

Figure 1

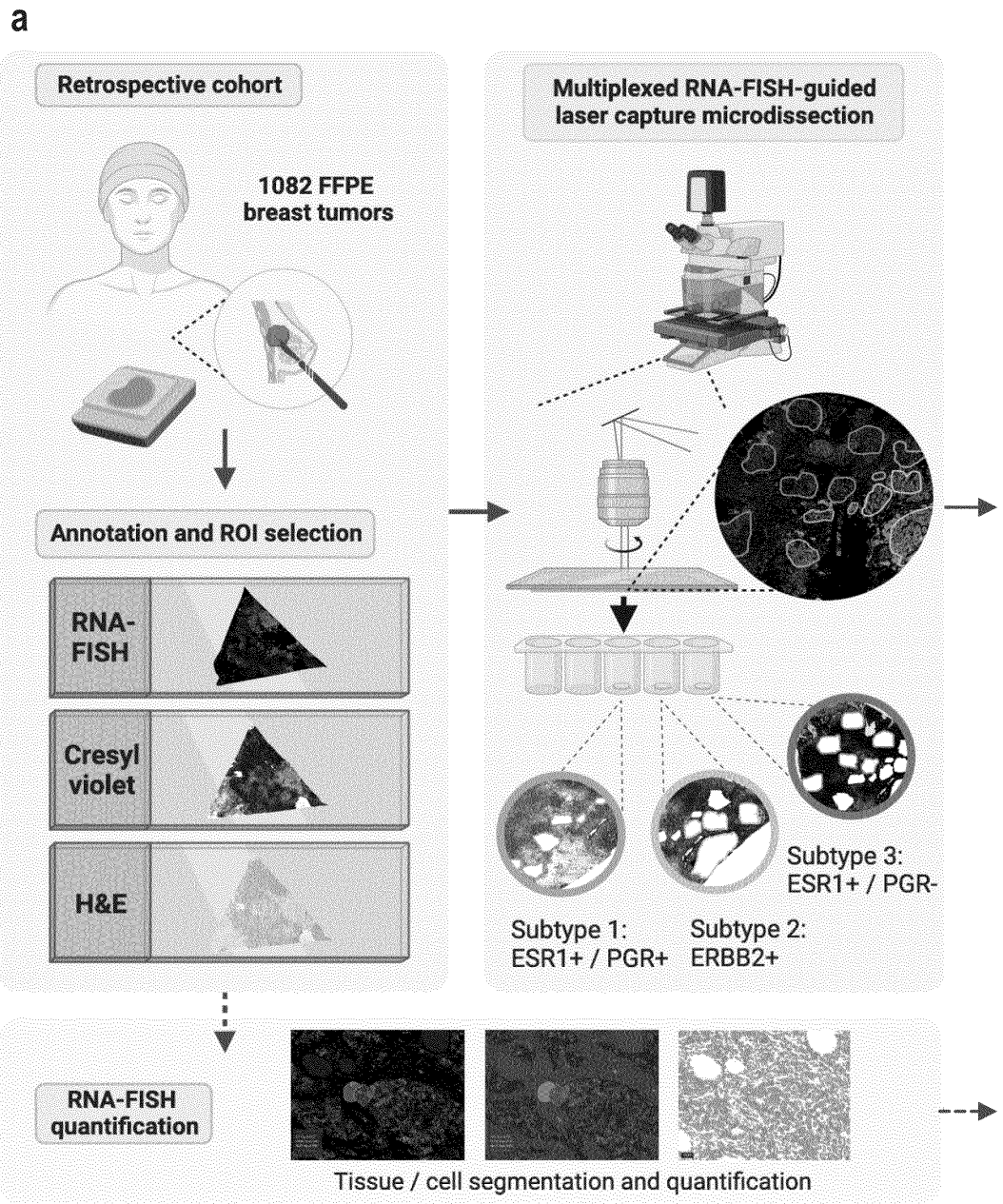


Figure 1 (cont.)

a (cont.)

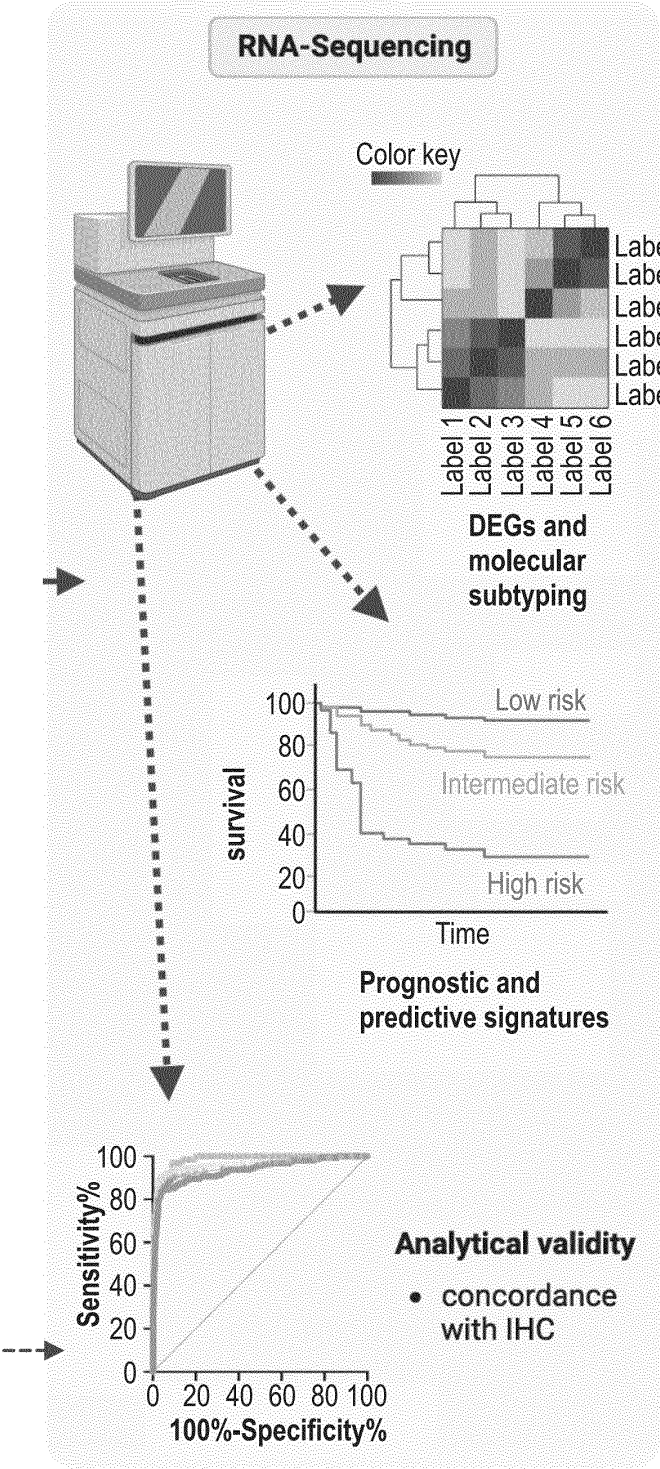
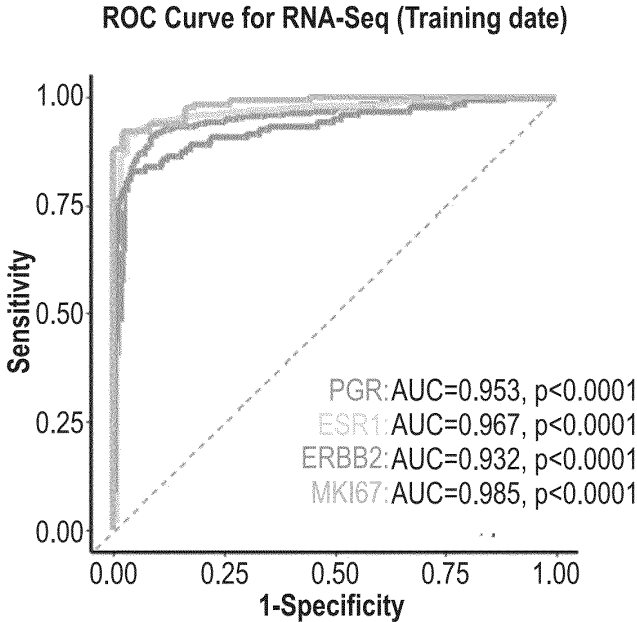


Figure 1 (cont.)

b



TPM thresholds (Maximum Cohen's K)	
PGR RNA-SEQ	≥ 1.4
ESR1 RNA-SEQ	≥ 5.0
ERBB2 RNA-SEQ	≥ 154.7
MKI67 RNA-SEQ	≥ 18.9

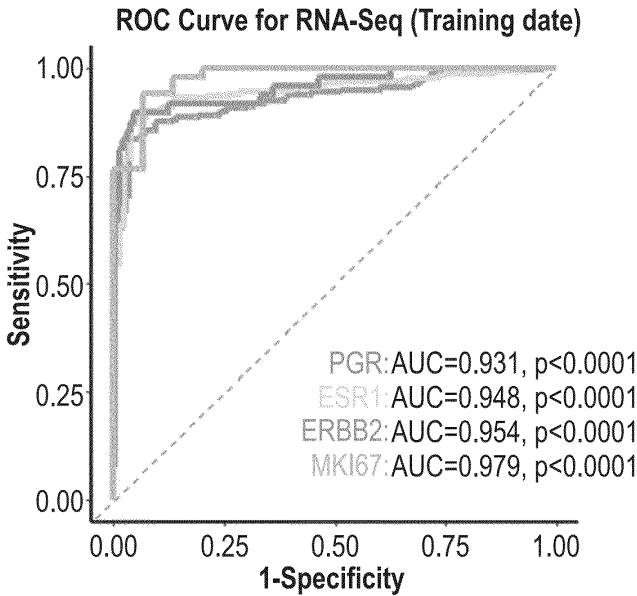


Figure 1 (cont.)

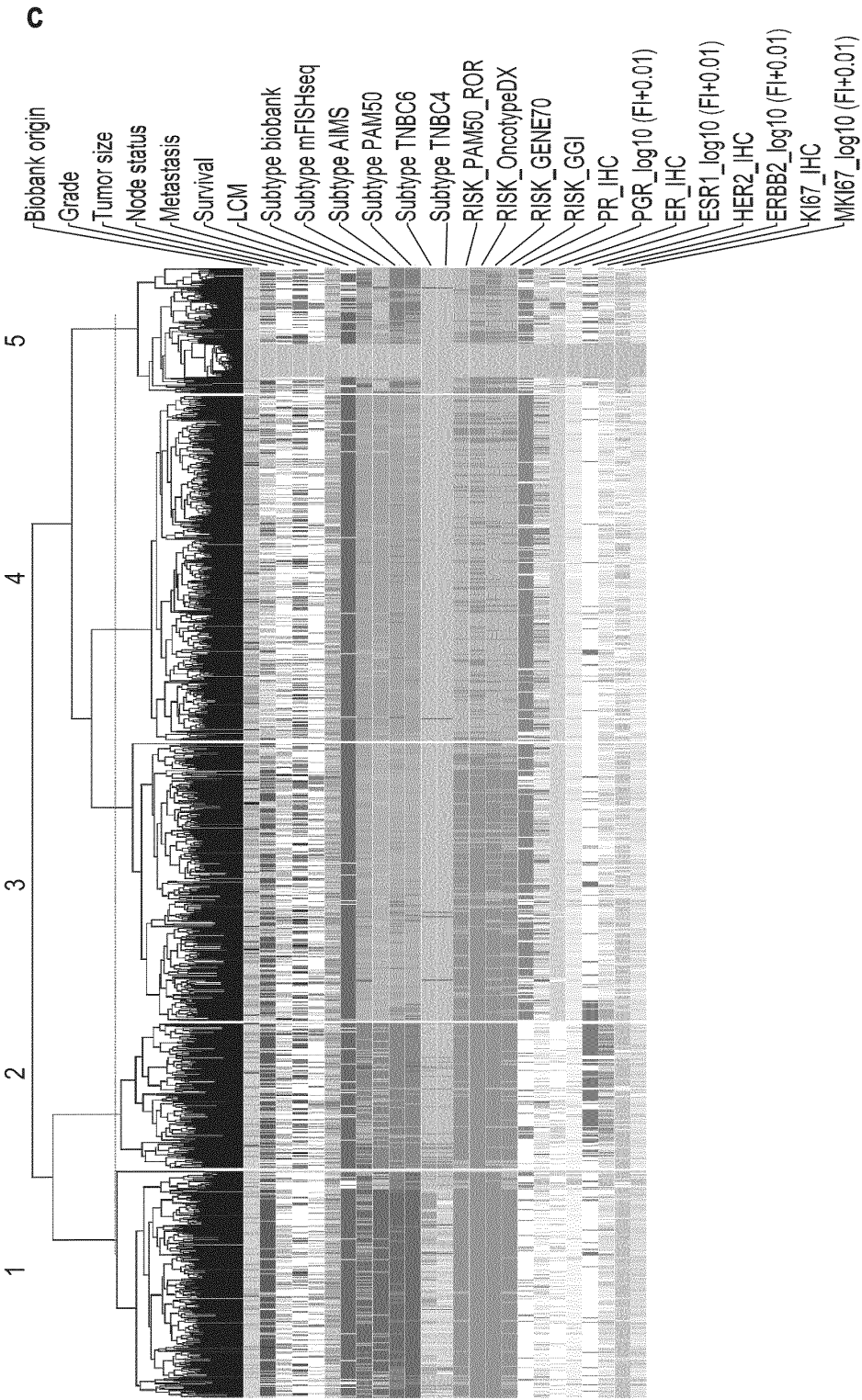


Figure 1 (cont.)

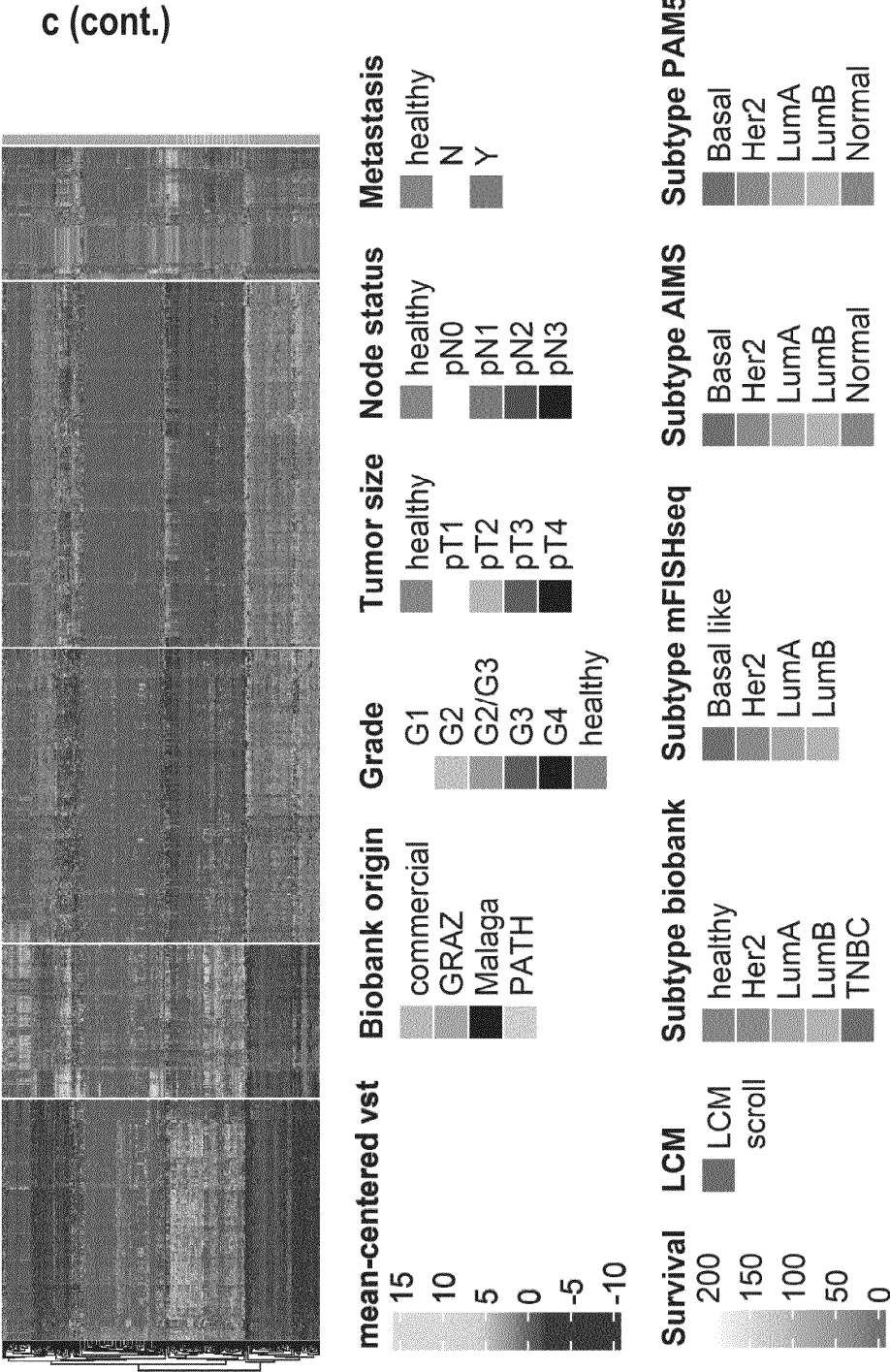


Figure 1 (cont.)

c (cont.)

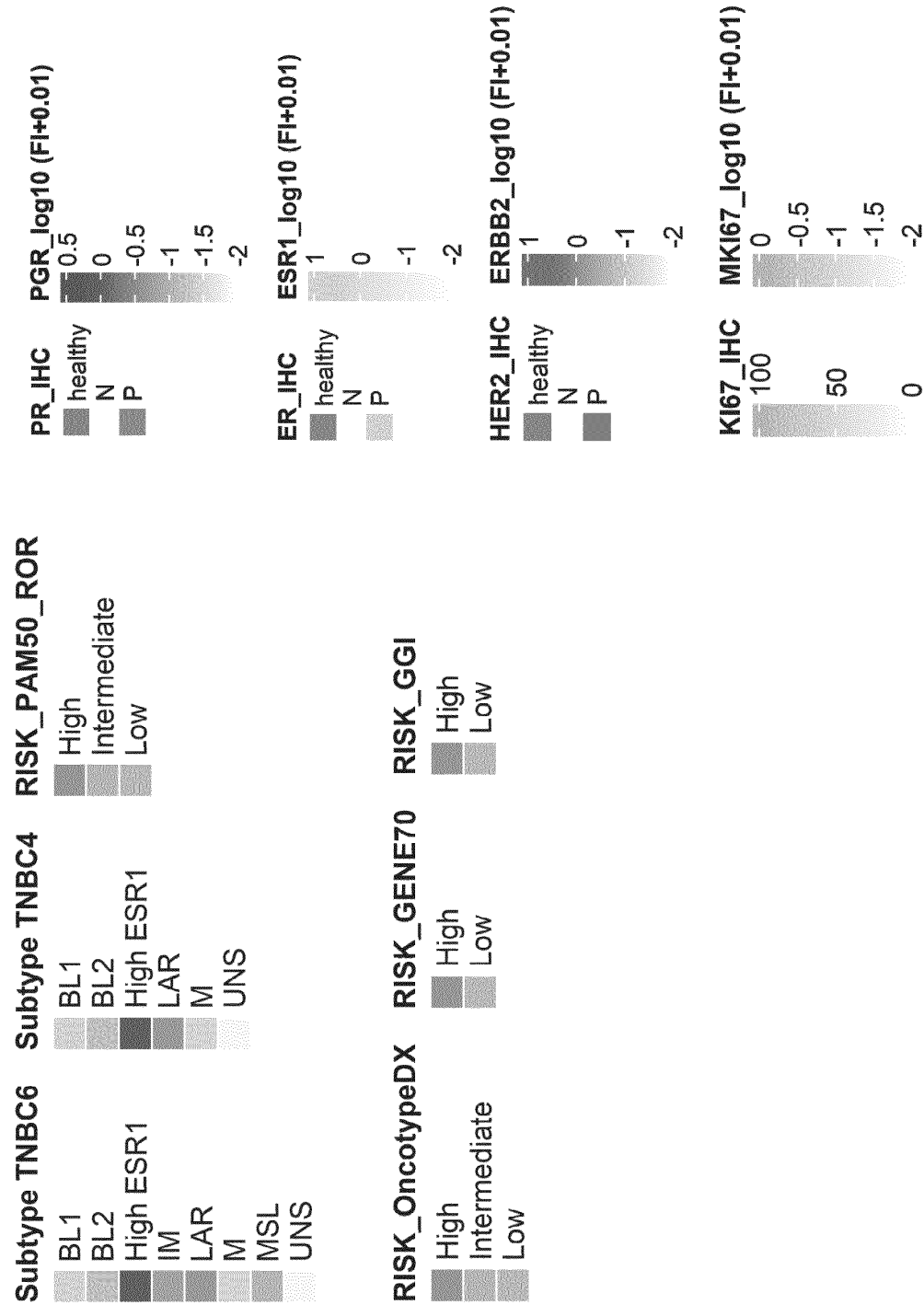


Figure 2

a

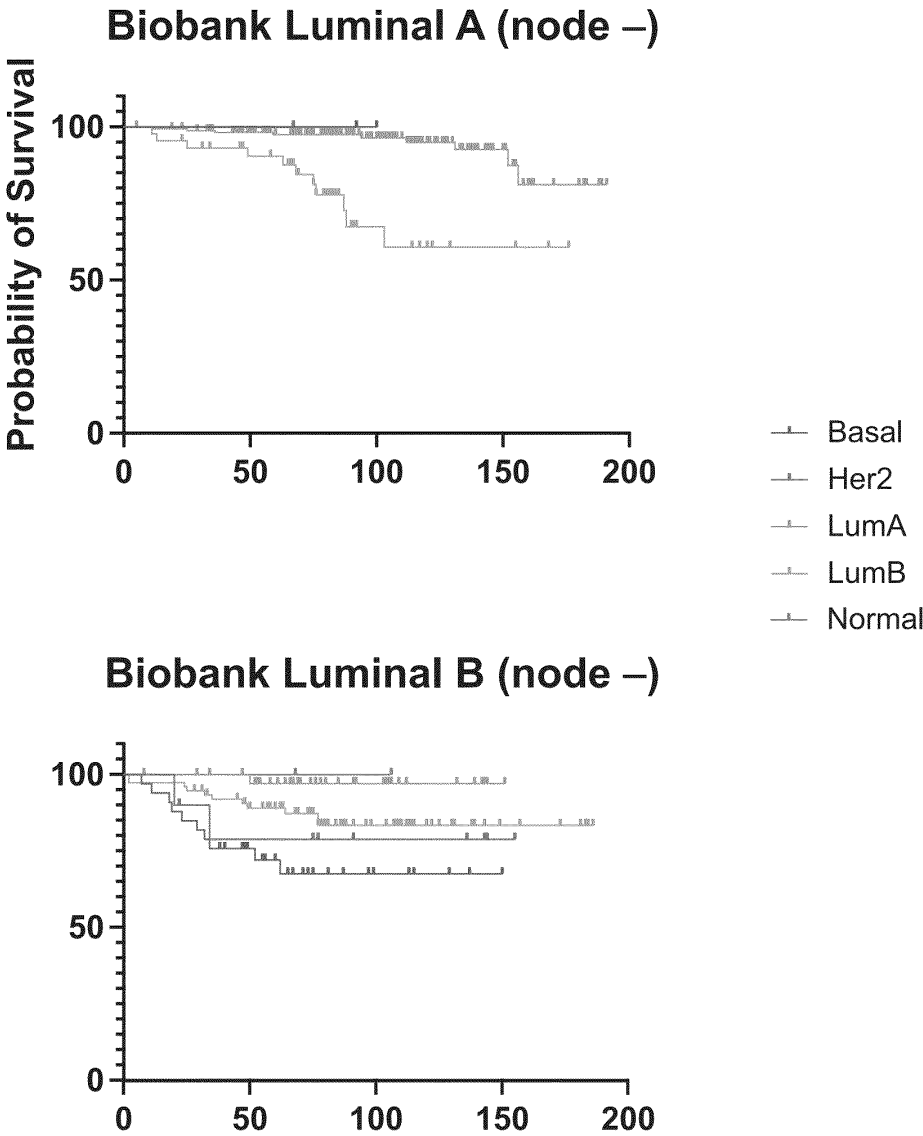


Figure 2 (cont.)

a (cont.)

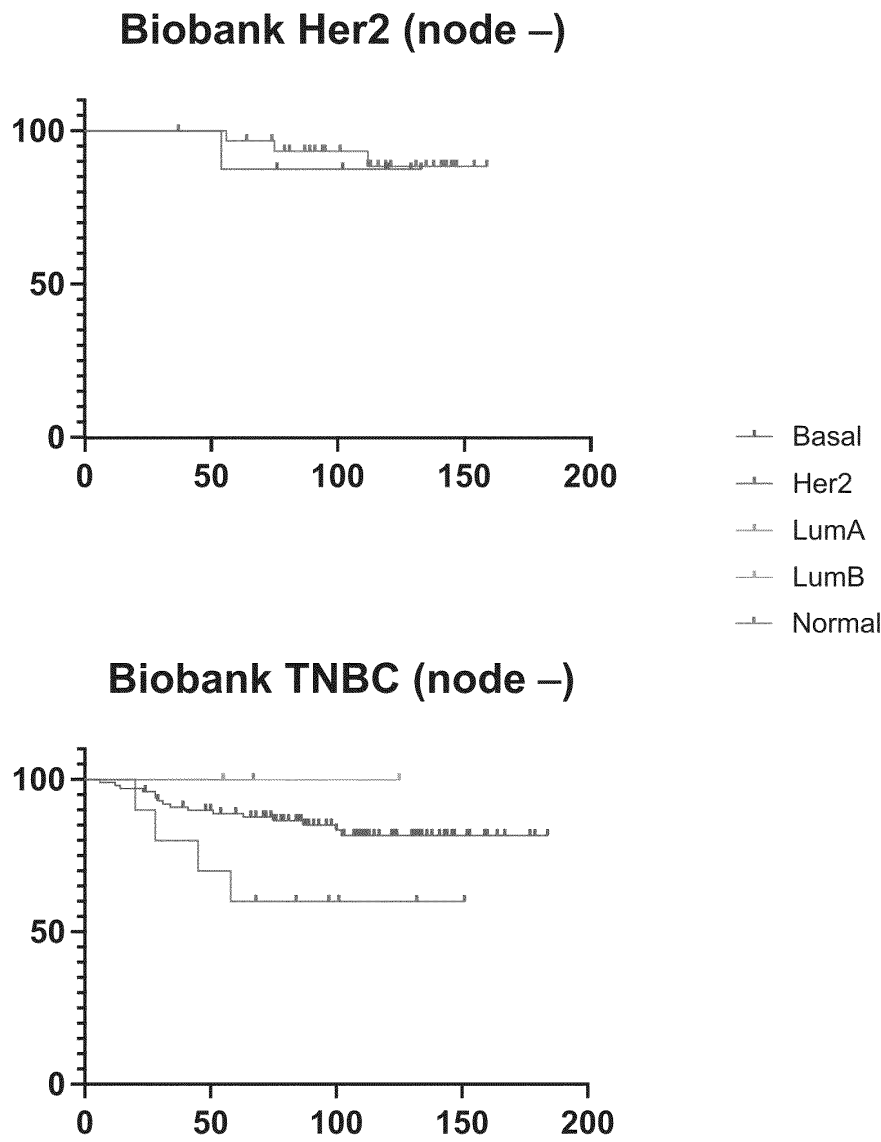


Figure 2 (cont.)

b

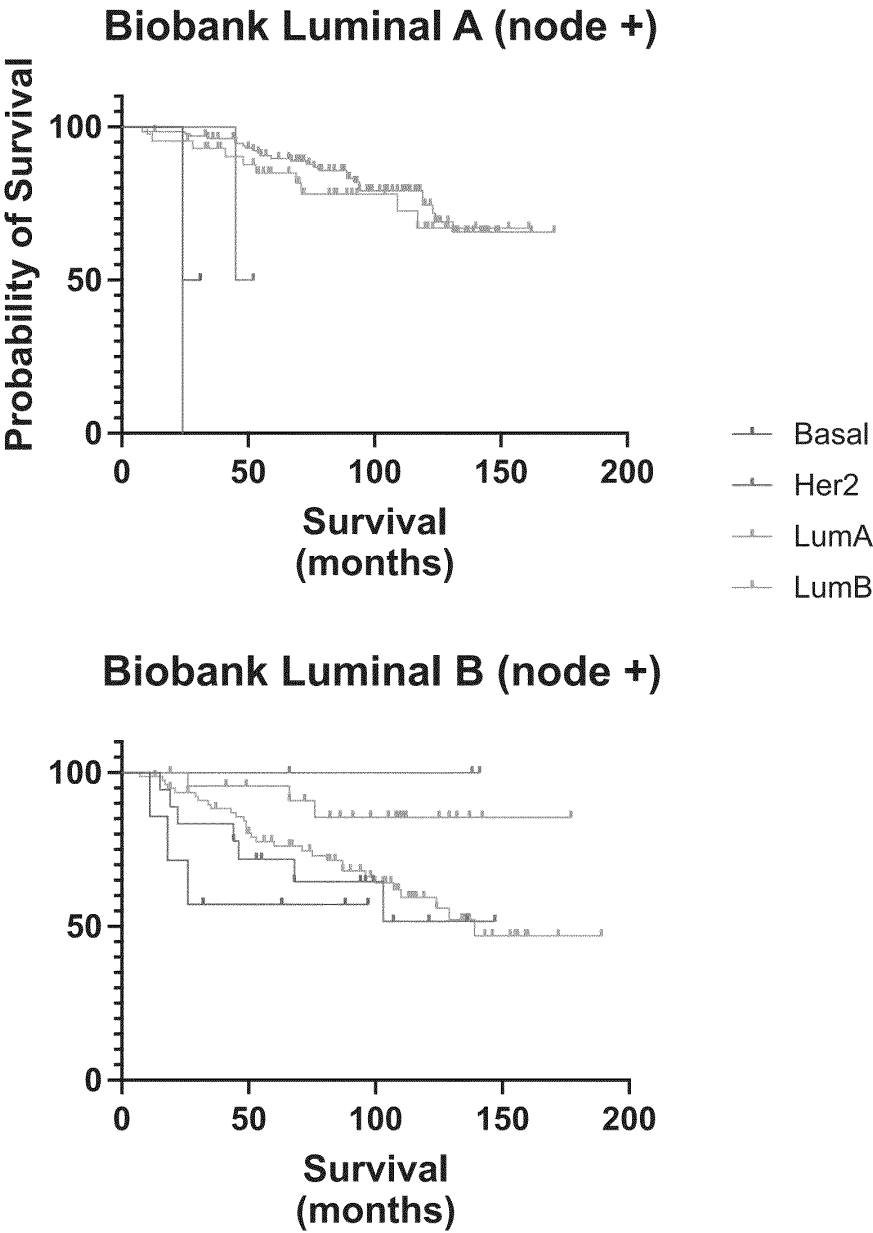


Figure 2 (cont.)

b (cont.)

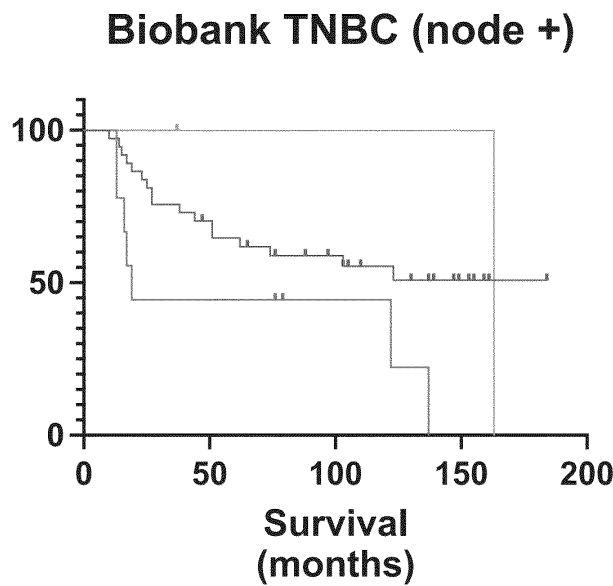
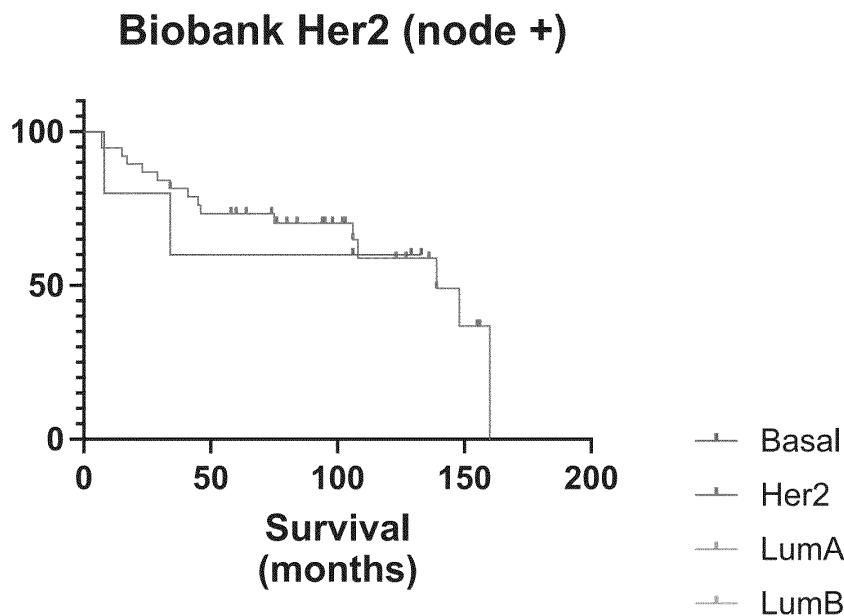


Figure 2 (cont.)

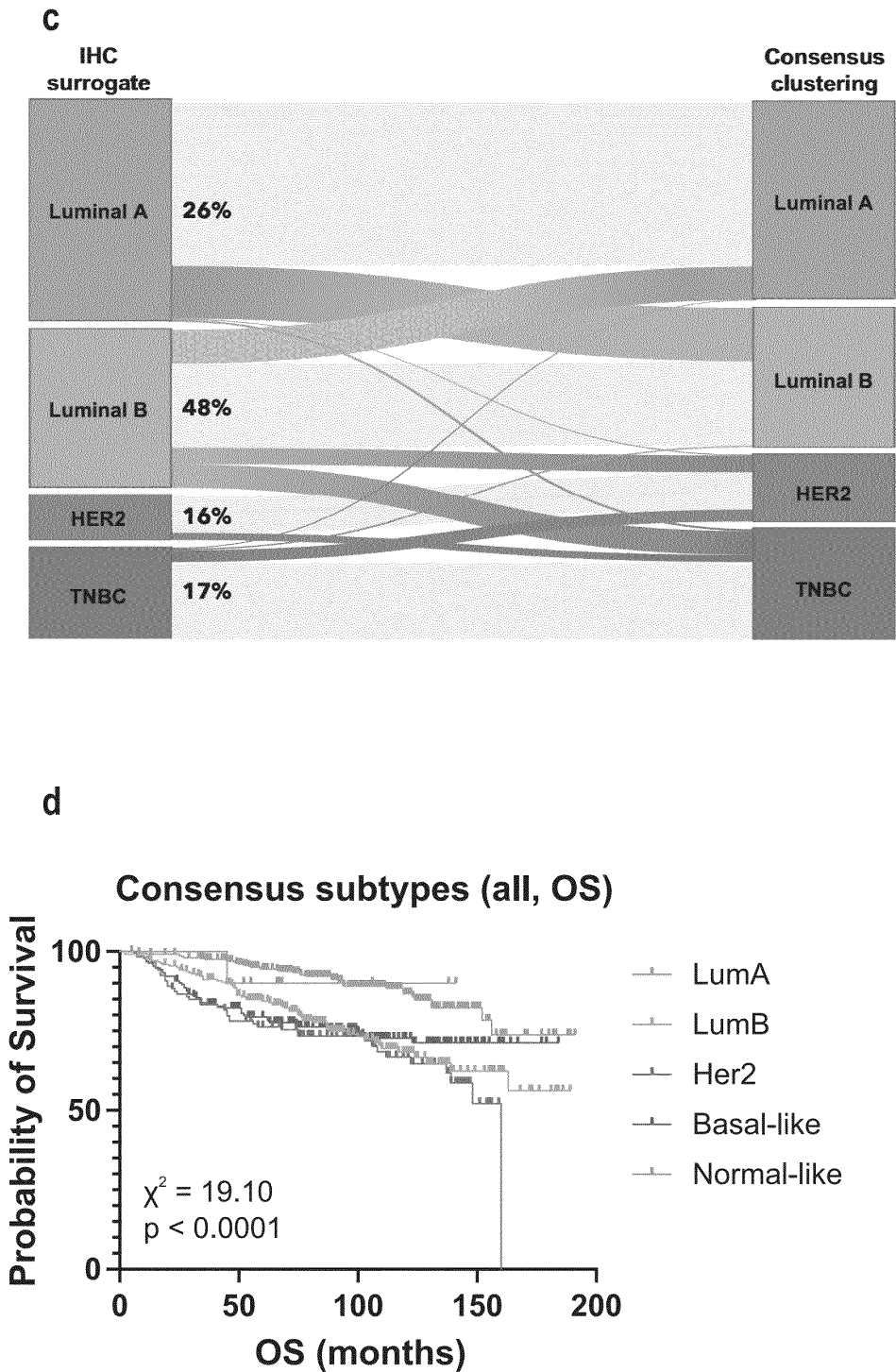


Figure 2 (cont.)

e

Univariate CPHM of ADC target genes

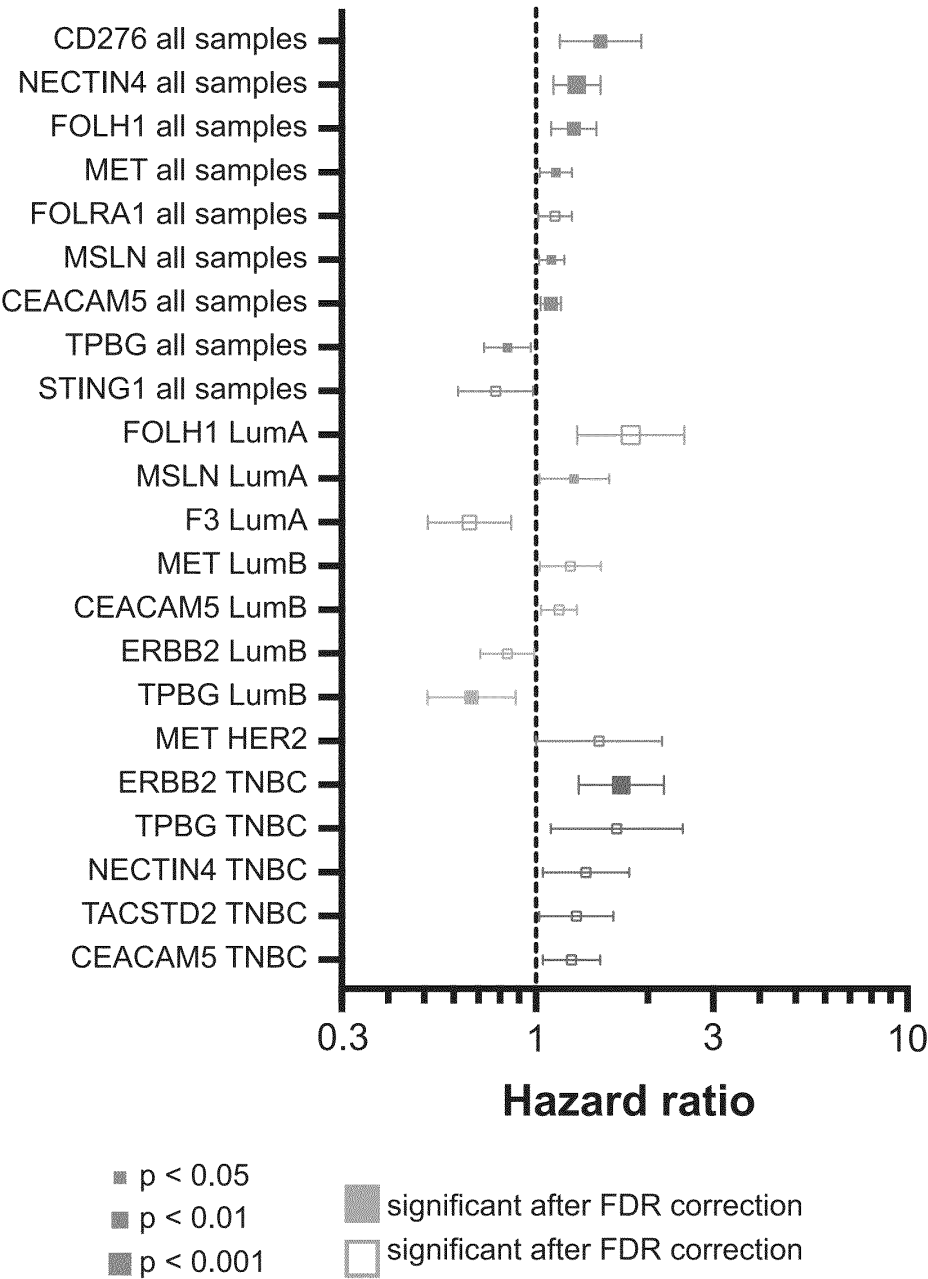


Figure 2 (cont.)

f

Multivariate CPHM of ADC target genes

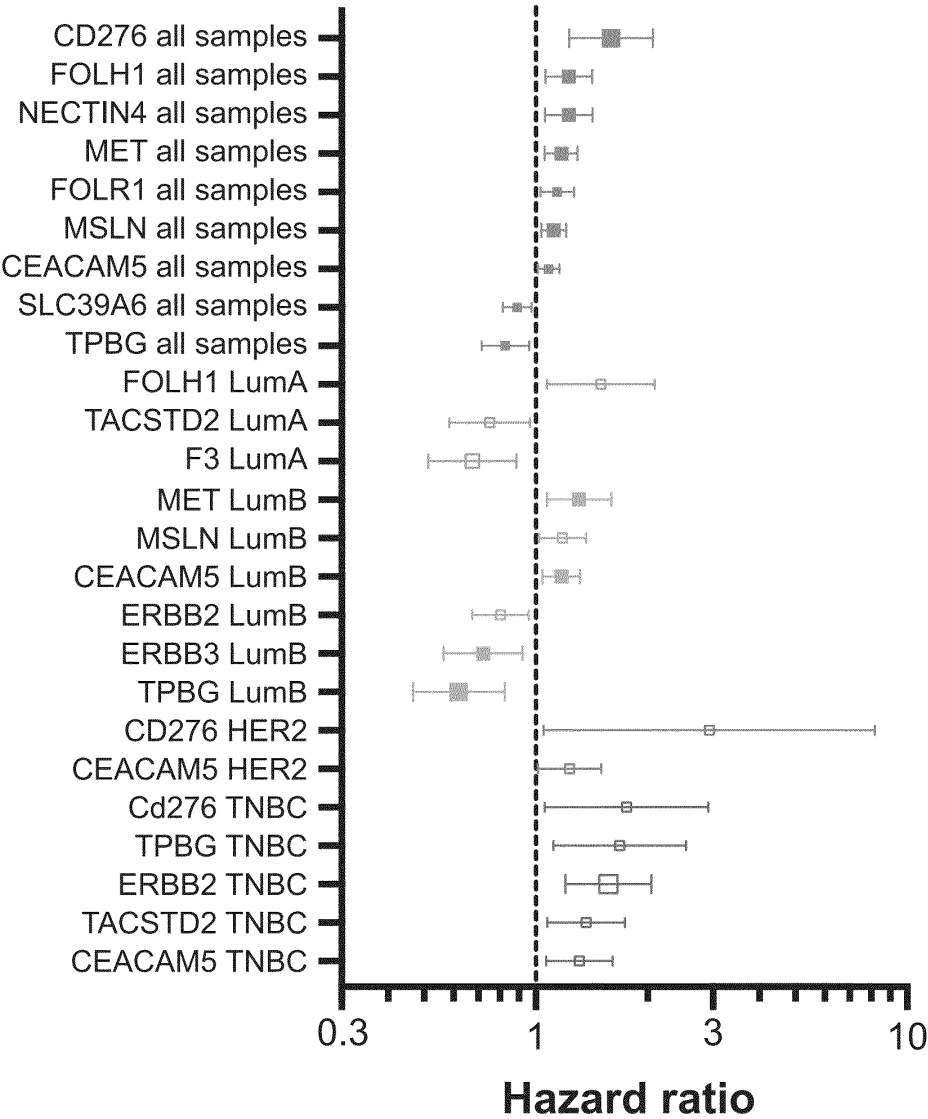


Figure 2 (cont.)

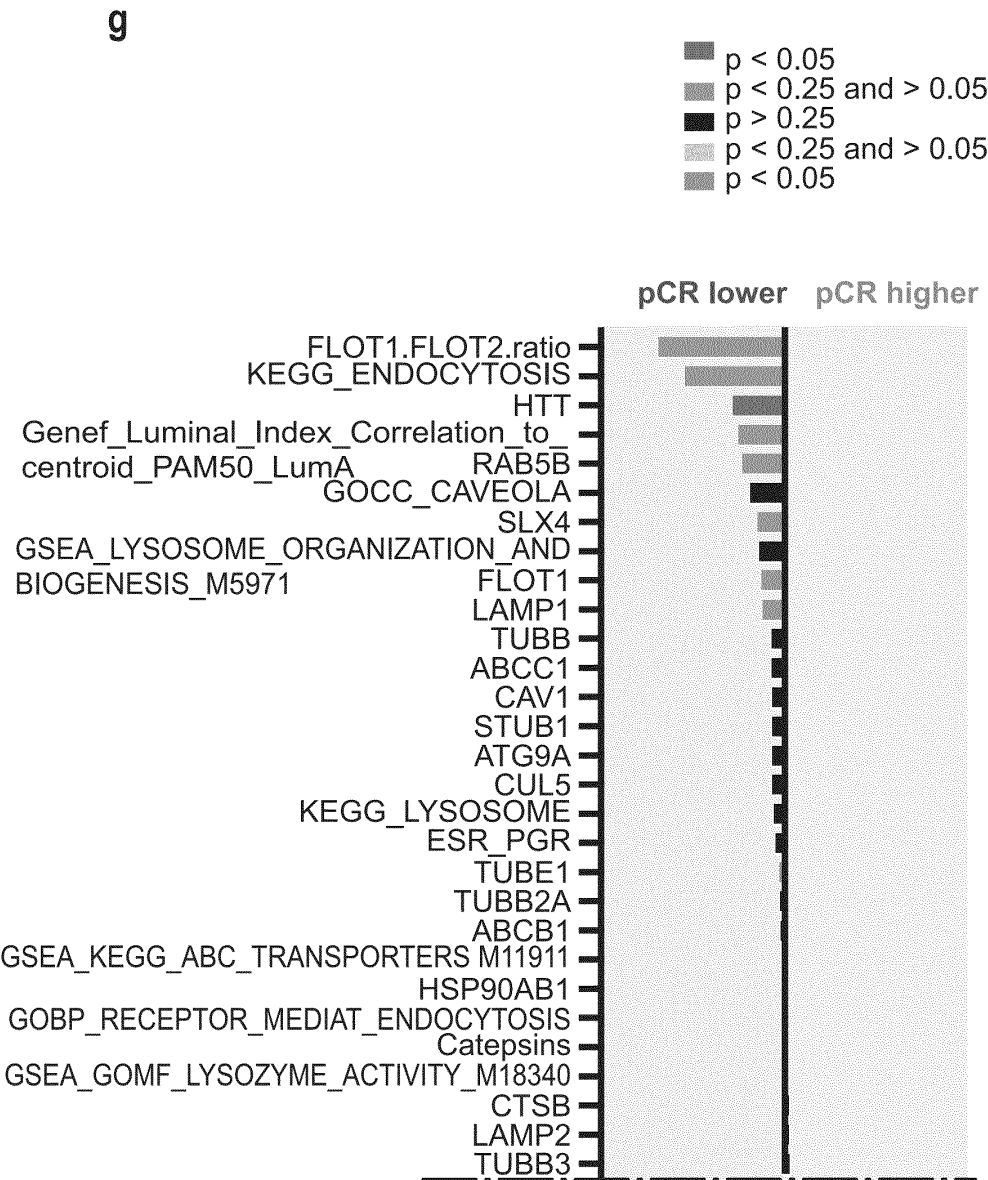


Figure 2 (cont.)

g (cont.)

