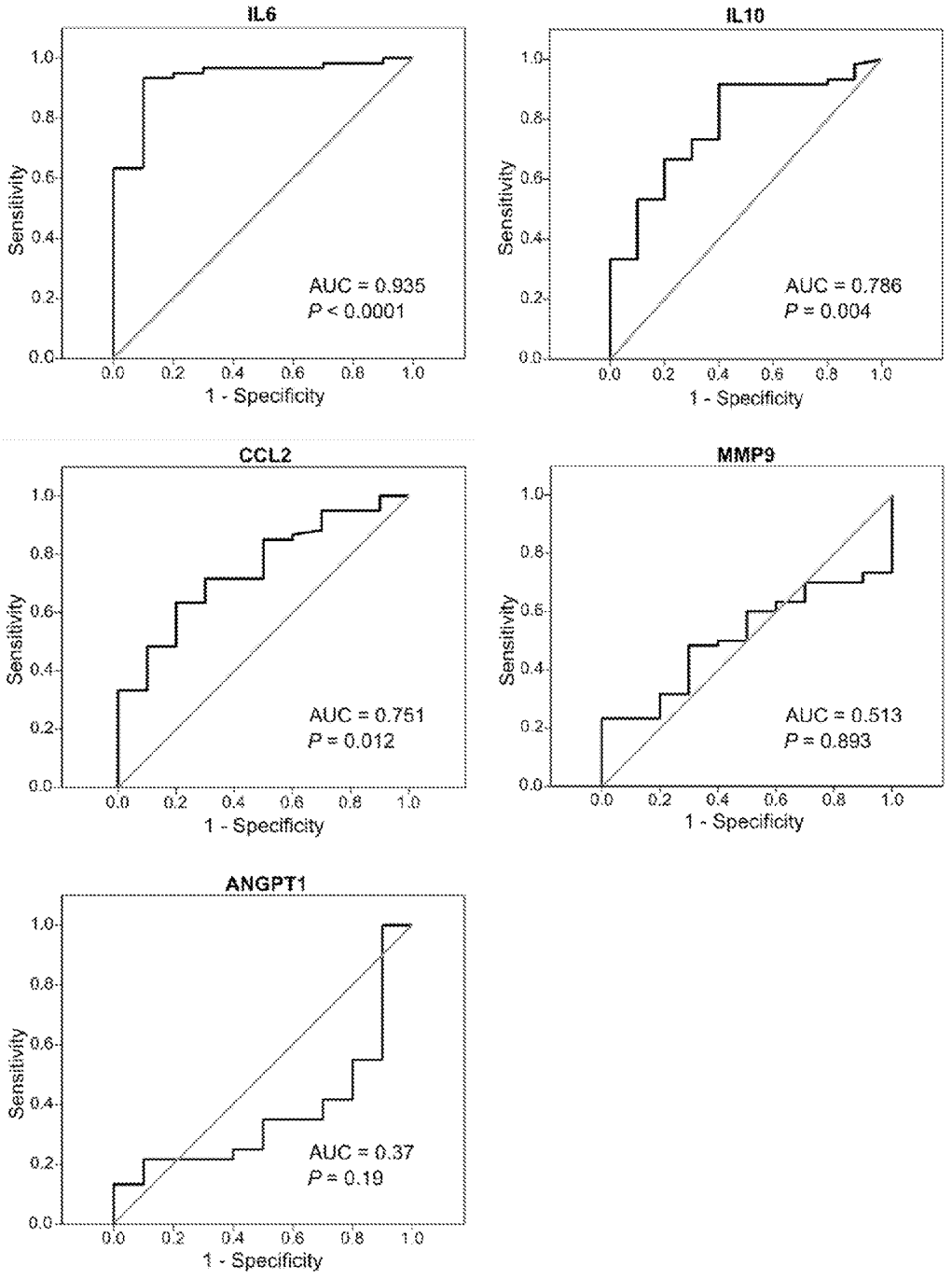
(B)

Priority list	TCGA COADREAD	TM5441 Microarray	No. of genes	Chosen	Gene names of selected candidates
1	Top 1% (+) correlated with STAT3	Top 1% downregulated	0	0	-
2	Top 1% (+) correlated with STAT3	Top 1% upregulated	1	1	LUM
3	Top 25% (+) correlated with STAT3	Top 1% downregulated	2	2	ANGPT1, IL1B
4	Top 25% (+) correlated with STAT3	Top 1% upregulated	0	0	-
5	Top 1% (+) correlated with STAT3	Top 25% downregulated	4	2	POSTN, TNC
6	Top 1% (+) correlated with STAT3	Top 25% upregulated	8	4	MMP9, MMP2, TIMP3, DCN
7	Top 25% (+) correlated with STAT3	Top 25% downregulated	15	5	VSIG4, CXCL5, CD36, ANGPT2, SERPINB5
8	Top 25% (+) correlated with STAT3	Top 25% upregulated	19	6	IL6, CCL2, LEP, VCAM1, CCL8, ITGAM
9	Top 1% (+) correlated with STAT3	Others	16	5	THBS1, FN1, COL5A1, MXRA5, C3
10	Top 25% (+) correlated with STAT3	Others	46	7	CXCL10, TGFB1, CD44, TIM3, TNFSF13B, CEACAM1, LAMB1
11	Others	Top 1% downregulated	0	0	-
12	Others	Top 25% downregulated	15	3	IL10, IL5, IL22
13	Others	Top 25% upregulated	19	0	-
14	Others	Others	2	0	-
15	Top 25% (-) correlated with STAT3	Others	7	0	-
16	Top 25% (-) correlated with STAT3	Top 25% upregulated	1	0	-
Total			155	35	

(A)



(B)



(C)

Biomarkers	IL-6 concentration	IL-10 concentration	CCL-2 concentration	MMP-9 concentration
Cut-off values for PPA/CAP	≥ 997 pg/mL	≥ 15 pg/mL	≥ 450 pg/mL	≥ 3 ng/mL
Cut-off values for APA	< 997 pg/mL	< 15 pg/mL	< 450 pg/mL	< 3 ng/mL

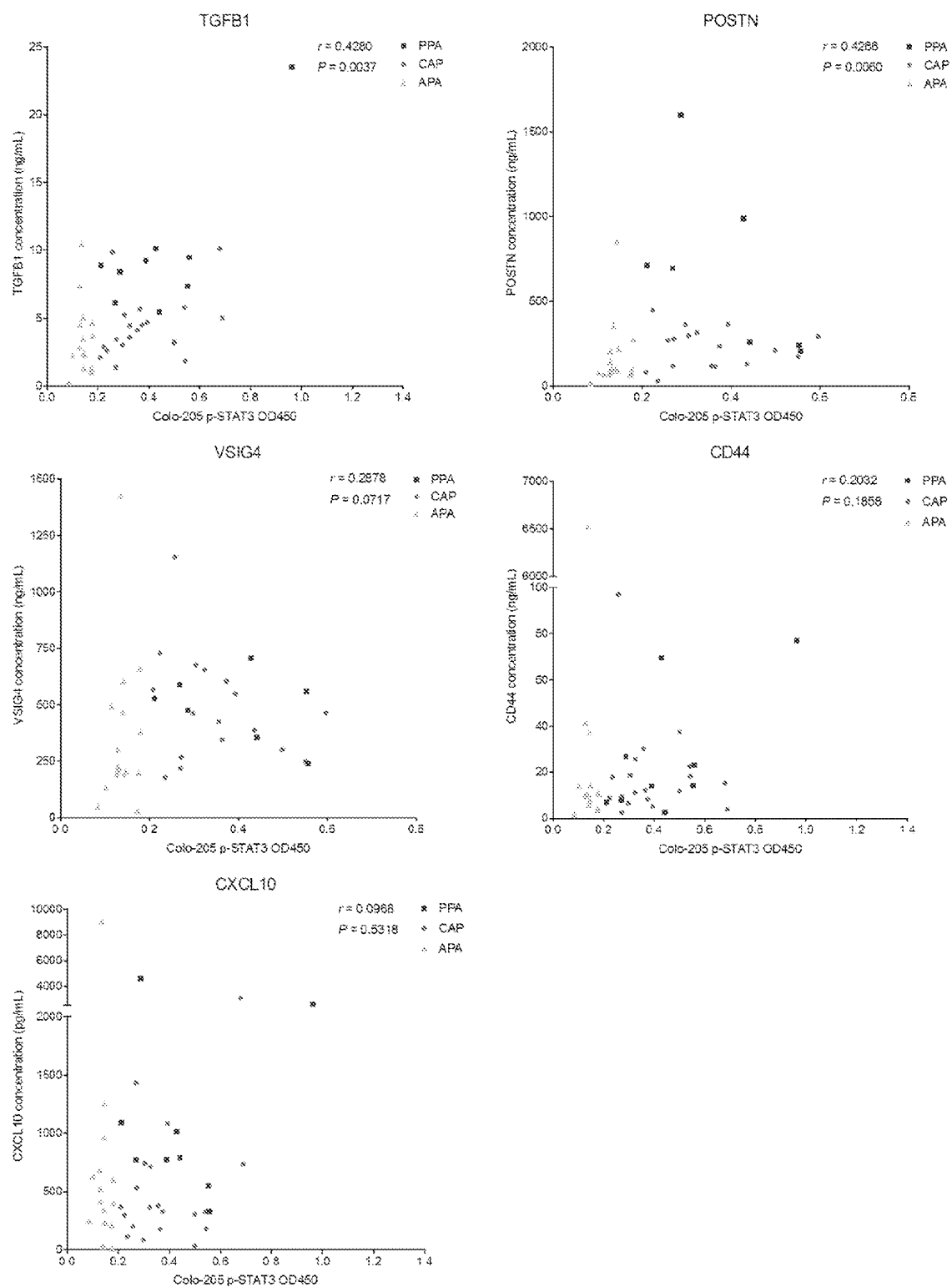
(D)