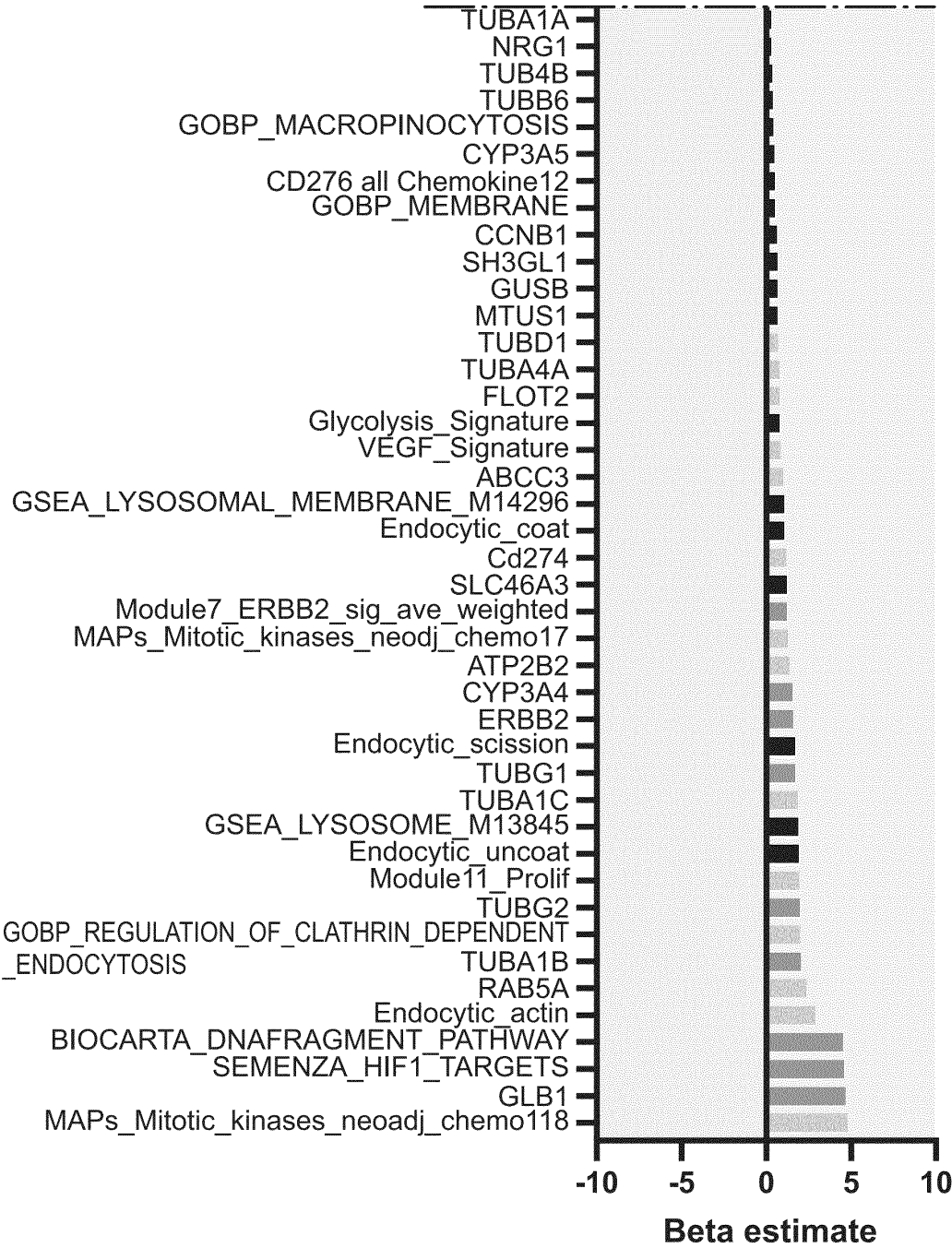


Figure 2 (cont.)

h

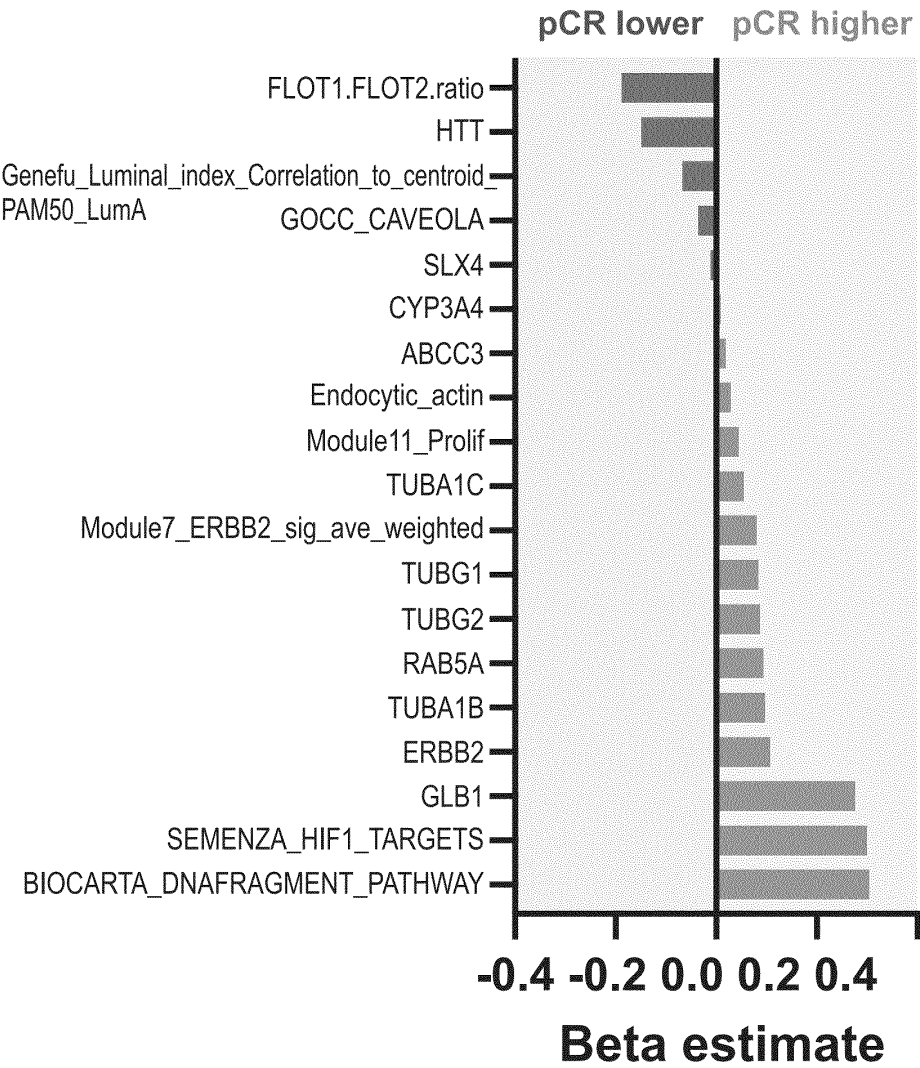


Figure 2 (cont.)

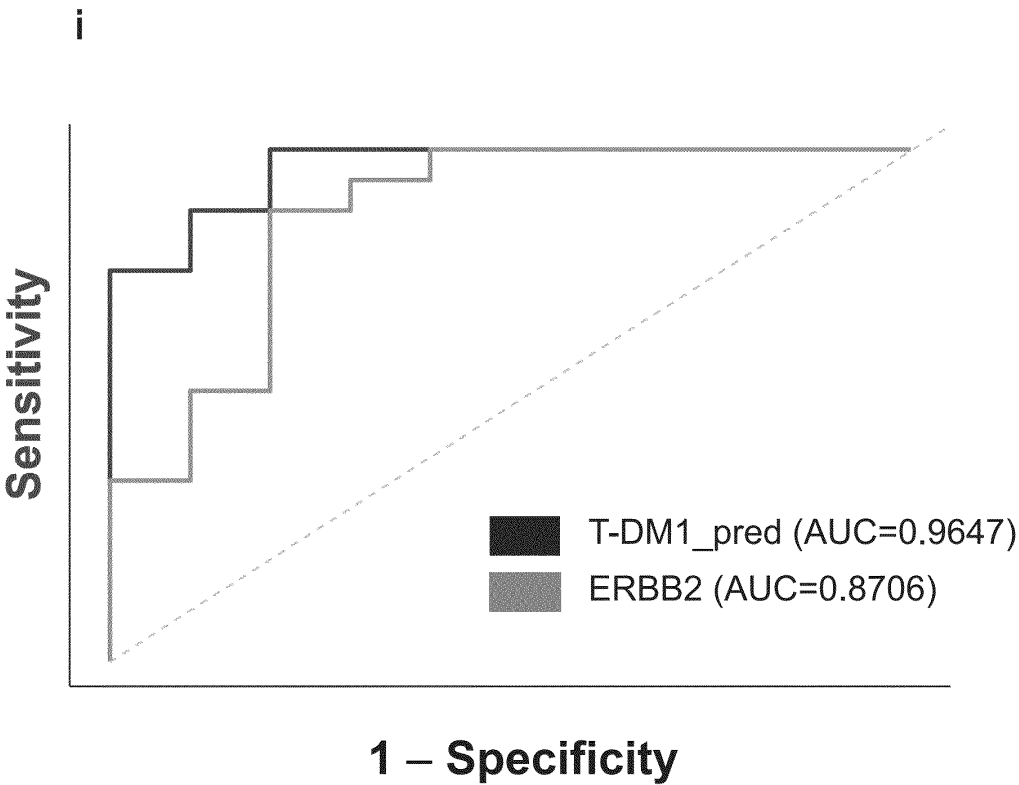


Figure 2 (cont.)

j

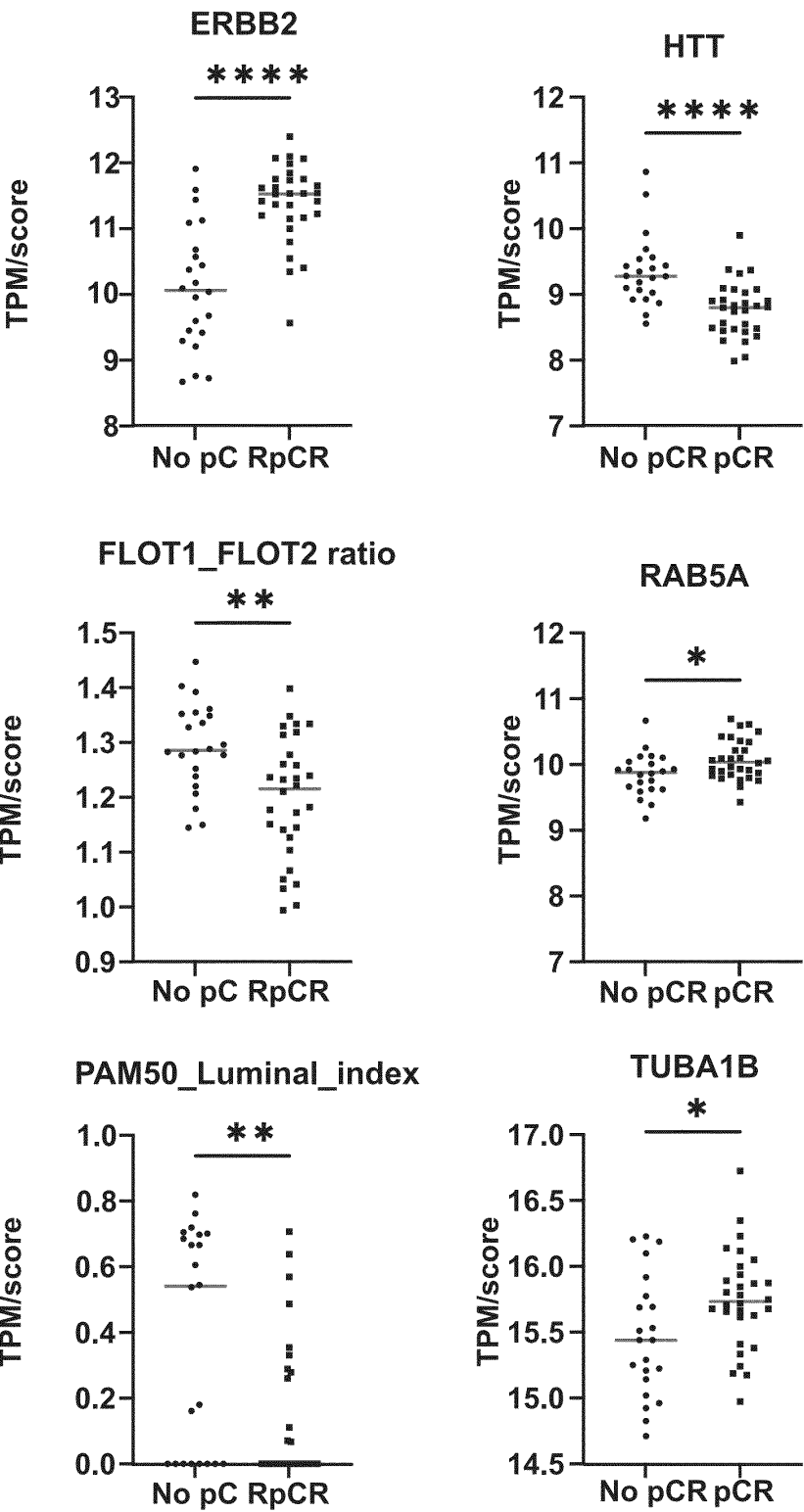
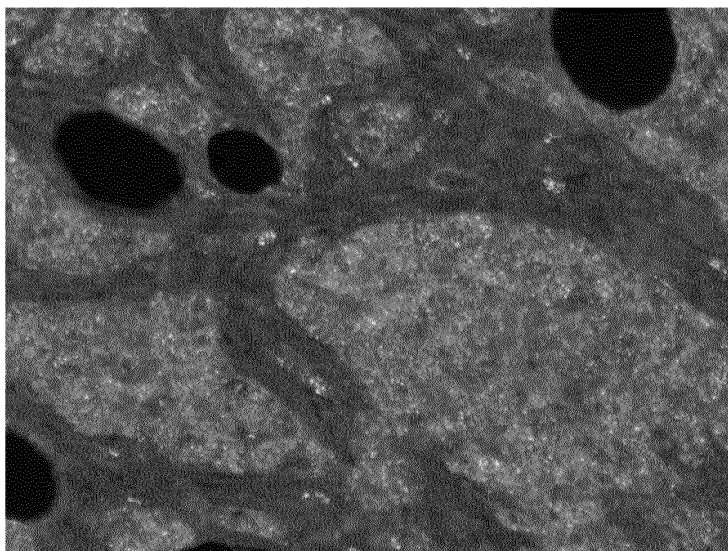
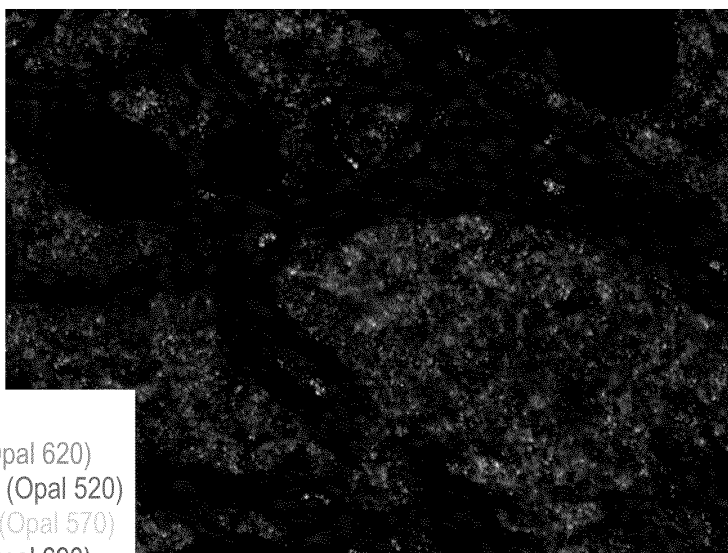


Figure 3

a

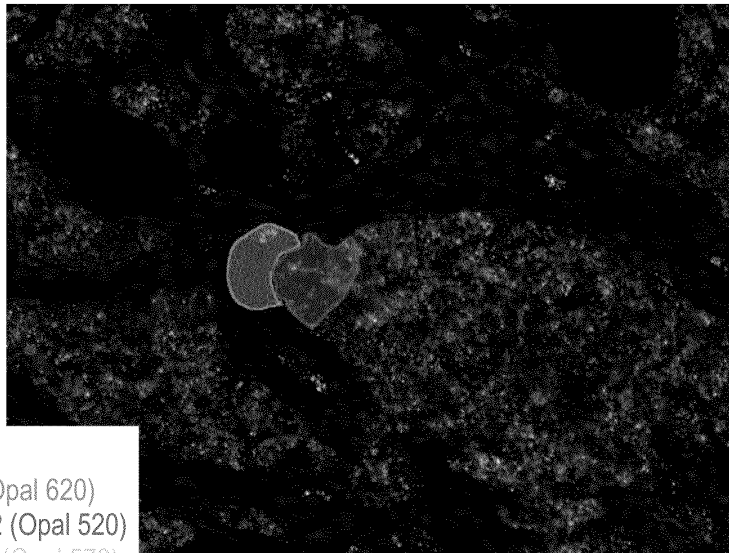


b

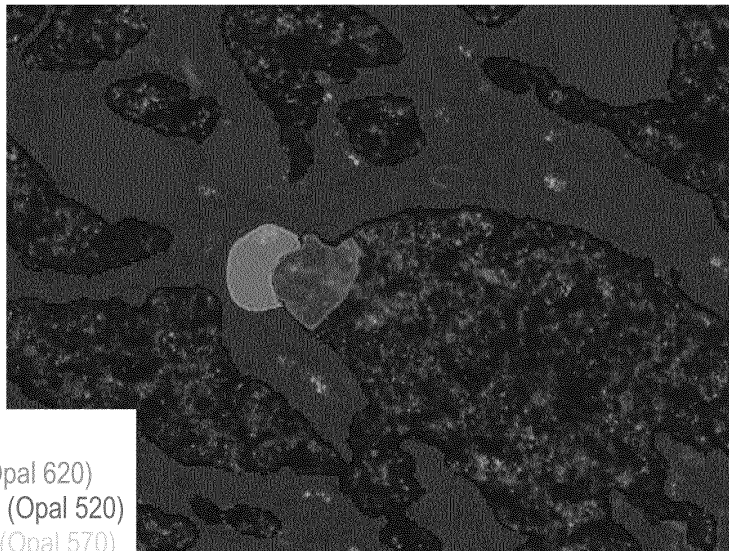


DAPI
ER (Opal 620)
HER2 (Opal 520)
Ki-67 (Opal 570)
PR (Opal 690)
Autofluorescence

Figure 3 (cont.)

c

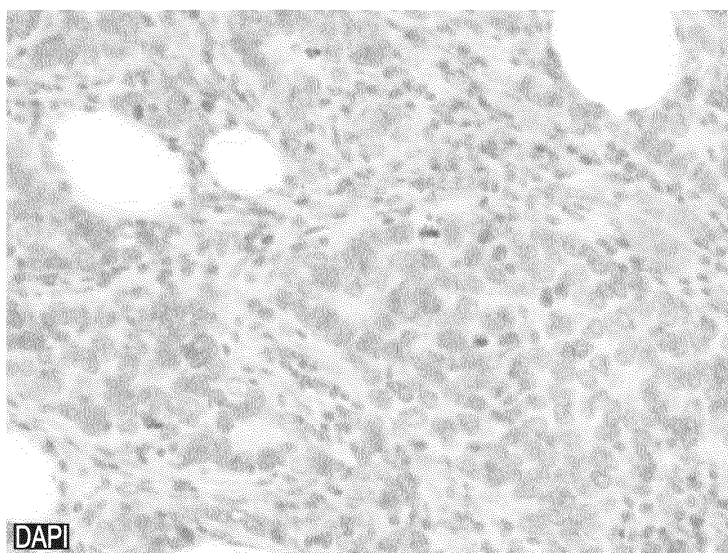
DAPI
ER (Opal 620)
HER2 (Opal 520)
Ki-67 (Opal 570)
PR (Opal 690)
Autofluorescence

d

DAPI
ER (Opal 620)
HER2 (Opal 520)
Ki-67 (Opal 570)
PR (Opal 690)
Autofluorescence

Figure 3 (cont.)

e



f

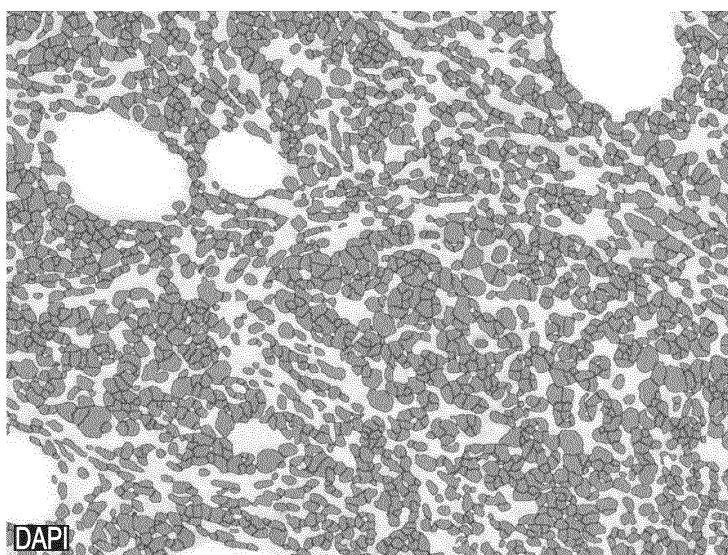


Figure 4

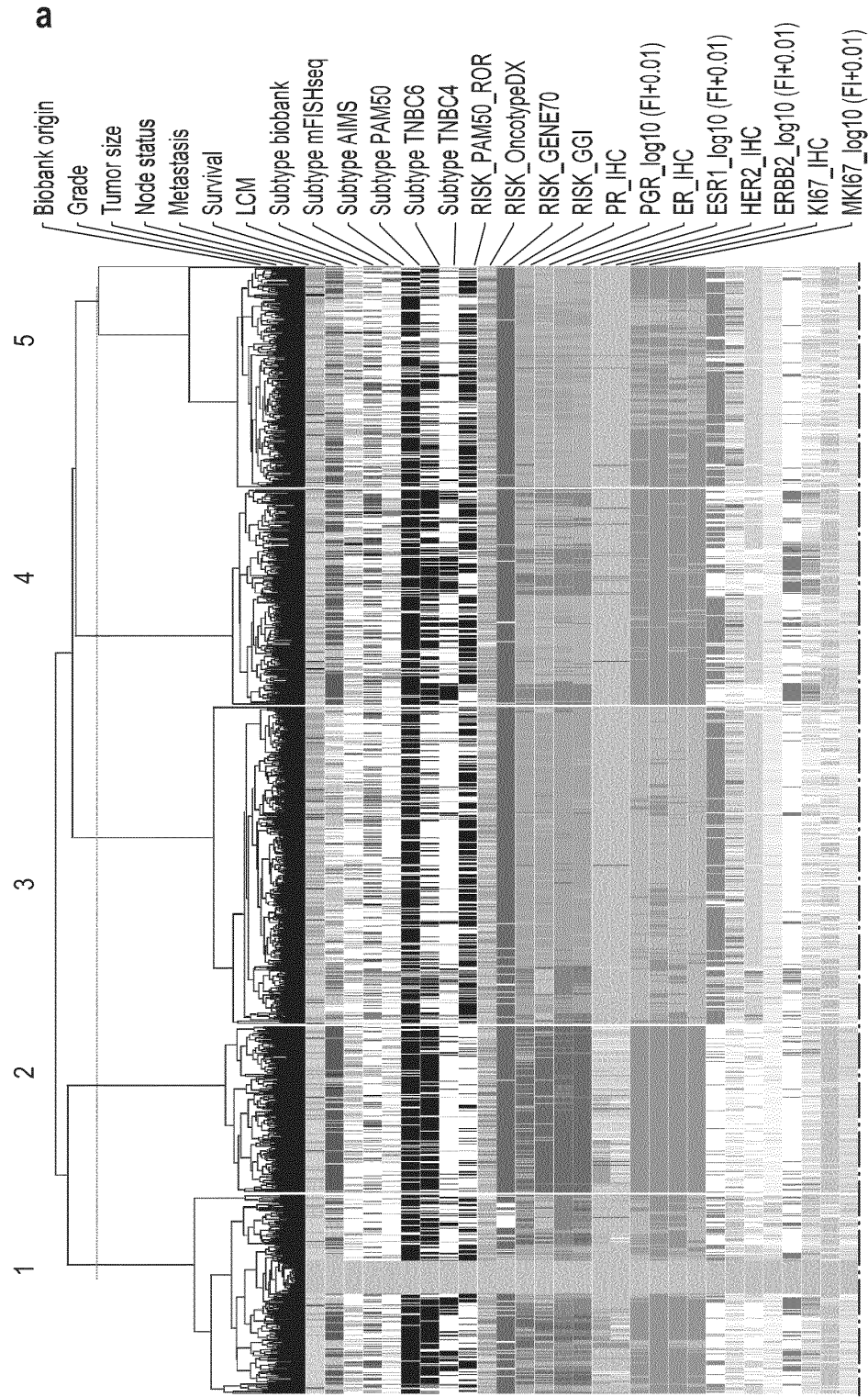


Figure 4 (cont.)

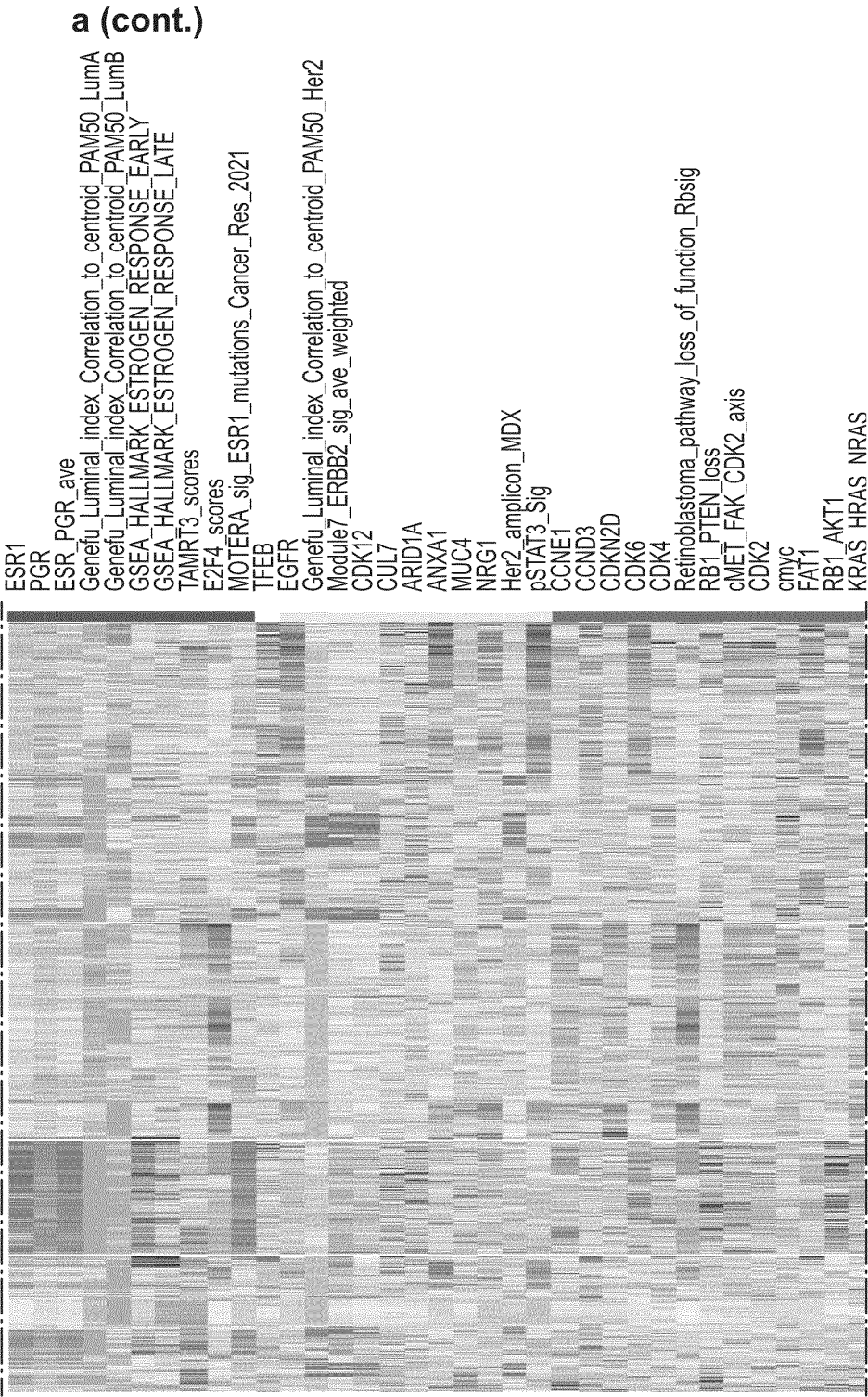


Figure 4 (cont.)

a (cont.)

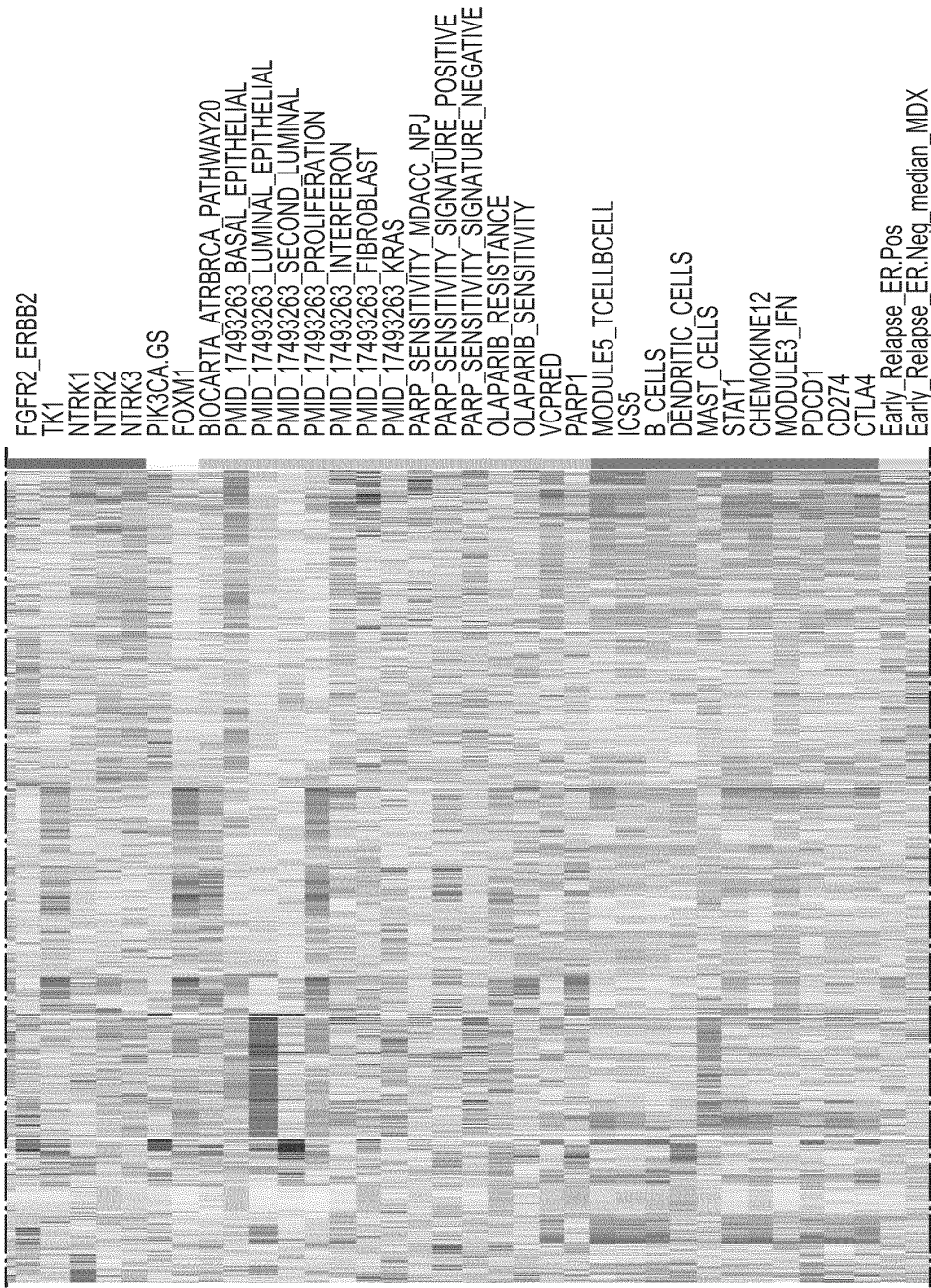


Figure 4 (cont.)

a (cont.)

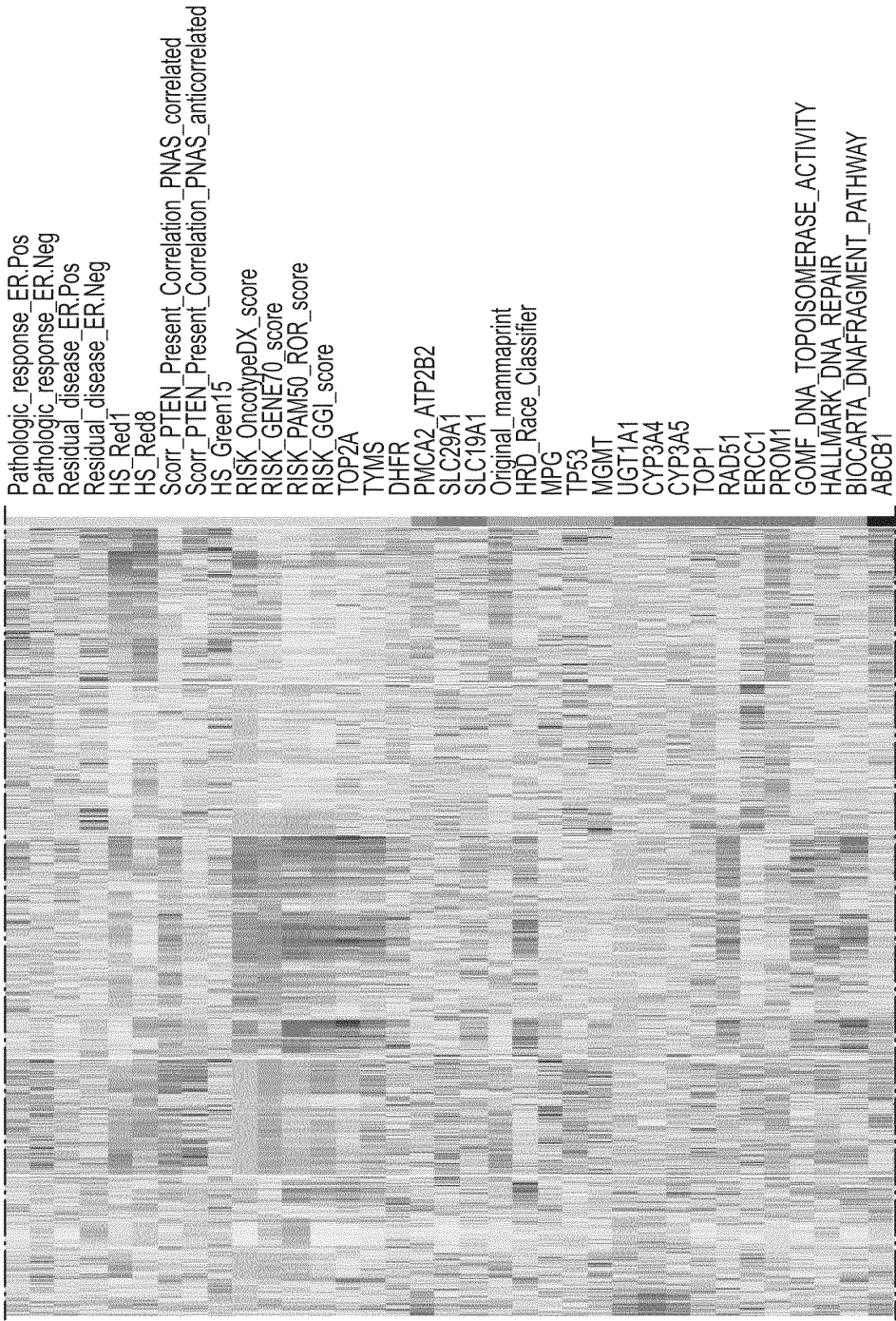


Figure 4 (cont.)

a (cont.)

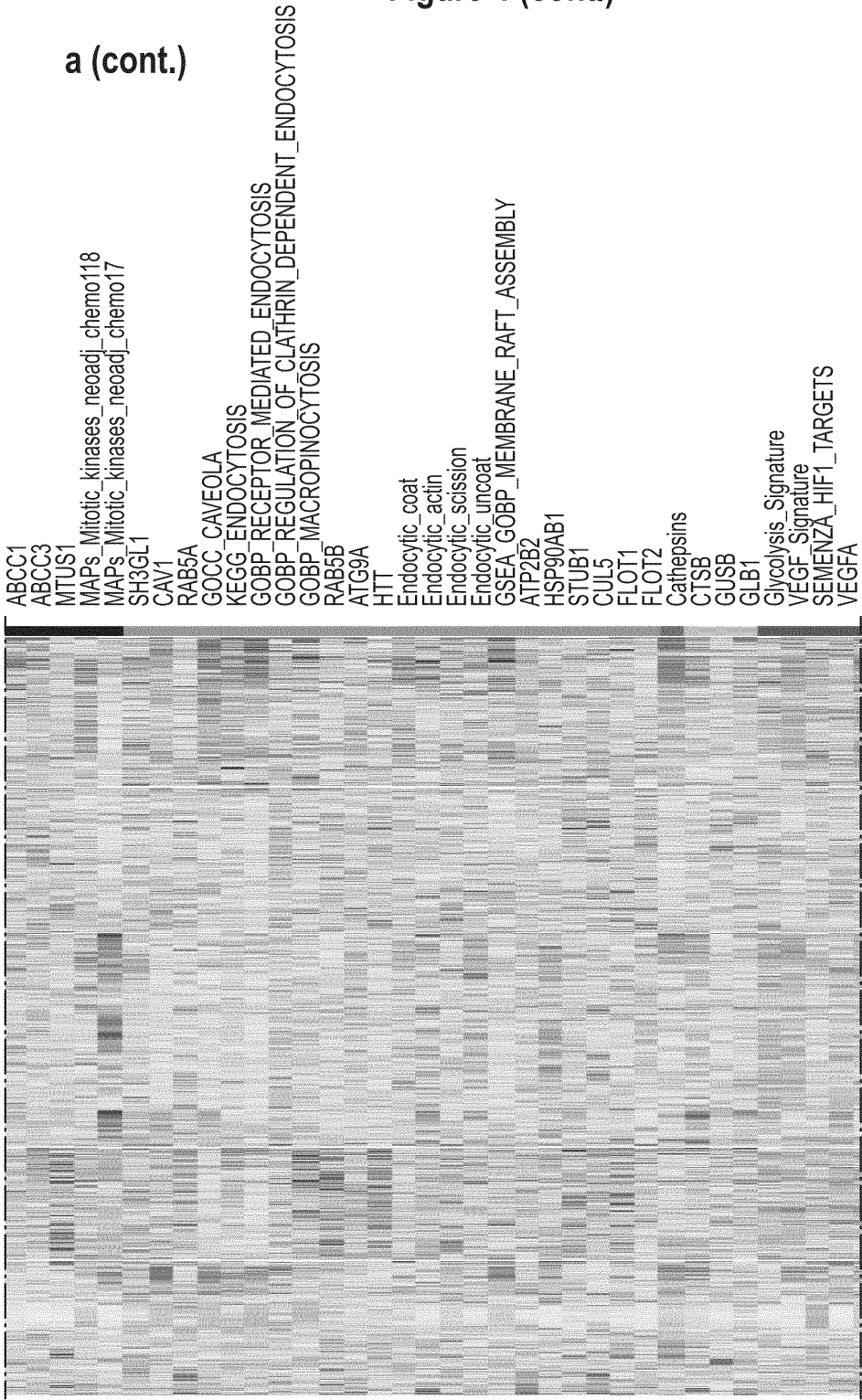


Figure 4 (cont.)

a (cont.)

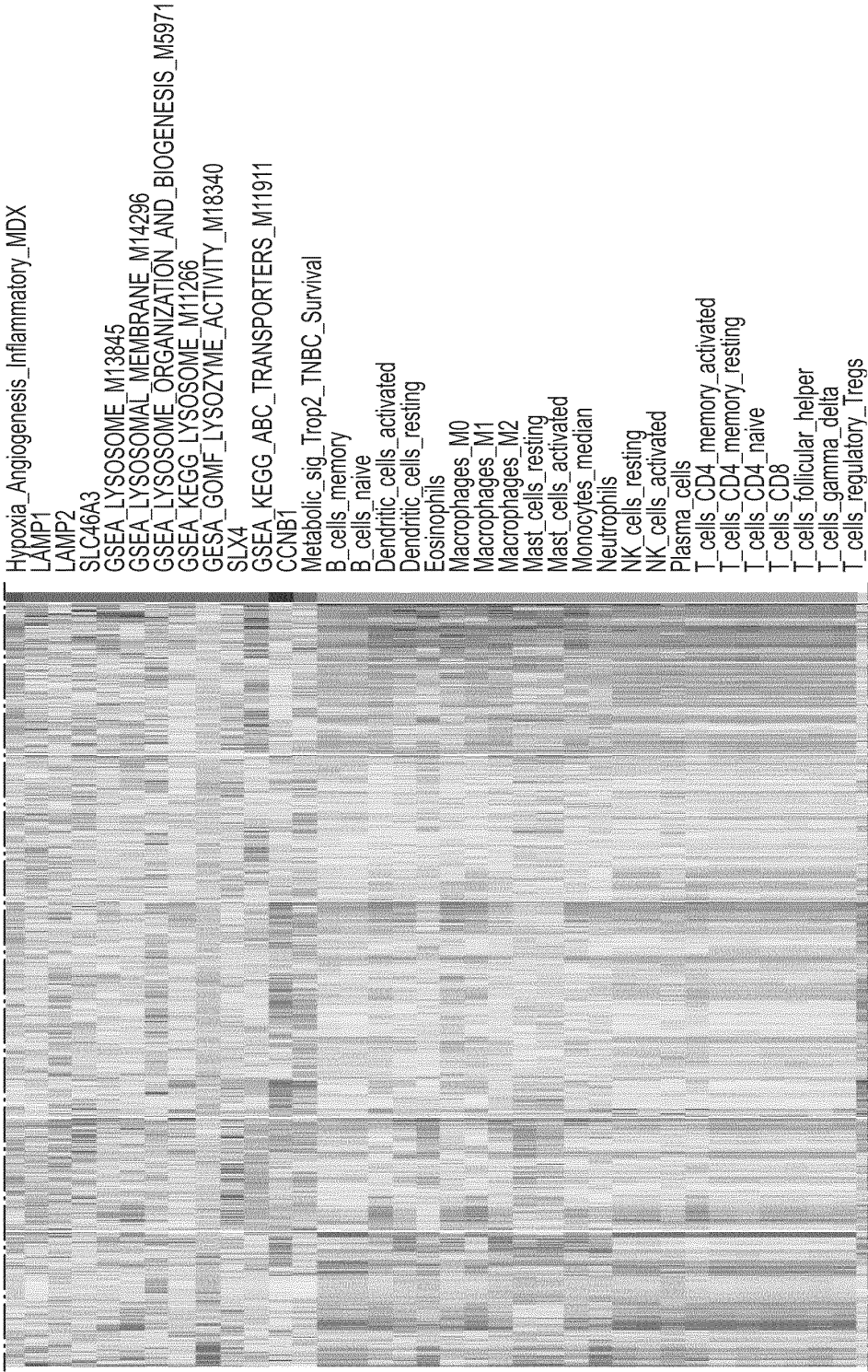


Figure 4 (cont.)

a (cont.)

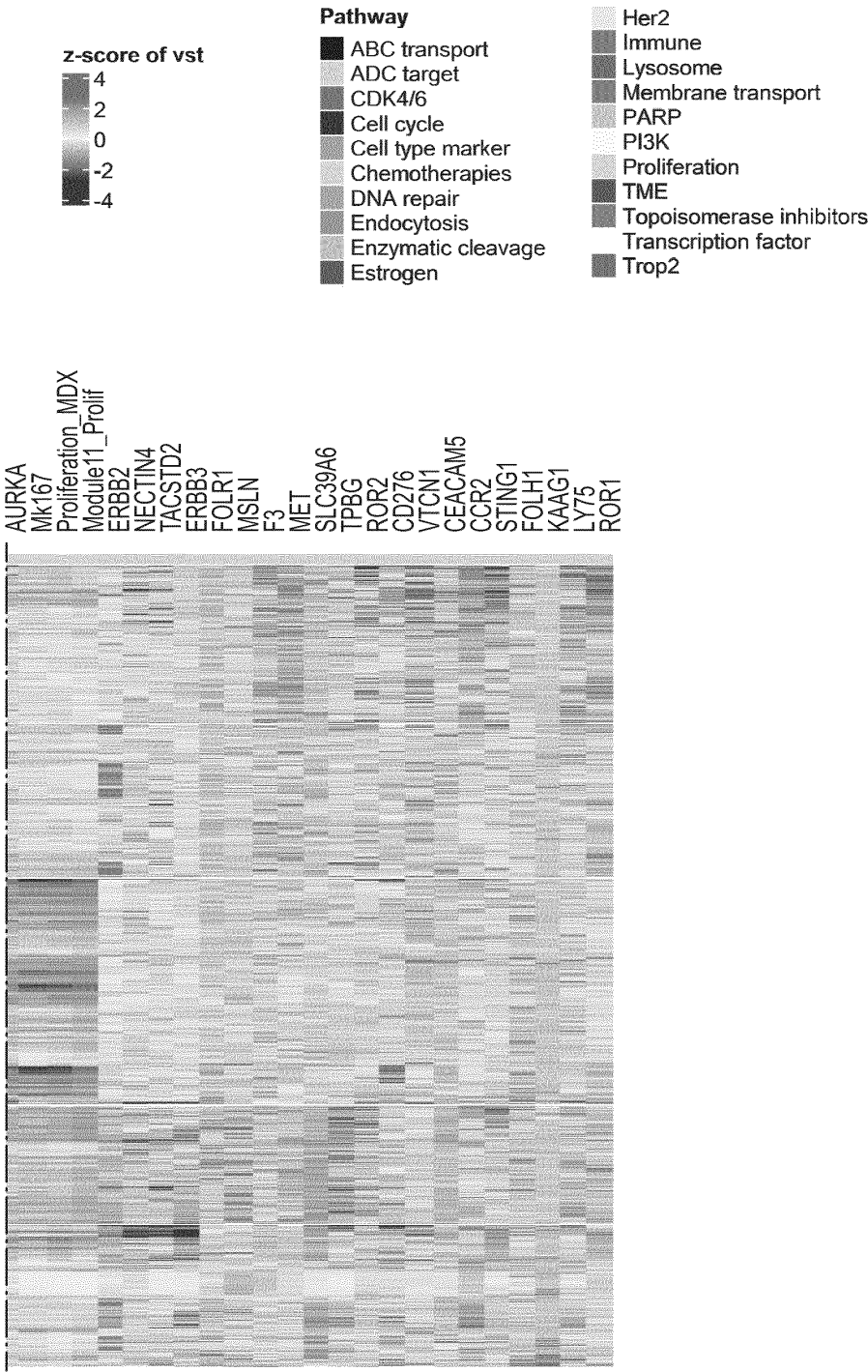
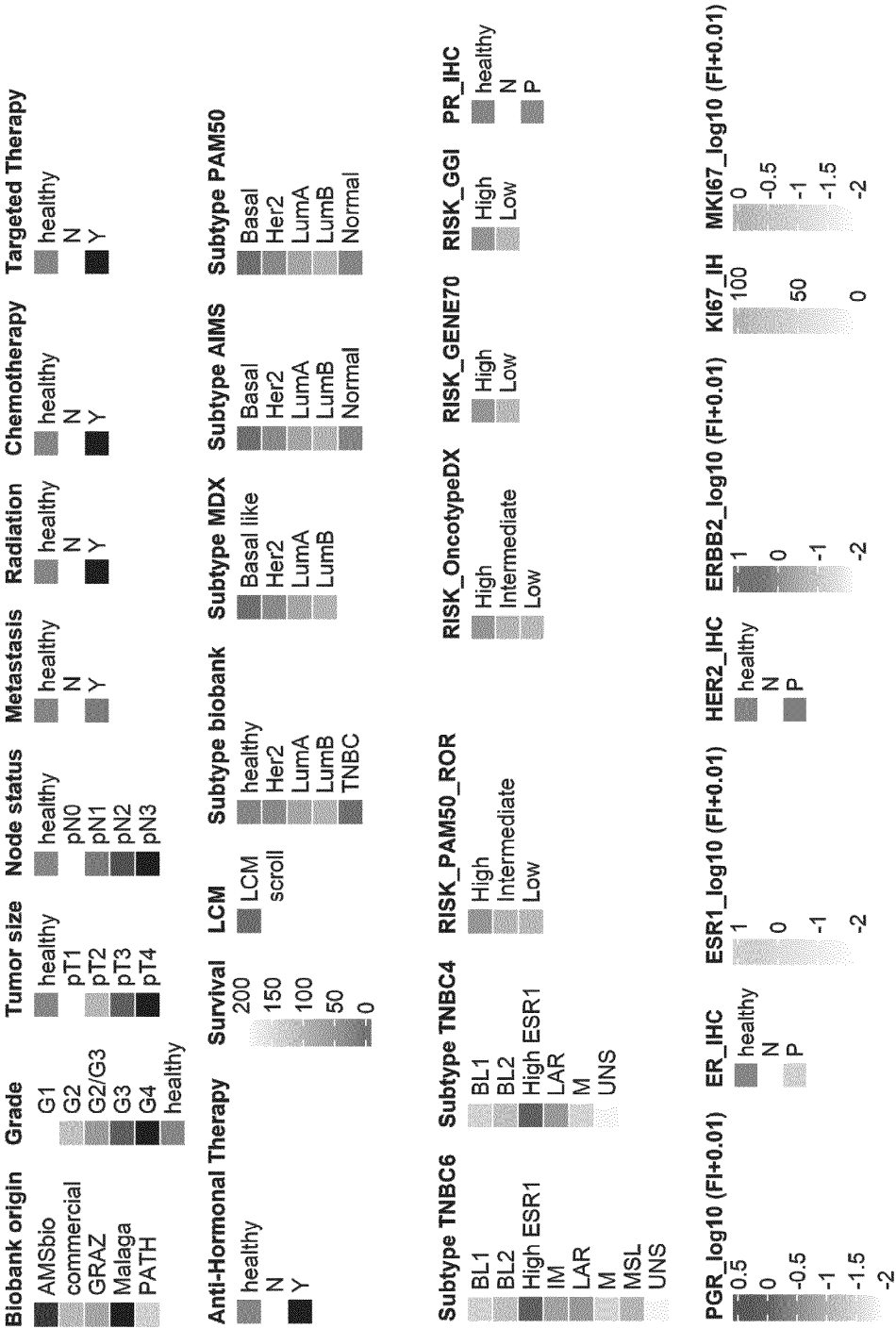


Figure 4 (cont.)

a (cont.)



b

Figure 4 (cont.)



Figure 4 (cont.)

b (cont.)

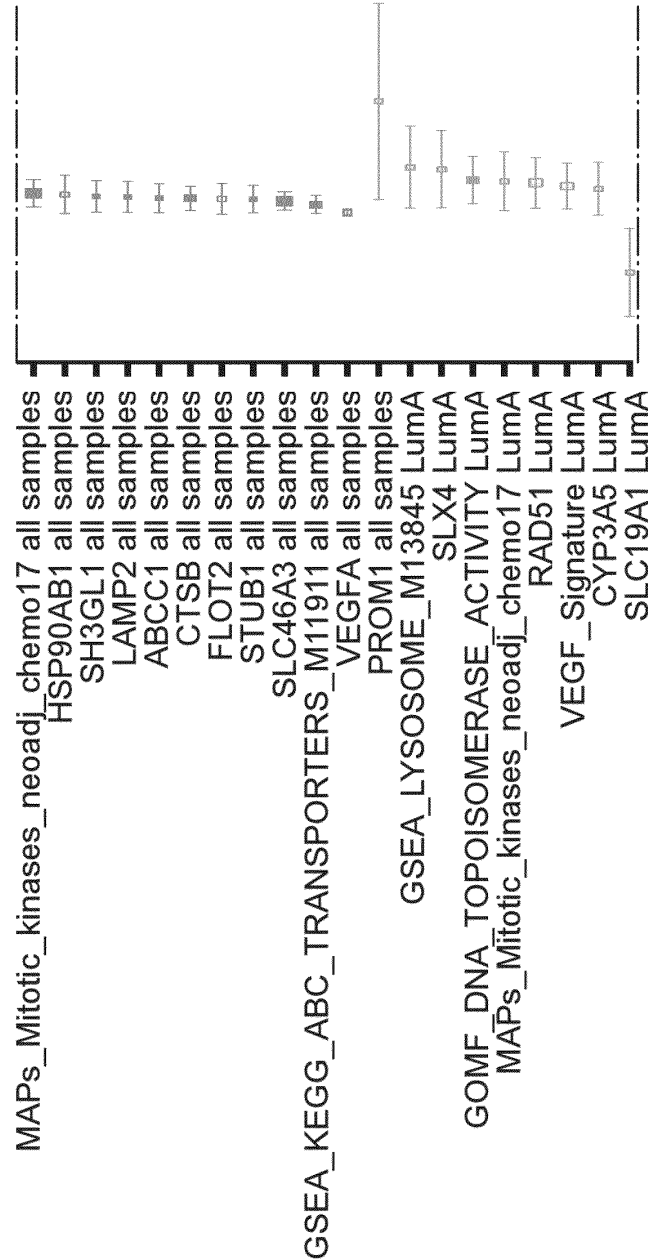
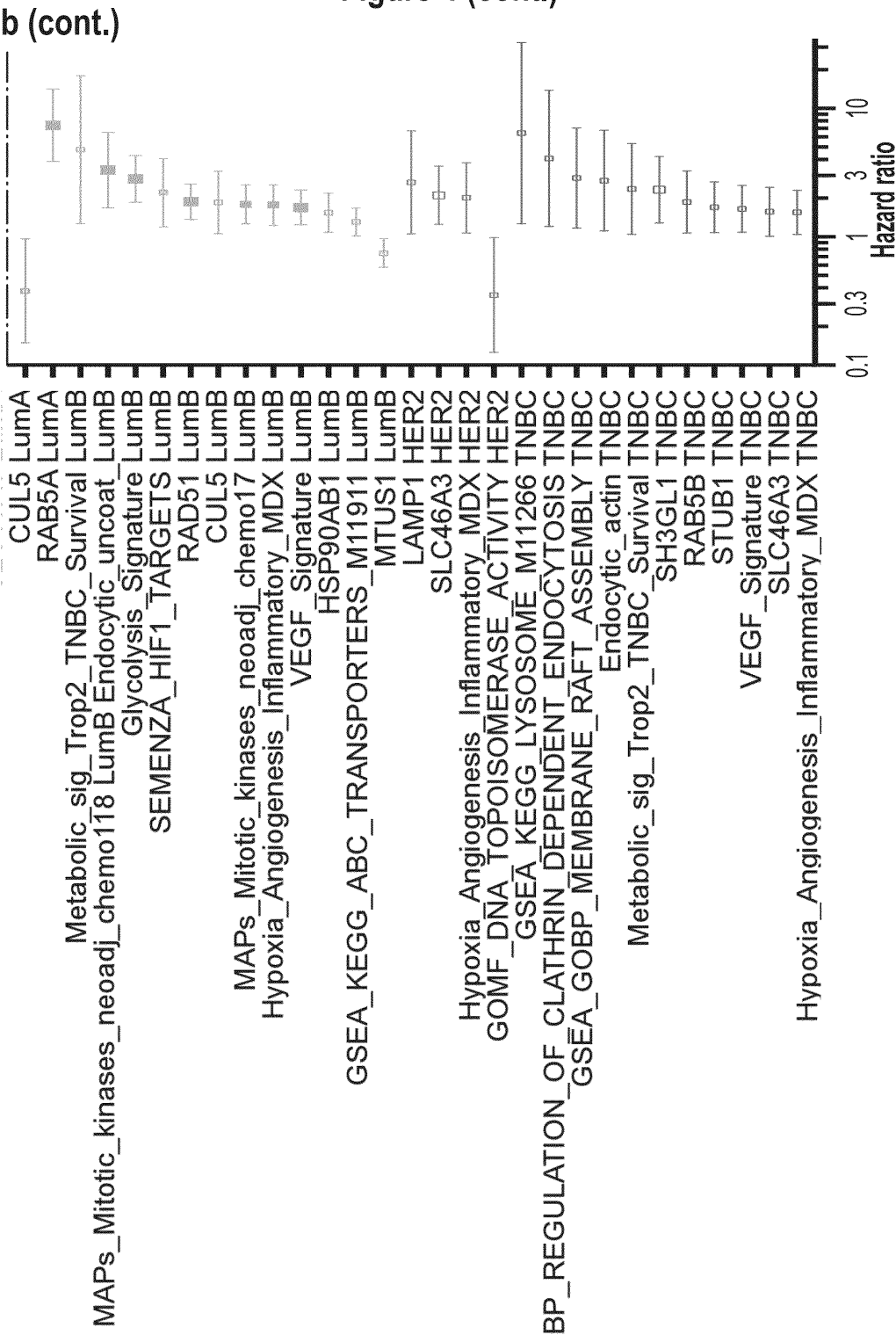


Figure 4 (cont.)



c

Figure 4 (cont.)

Multivariate CPHM of
ADC related gene signatures

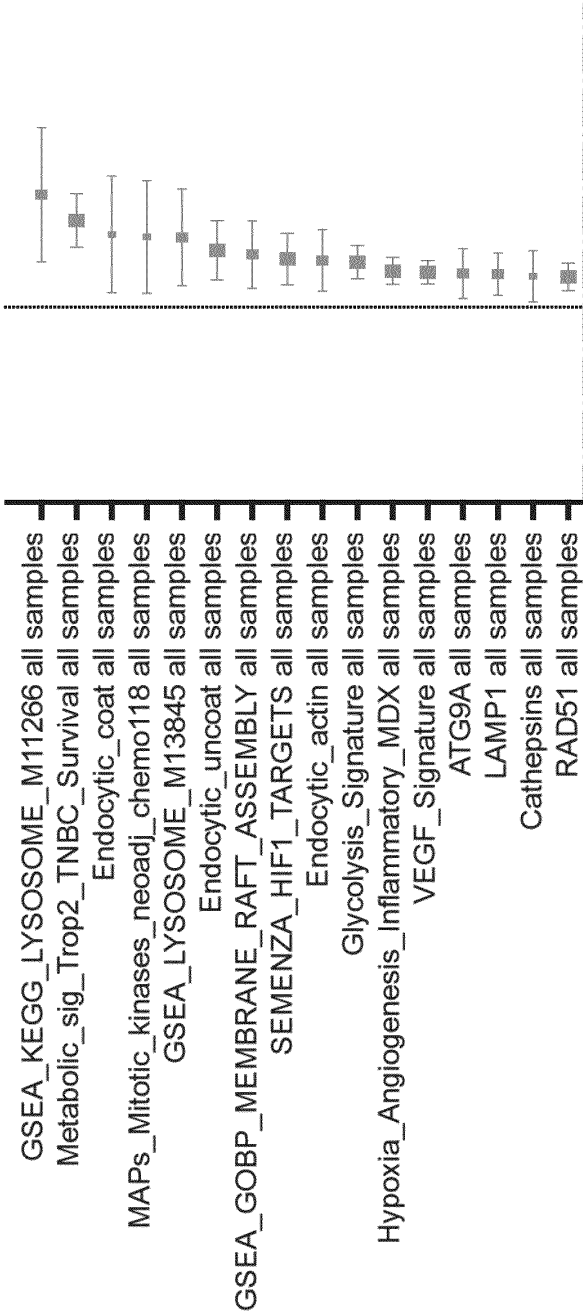
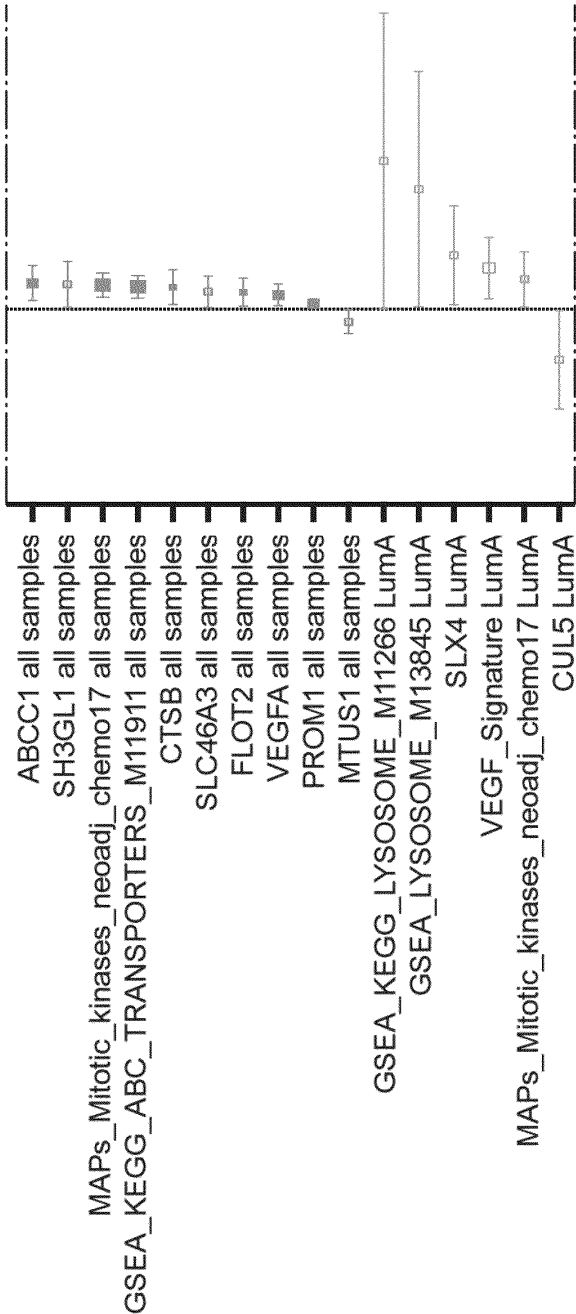


Figure 4 (cont.)

c (cont.)



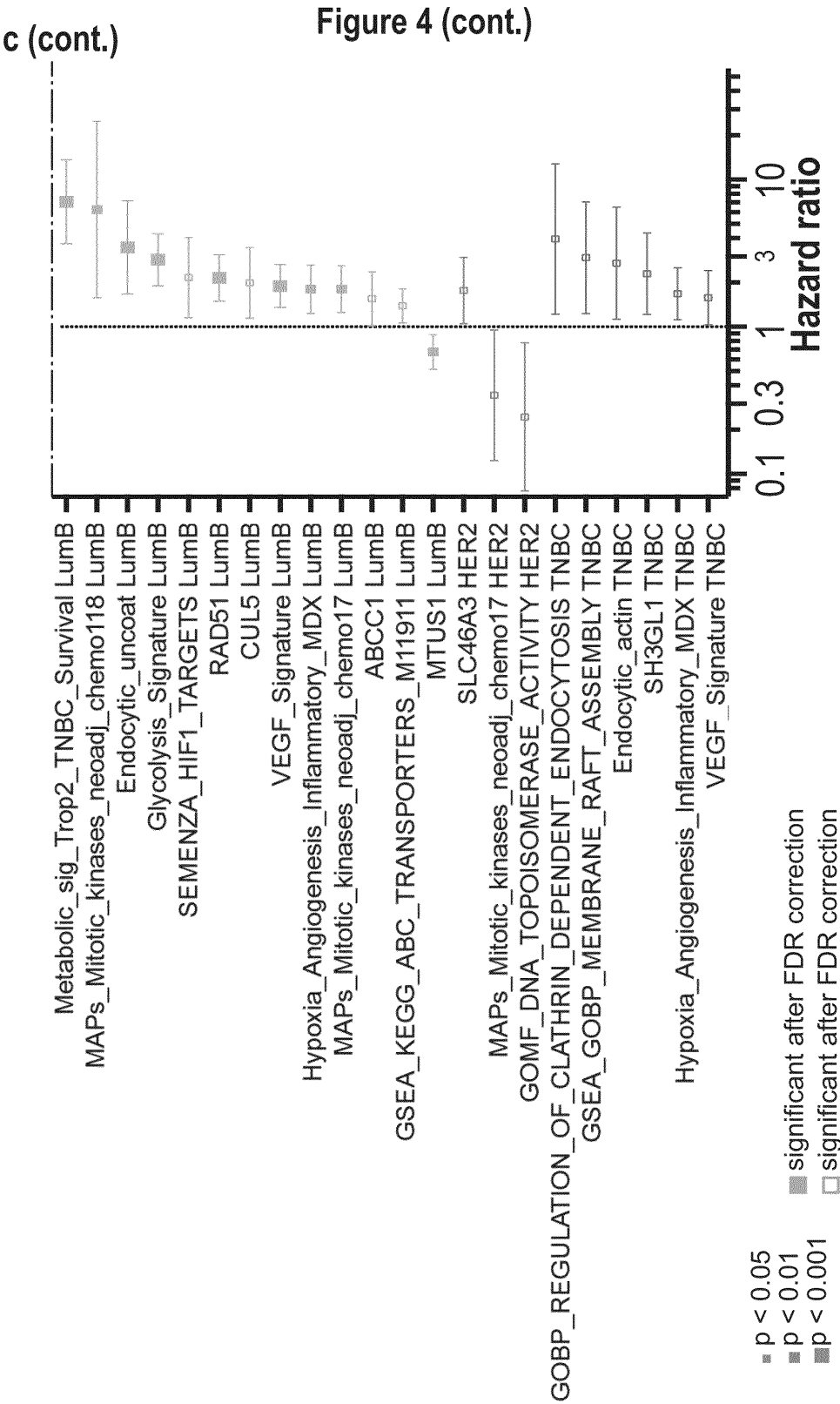


Figure 5

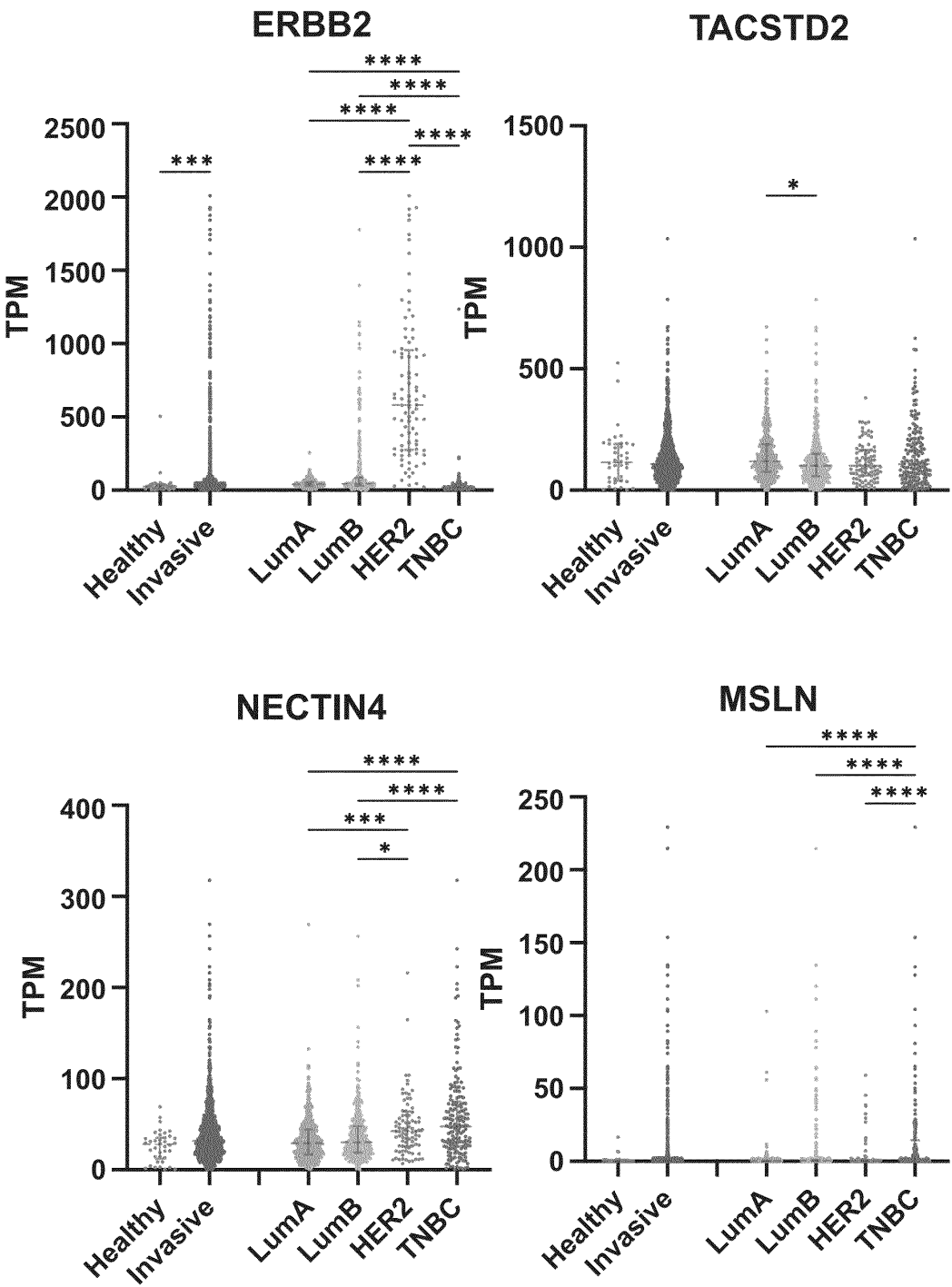


Figure 5 (cont.)

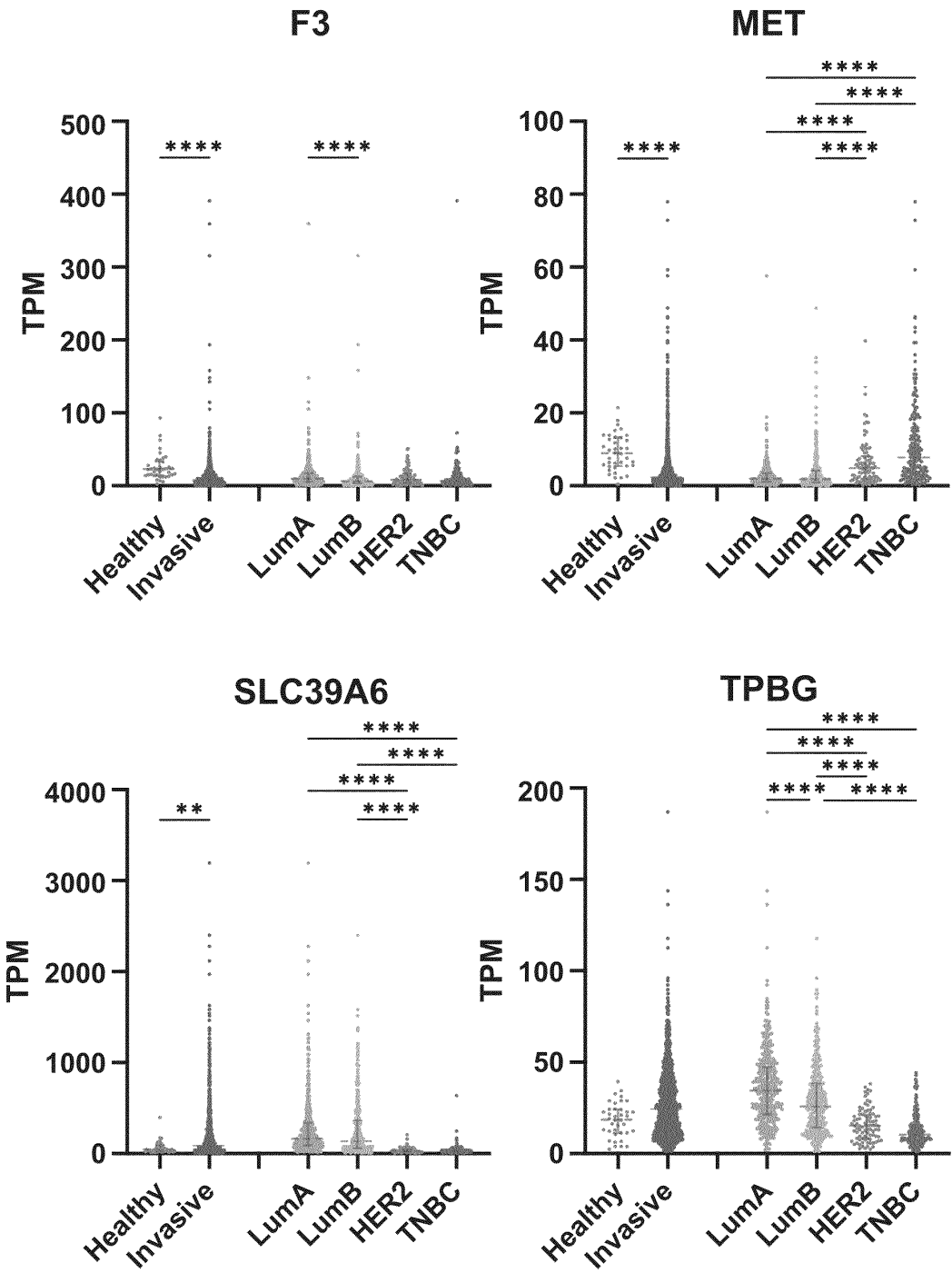


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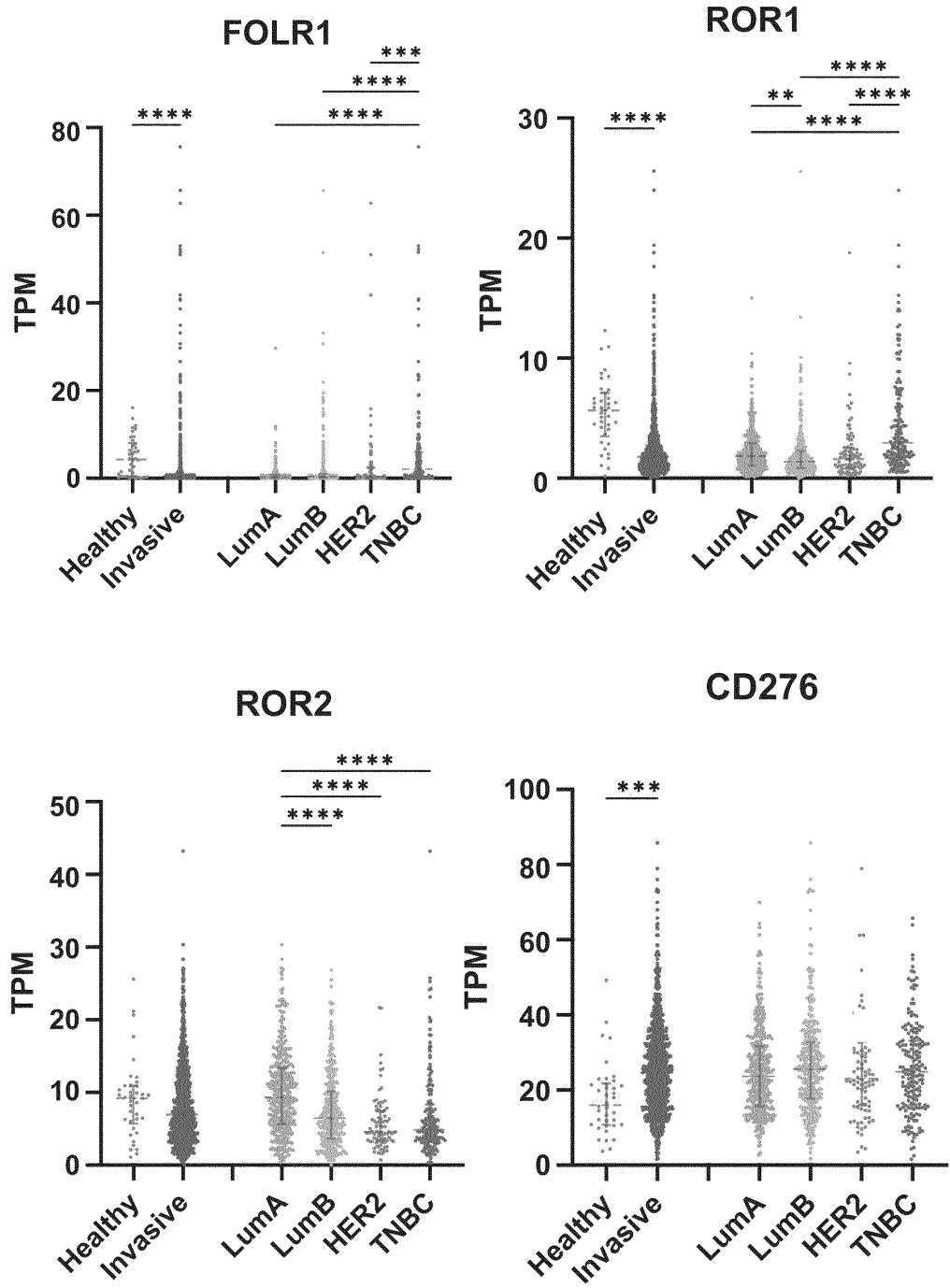


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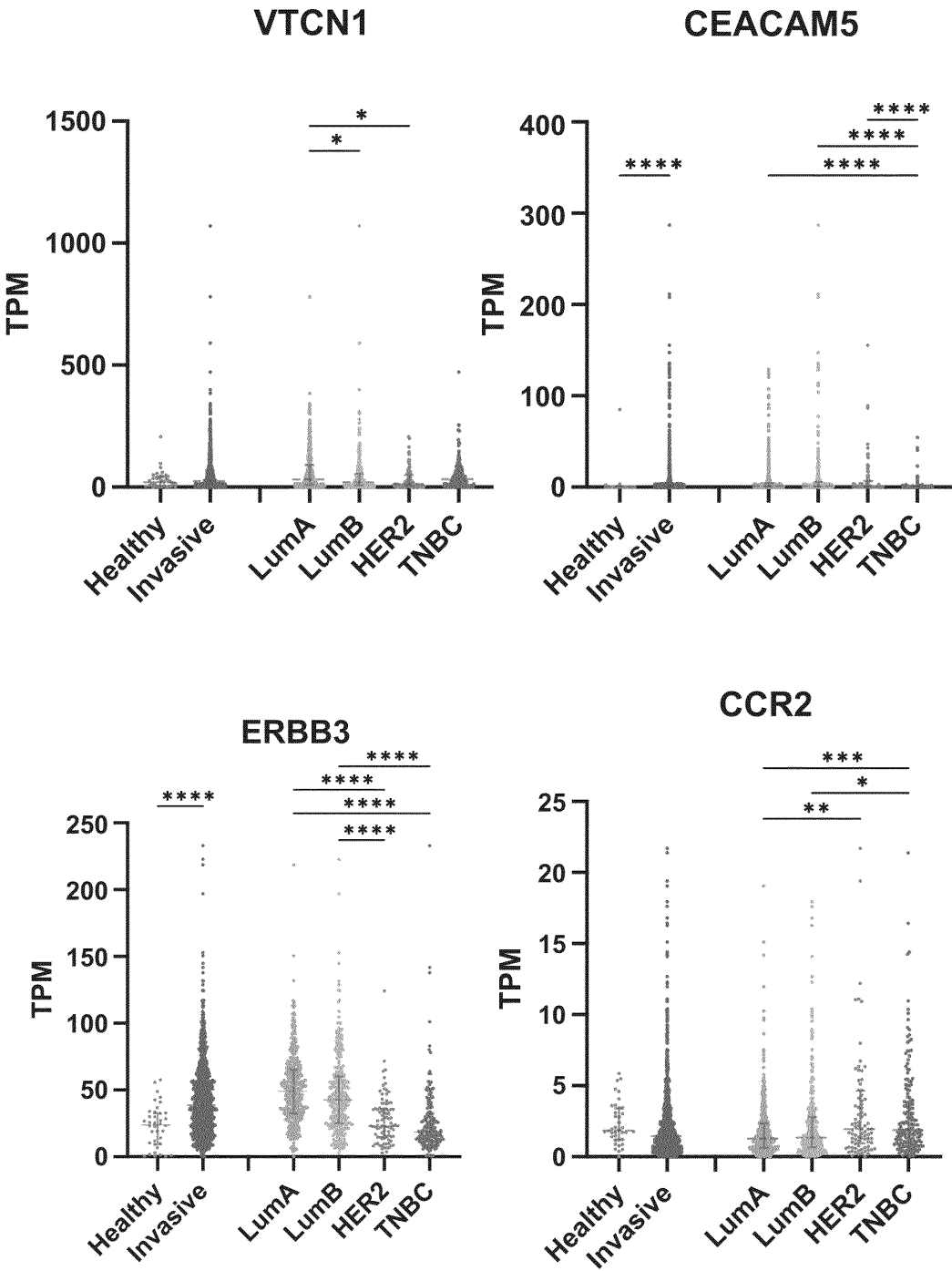


Figure 5 (cont.)

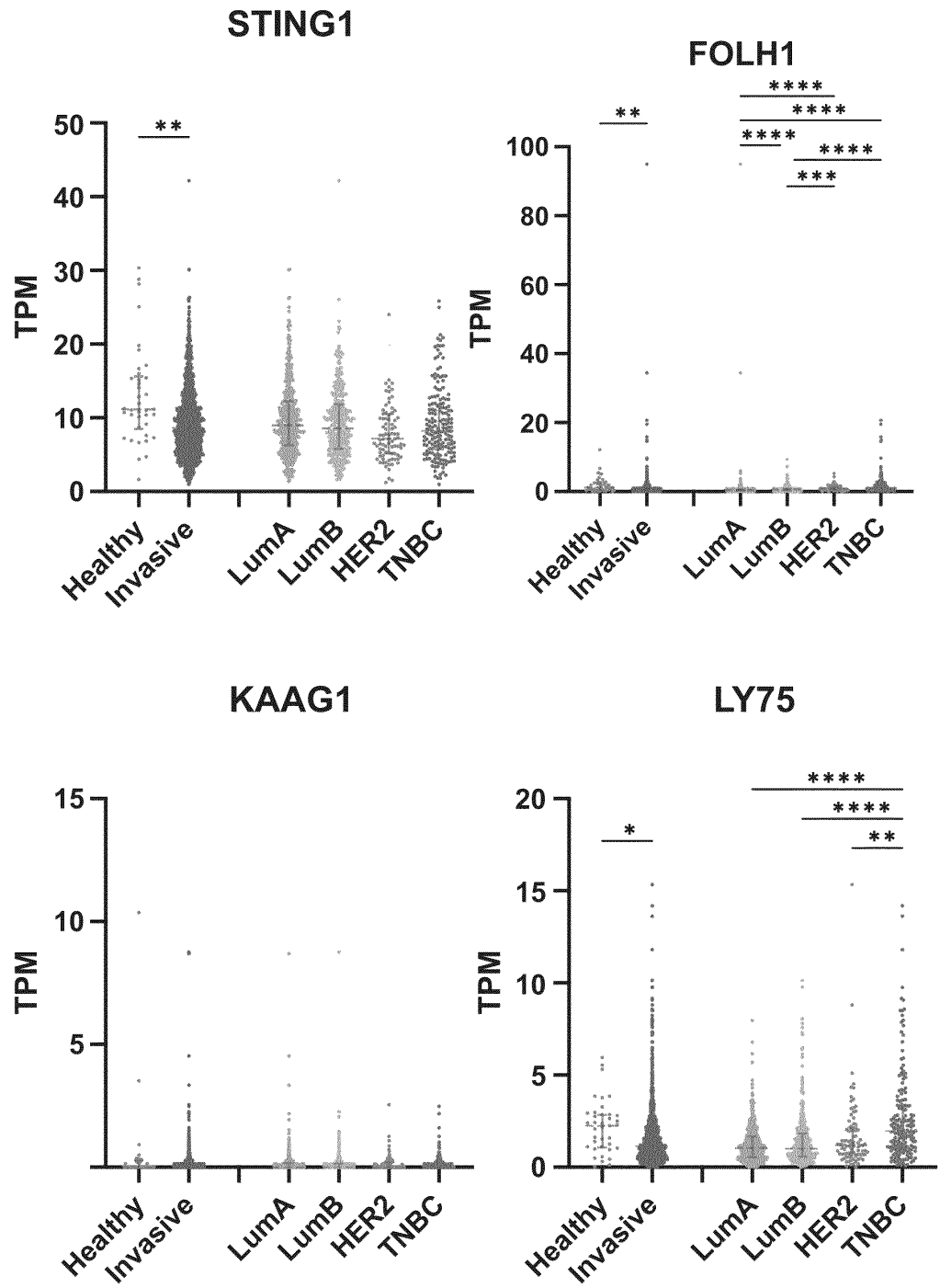


Figure 6

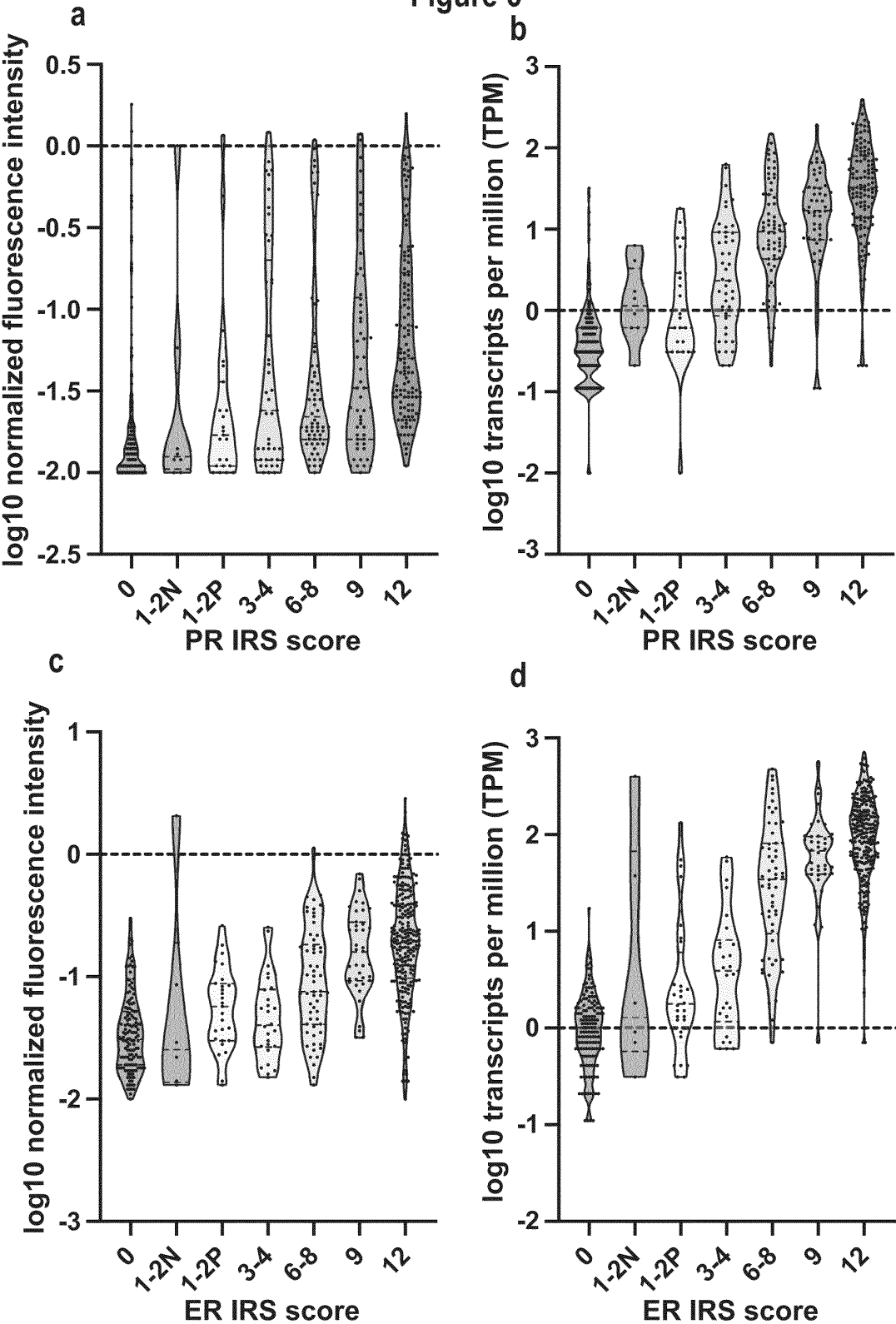


Figure 6 (cont.)

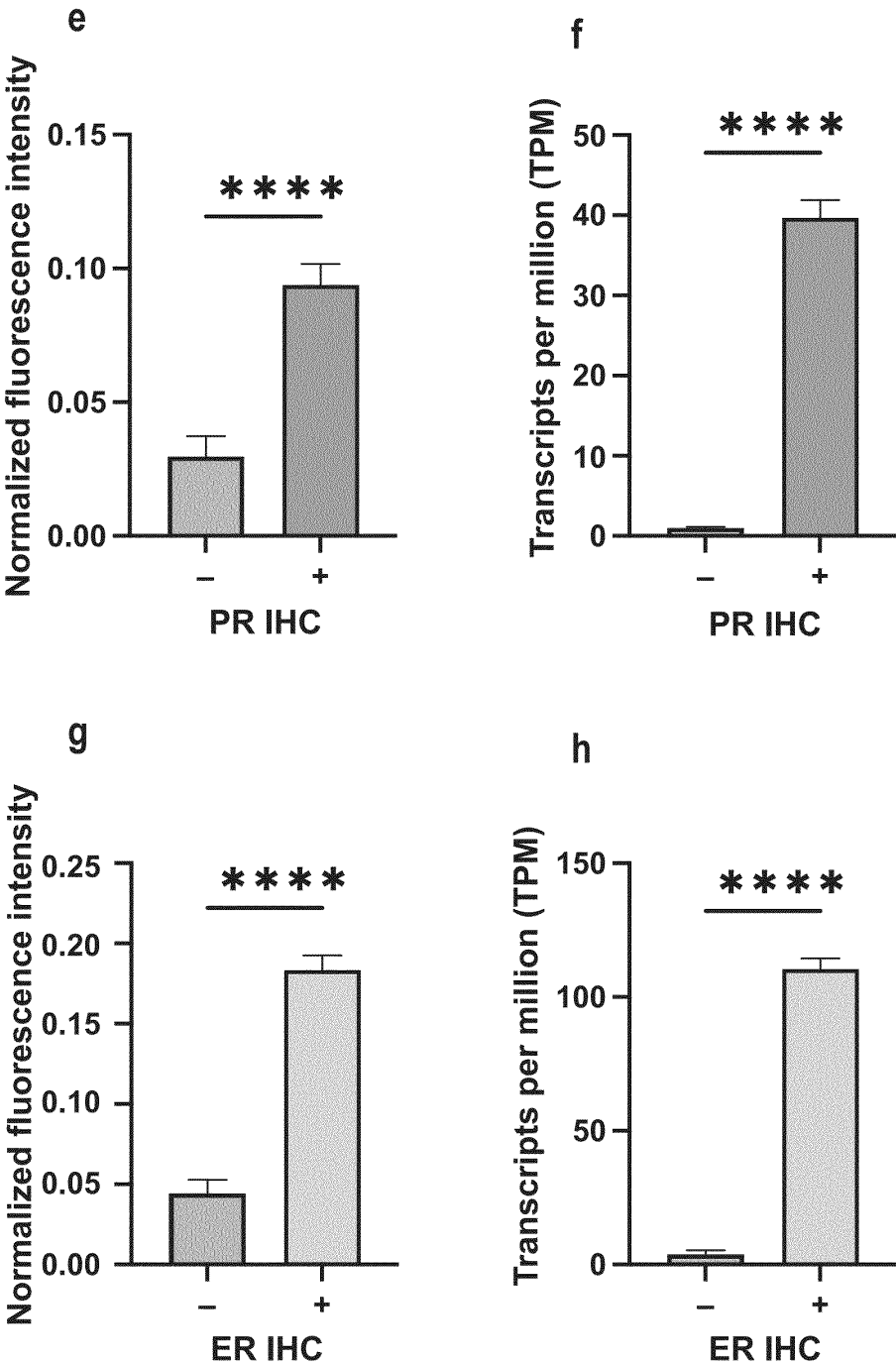


Figure 6 (cont.)