No. of biomarker	p-STAT3 surrogate biomarker	APA Accuracy	PPA/CAP Accuracy	Overall Accuracy	Cut-off (PPA/CAP)	Cut-off (APA)
1	IL6	80%	95%	92.86%		
	IL10	60%	88.33%	84.29%		
	CCL2	30%	95%	85.71%		
	MMP9	70%	48.33%	51.43%		
2	IL6, IL10	100%	86.67%	88.57%	2 (+) biomarkers	0 or 1 (+) biomarker
	IL6, CCL2	90%	91.67%	91.43%		
	IL10, CCL2	70%	85%	82.86%		
	IL6, MMP9	50%	98.33%	91.43%	1 or 2 (+) biomarkers	0 (+) biomarker
	IL10, MMP9	50%	95%	88.57%		
	CCL2, MMP9	20%	100%	88.57%		
3	IL6, IL10, CCL2	60%	96.67%	91.43%	2 or 3 (+) biomarkers	0 or 1 (+) biomarker
	IL6, IL10, MMP9	80%	93.33%	91.43%		
	IL6, CCL2, MMP9	70%	96.67%	92.86%		
	IL10, CCL2, MMP9	50%	93.33%	87.14%		
4	IL6, IL10, CCL2, MMP9	90%	93.33%	92.86%	3 or 4 (+) biomarkers	0, or 1, or 2 (+) biomarker

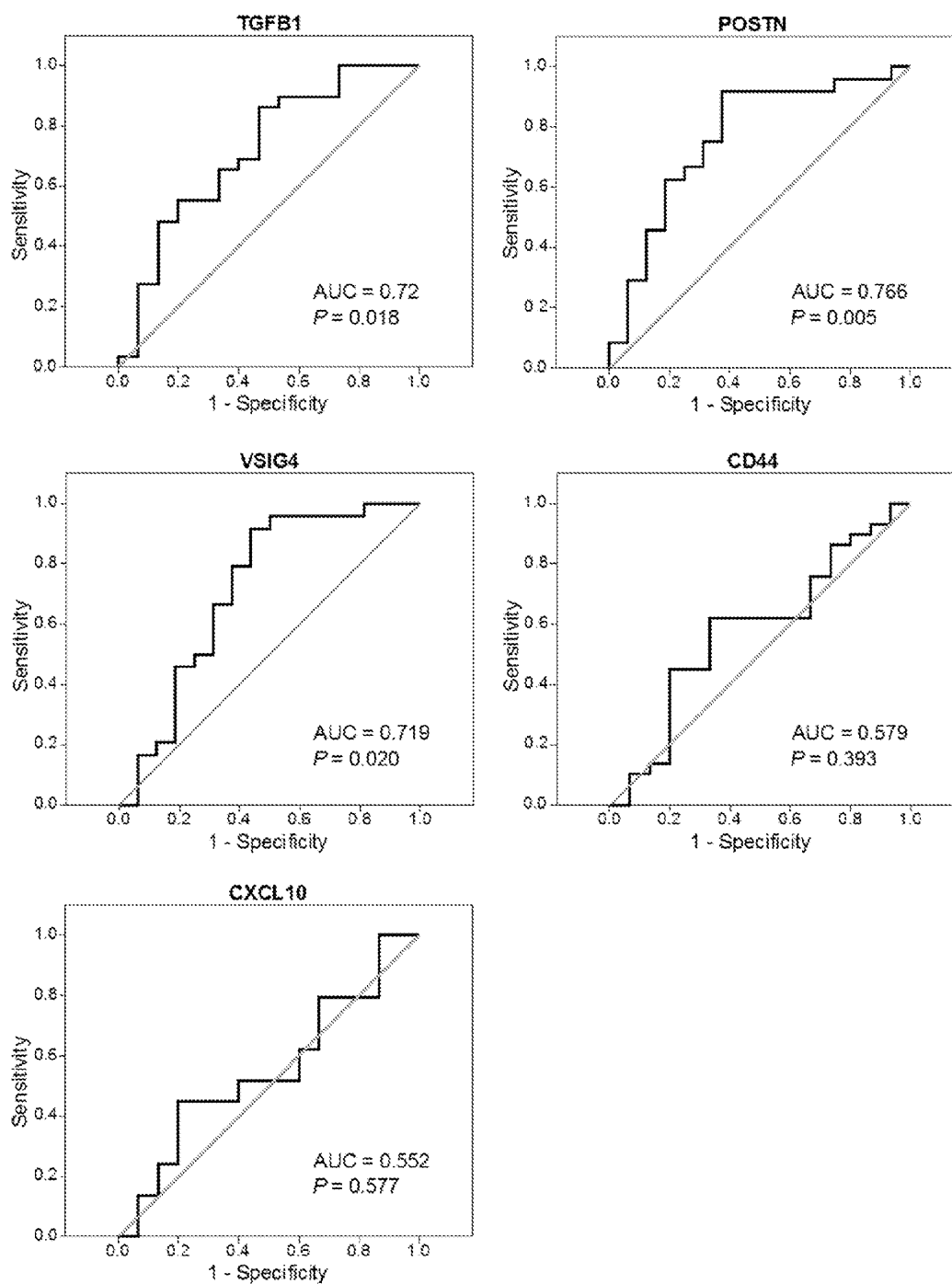
(E)