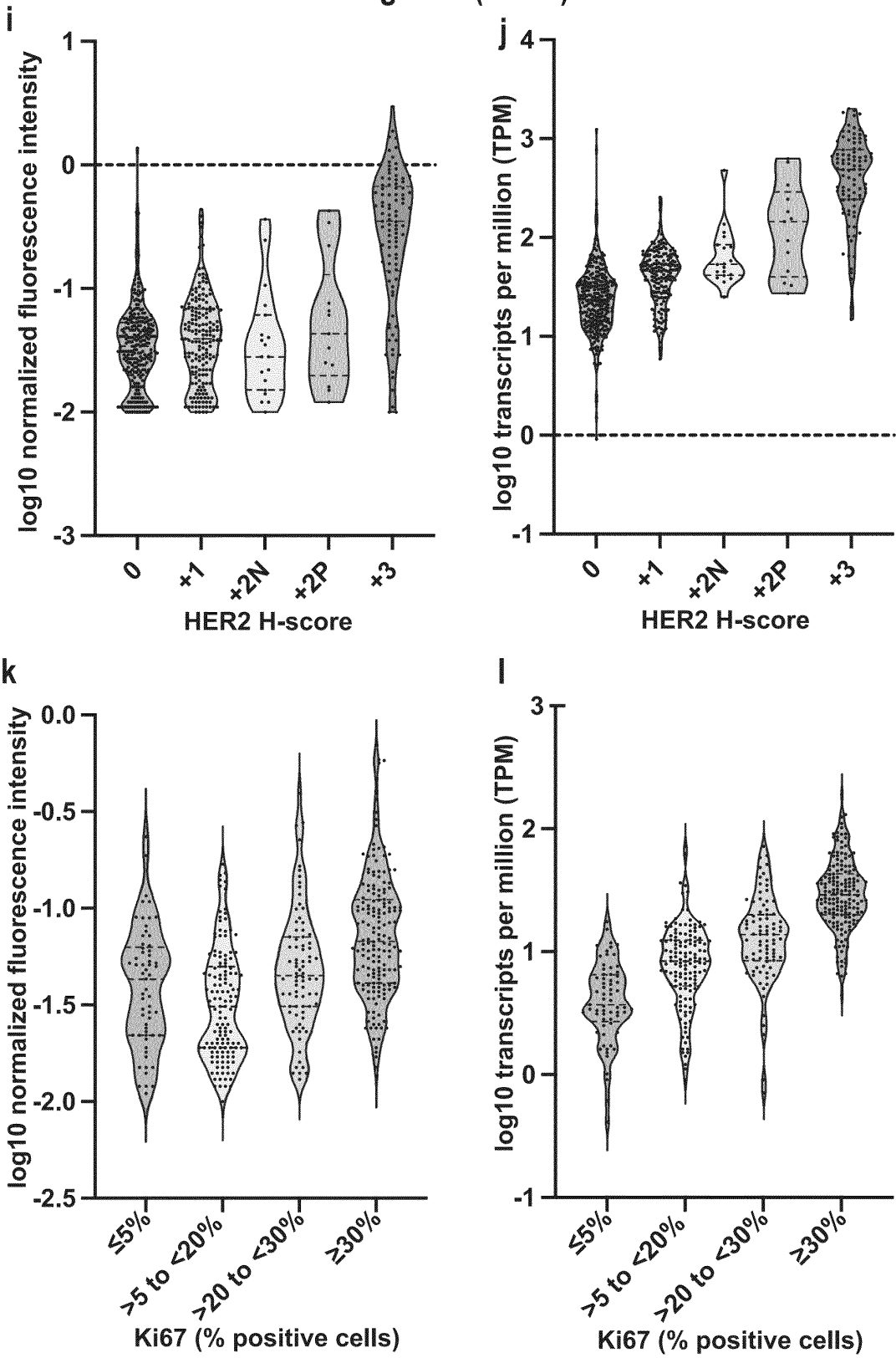


Figure 6 (cont.)

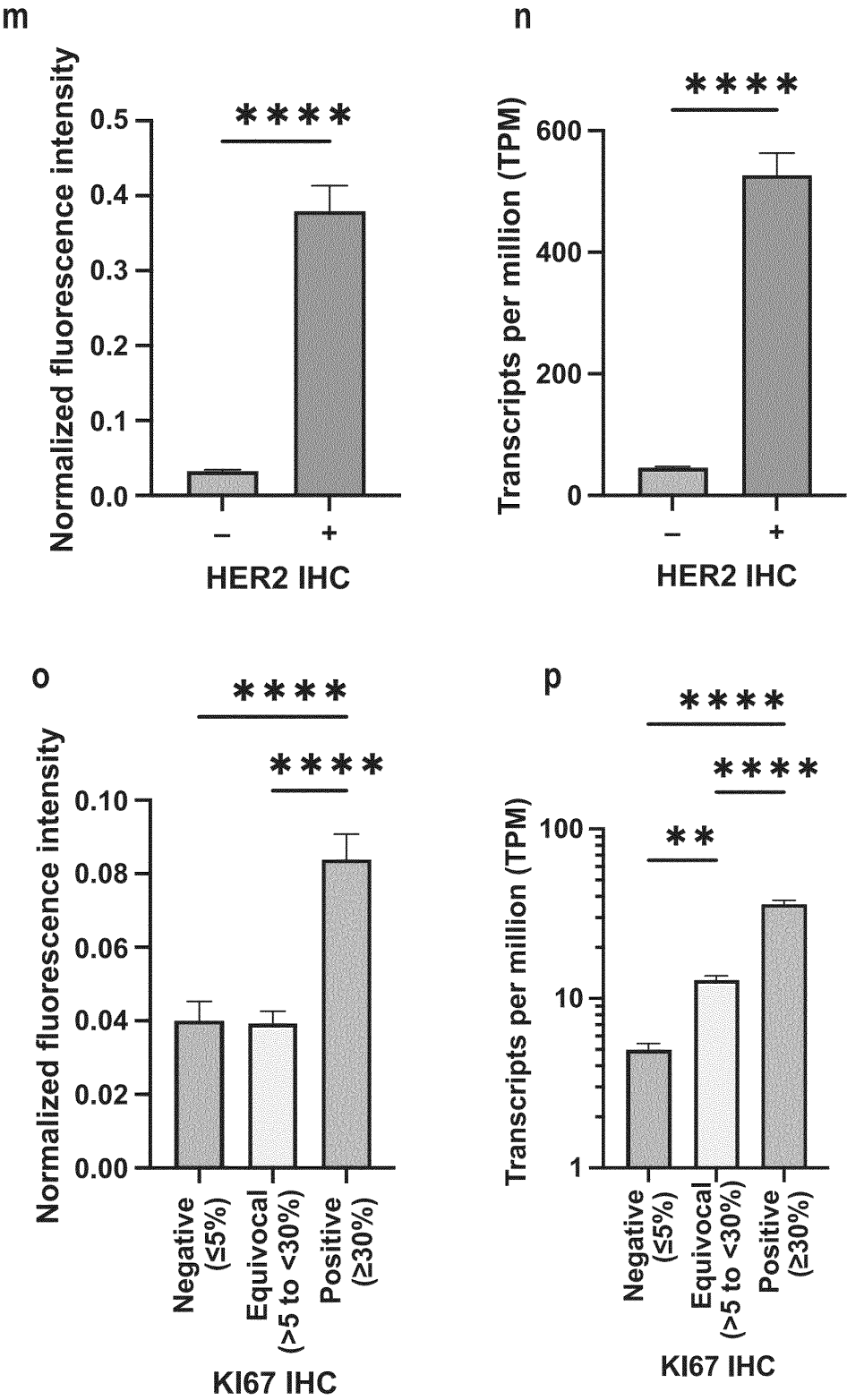
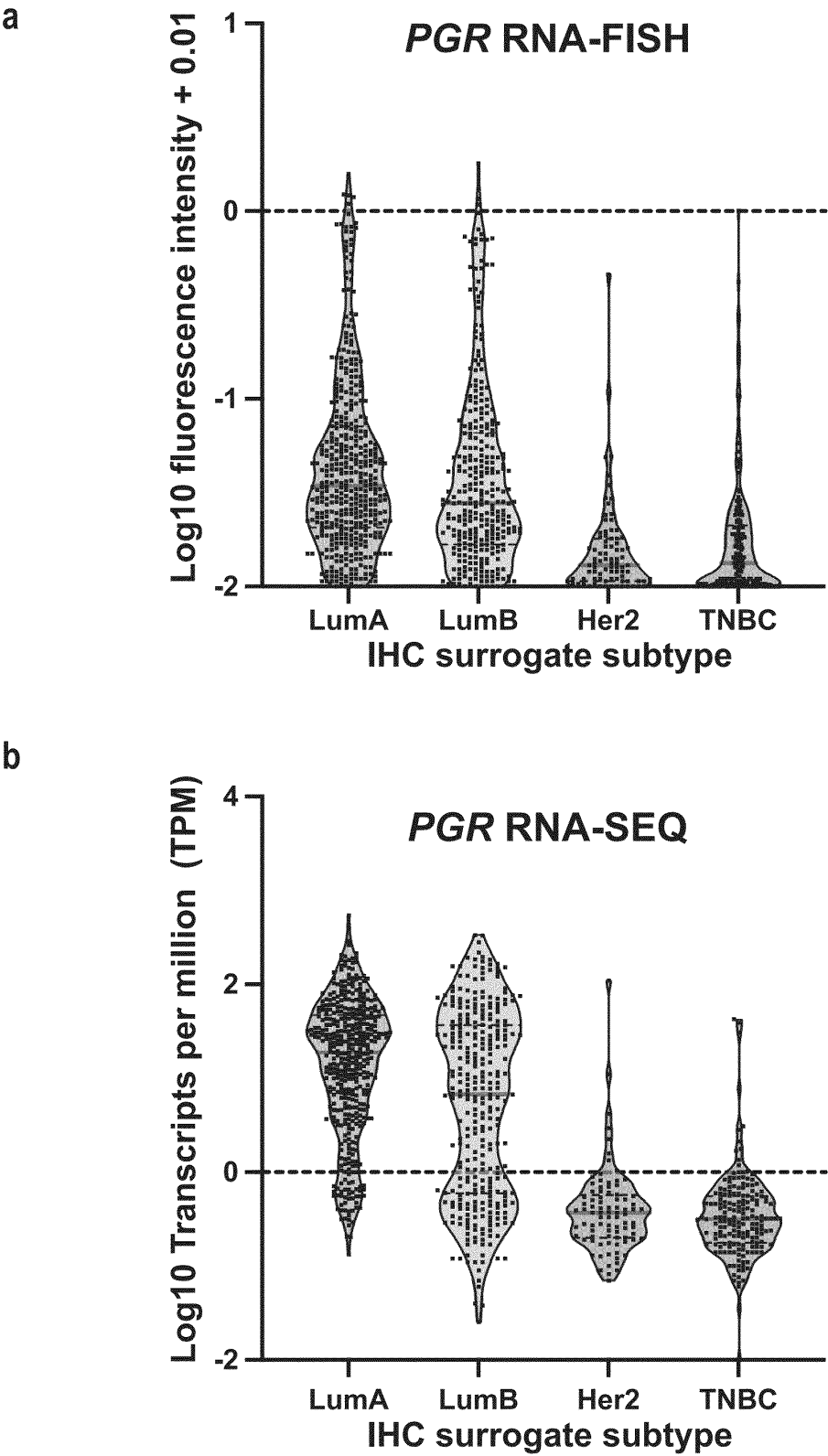
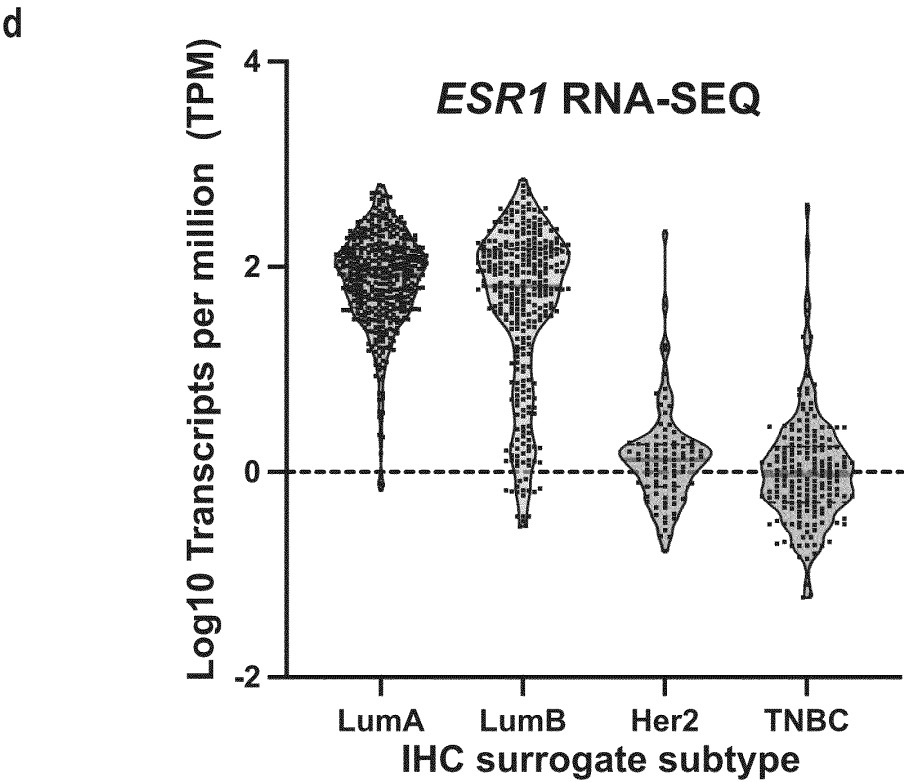
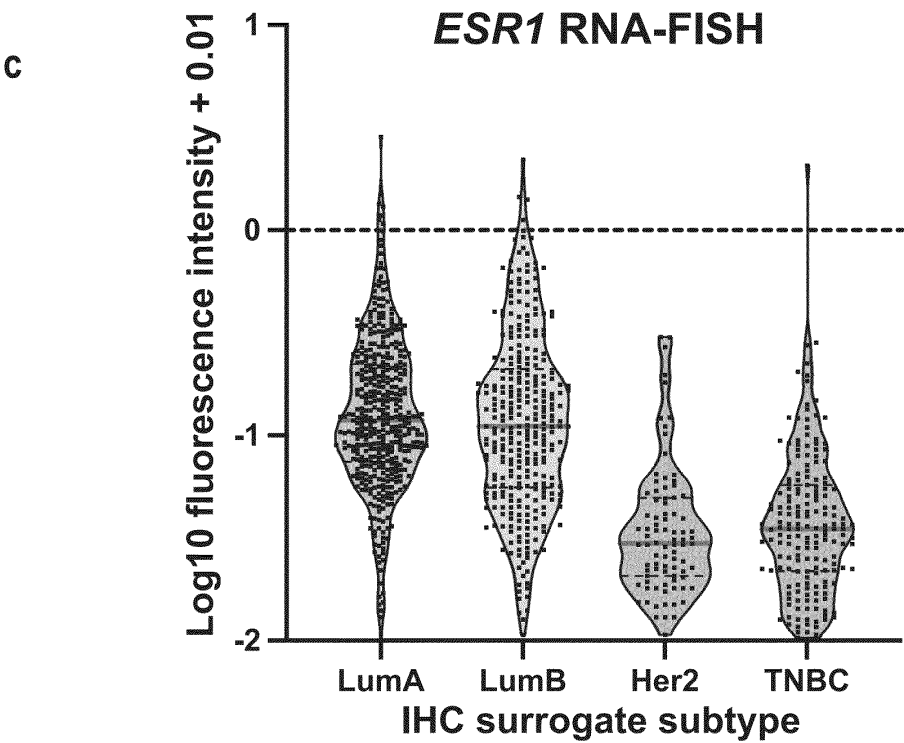


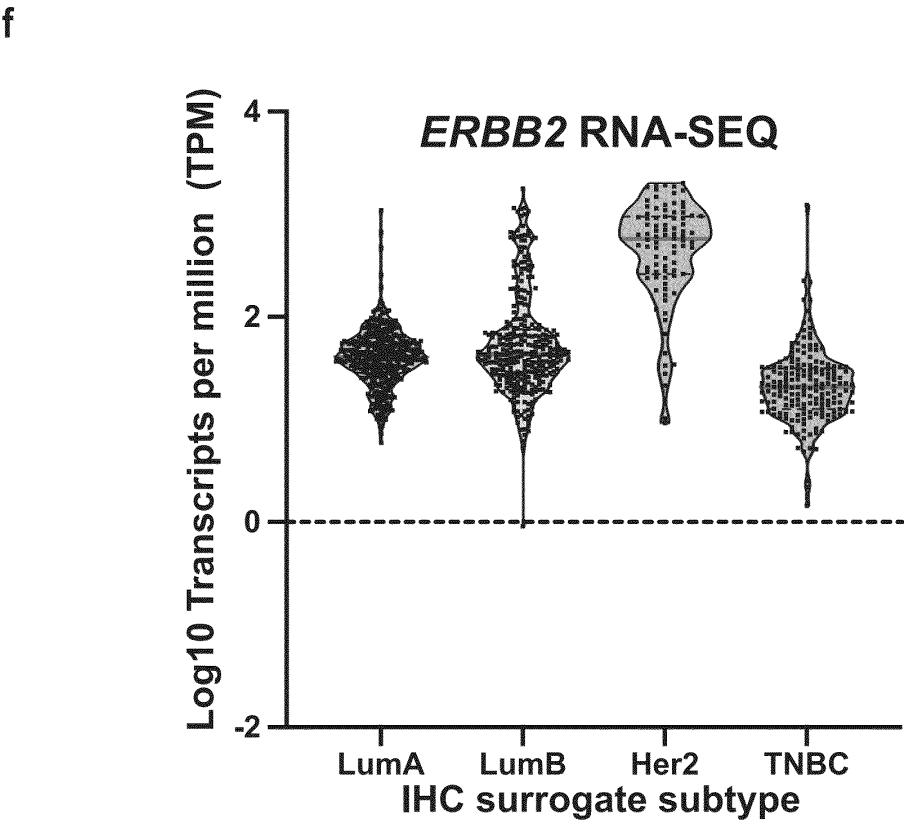
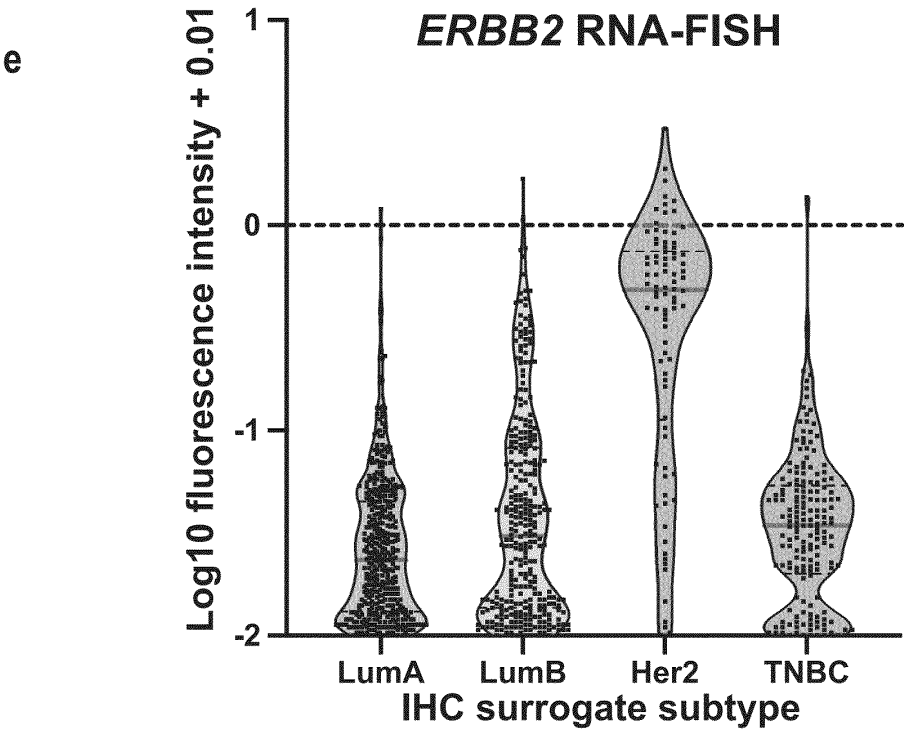
Figure 7



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Figure 7 (cont.)



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Figure 7 (cont.)



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Figure 7 (cont.)

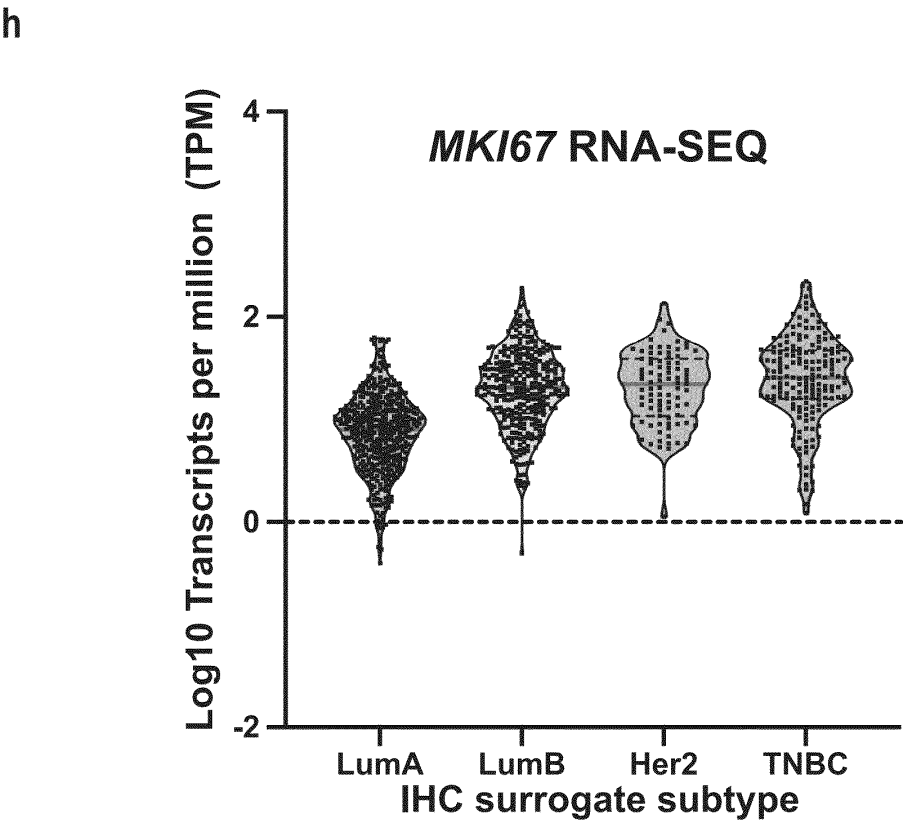
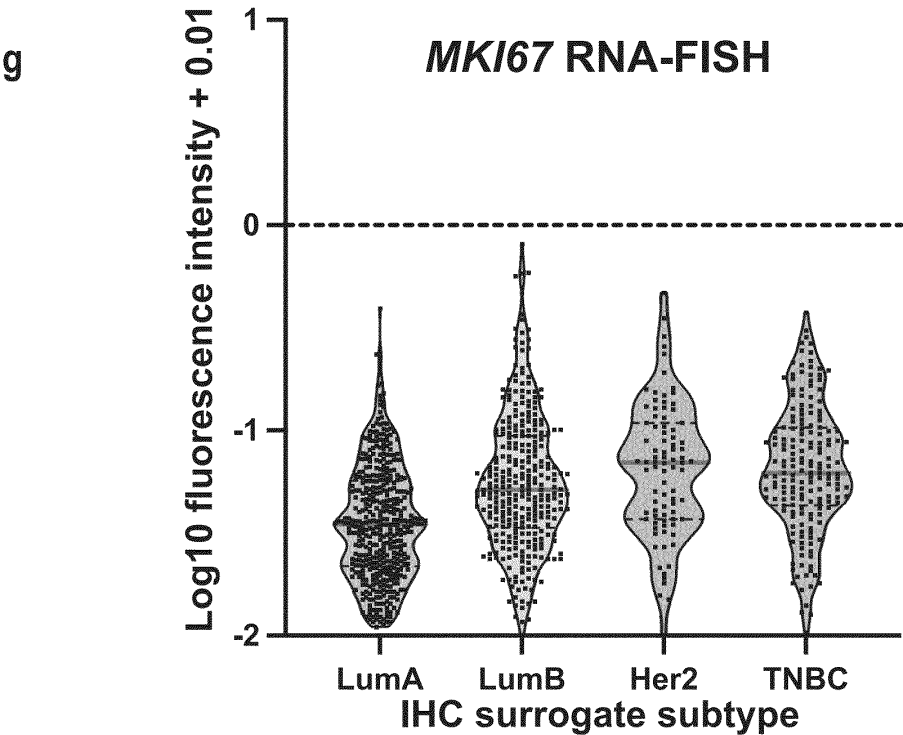
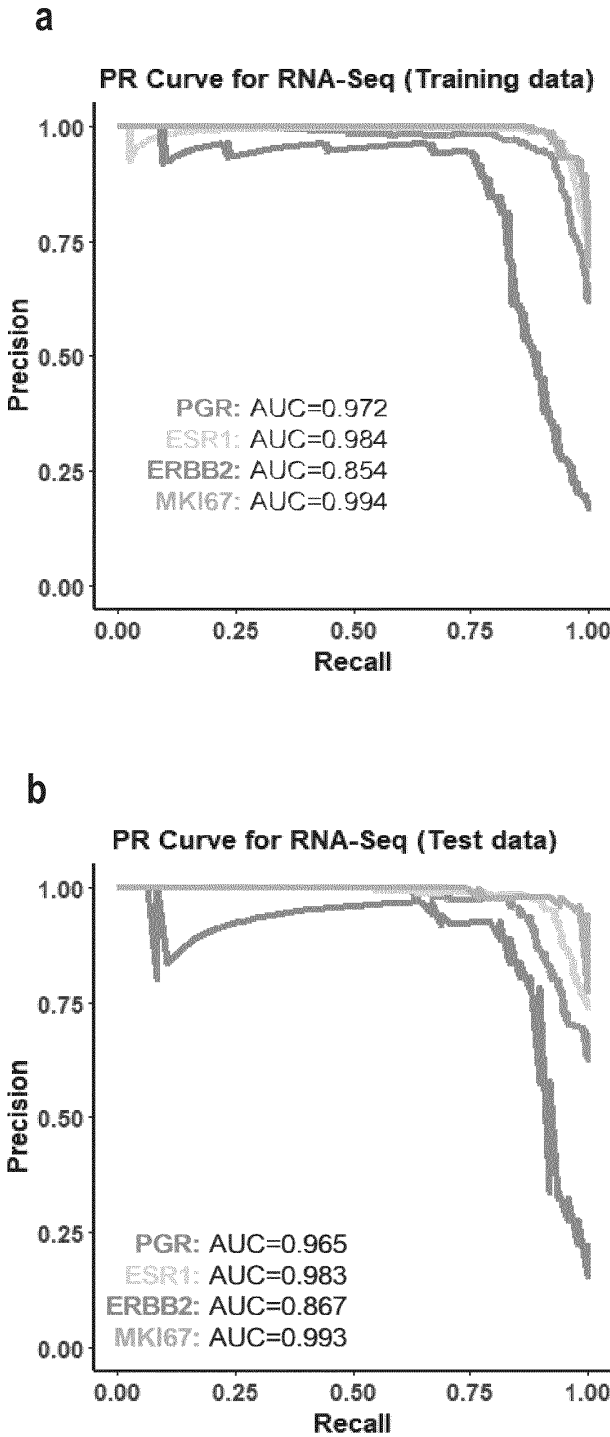
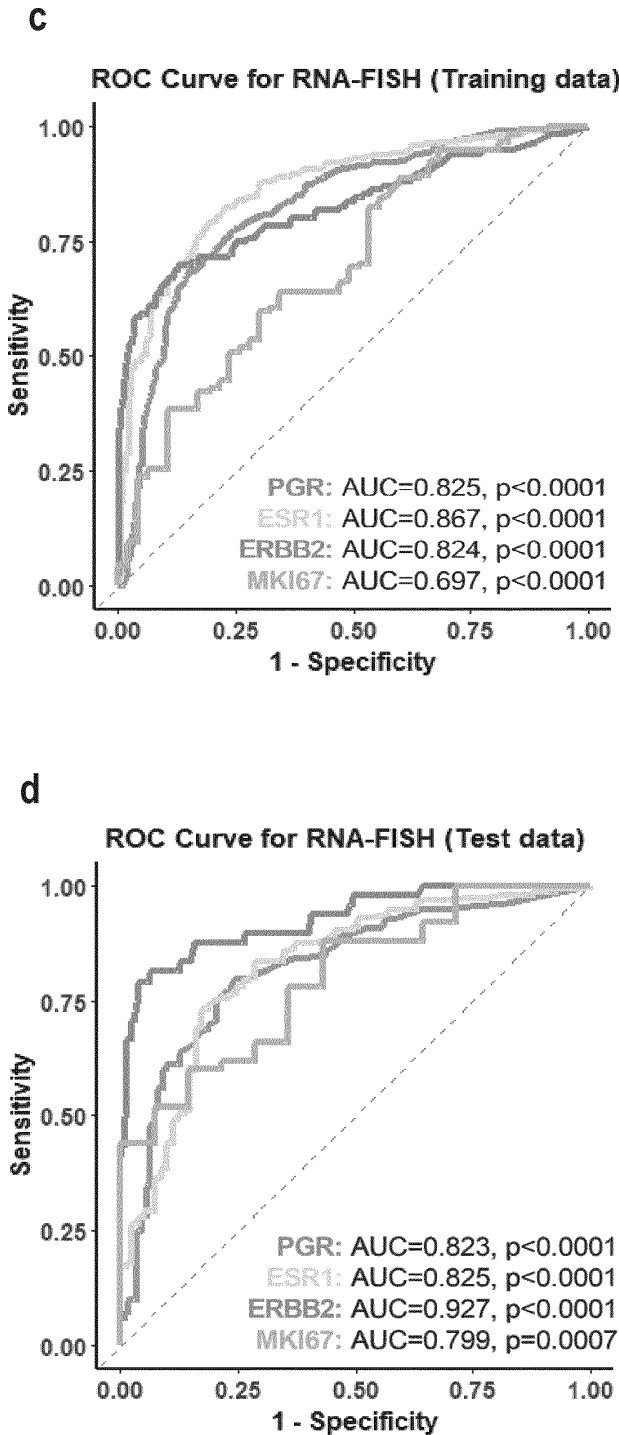


Figure 8

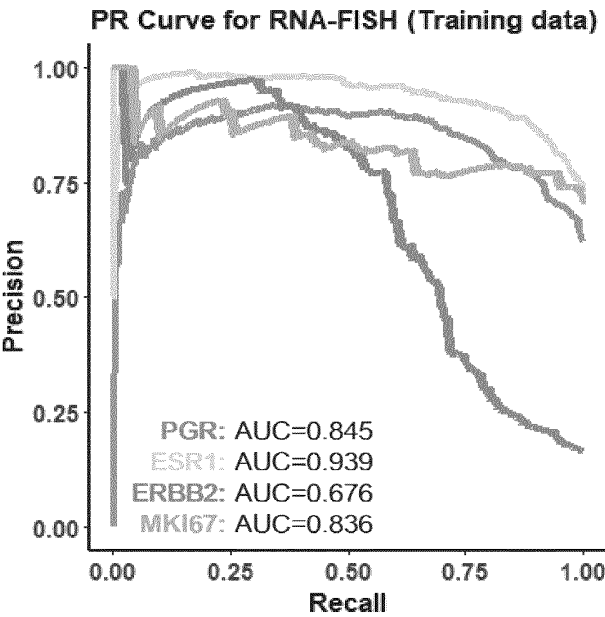


50 / 186
Figure 8 (cont.)

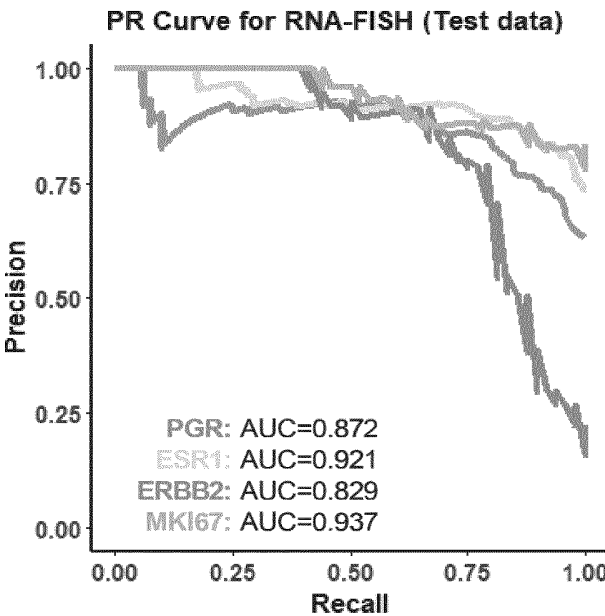


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Figure 8 (cont.)

e



f



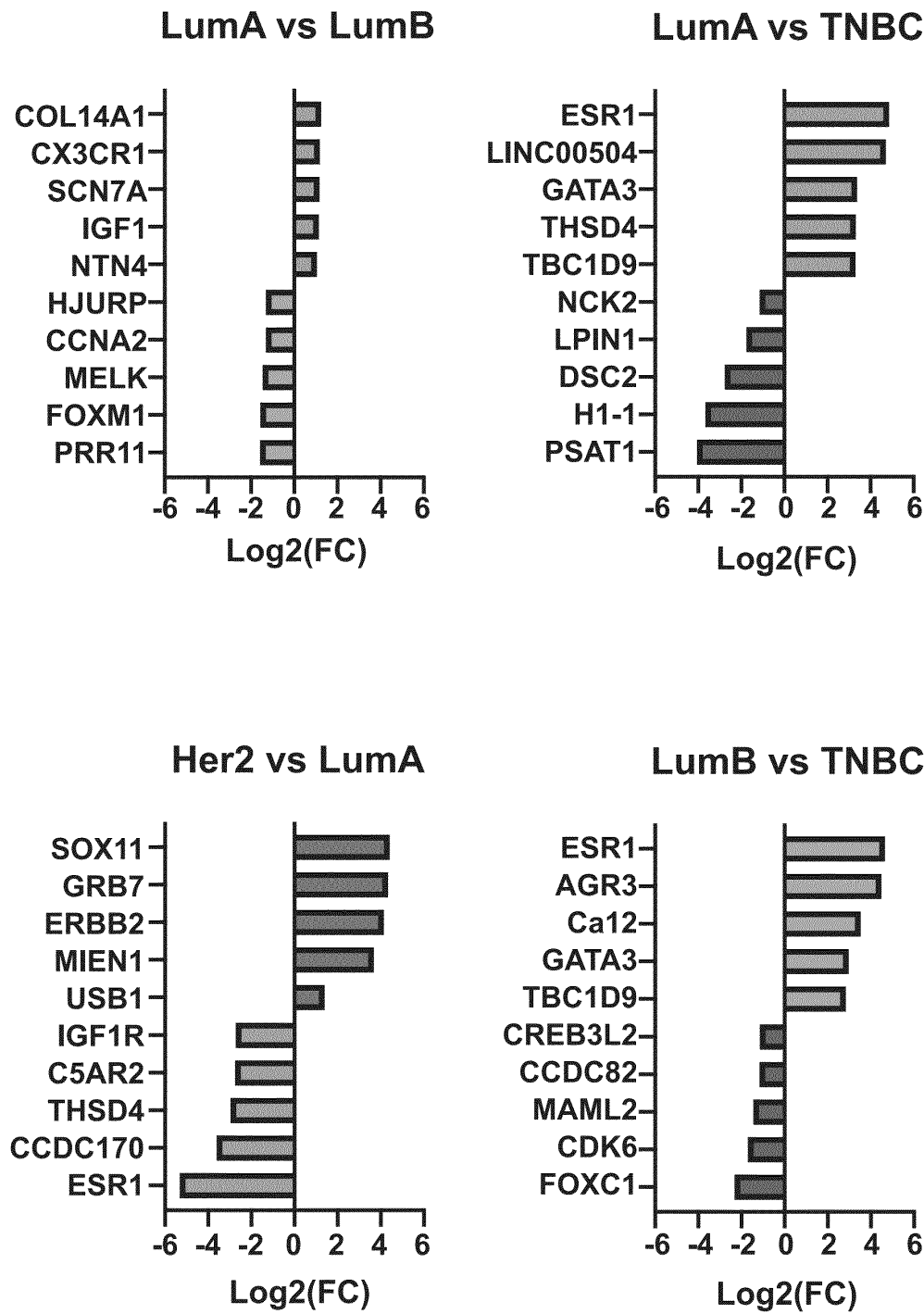
52 / 186
Figure 8 (cont.)

g

Flourescent SI thresholds (Maximum Cohen’s K)	
PGR RNA-FISH	≥ 0.011
ESR1 RNA-FISH	≥ 0.038
ERBB2 RNA-FISH	≥ 0.123
MKI67 RNA-FISH	≥ 0.05

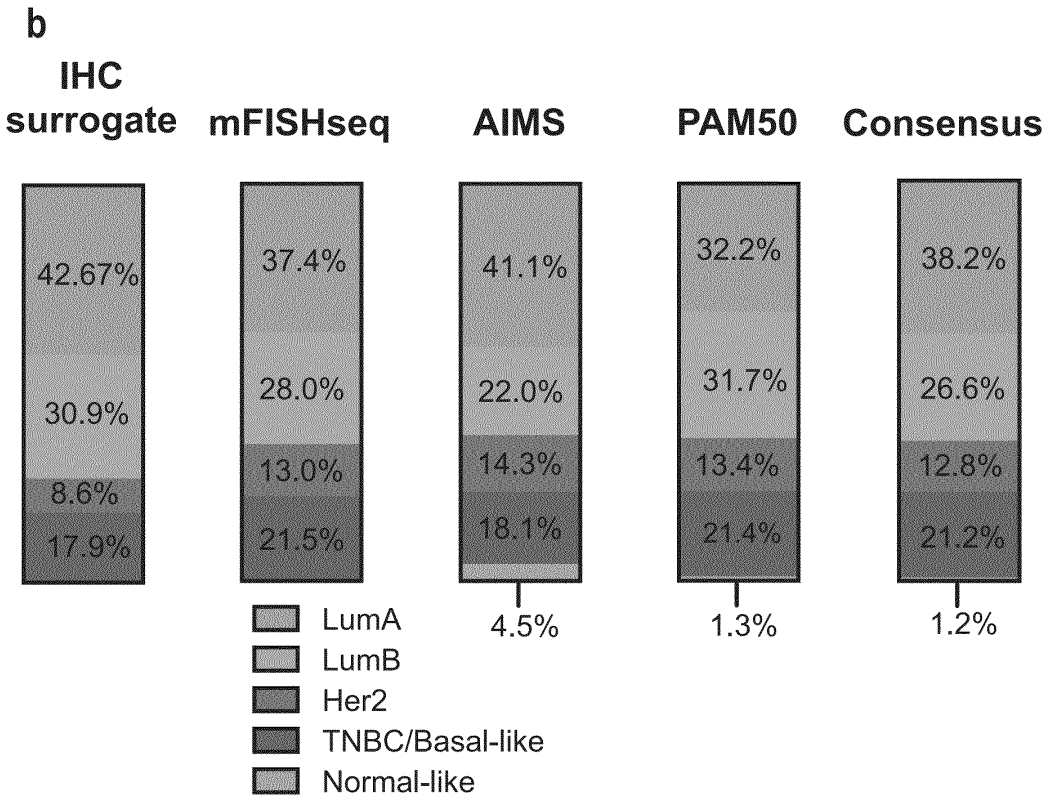
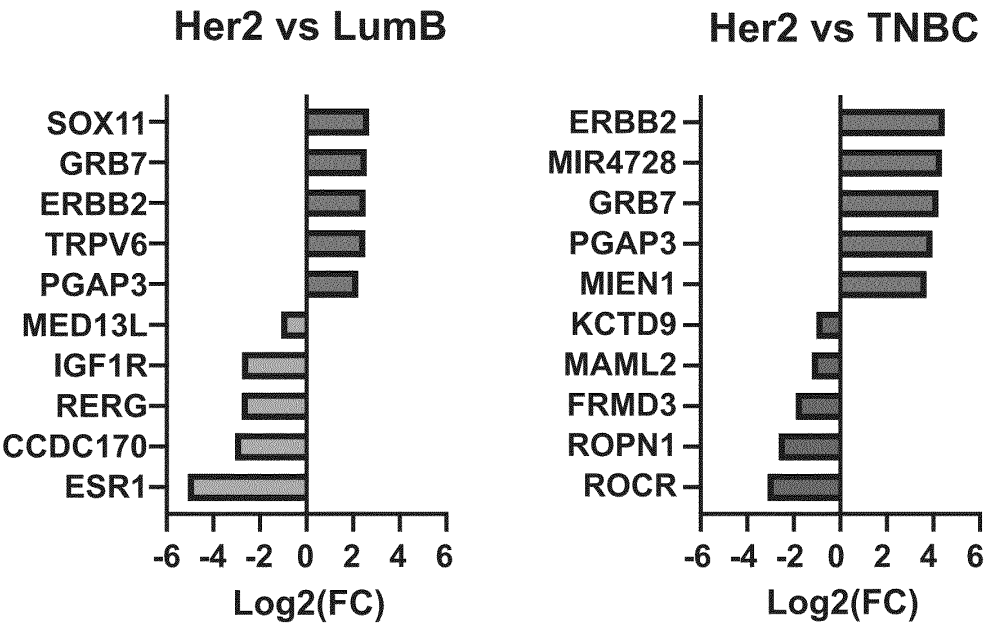
Figure 9

a



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Figure 9 (cont.)

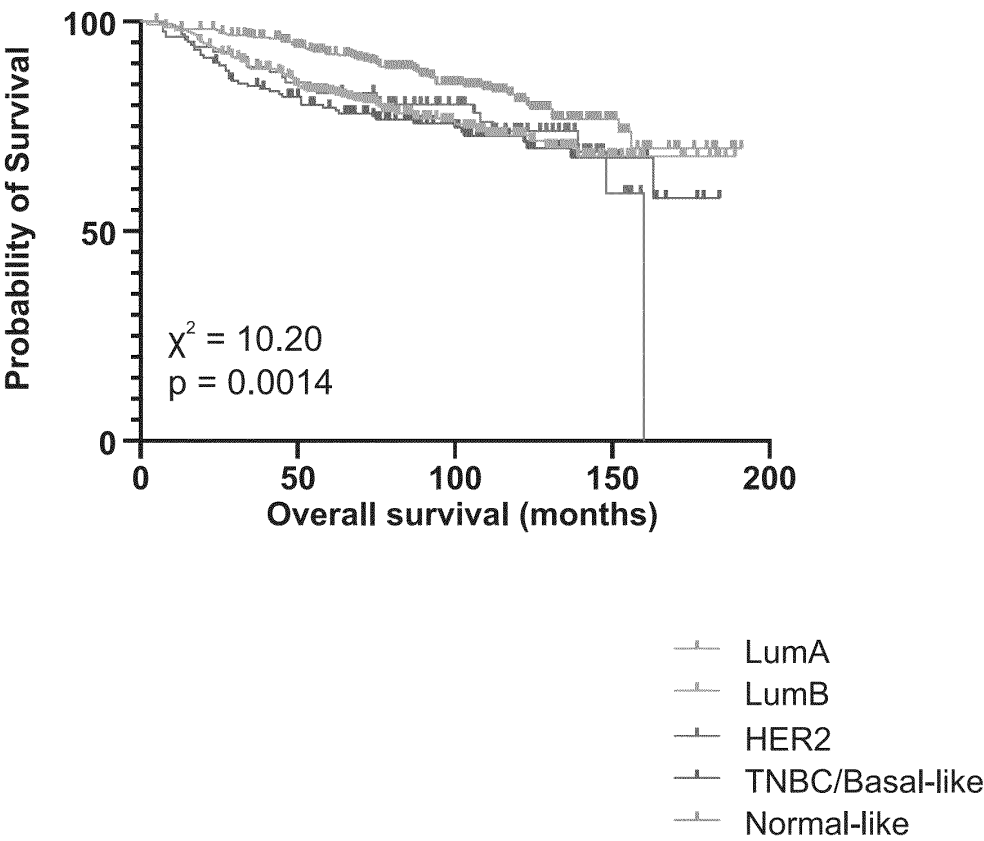
a (cont.)



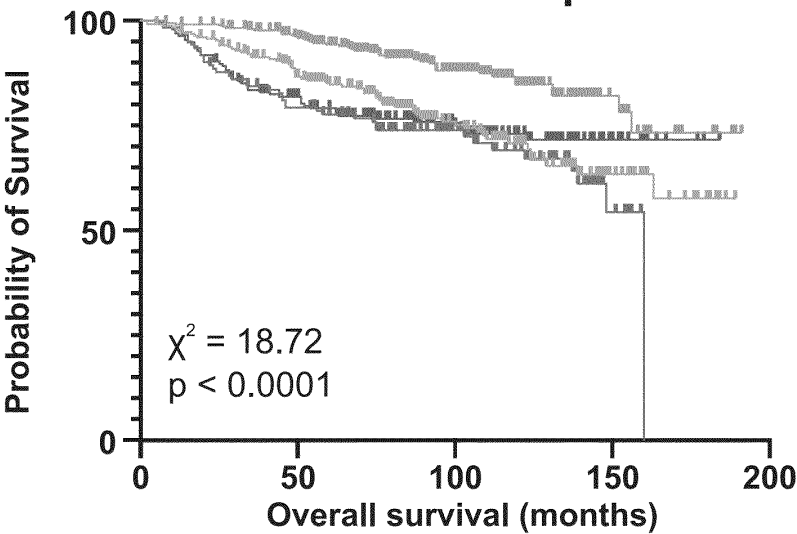
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Figure 9 (cont.)

c

IHC surrogate

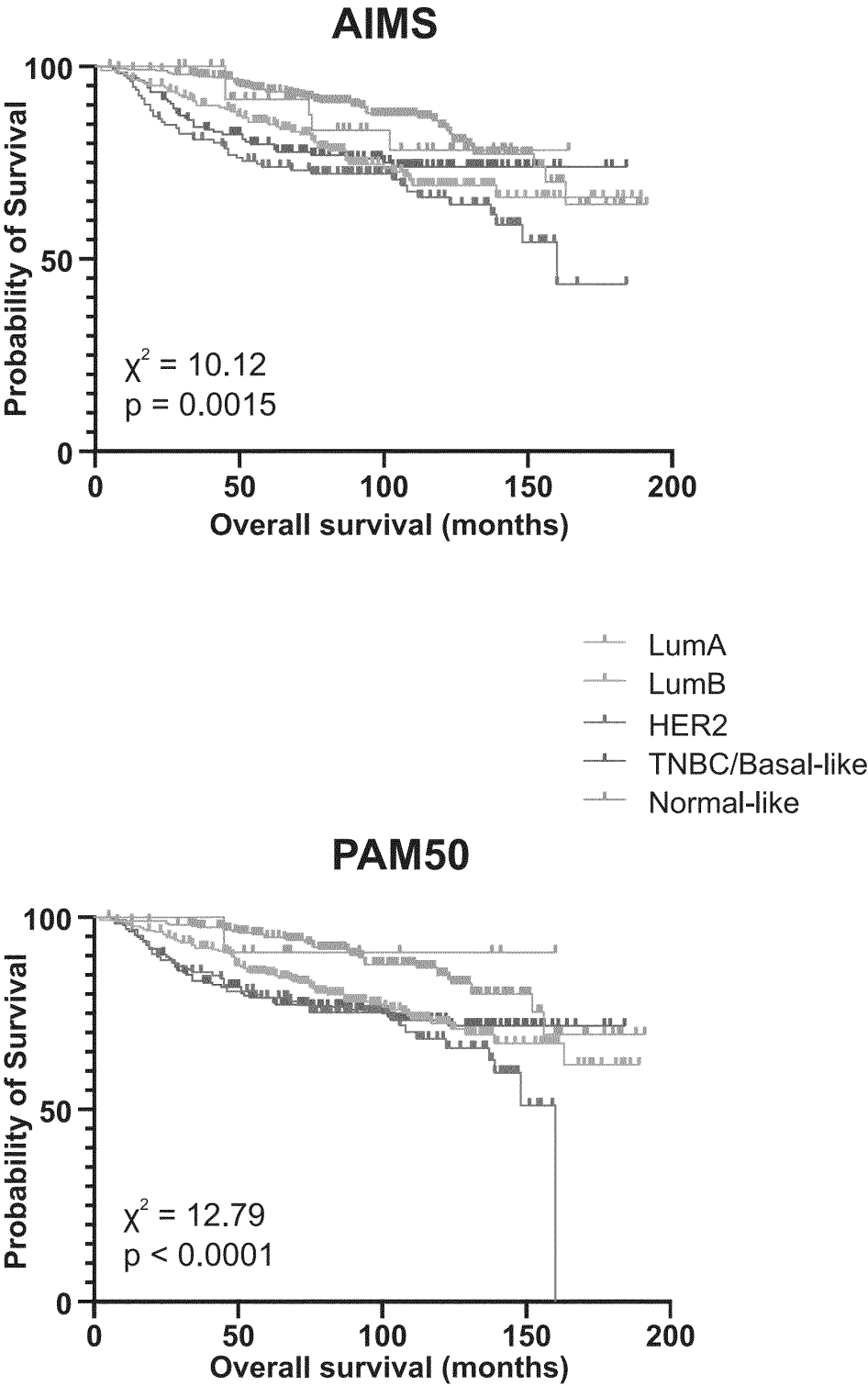


mFISHSeq



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Figure 9 (cont.)

c (cont.)



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Figure 9 (cont.)

d

Concordance all samples (Cohen's Kappa)					
IHC surrogate					
MDX293	0.567				
AIMS	0.519	0.731			
PAM50	0.539	0.748	0.744		
Consensus	0.573	0.869	0.856	0.876	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

Concordance Her2 (Cohen's Kappa)					
IHC surrogate					
MDX293	0.618				
AIMS	0.565	0.795			
PAM50	0.584	0.837	0.773		
Consensus	0.635	0.93	0.861	0.924	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

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Figure 9 (cont.)

d (cont.)

Concordance Luminal A (Cohen's Kappa)					
IHC surrogate					
MDX293	0.615				
AIMS	0.605	0.717			
PAM50	0.594	0.668	0.722		
Consensus	0.632	0.832	0.874	0.843	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

Concordance Basal-like (Cohen's Kappa)					
IHC surrogate					
MDX293	0.704				
AIMS	0.638	0.891			
PAM50	0.688	0.968	0.894		
Consensus	0.706	0.979	0.9	0.976	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

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Figure 9 (cont.)

d (cont.)

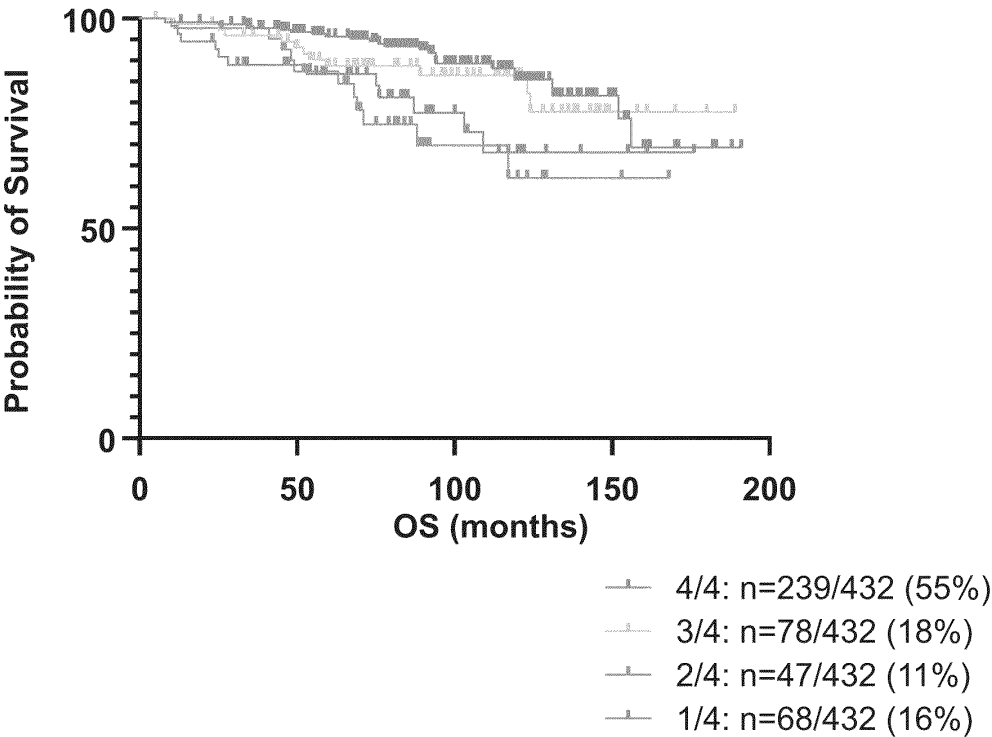
Concordance Luminal B (Cohen's Kappa)					
IHC surrogate					
MDX293	0.384				
AIMS	0.36	0.663			
PAM50	0.365	0.631	0.683		
Consensus	0.387	0.809	0.861	0.81	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

Concordance Normal-like (Cohen's Kappa)					
IHC surrogate					
MDX293					
AIMS					
PAM50			0.395		
Consensus			0.403	0.96	
	IHC surrogate	MDX293	AIMS	PAM50	Consensus

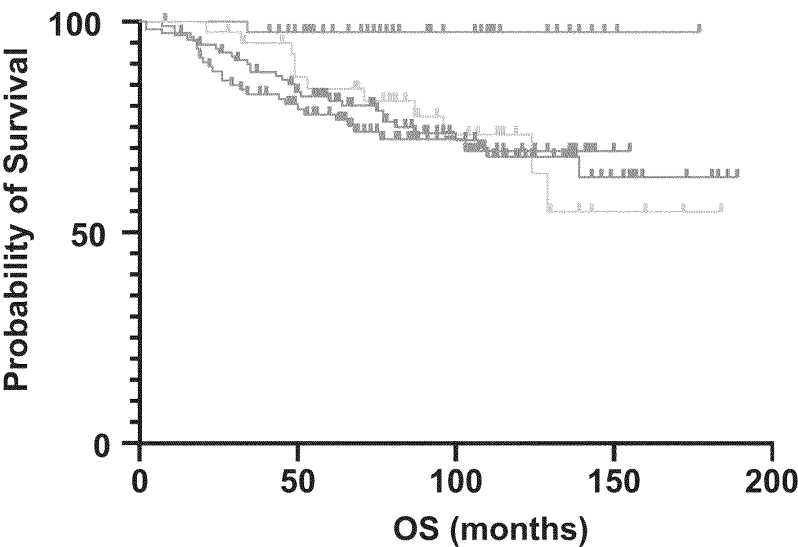
60 / 186
Figure 9 (cont.)

e

LumA - Discordant samples

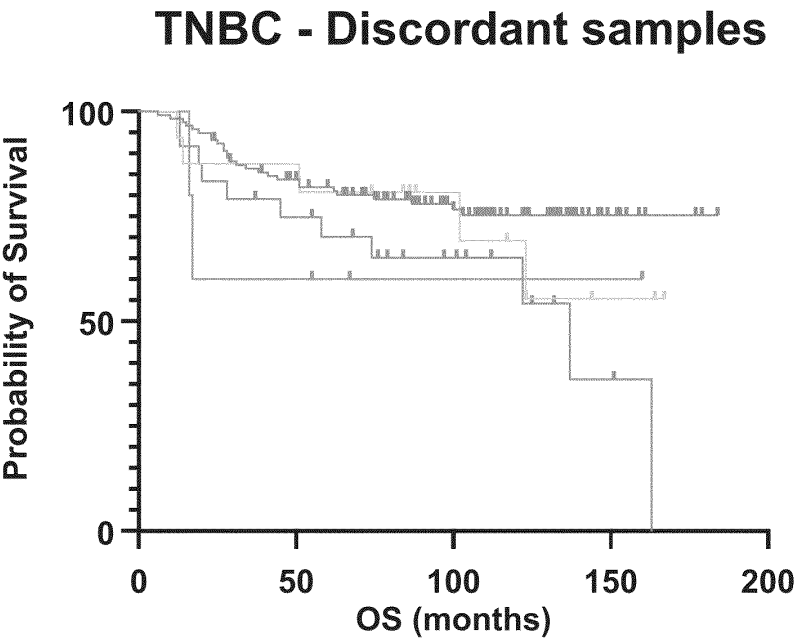
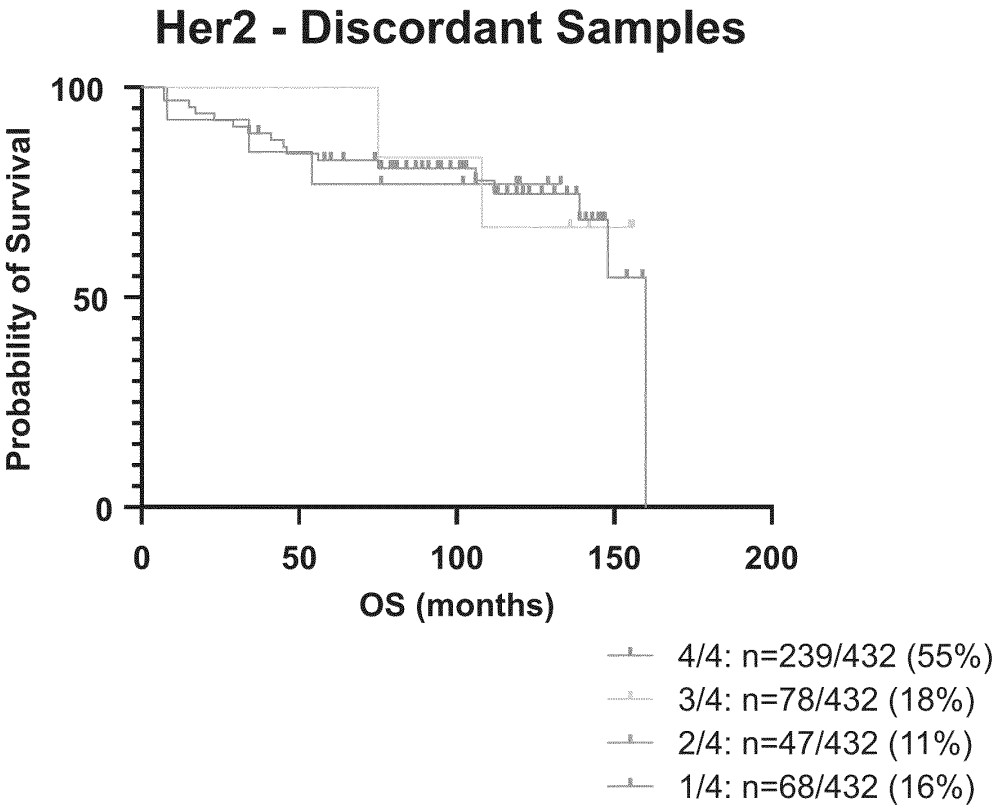


LumB - Discordant samples



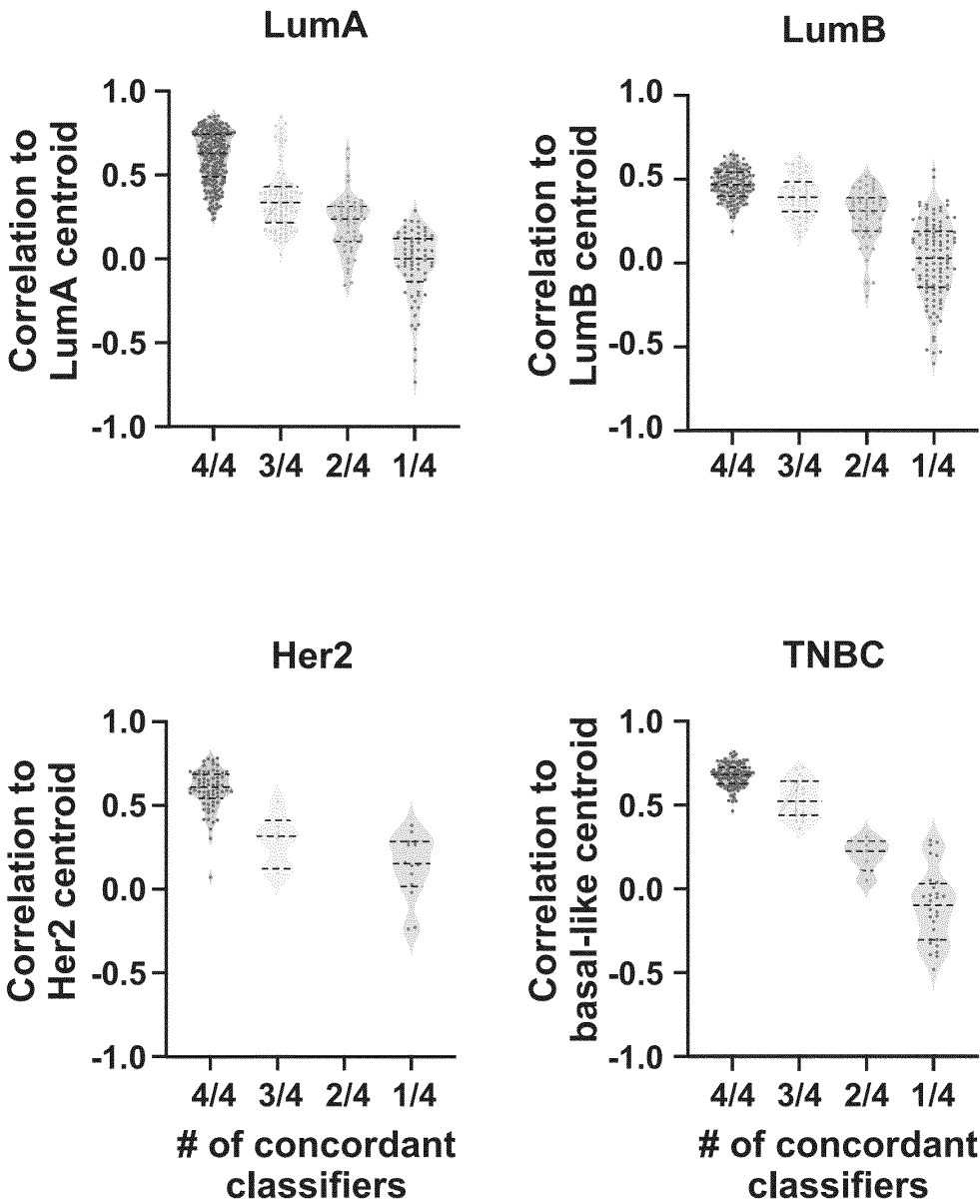
61 / 186
Figure 9 (cont.)

e (cont.)



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Figure 9 (cont.)

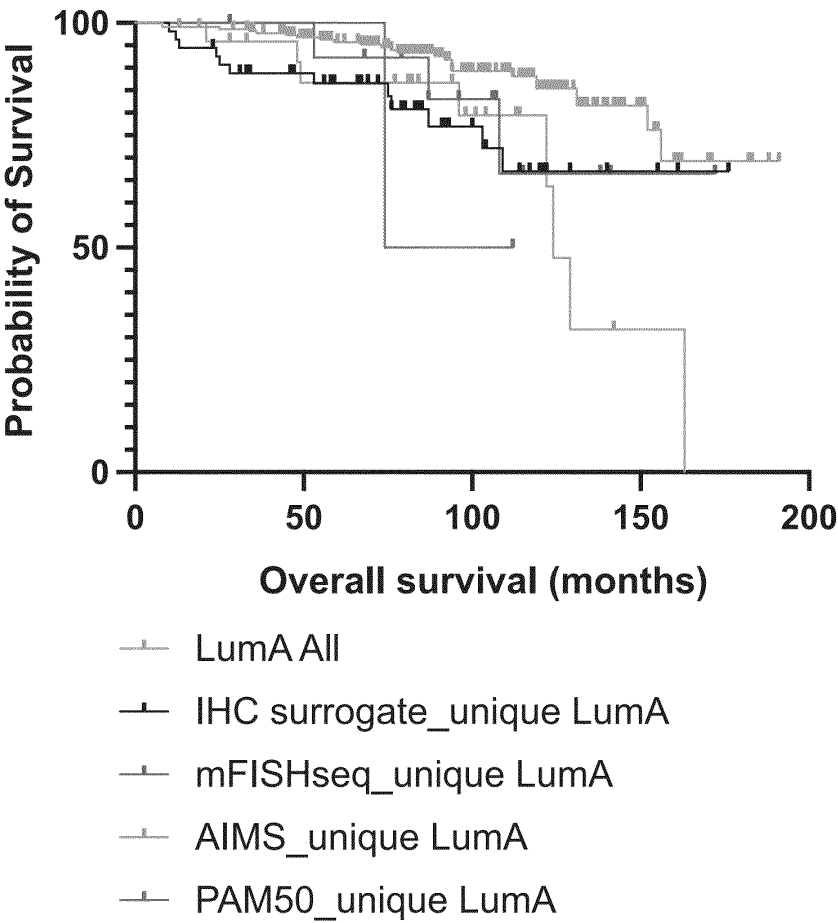
f



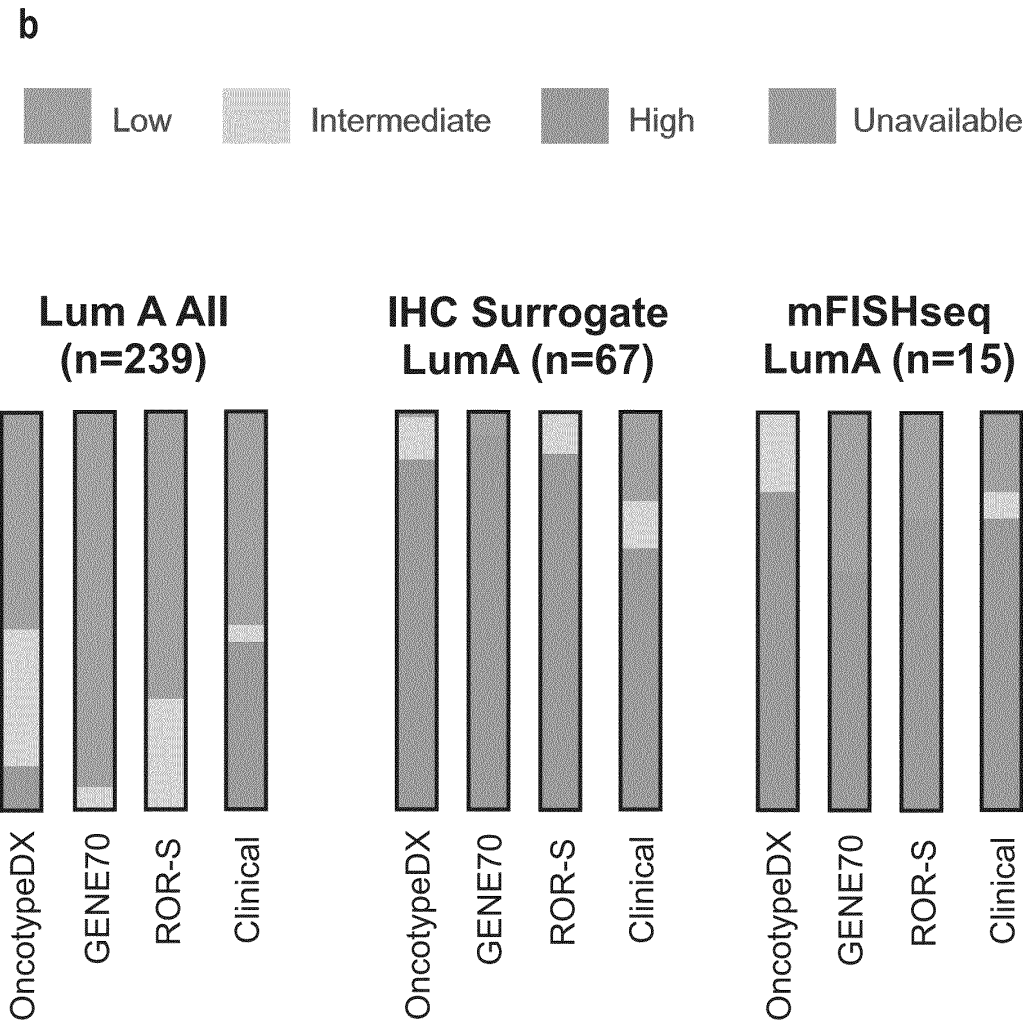
63 / 186
Figure 10

a

Unique LumA for each classifier_OS (all)

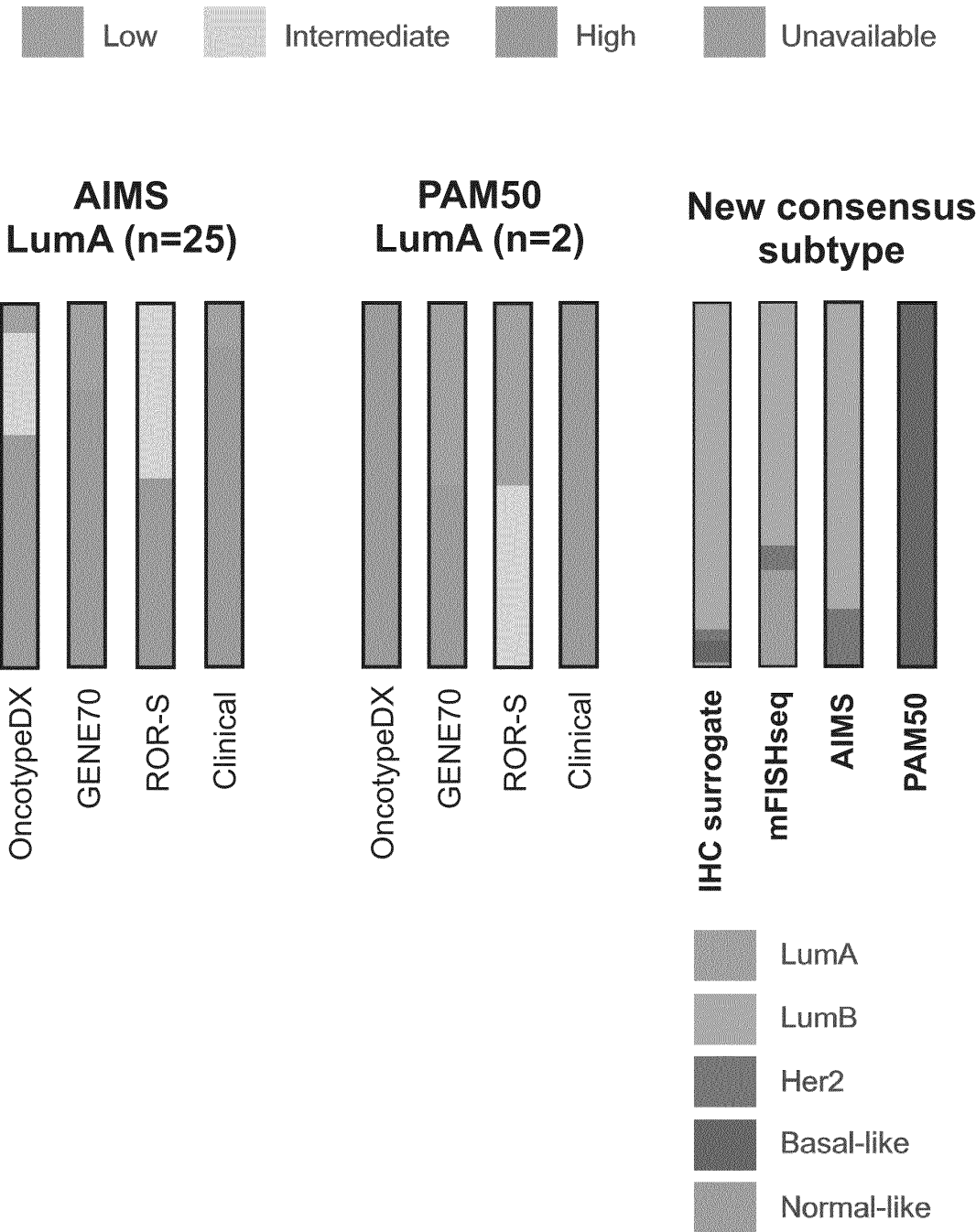


64 / 186
Figure 10 (cont.)



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Figure 10 (cont.)

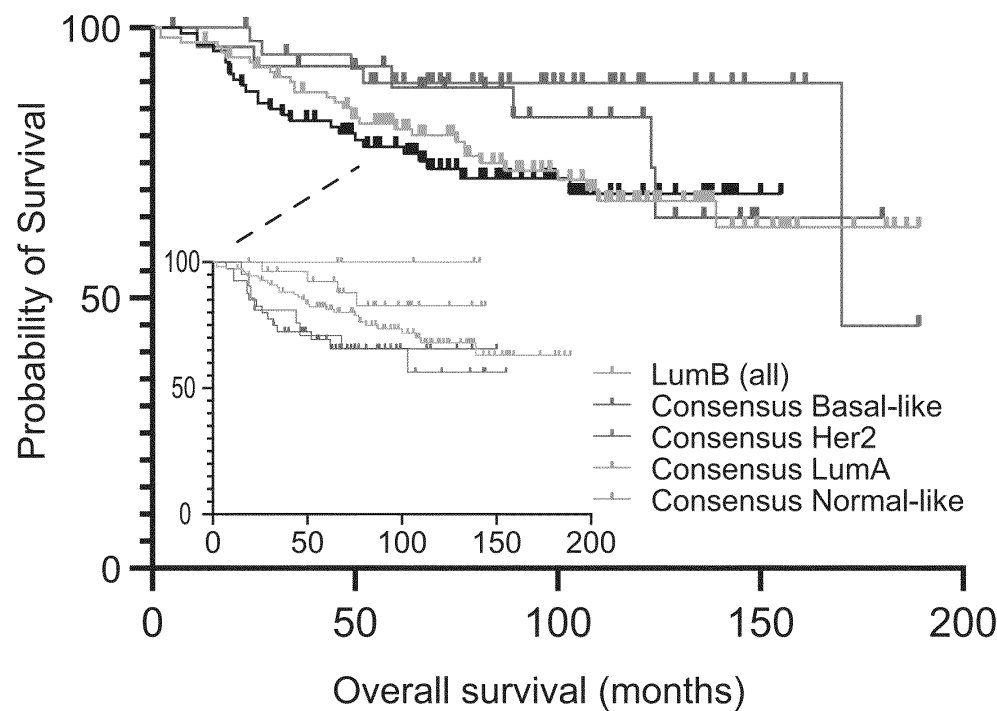
b (cont.)



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Figure 10 (cont.)

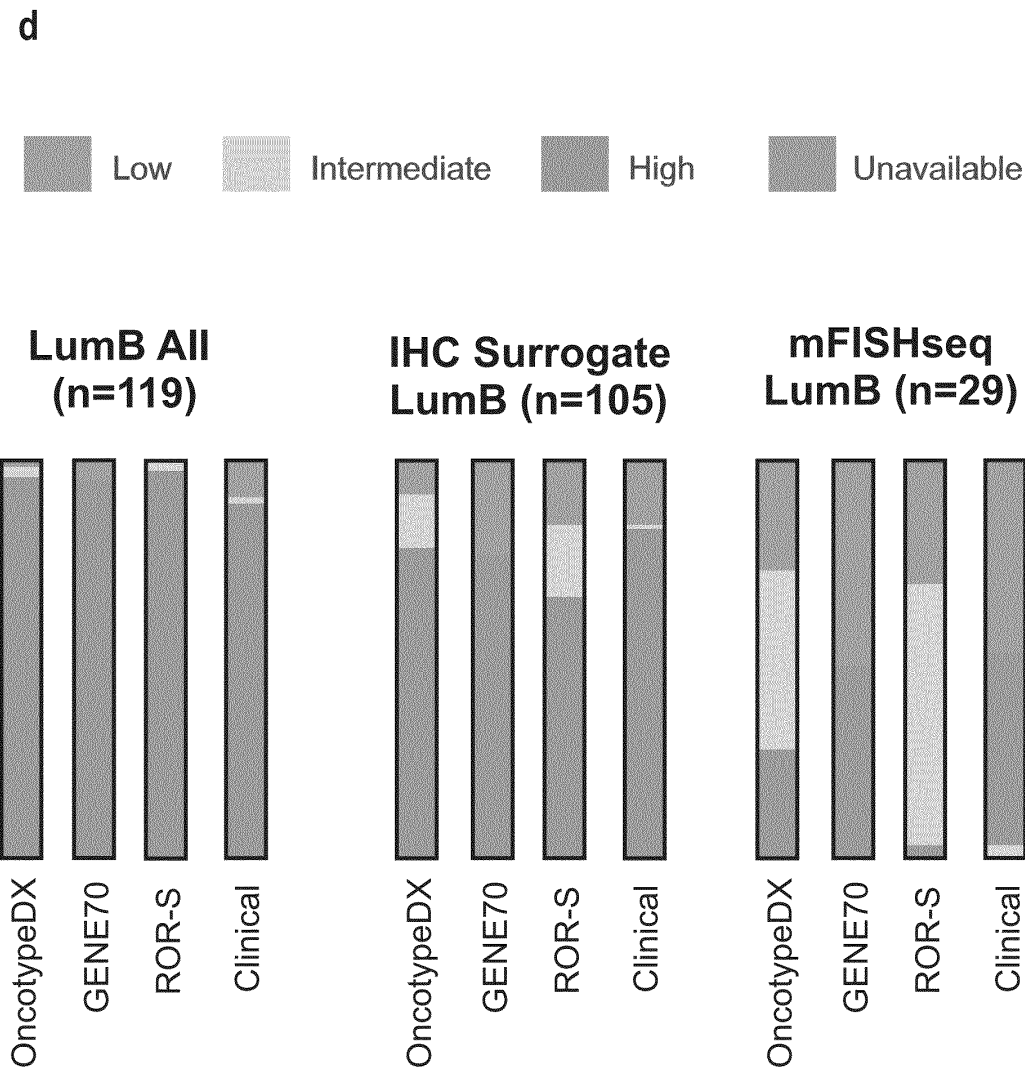
c

Unique LumB for each classifier_OS (all)



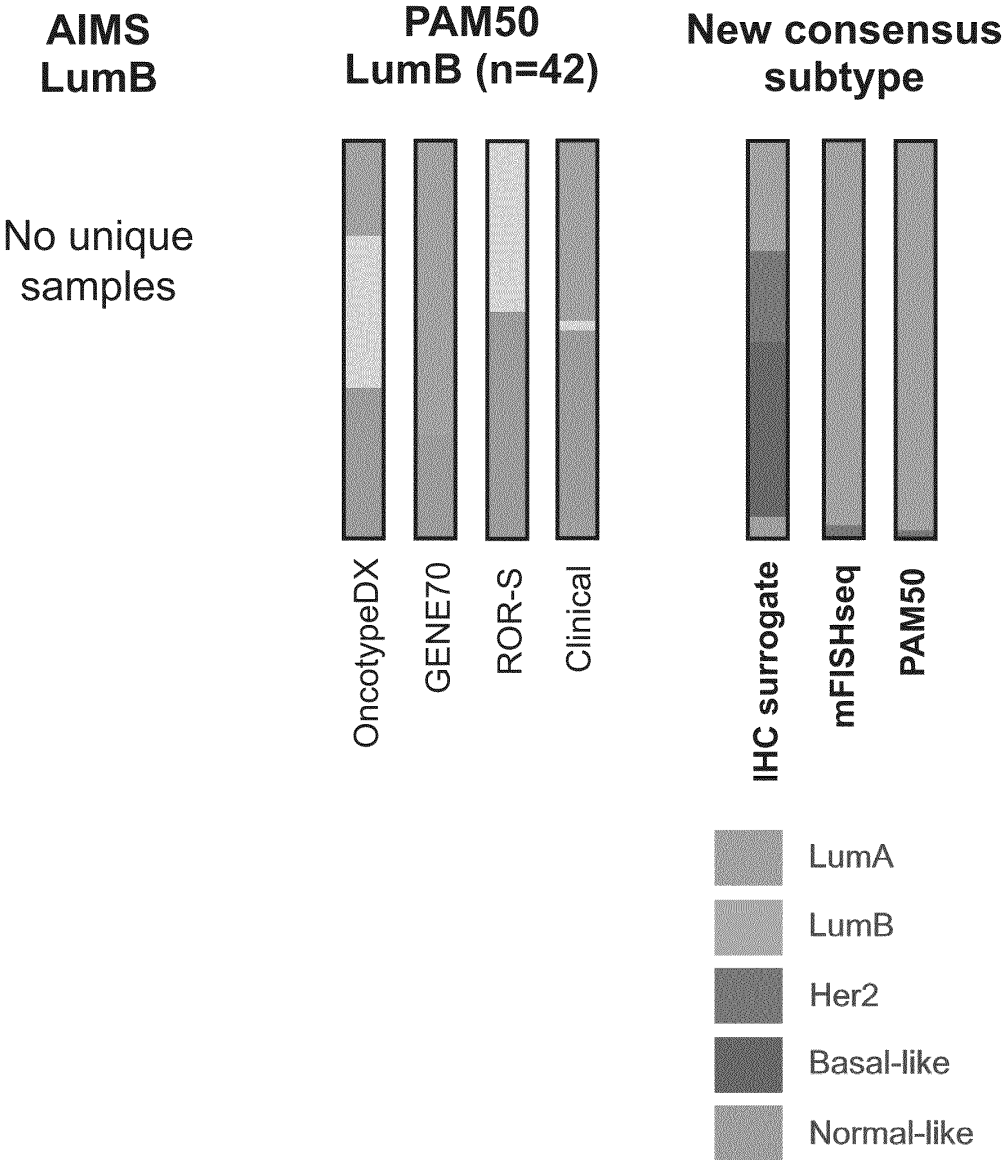
- LumB All
- IHC surrogate_unique LumB
- mFISHseq_unique LumB
- AIMS_unique LumB
- PAM50_unique LumB

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Figure 10 (cont.)



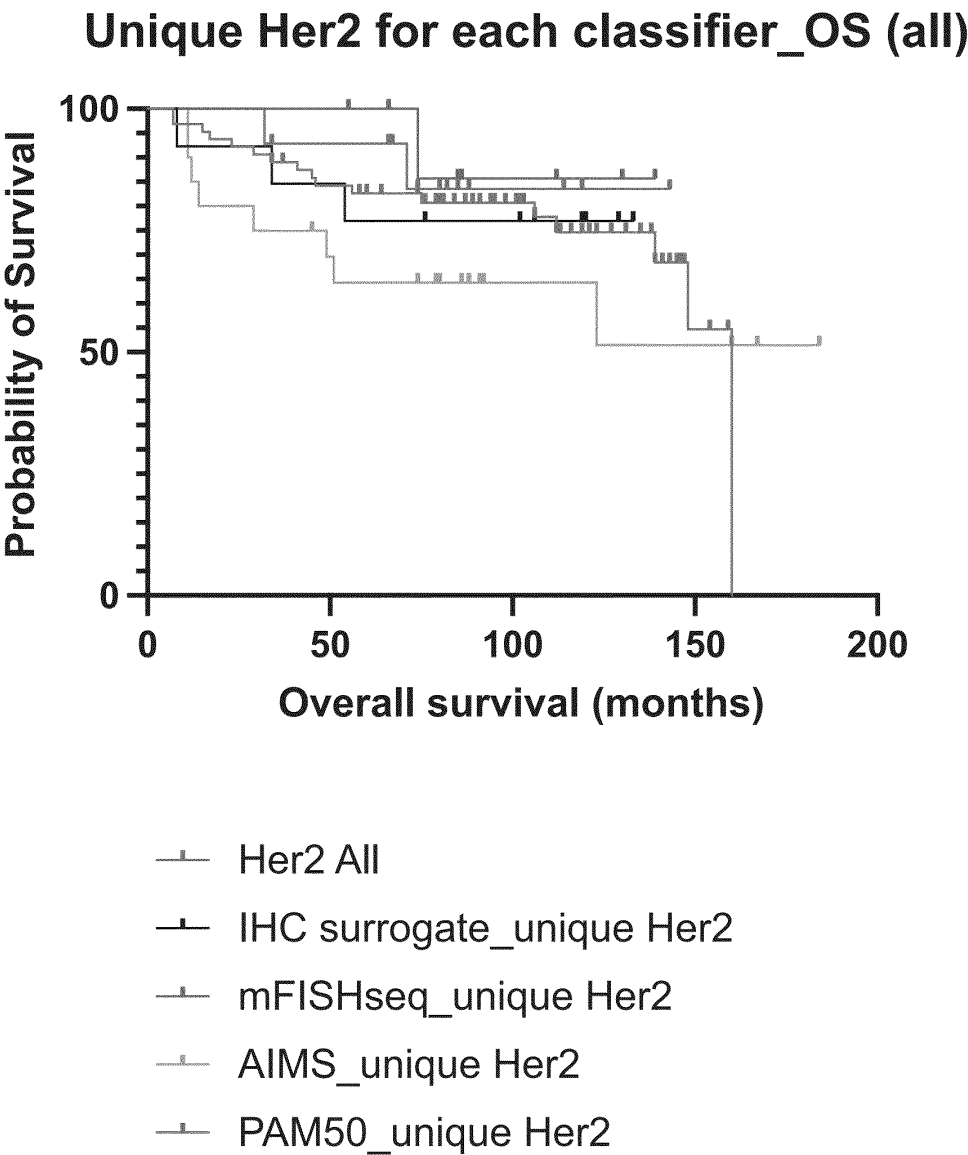
68 / 186
Figure 10 (cont.)

d (cont.)



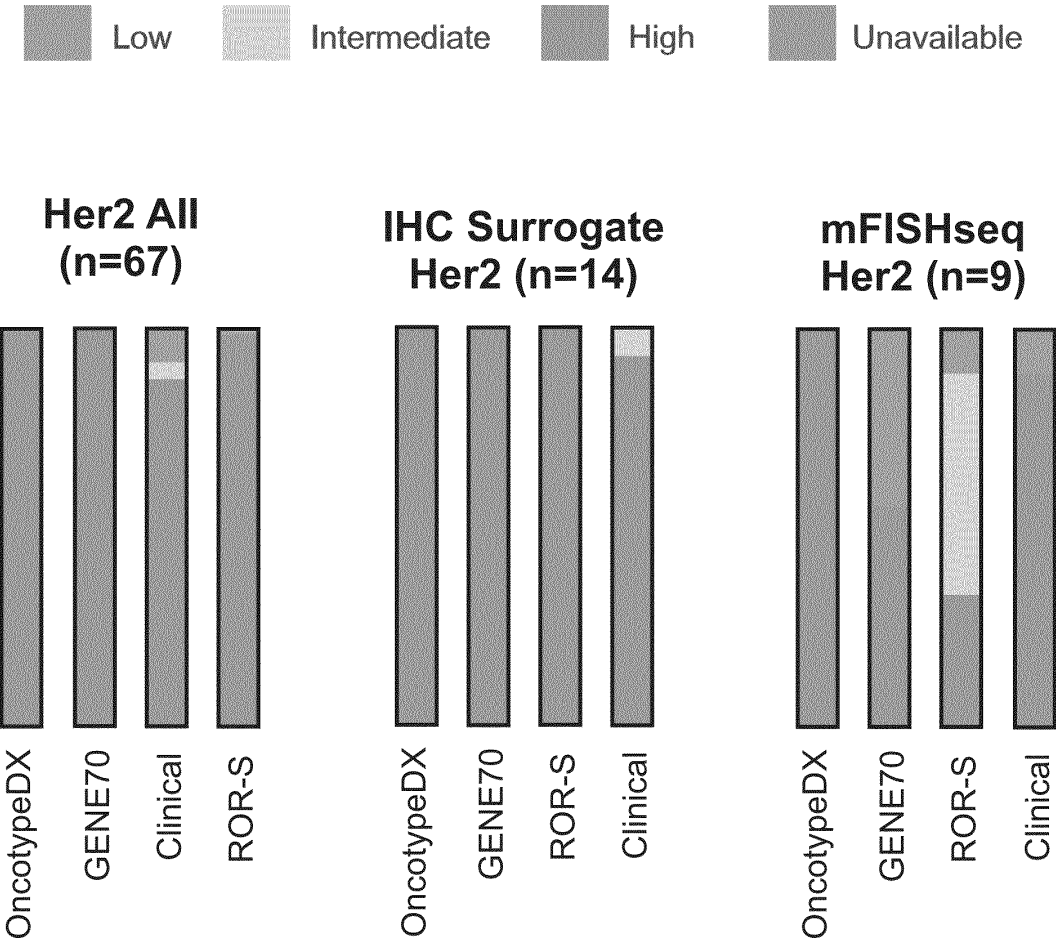
69 / 186
Figure 10 (cont.)

e



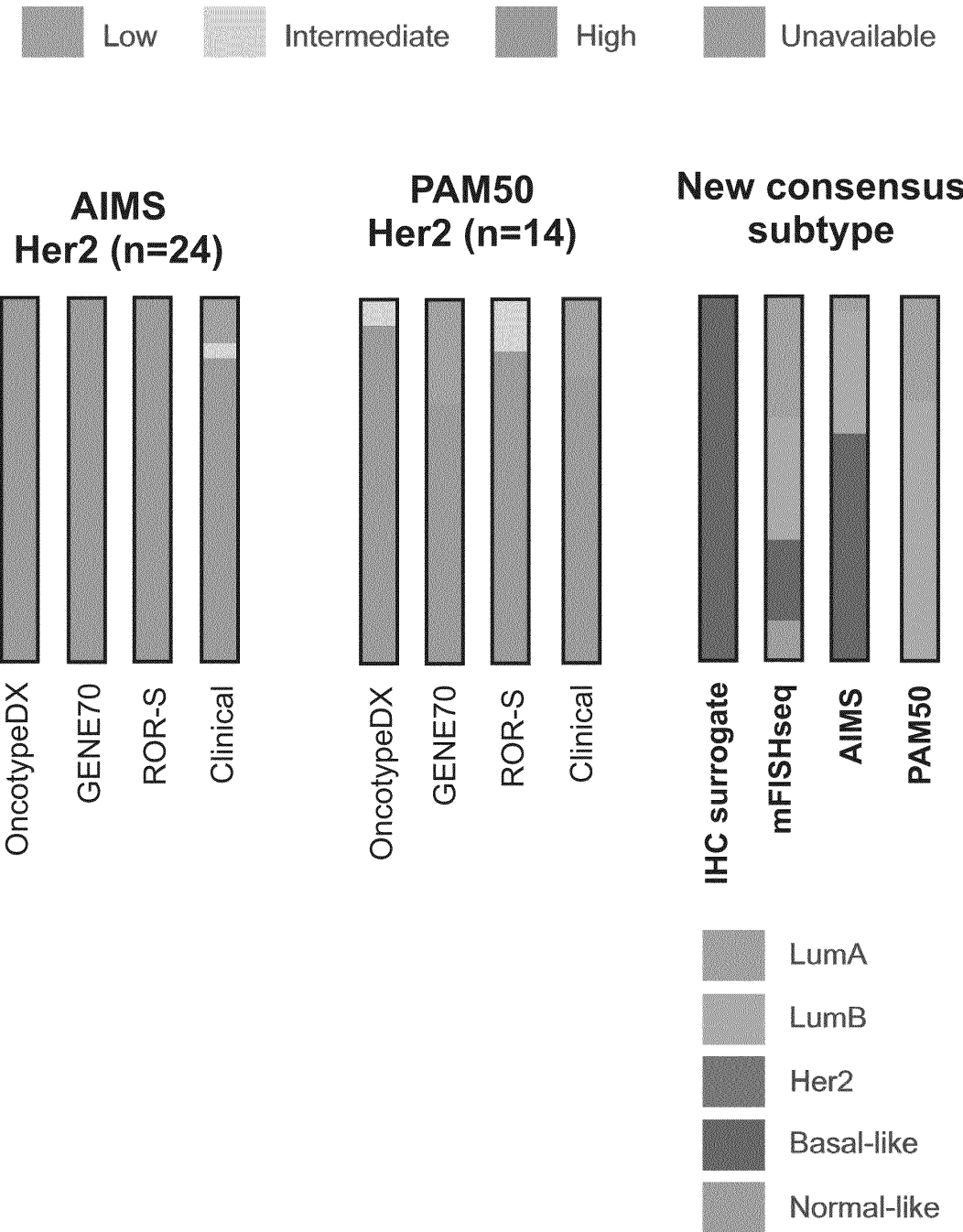
70 / 186
Figure 10 (cont.)

f



71 / 186
Figure 10 (cont.)

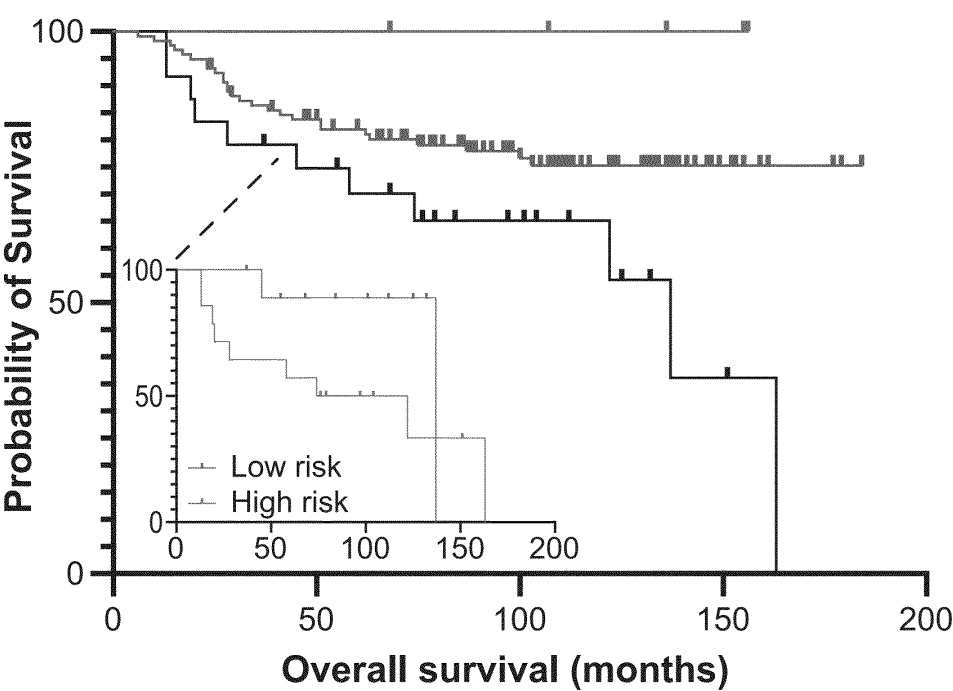
f (cont.)