Biomarkers	PAI-1 concentration	p-STAT3 (Y705) OD450	IL-6 concentration	IL-10 concentration	CCL-2 concentration	MMP-9 concentration
Cut-off values	20 ng/mL	0.2	997 pg/mL	15 pg/mL	450 pg/mL	3 ng/mL
Range			± 5%			

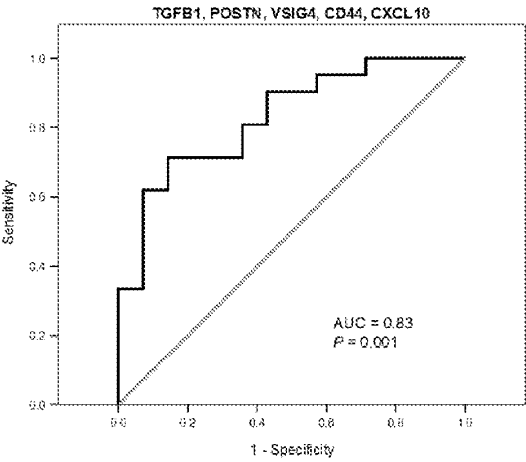
(A)



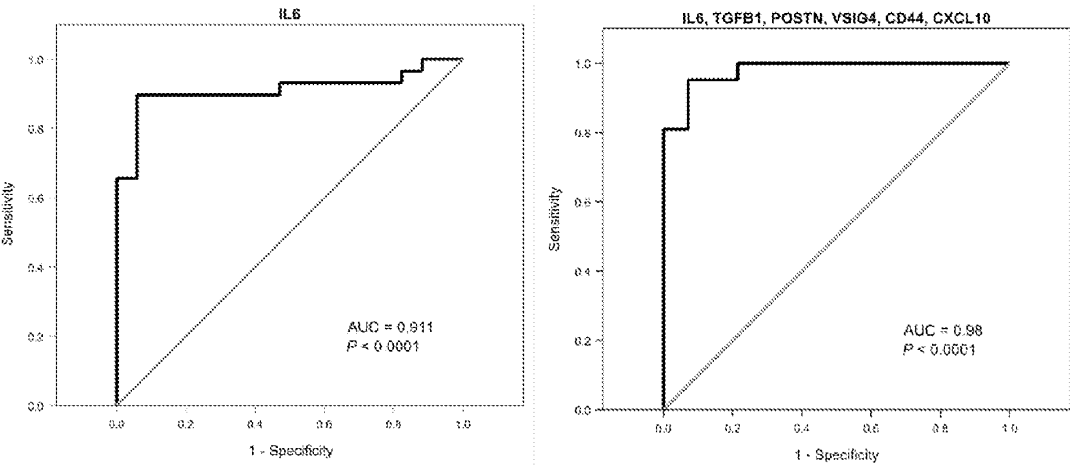
(B)



(C)



(D)



(E)

No. of biomarker	p-STAT3 surrogate biomarker	AUC	P-value
1	TGFB1	0.720	0.018
	POSTN	0.766	0.005
	VSIG4	0.719	0.020
	CD44	0.579	0.393
	CXCL10	0.552	0.577
	IL6	0.911	< 0.0001
5	TGFB1, POSTN, VSIG4, CD44, CXCL10	0.830	0.001
6	IL6, TGFB1, POSTN, VSIG4, CD44, CXCL10	0.980	< 0.0001