72 / 186
Figure 10 (cont.)

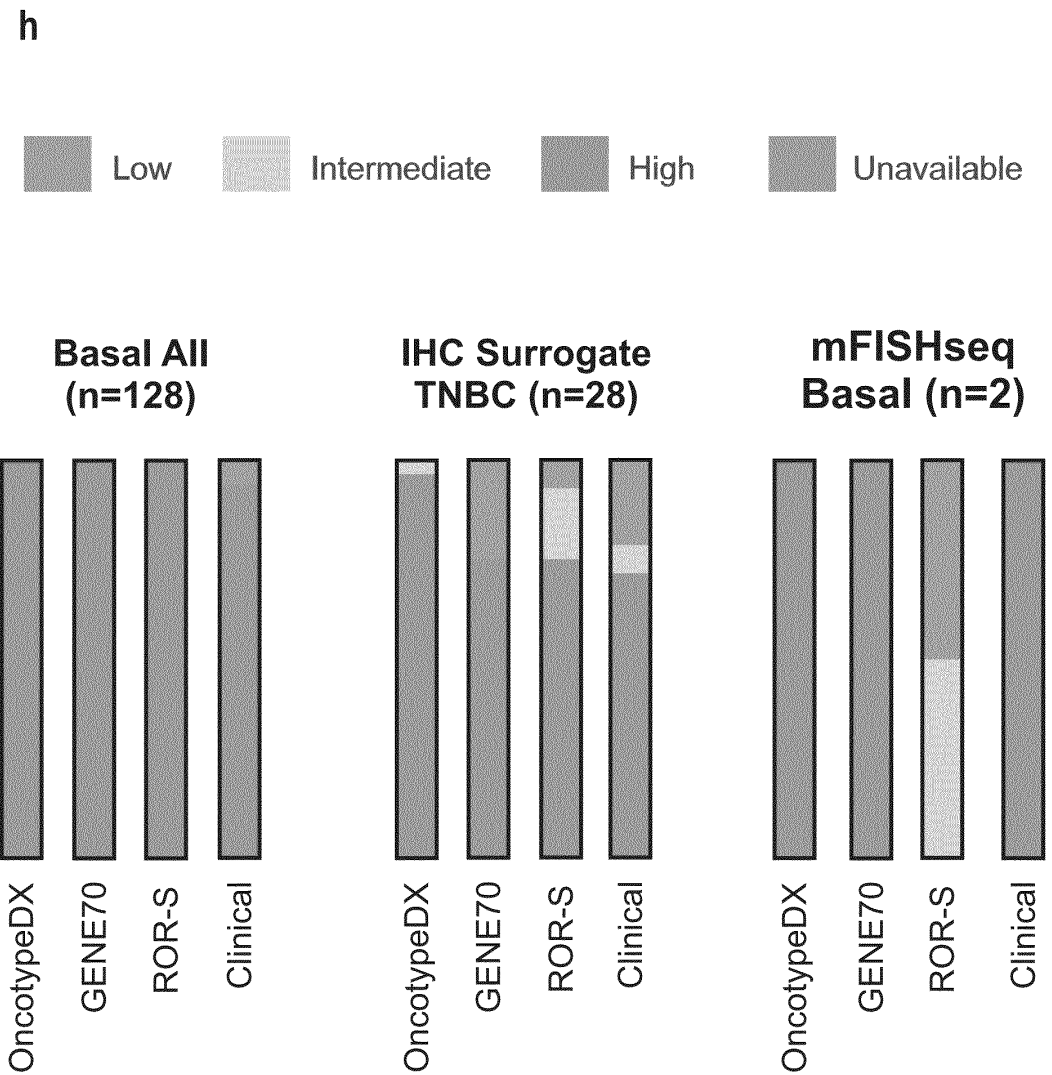
g

Unique Basal-like for each classifier_OS (all)



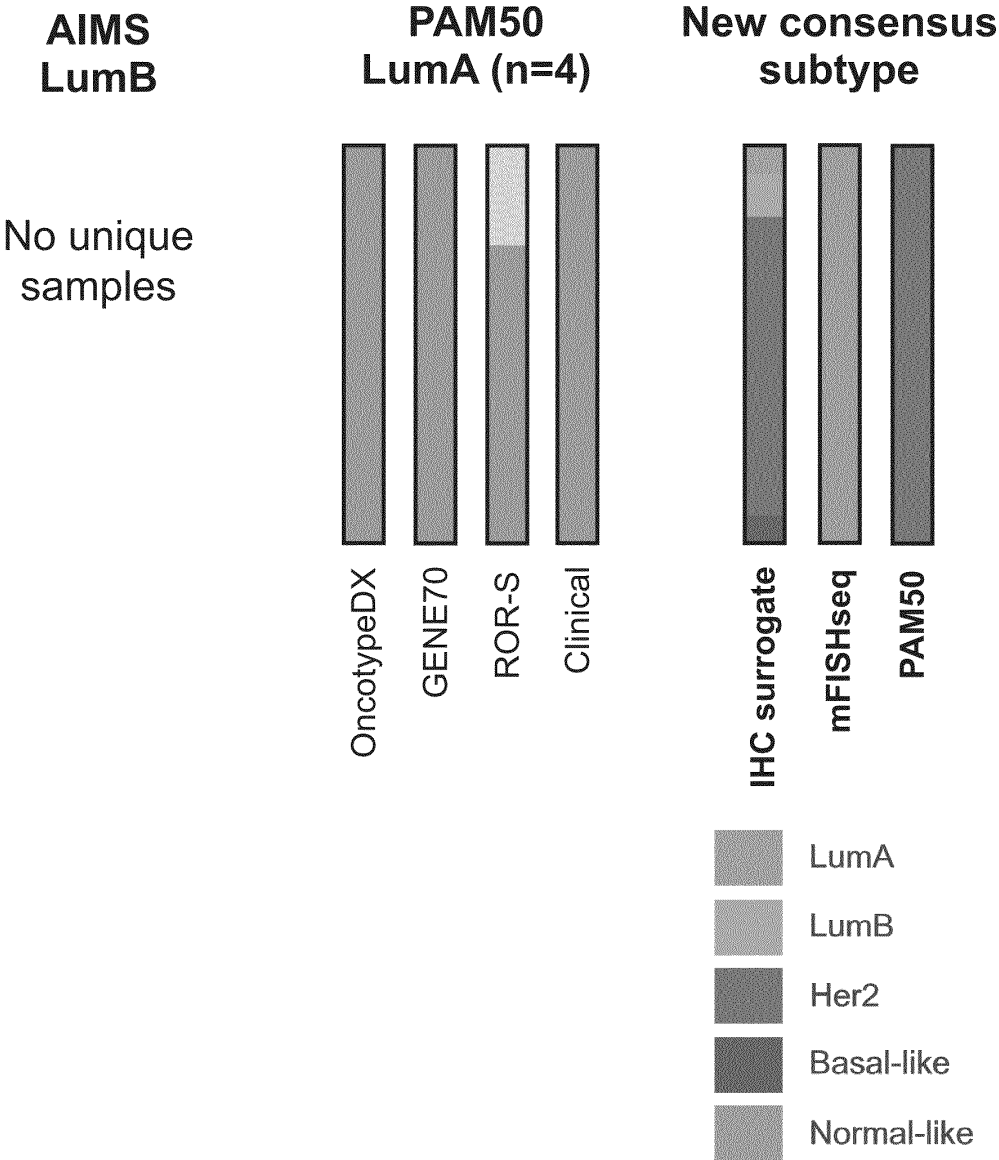
- Basal-like All
- IHC surrogate_unique TNBC
- mFISHseq_unique Basal-like
- AIMS_unique Basal-like
- PAM50_unique Basal-like

73 / 186
Figure 10 (cont.)

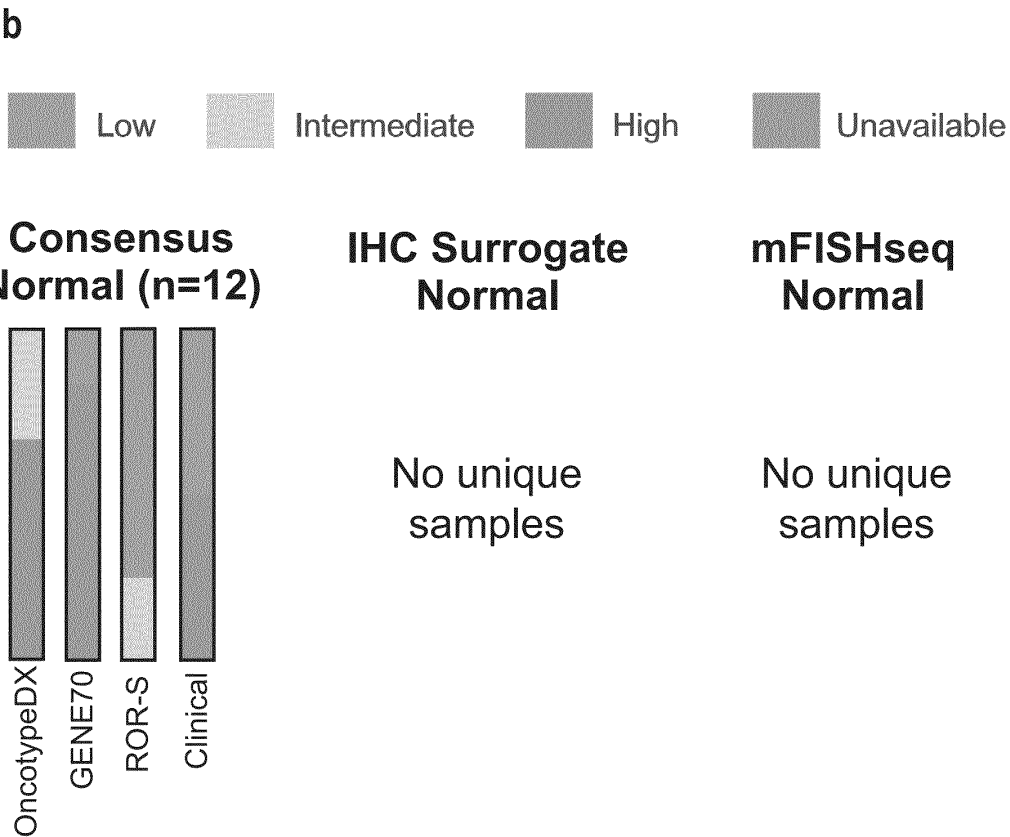
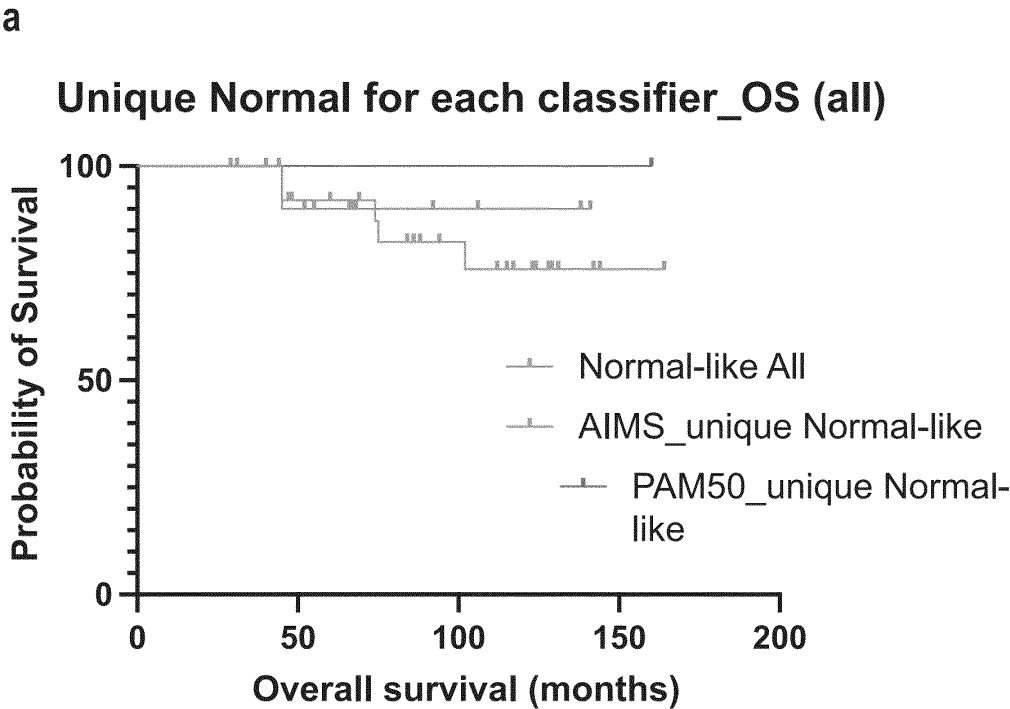


74 / 186
Figure 10 (cont.)

h (cont.)

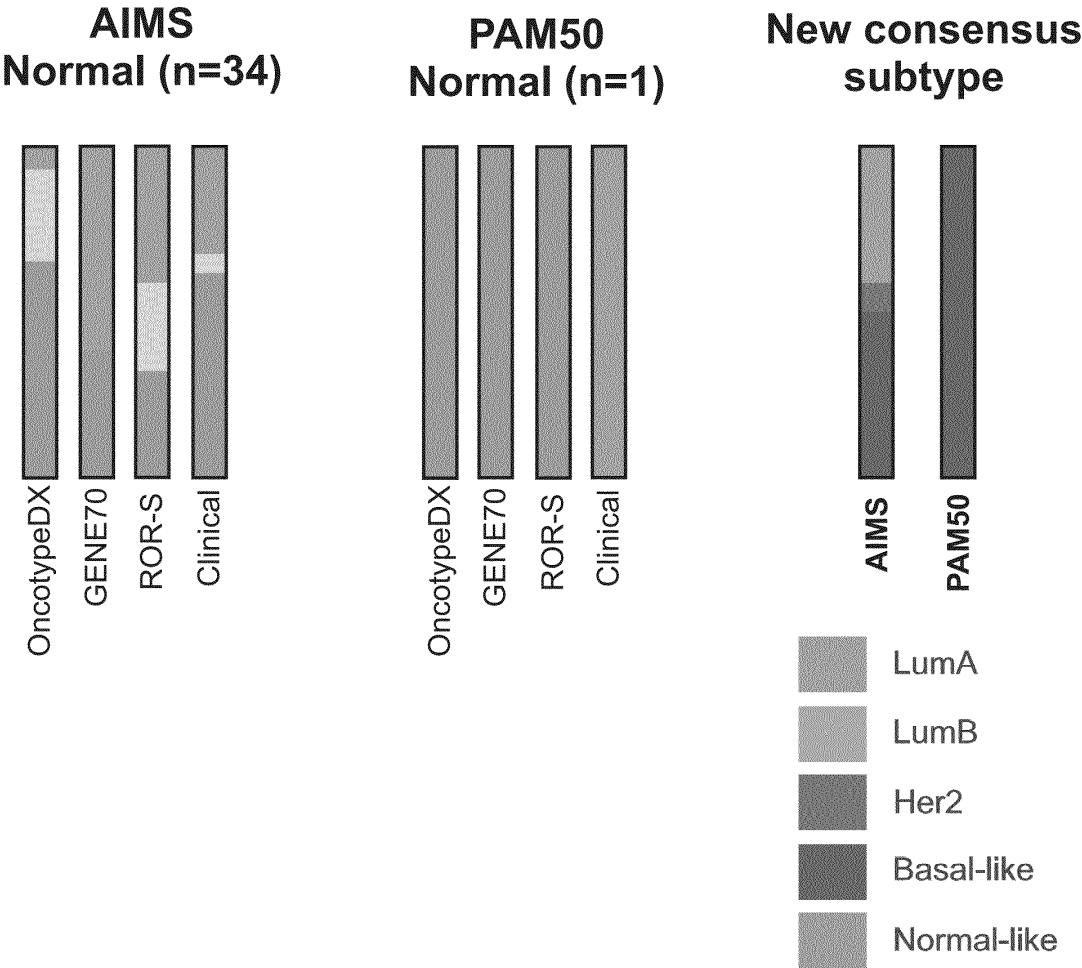


75 / 186
Figure 11

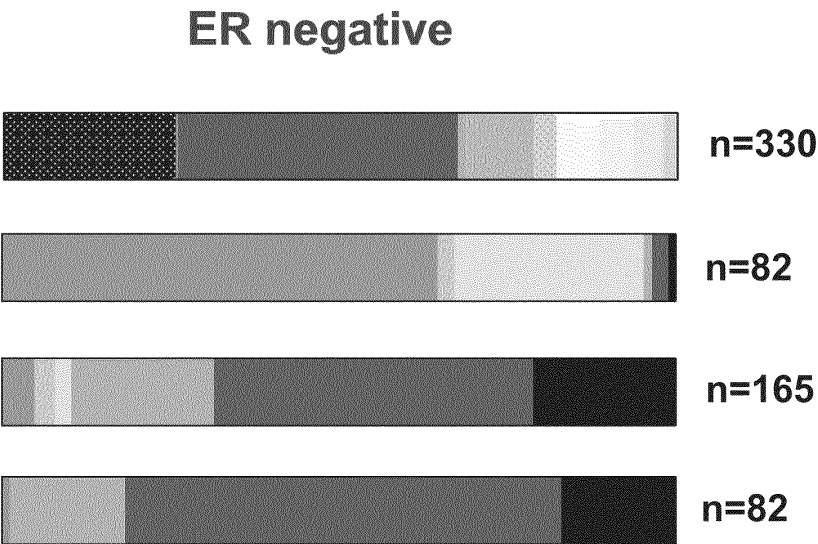
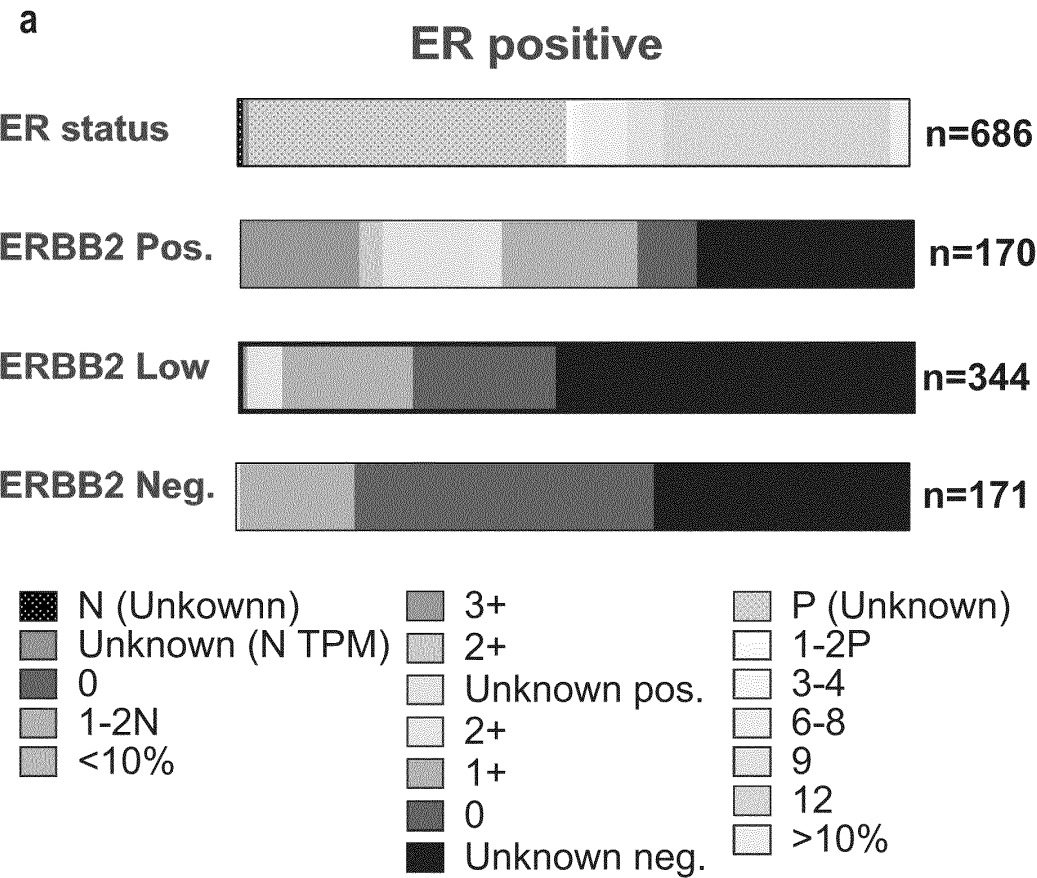


76 / 186
Figure 11 (cont.)

b (cont.)



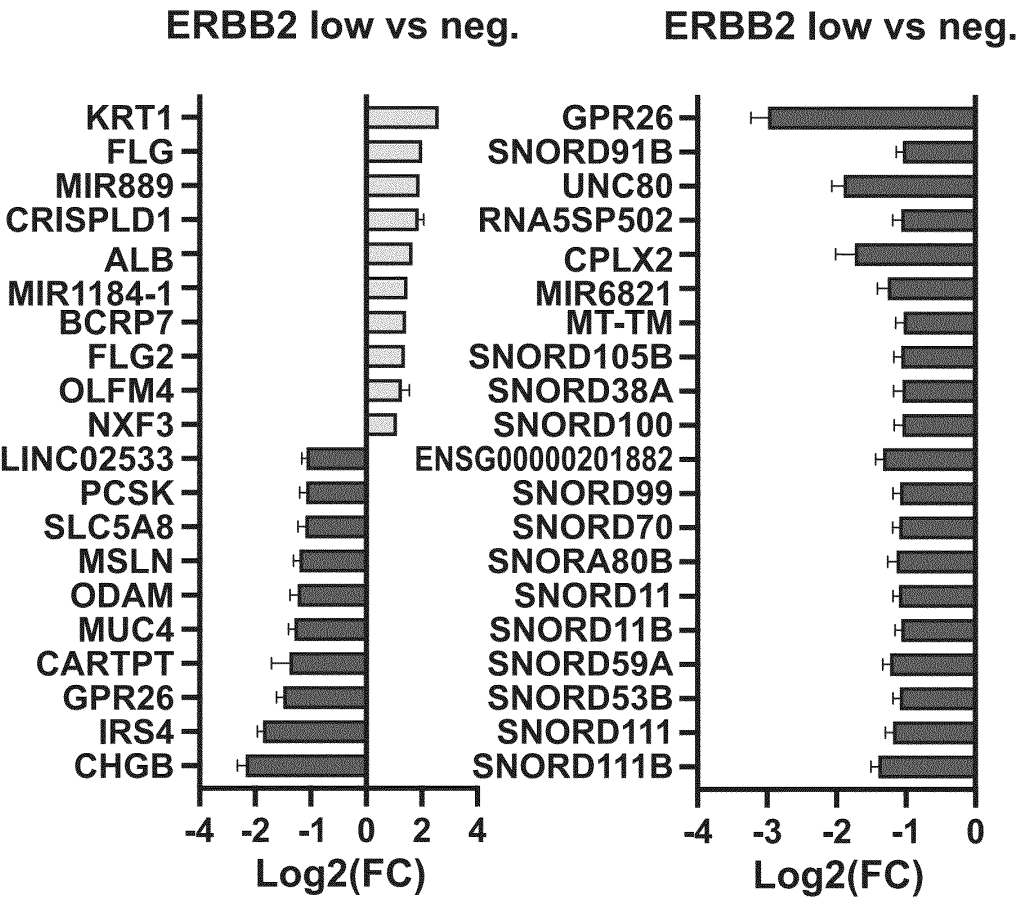
77 / 186
Figure 12



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Figure 12 (cont.)

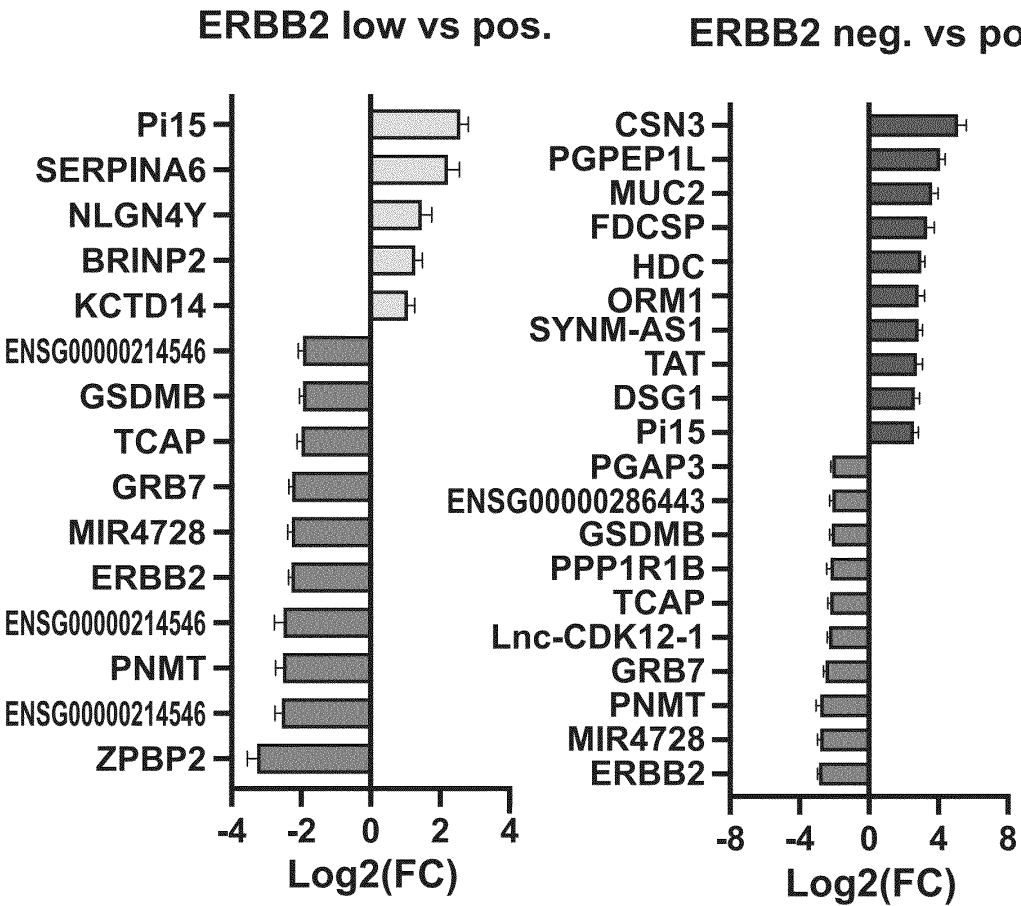
b

ER positive



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Figure 12 (cont.)

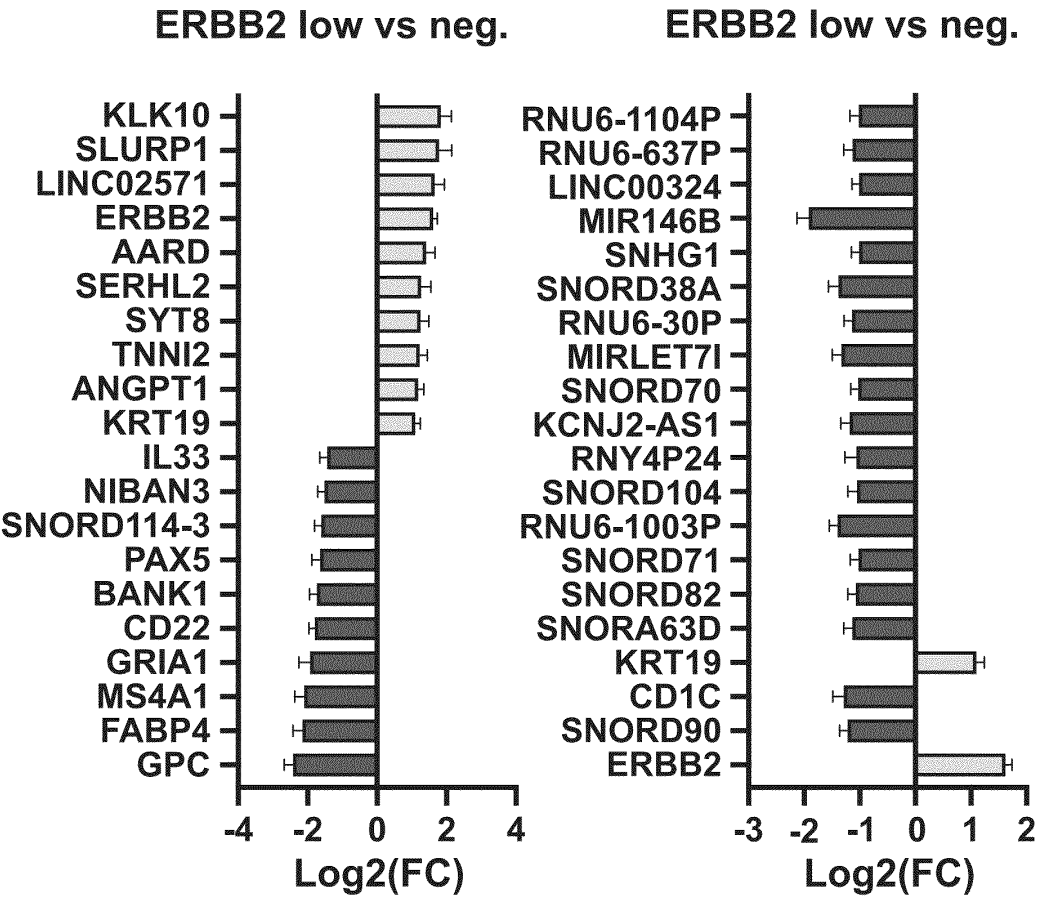
b (cont.)



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Figure 12 (cont.)

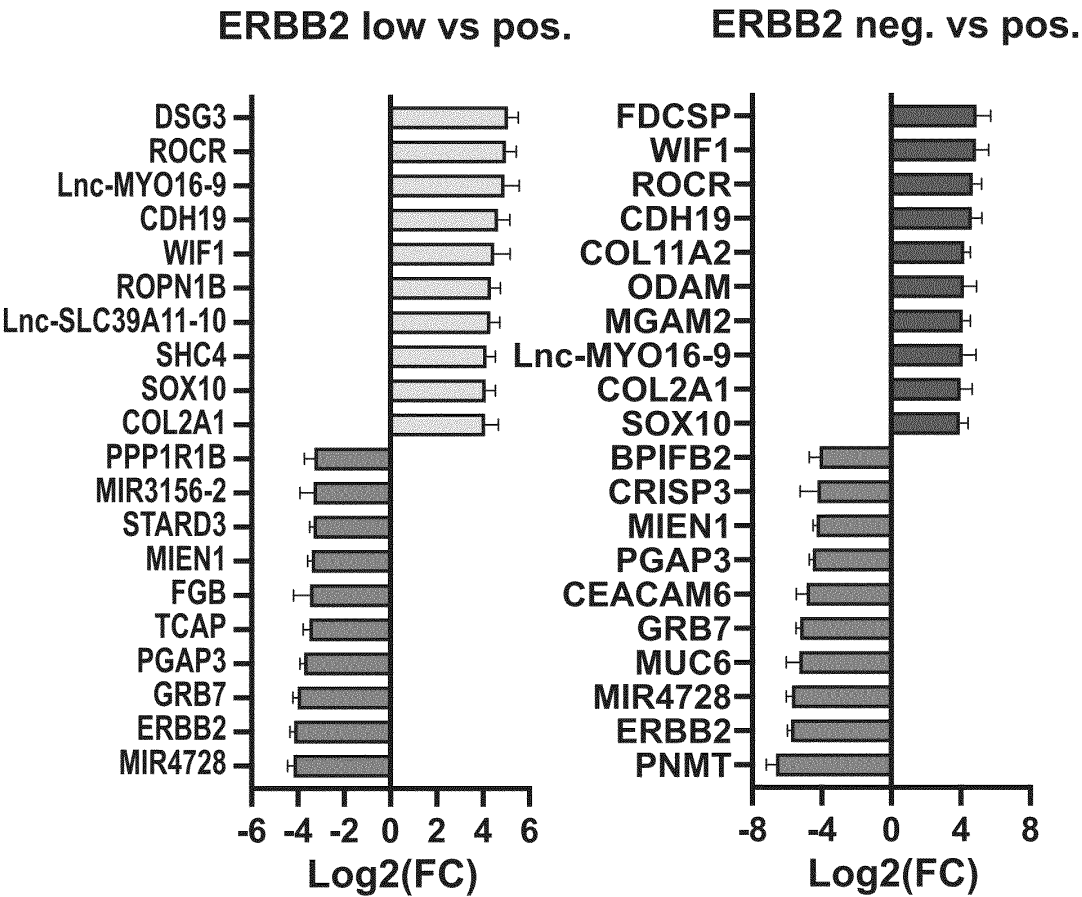
b (cont.)

ER negative



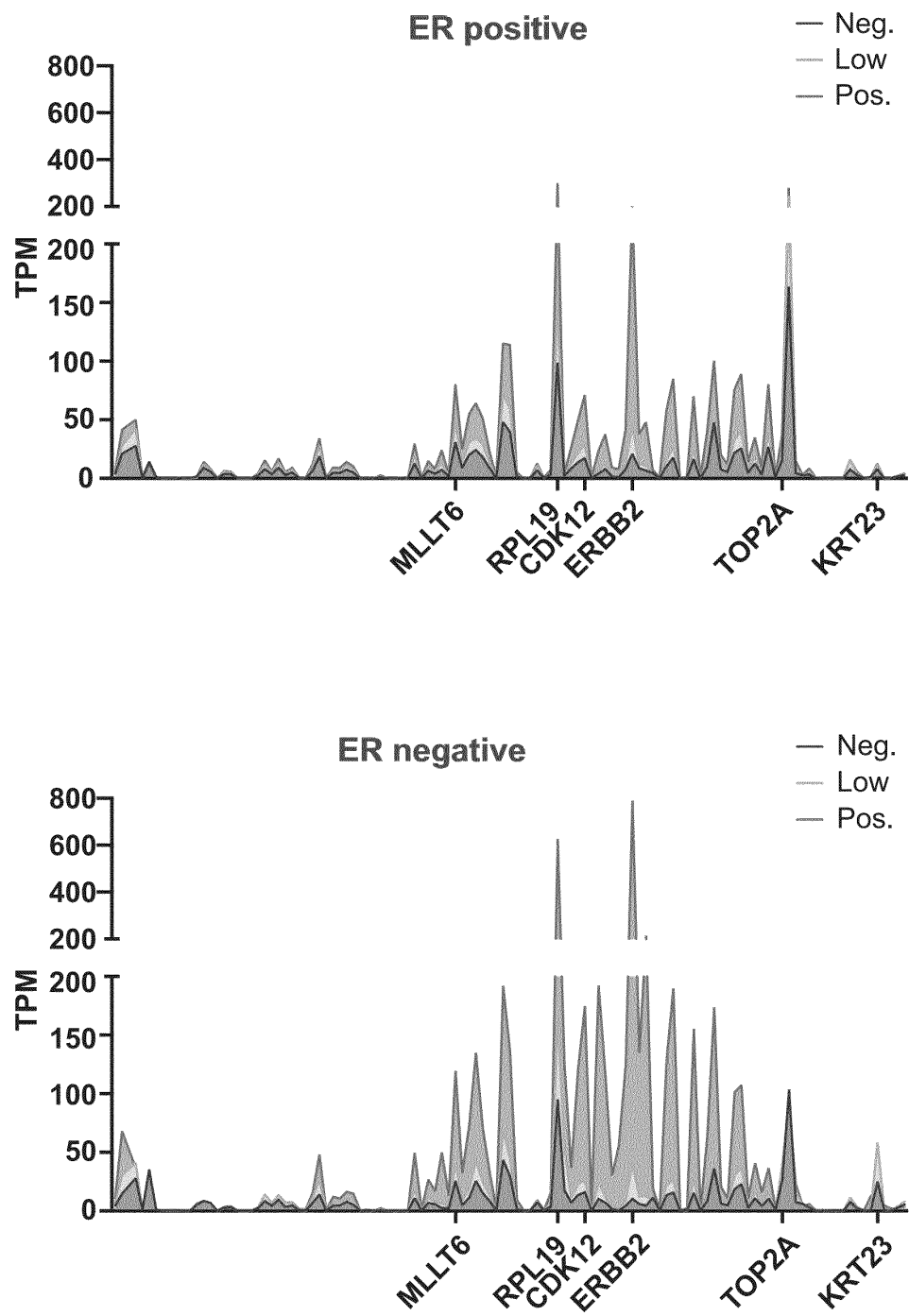
81 / 186
Figure 12 (cont.)

b (cont.)



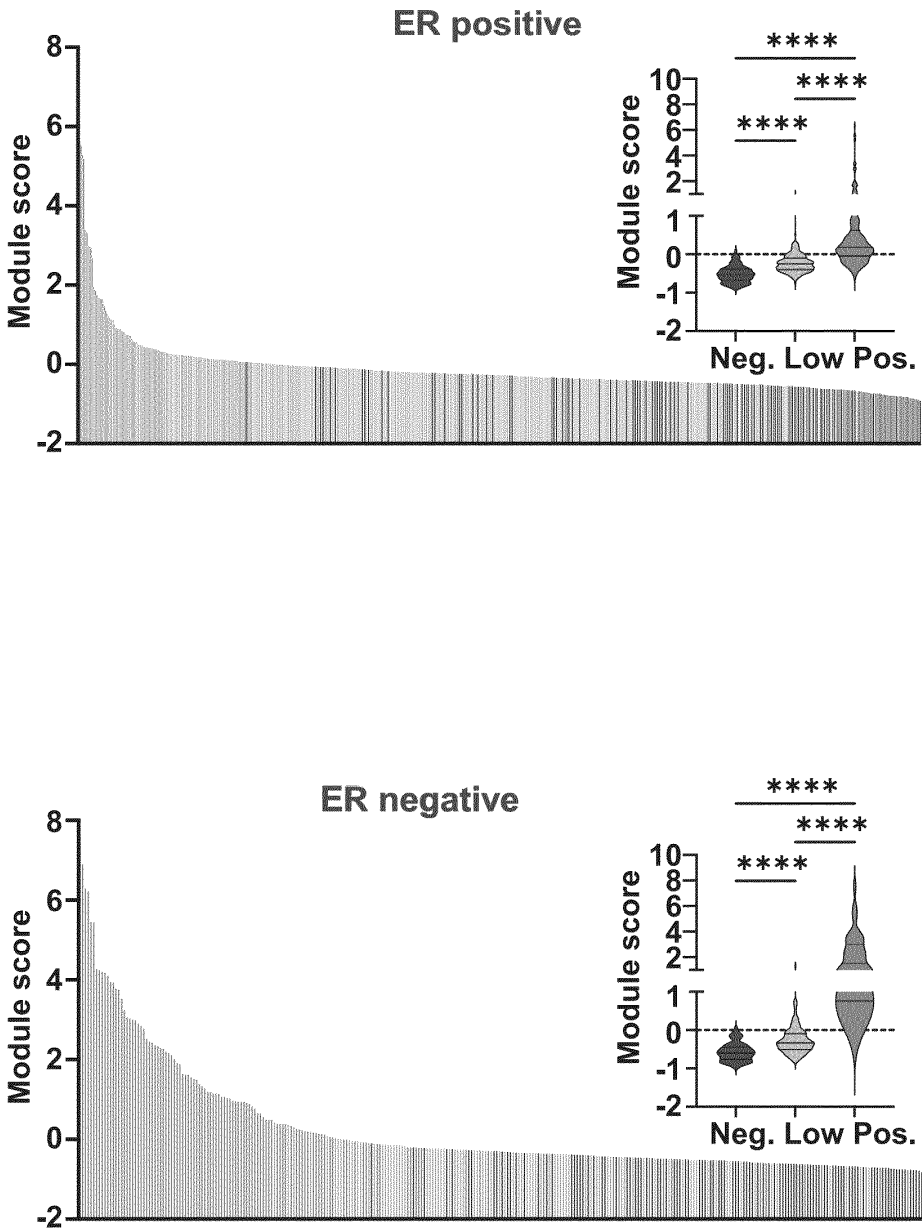
82 / 186
Figure 12 (cont.)

C



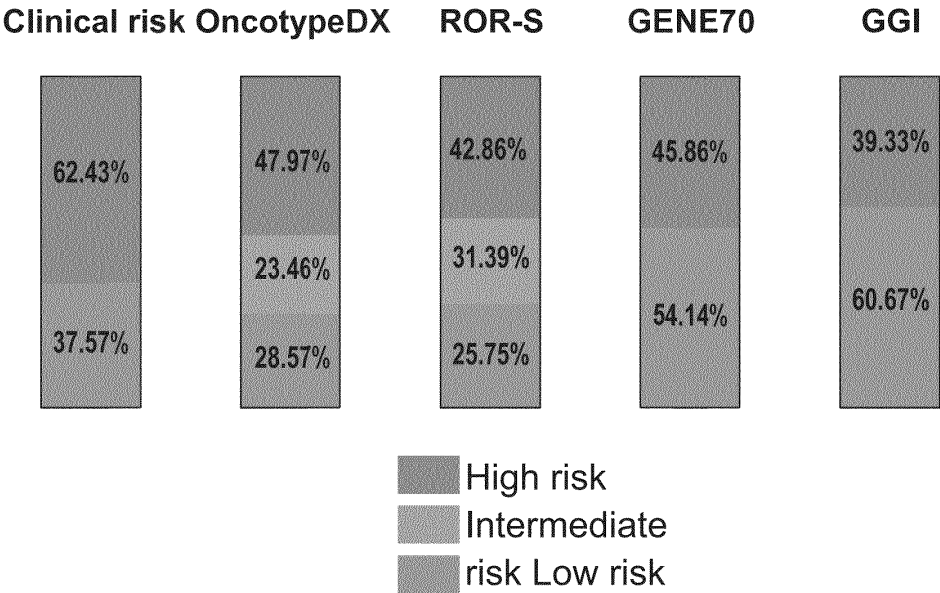
83 / 186
Figure 12 (cont.)

d

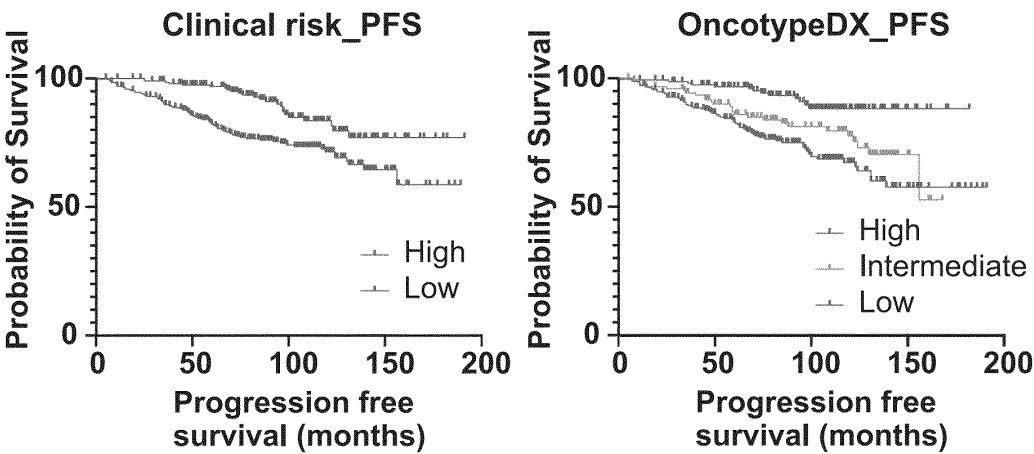


84 / 186
Figure 13

a

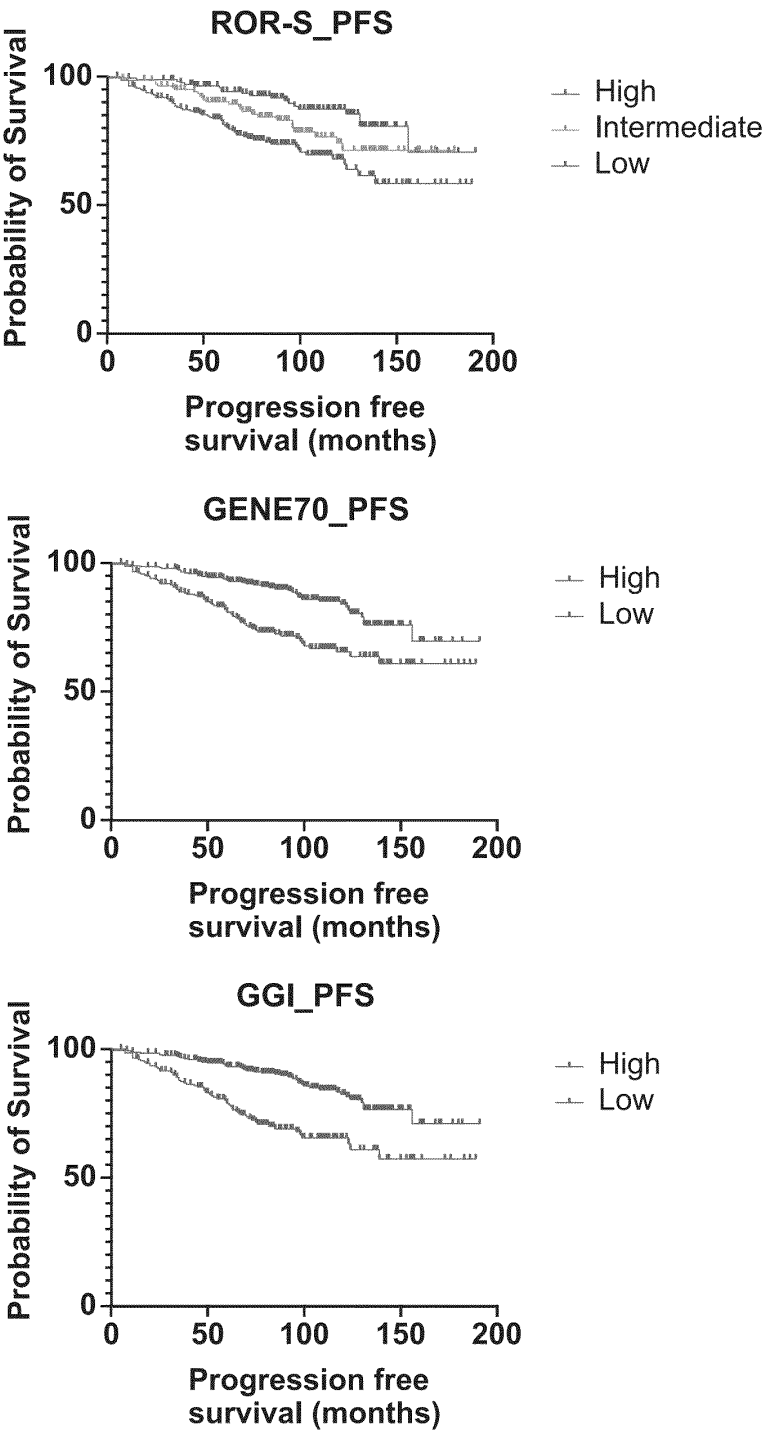


b



85 / 186
Figure 13 (cont.)

b (cont.)



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Figure 13 (cont.)

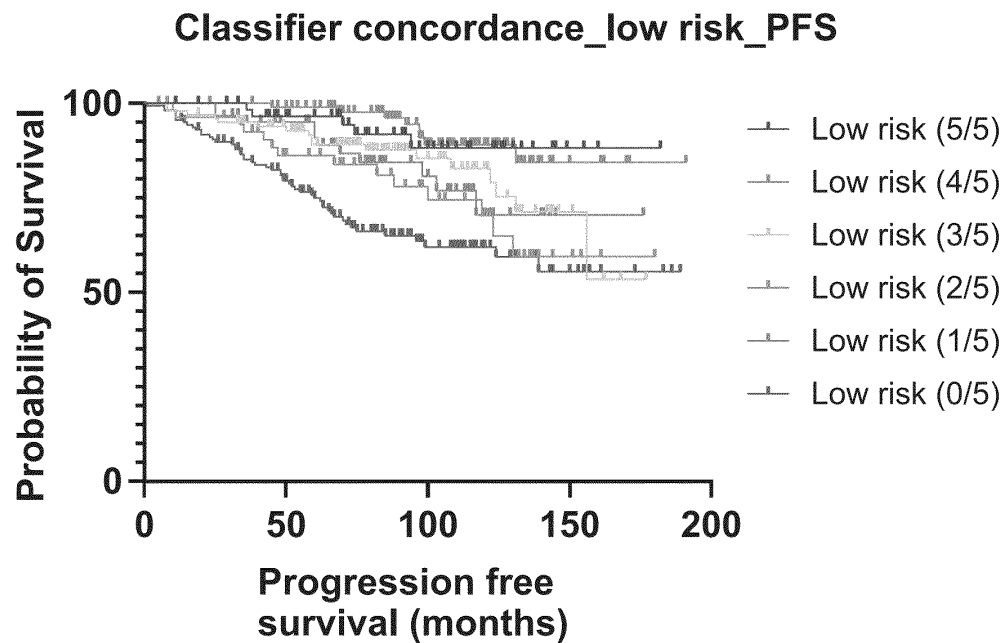
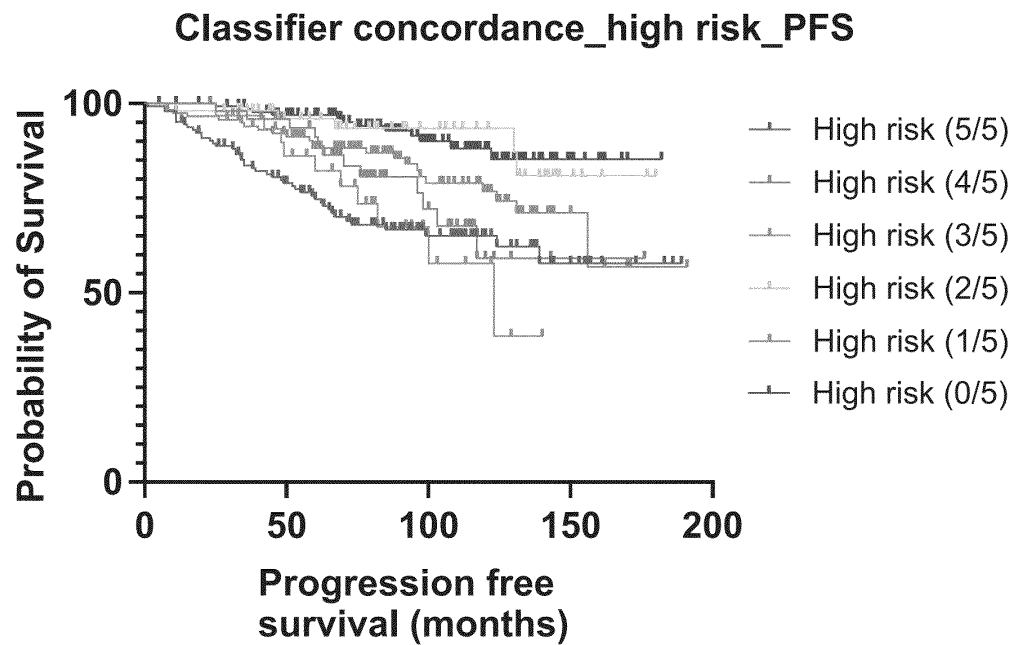
C

Concordance all samples (Cohen's Kappa)					
Clinical risk					
GGI	0.367				
GENE70	0.364	0.724			
OncoDX	0.209	0.458	0.43		
ROR-S	0.268	0.494	0.46	0.431	
	Clinical risk	GGI	GENE70	OncoDX	ROR-S

Concordance all samples (Cohen's Kappa) - high vs intermediate/low					
Clinical risk					
GGI	0.367				
GENE70	0.364	0.724			
OncoDX	0.288	0.74	0.653		
ROR-S	0.343	0.796	0.668	0.72	
	Clinical risk	GGI	GENE70	OncoDX	ROR-S

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Figure 13 (cont.)

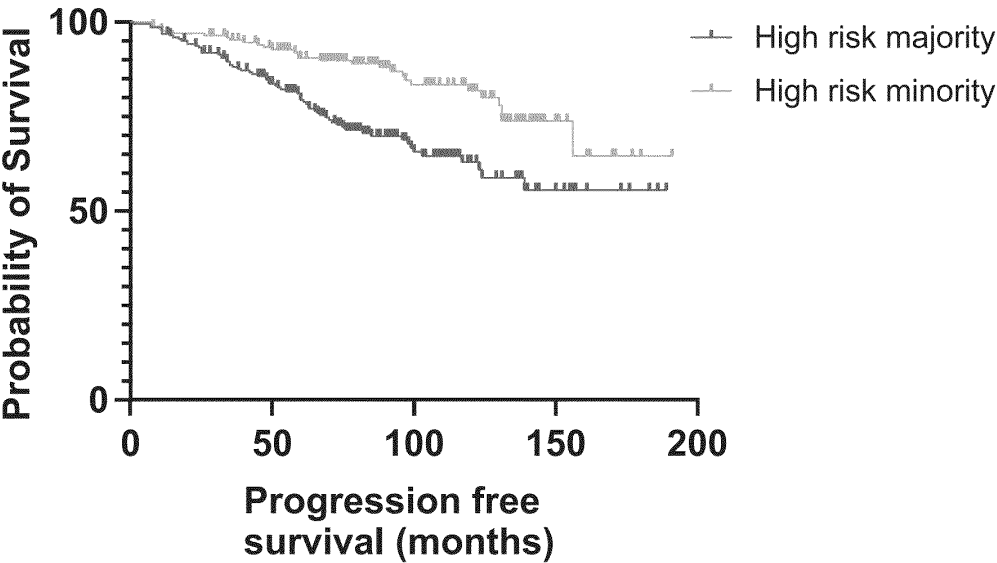
d



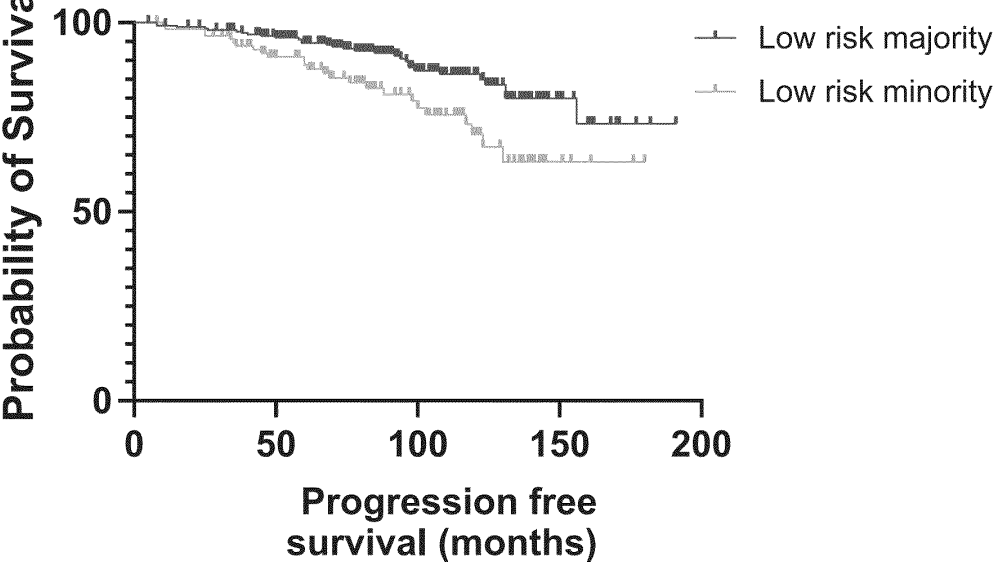
88 / 186
Figure 13 (cont.)

e

Majority vs minority concordance_high risk_PFS



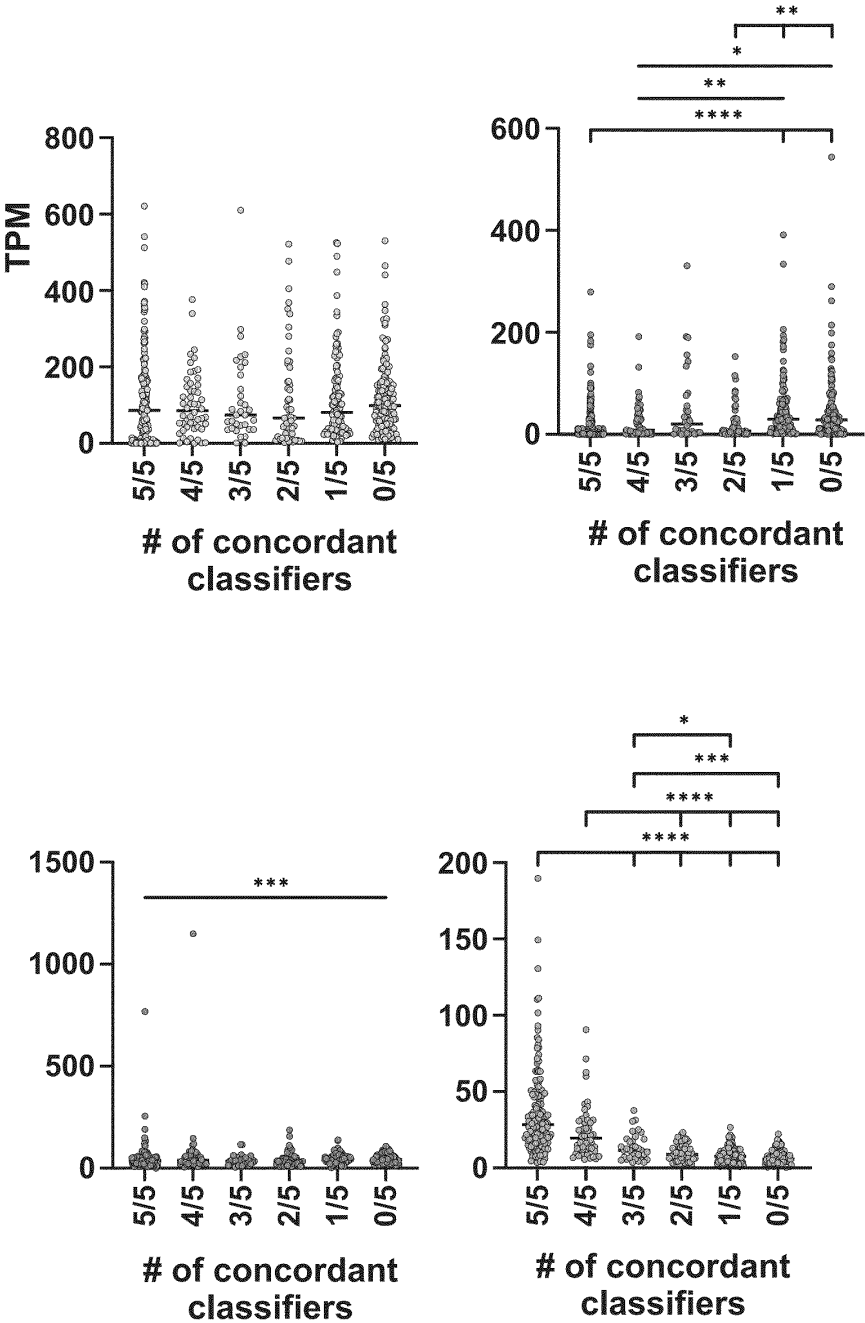
Majority vs minority concordance_low risk_PFS



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Figure 13 (cont.)

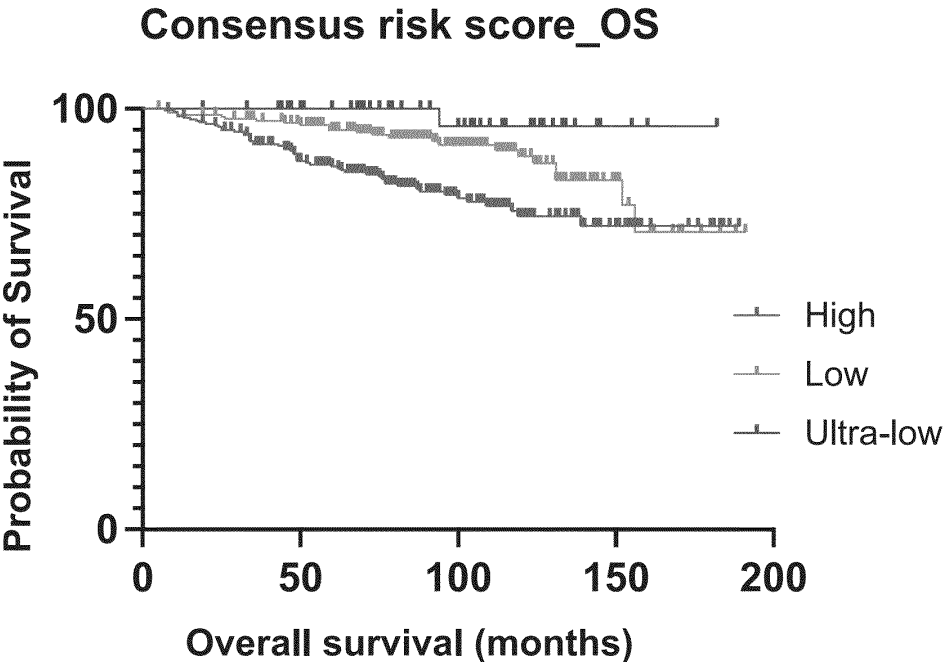
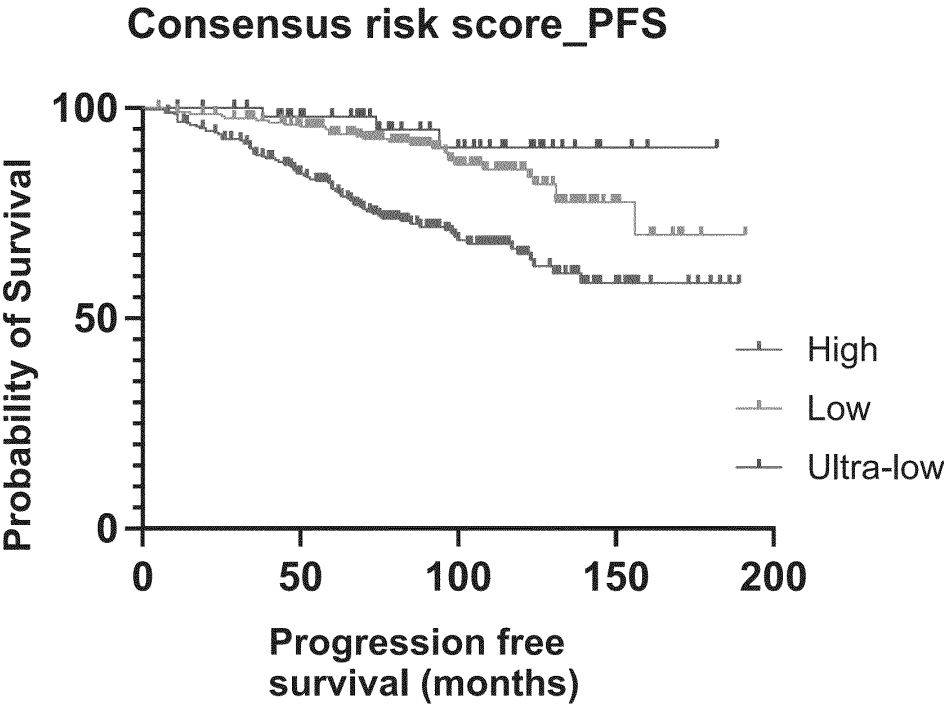
f

High risk classification



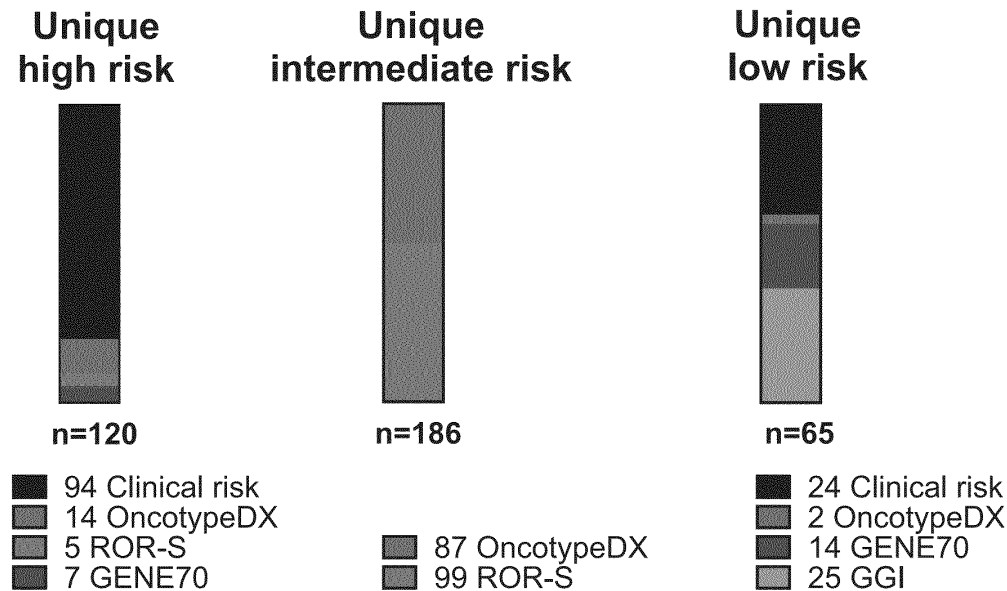
90 / 186
Figure 13 (cont.)

g

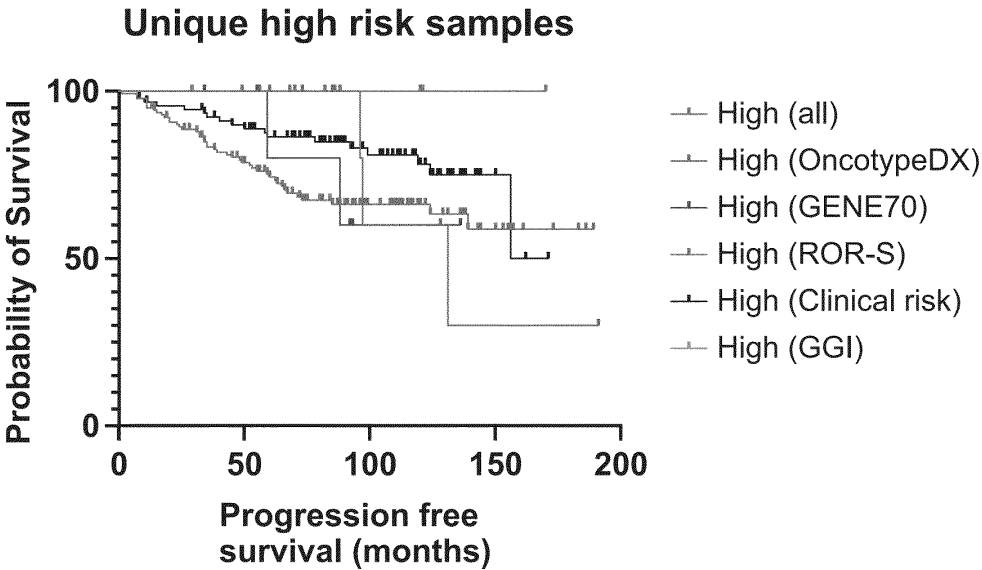


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Figure 14

a

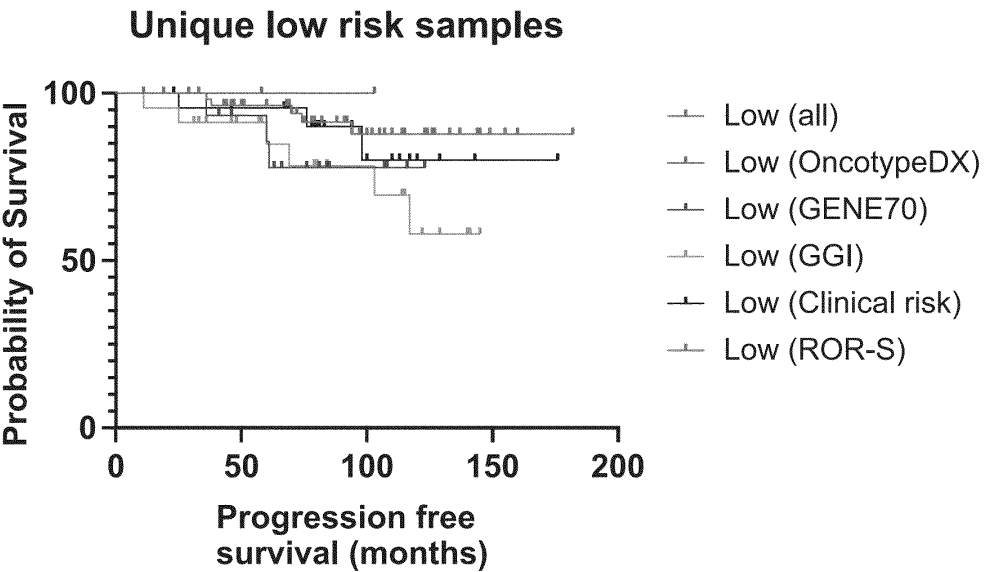
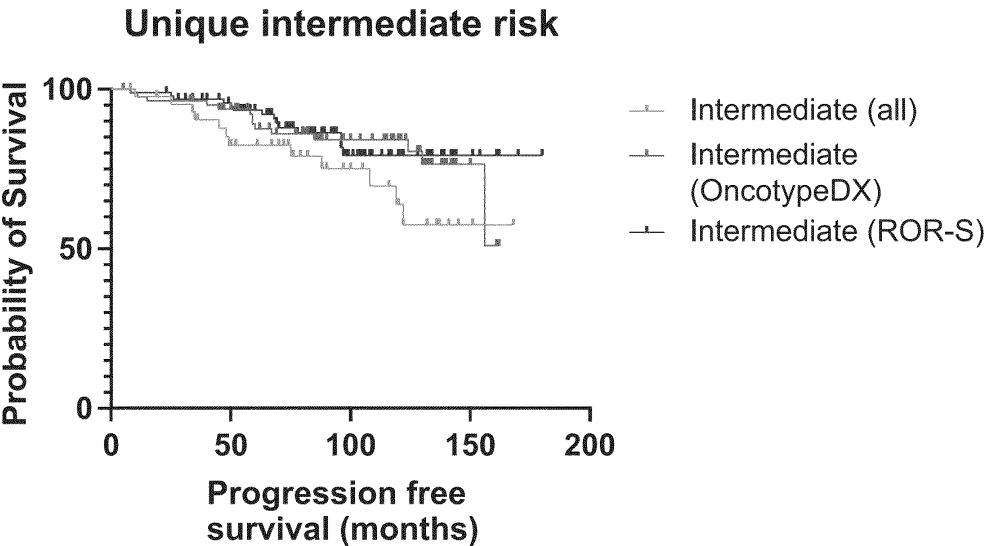


b



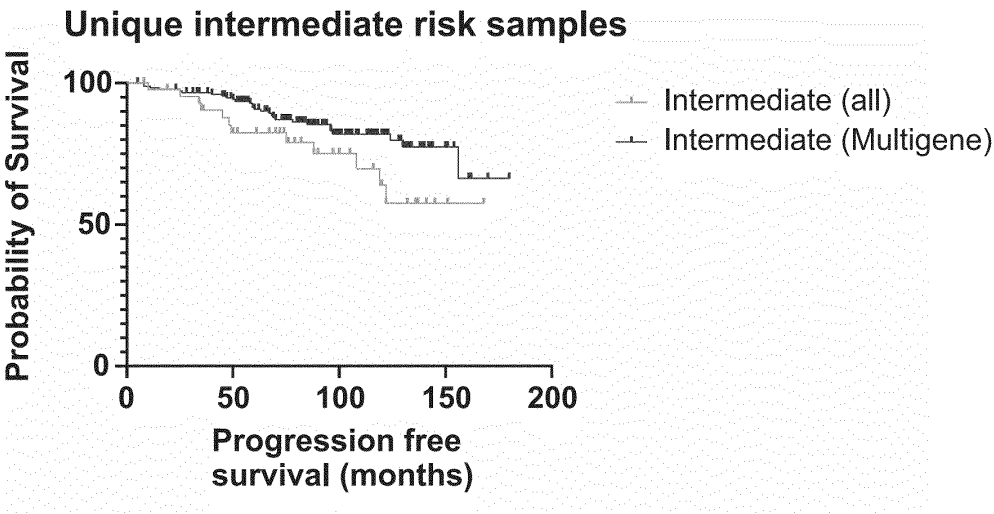
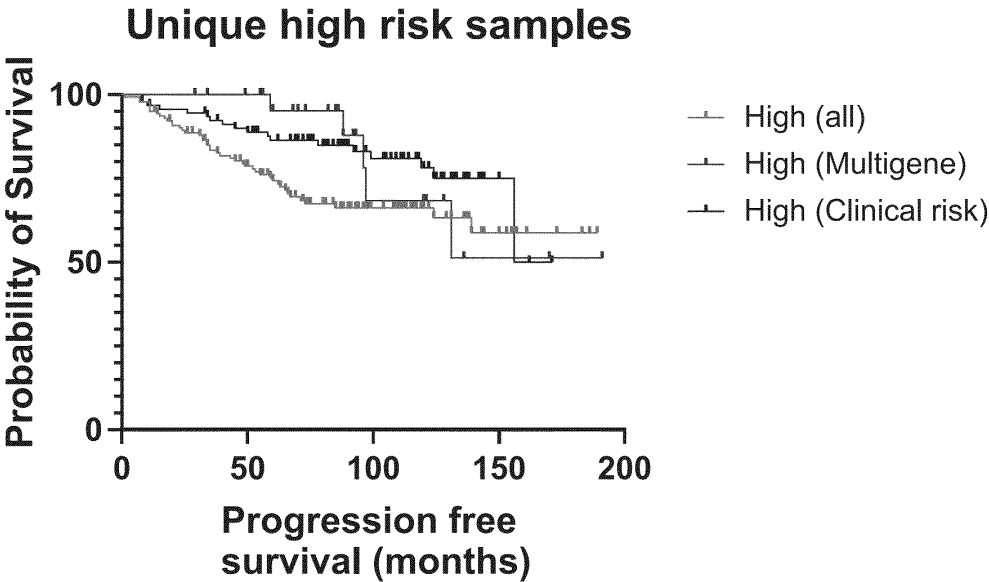
92 / 186
Figure 14 (cont.)

b (cont.)



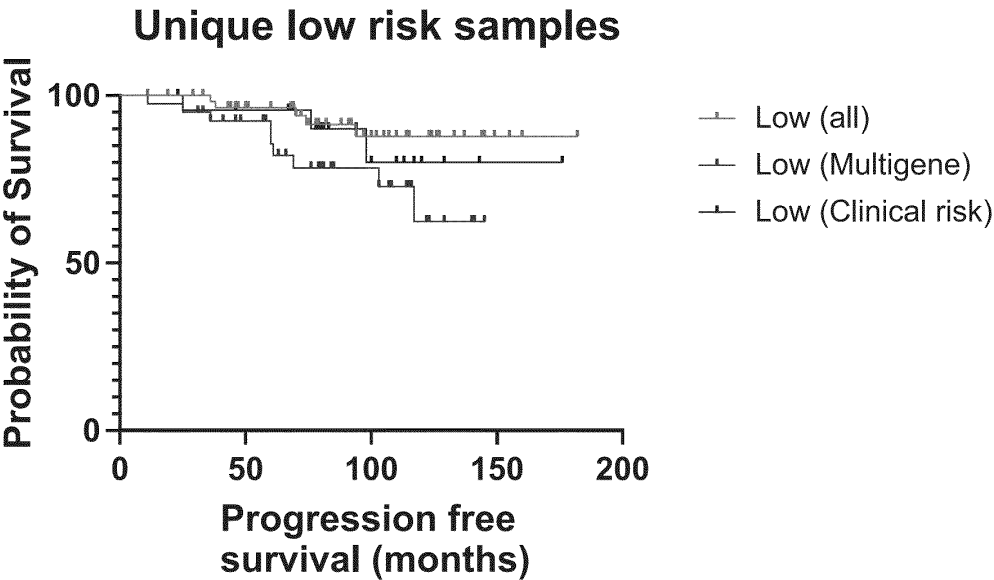
93 / 186
Figure 14 (cont.)

c

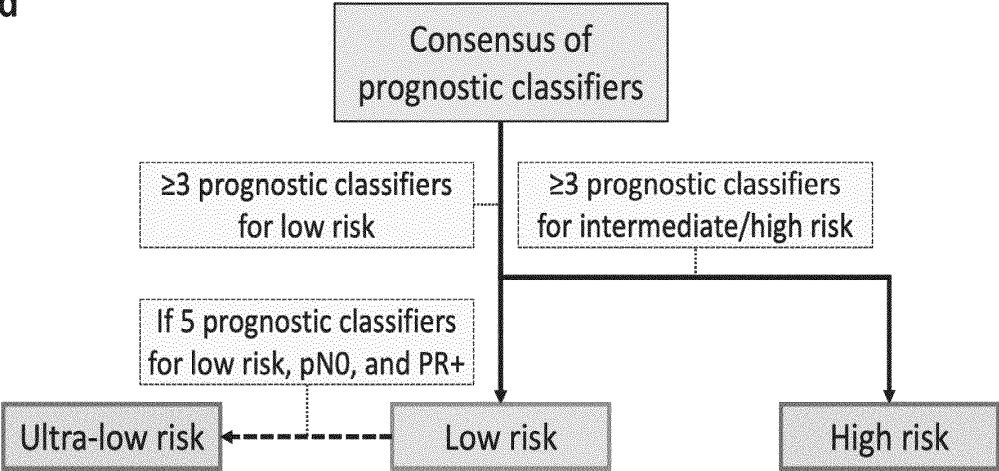


94 / 186
Figure 14 (cont.)

c (cont.)



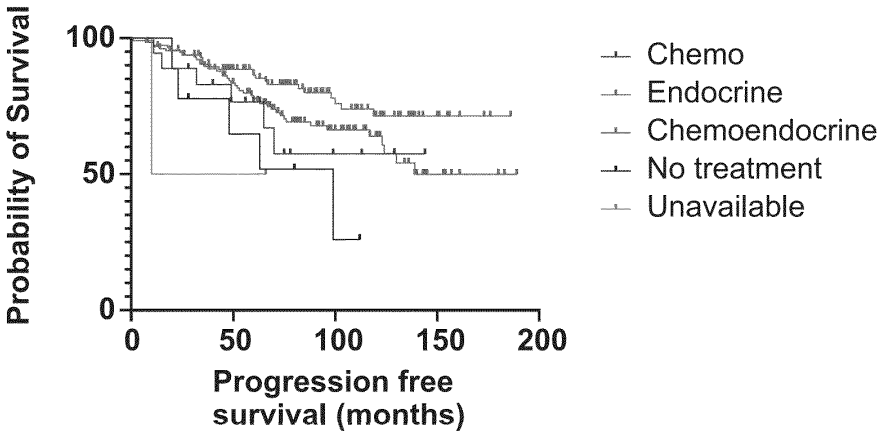
d



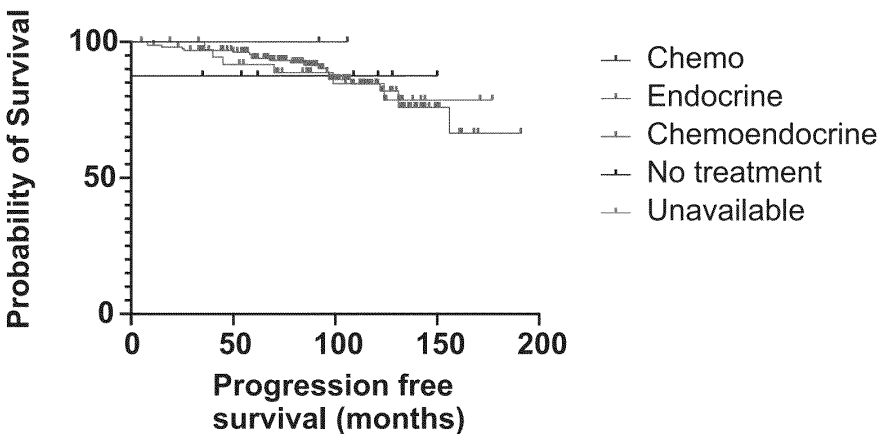
95 / 186
Figure 14 (cont.)

e

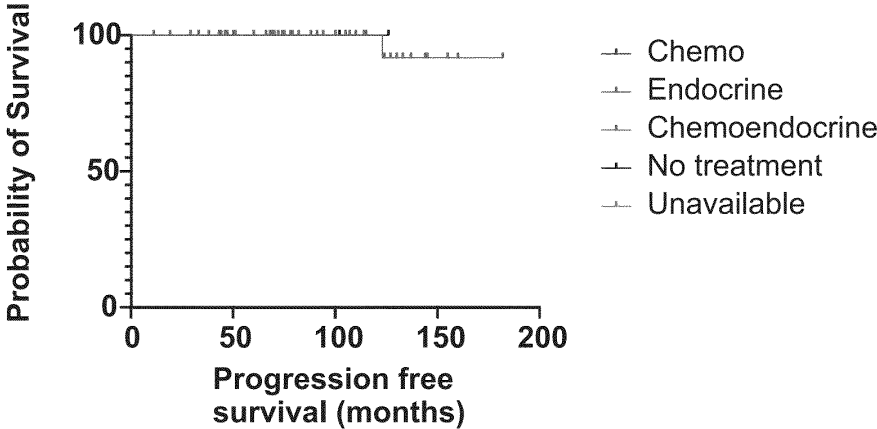
Consensus high risk x treatment category_PFS



Consensus high risk x treatment category_PFS



Consensus high risk x treatment category_PFS



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Figure 15

Variable	N	Hazard ratio	p
Metabolic_sig_Trop2_TNBC_Survival	933		<0.001
VEGF_Signature	933		<0.001
RISK_OncotypeDX_score	933		<0.001
RISK_GENE70_score	933		<0.001
RISK_PAM50_ROR_score	933		<0.001
Glycolysis_Signature	933		<0.001
Hypoxia_Angiogenesis_Inflammatory_MDX	933		<0.001
RISK_GGI	933		<0.001
RAD51	933		<0.001
CCNB1	933		<0.001
RISK_GGI_score	933		<0.001
Module11_Prolif	933		<0.001
Retinoblastoma_pathway_loss_of_function_Rbsig	933		<0.001
PMID_17493263_proliferation	933		<0.001
MAPs_Mitotic_kinases_neoadj_chemo17	933		<0.001
AURKA	933		<0.001
RISK_GENE70	933		<0.001
Genefu_Luminal_index_Correlation_to_centroid_PAM50_Luma	933		<0.001
E2F4_scores	933		<0.001
Genefu_Correlation_to_centroid_PAM50_Her2	933		<0.001
Proliferation_MDX	933		<0.001
Genefu_Correlation_to_centroid_PAM50_Normal	933		<0.001
CCNE1	933		<0.001

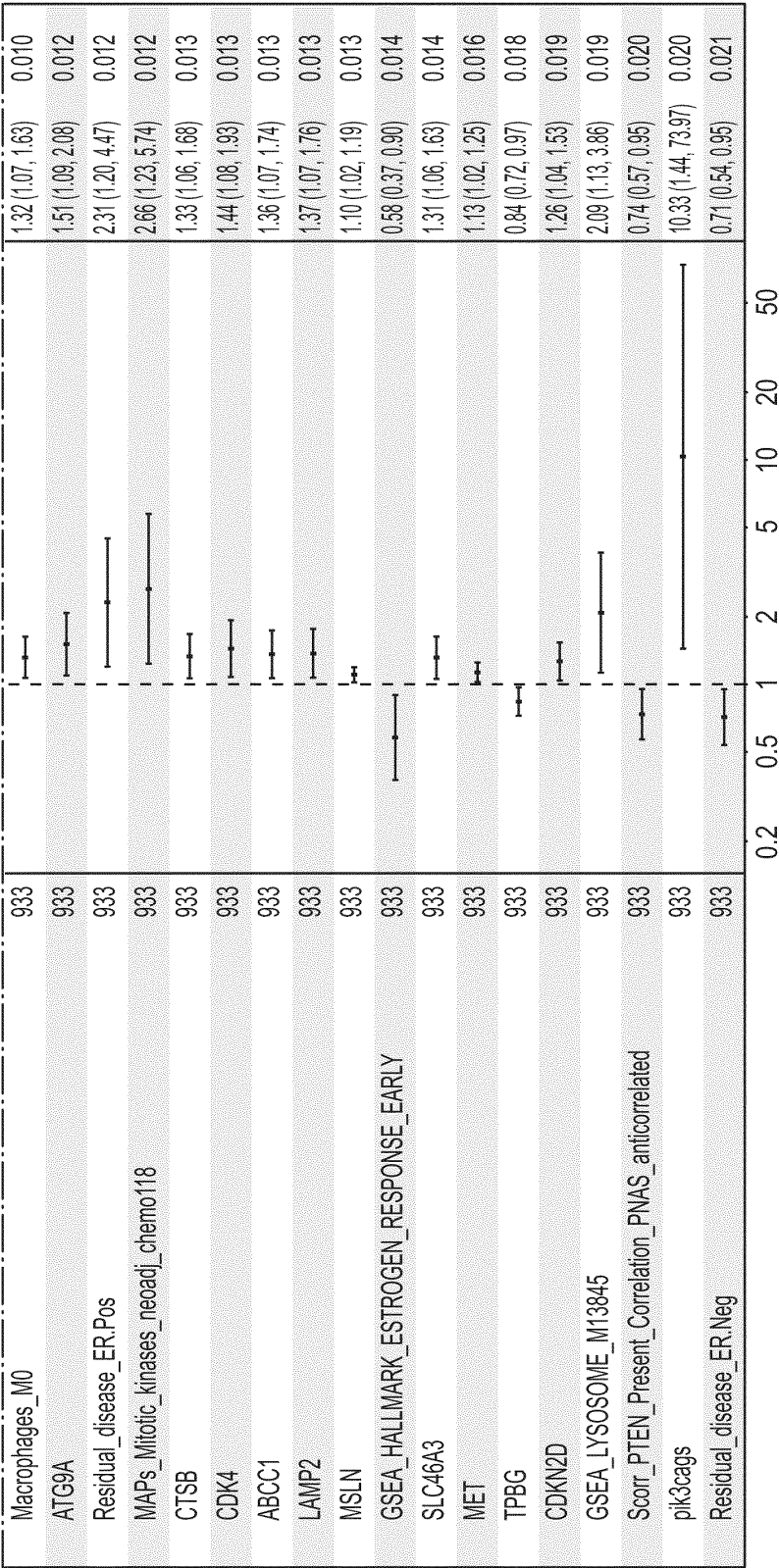
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Figure 15 (cont.)

Endocytic_uncoat	933				2.55 (1.70, 3.83)	<0.001
PGR	933				0.89 (0.84, 0.93)	<0.001
RISK_PAM50_ROR	530	High			Reference	
	182	Intermediate			0.62 (0.42, 0.92)	0.017
	221	Low			0.38 (0.25, 0.59)	<0.001
TK1	933				1.34 (1.18, 1.54)	<0.001
PMID_17493263_second_luminal	933				2.18 (1.53, 3.09)	<0.001
MKI67	933				1.27 (1.14, 1.42)	<0.001
FOXM1	933				1.24 (1.12, 1.37)	<0.001
RISK_OncotypeDX_Sparano.etal.2018.in.TAILORx.intermediate..11to.26.	603	High			Reference	
	159	Intermediate			0.69 (0.46, 1.04)	0.075
	171	Low			0.33 (0.19, 0.56)	<0.001
TAMR13_scores	933				0.82 (0.74, 0.90)	<0.001
MOTERA_sig_ESR1_mutations_Cancer_Res_2021	933				0.75 (0.64, 0.87)	<0.001
BIOCARTA_ATRBRCA_PATHWAY20	933				2.31 (1.49, 3.57)	<0.001
SEMENZA_HIF1_TARGETS	933				1.92 (1.36, 2.73)	<0.001
Endocytic_actin	933				2.14 (1.42, 3.23)	<0.001
ARID1A	933				0.47 (0.31, 0.70)	<0.001
cMET_FAK_CDK2_axis	933				1.39 (1.16, 1.67)	<0.001
ESR_PGR_ave	933				0.91 (0.86, 0.96)	<0.001
Endocytic_coat	933				4.00 (1.83, 8.75)	<0.001
NECTIN4	933				1.29 (1.12, 1.49)	<0.001
TYMS	933				1.24 (1.10, 1.41)	<0.001
GSEA_KEGG_ABC_TRANSPORTERS_M11911	933				1.28 (1.11, 1.48)	<0.001

Figure 15 (cont.)

Genefu_Correlation_to_centroid_PAM50_Basal	933		1.62 (1.22, 2.16)	<0.001
HSP90AB1	933		1.44 (1.16, 1.79)	<0.001
olaparib_Sensitivity	933		1.73 (1.25, 2.40)	<0.001
FOLH1	933		1.26 (1.10, 1.46)	0.001
HRD_Race_Classifier	933		2.40 (1.42, 4.07)	0.001
MUC4	933		1.14 (1.05, 1.24)	0.002
TOP2A	933		1.18 (1.06, 1.30)	0.002
LAMP1	933		1.58 (1.19, 2.10)	0.002
CD276	933		1.49 (1.16, 1.92)	0.002
HS_Red1	933		1.62 (1.20, 2.20)	0.002
Scorr_PTEN_Present_Correlation_PNAS_correlated	933		1.82 (1.25, 2.66)	0.002
olaparib_Resistance	933		1.65 (1.19, 2.29)	0.002
GSEA_KEGG_LYSOSOME_M11266	933		3.95 (1.63, 9.60)	0.002
FLOT2	933		1.33 (1.10, 1.61)	0.003
HALLMARK_DNA_REPAIR	933		4.00 (1.58, 10.10)	0.003
CEACAM5	933		1.10 (1.03, 1.17)	0.005
EGFR	933		1.14 (1.04, 1.25)	0.005
BIOCARTA_DNAFRAGMENT_PATHWAY	933		1.60 (1.14, 2.26)	0.007
GSEA_GOBP_MEMBRANE_RAFT_ASSEMBLY	933		1.84 (1.18, 2.87)	0.007
HS_Green15	933		5.44 (1.55, 19.15)	0.008
Mast_cells	933		0.86 (0.76, 0.96)	0.009
Genefu_Luminal_index_Correlation_to_centroid_PAM50_LumB	933		1.99 (1.19, 3.34)	0.009
CDK2	933		1.45 (1.09, 1.91)	0.009
VEGFA	933		1.21 (1.05, 1.39)	0.010

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Figure 15 (cont.)



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Figure 16

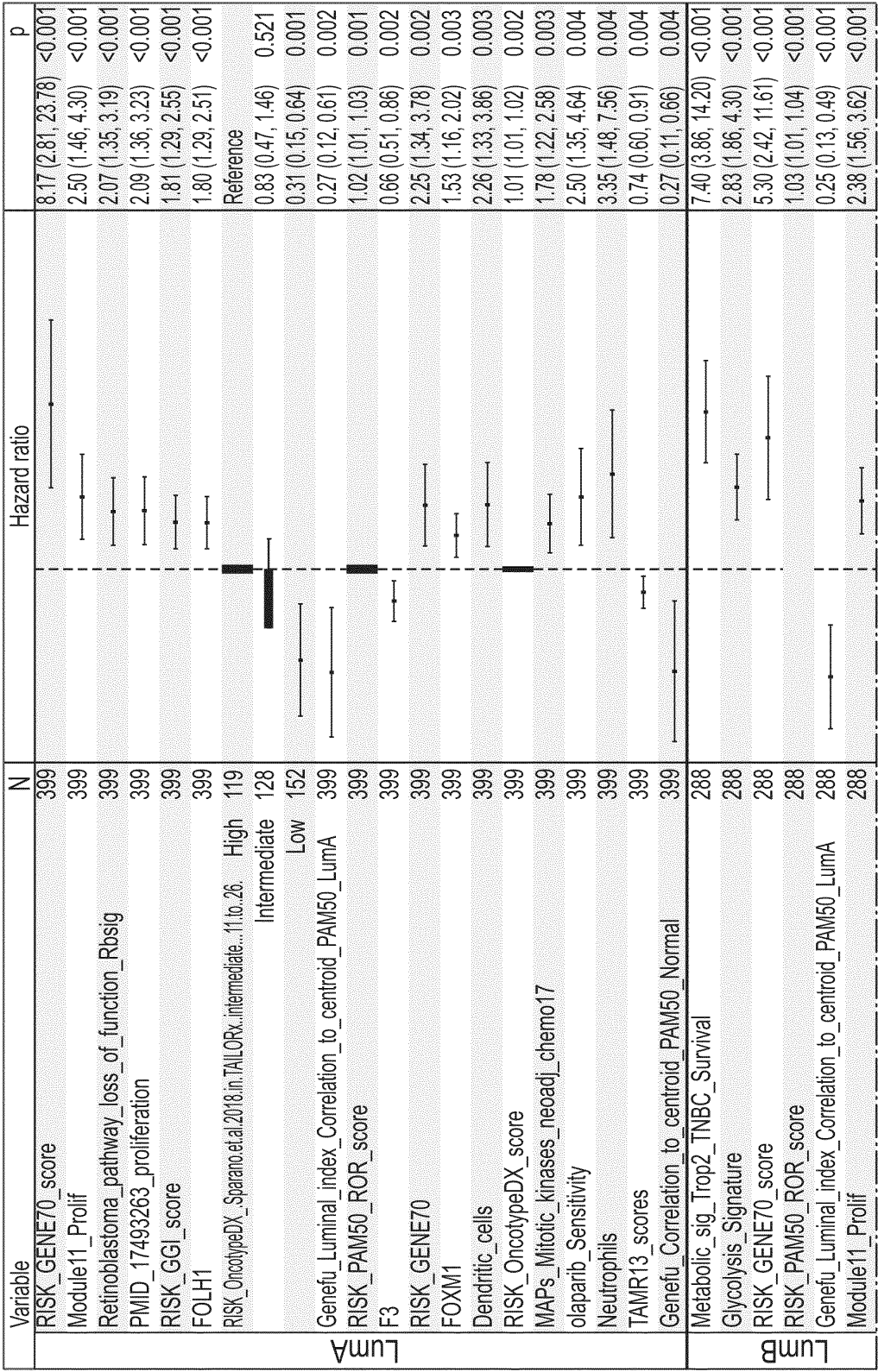
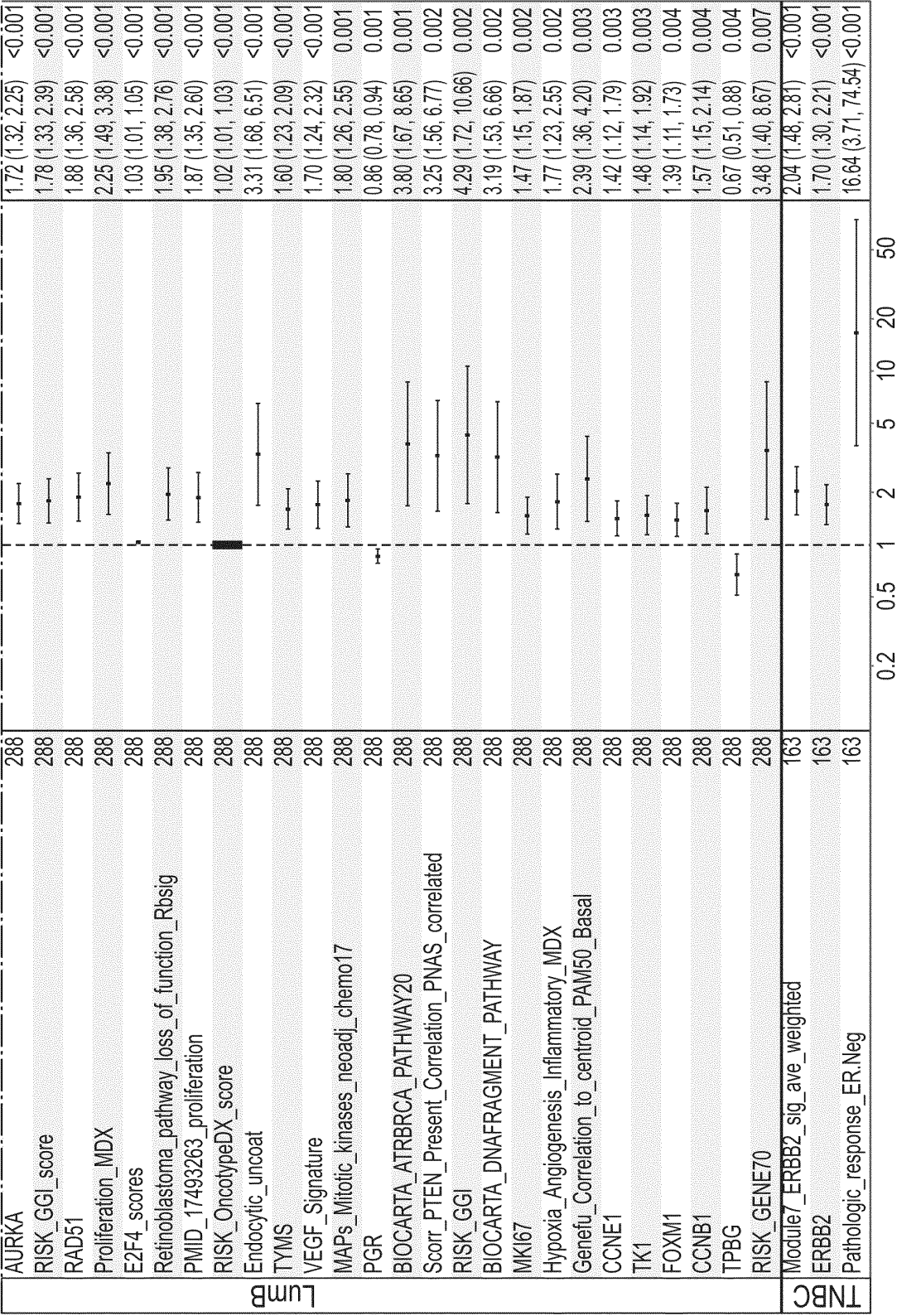
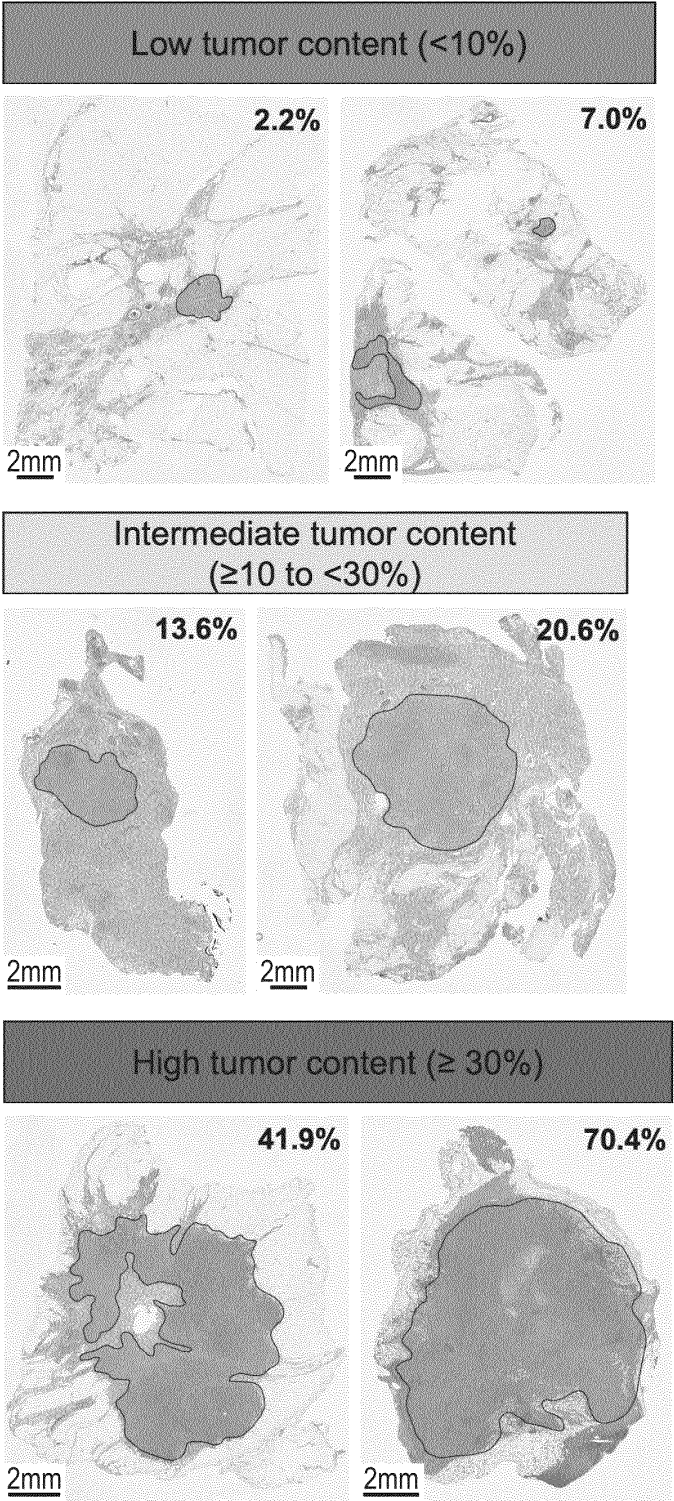


Figure 16 (cont.)

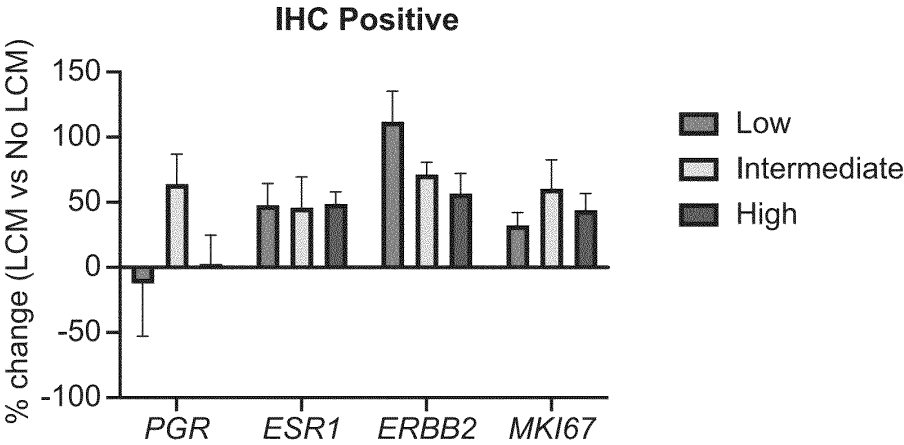


a

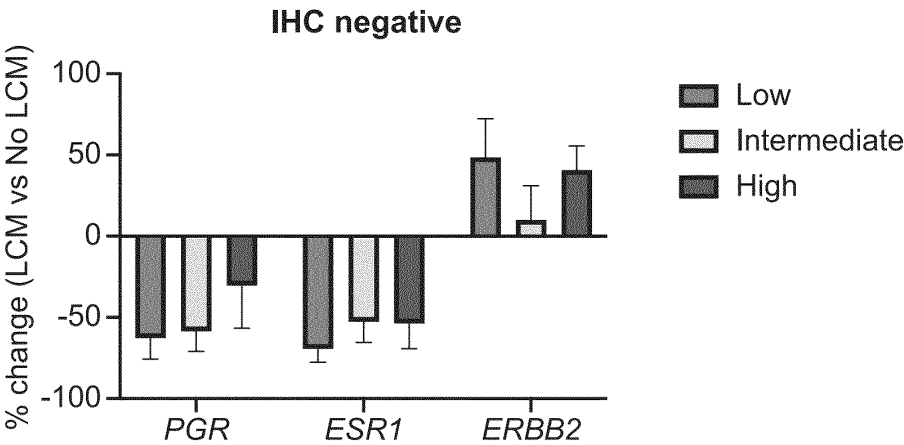


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Figure 17 (cont.)

b

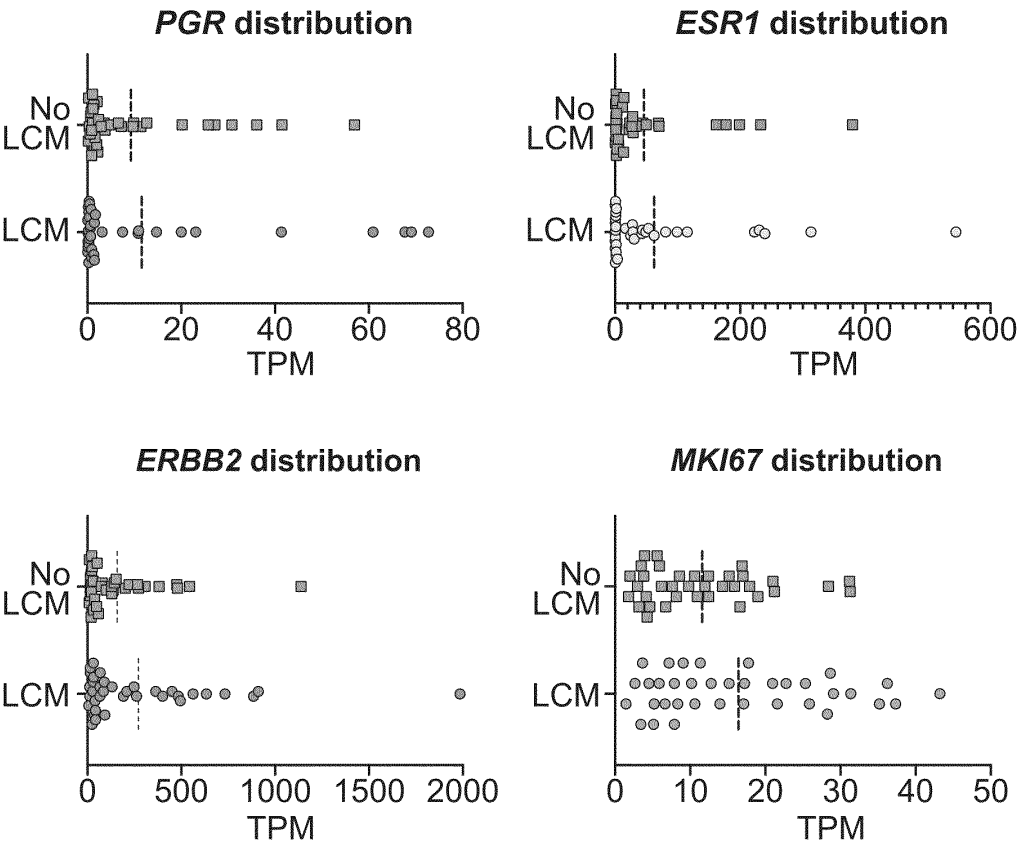


c



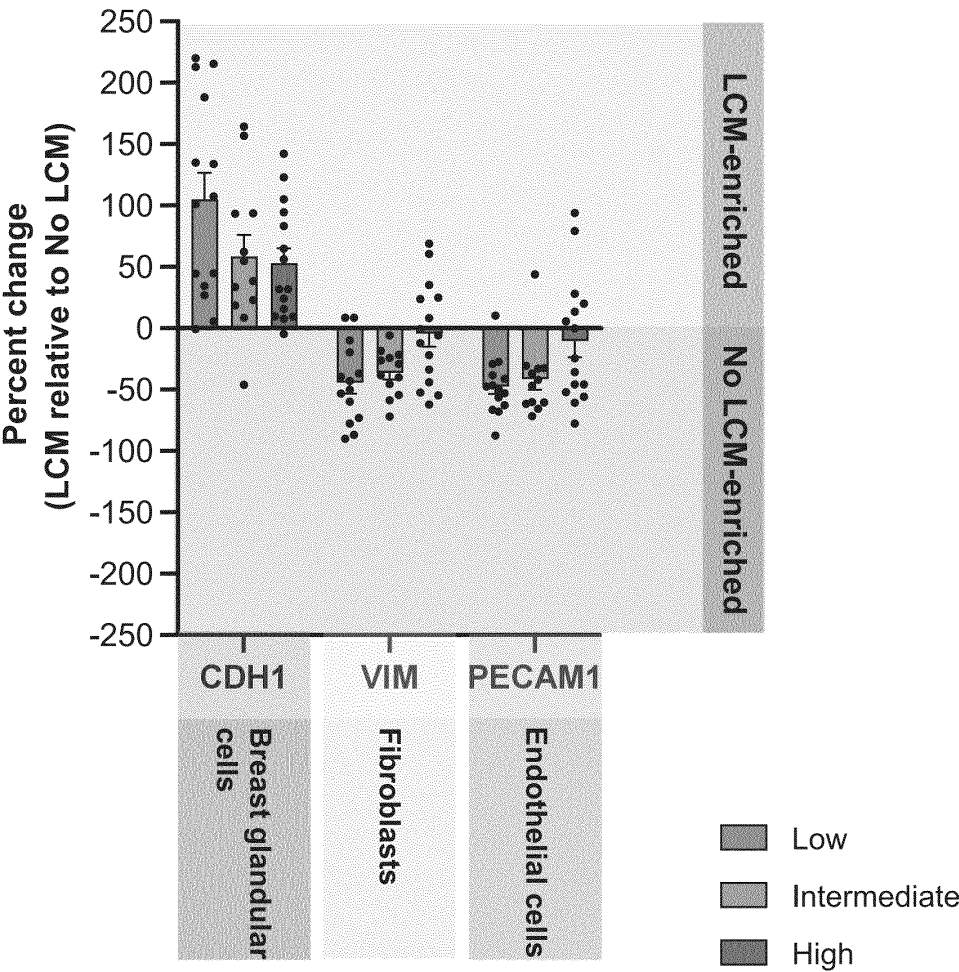
104 / 186
Figure 17 (cont.)

d

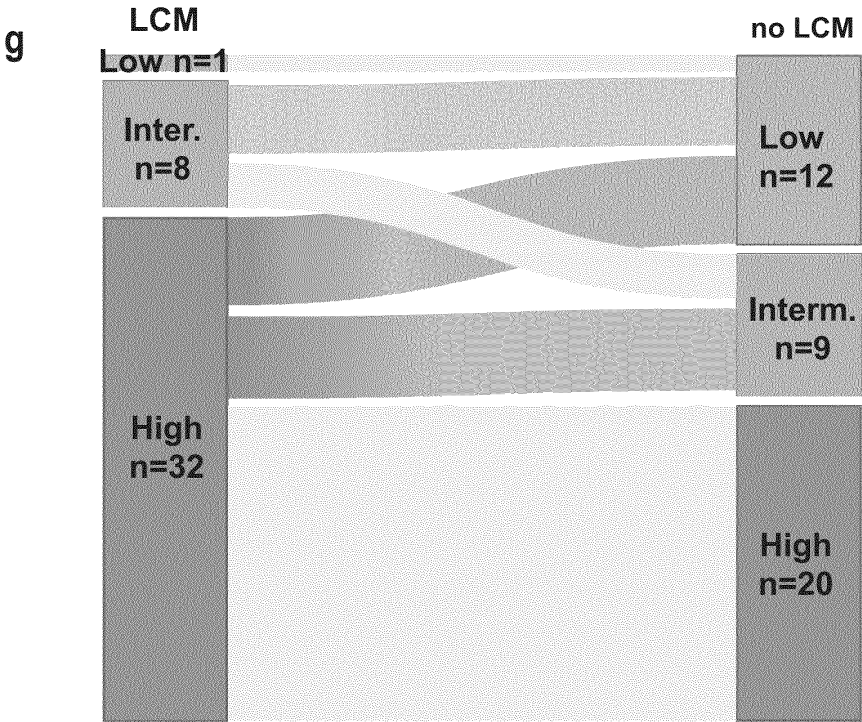
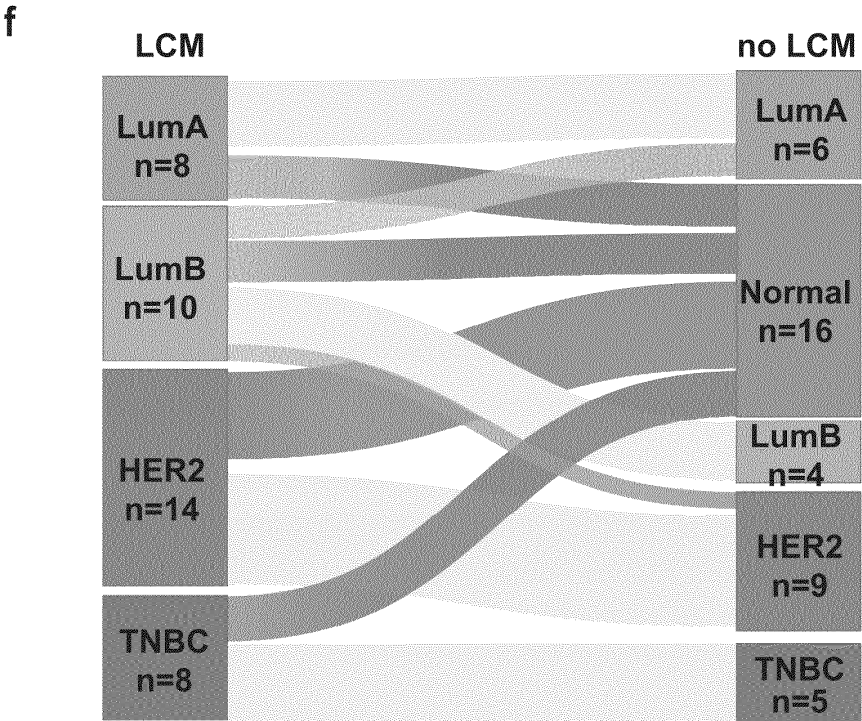


105 / 186
Figure 17 (cont.)

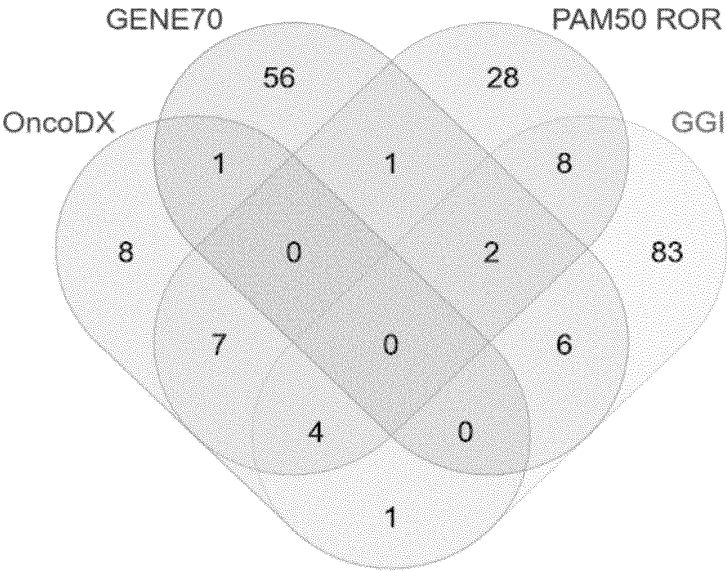
e



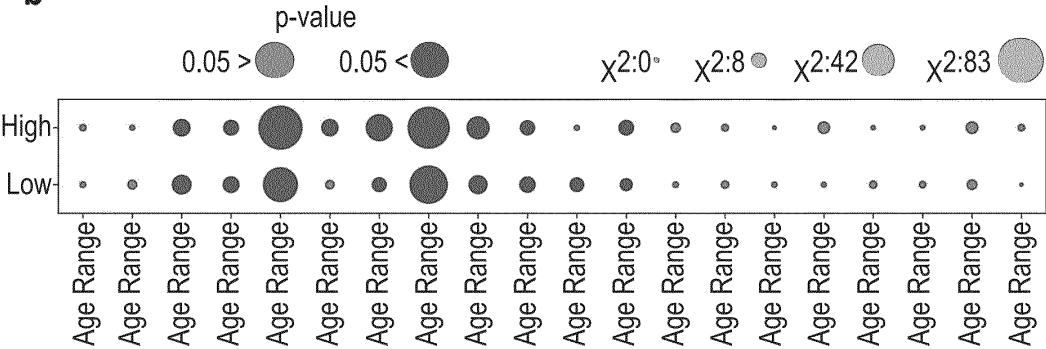
106 / 186
Figure 17 (cont.)



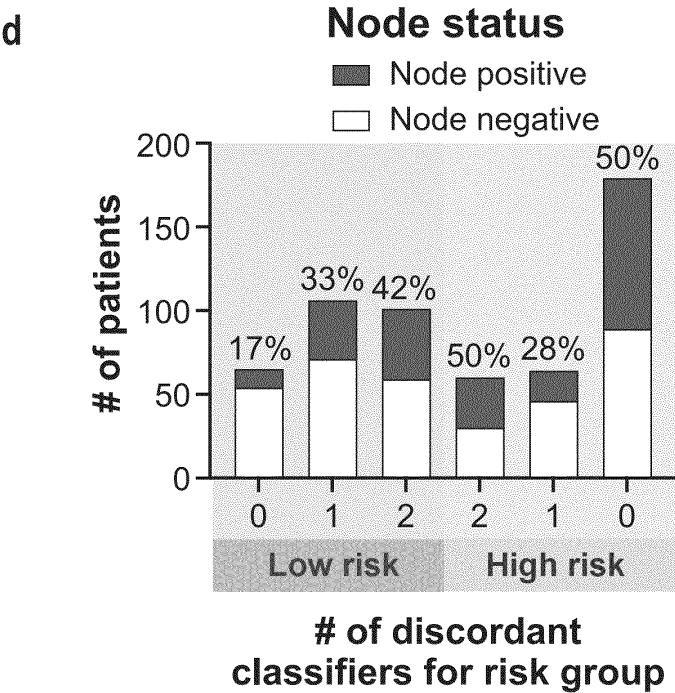
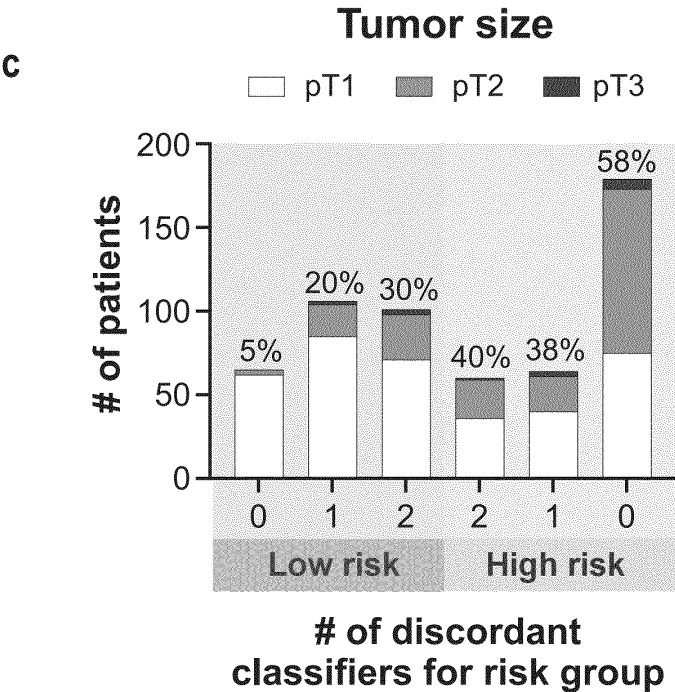
a



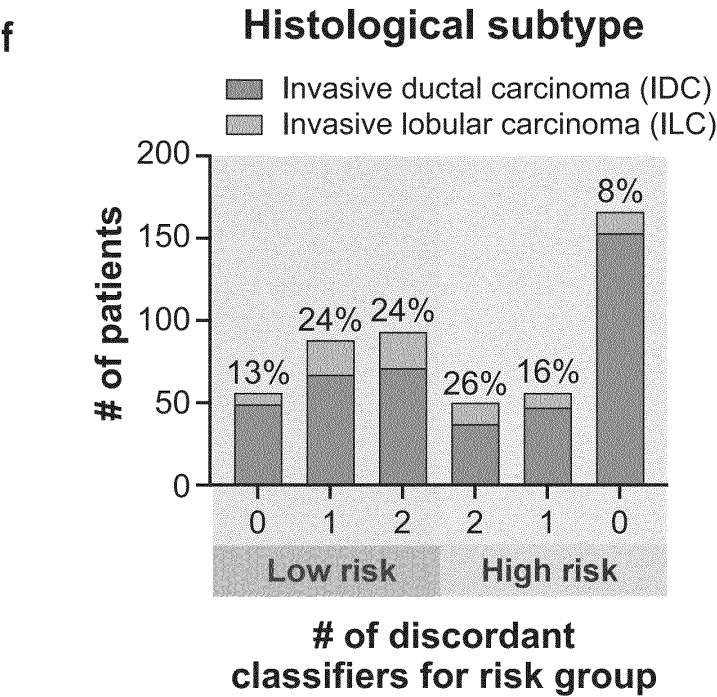
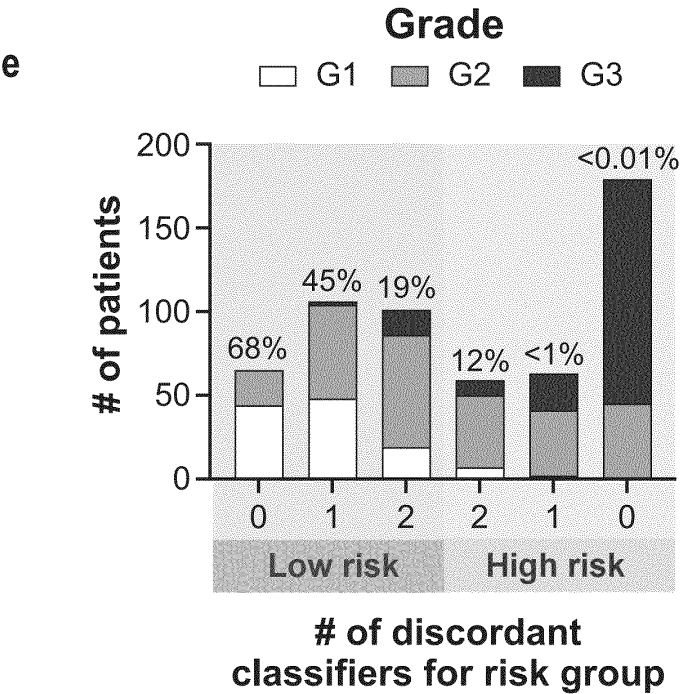
b



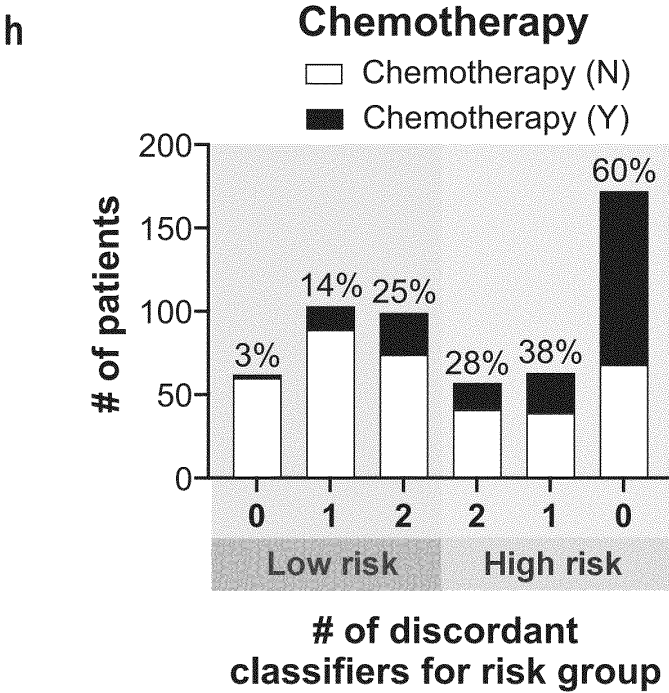
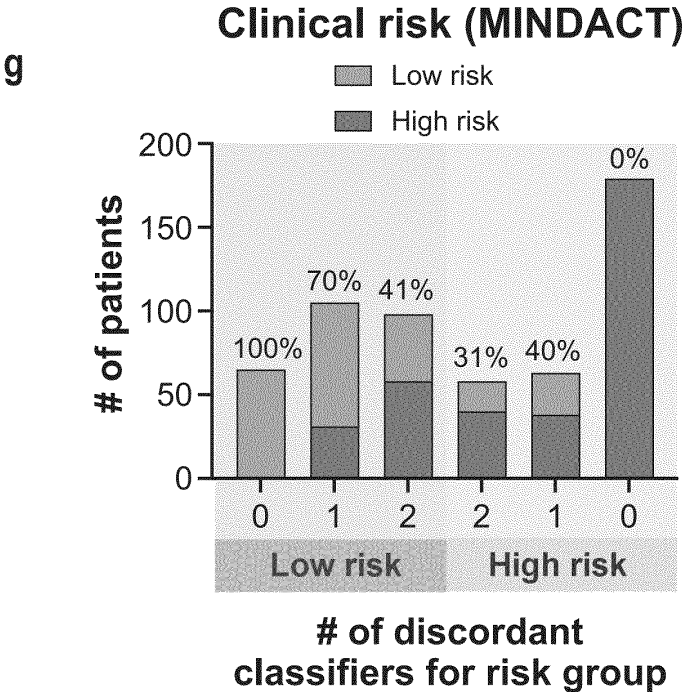
108 / 186
Figure 18 (cont.)



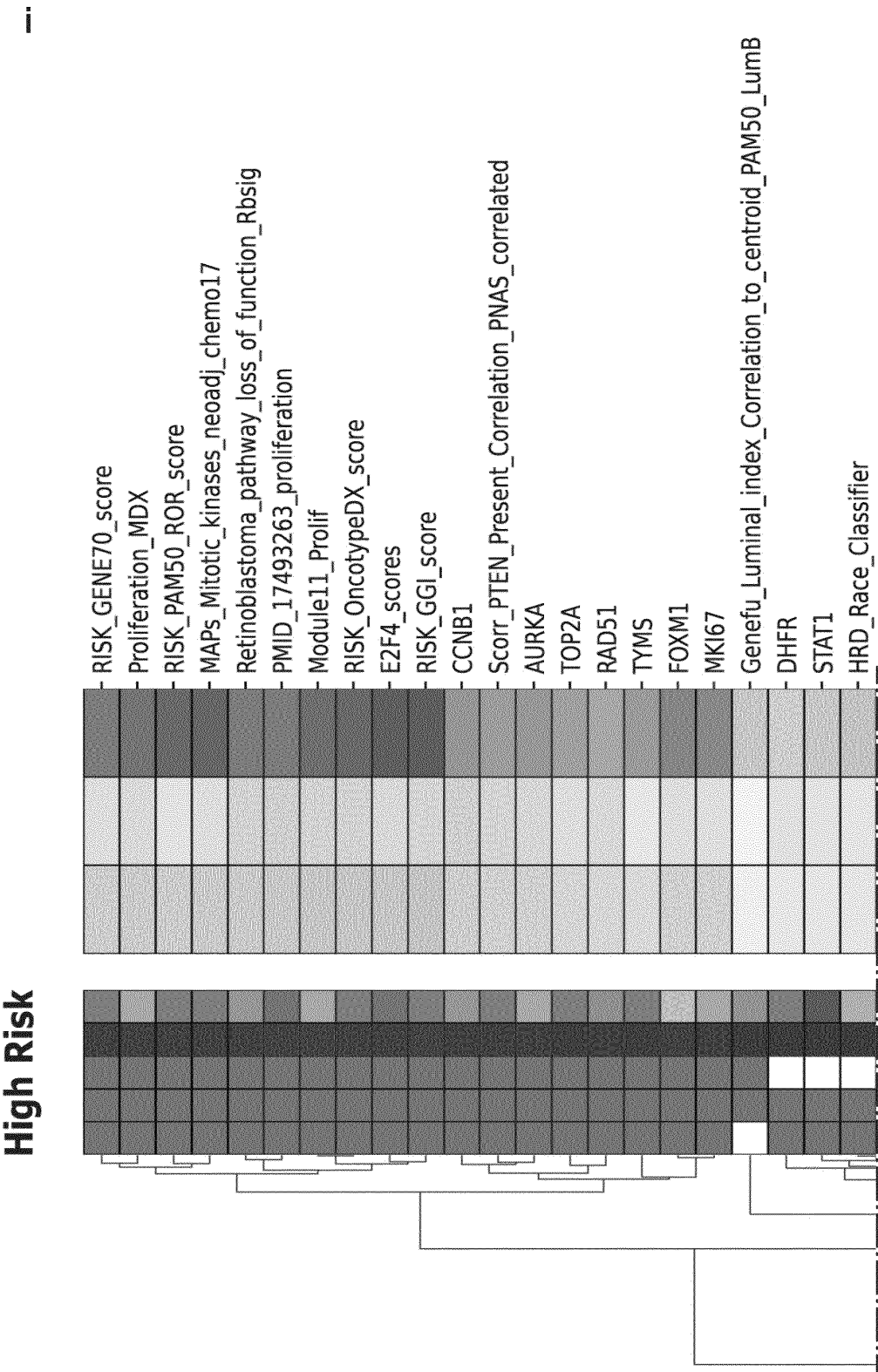
109 / 186
Figure 18 (cont.)



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Figure 18 (cont.)

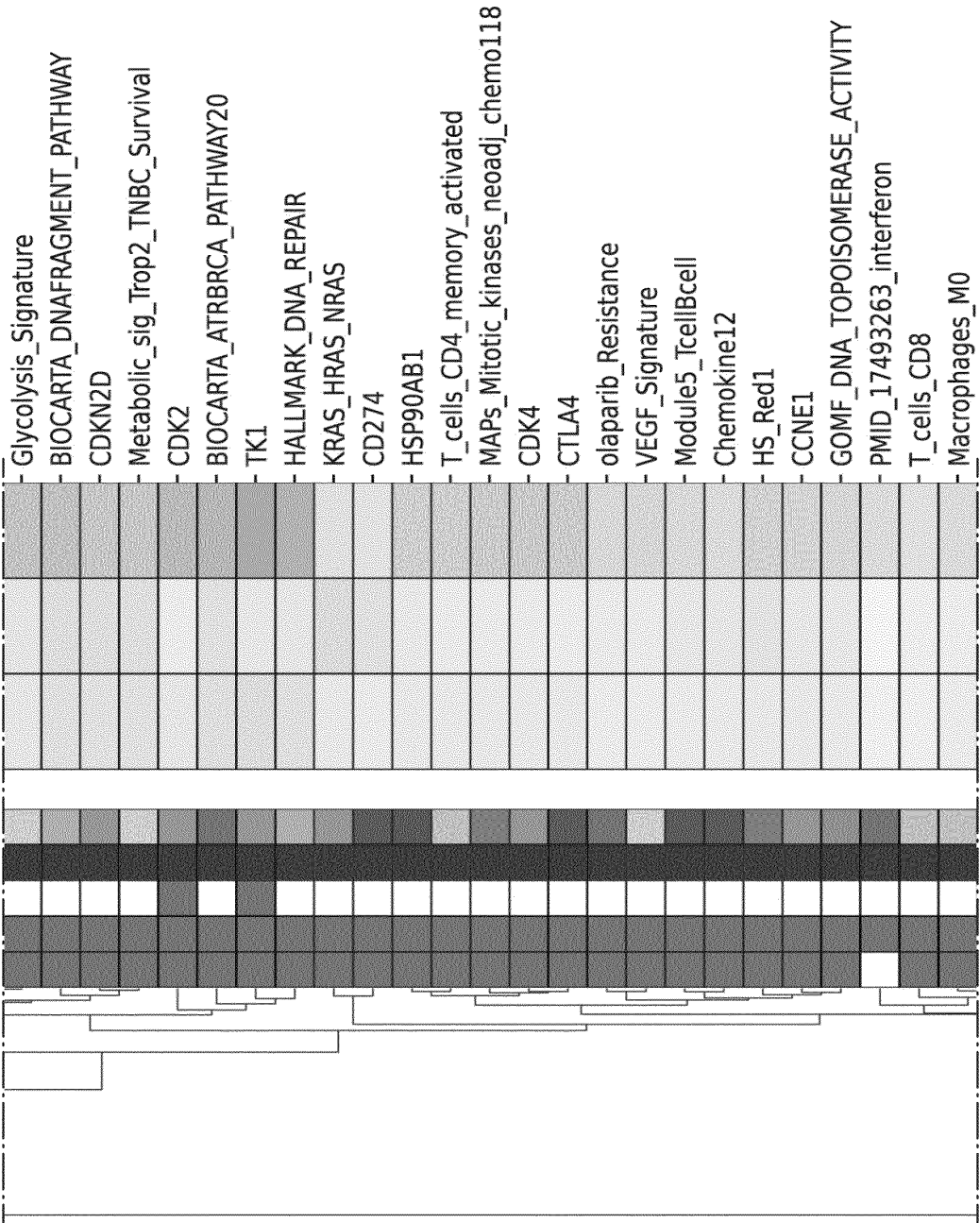


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Figure 18 (cont.)



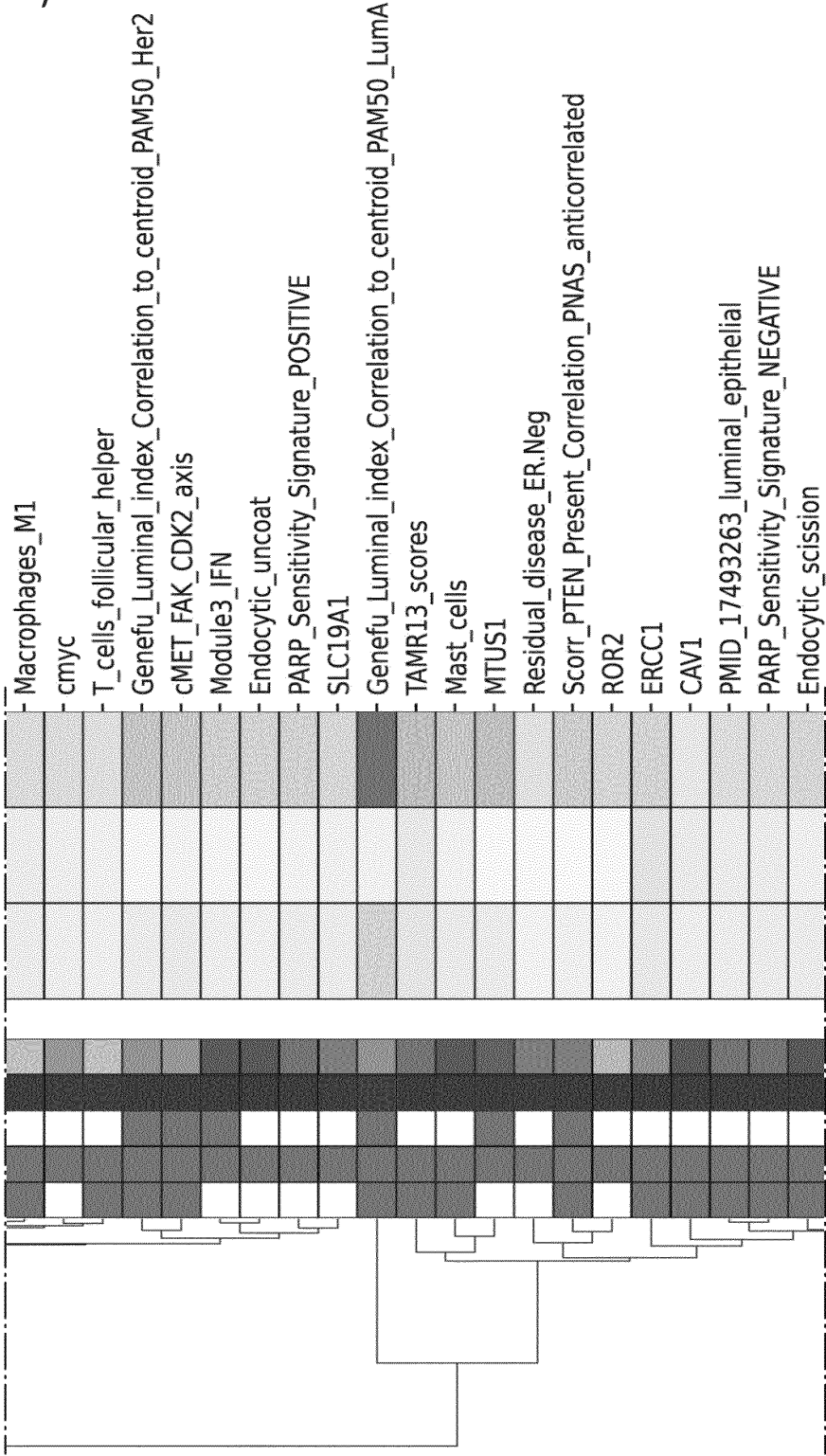
112 / 186
Figure 18 (cont.)

i (cont.)



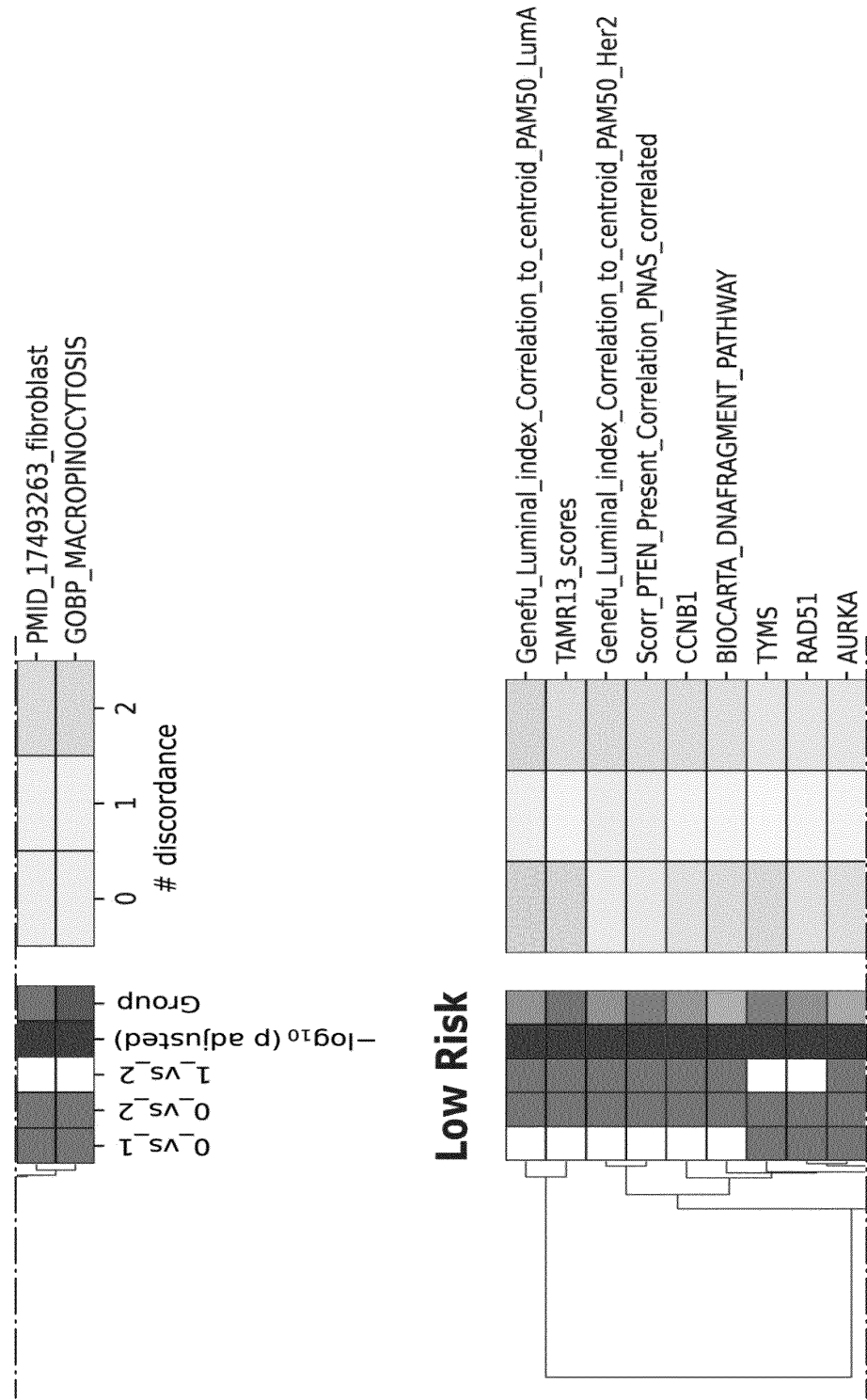
113 / 186
Figure 18 (cont.)

i (cont.)



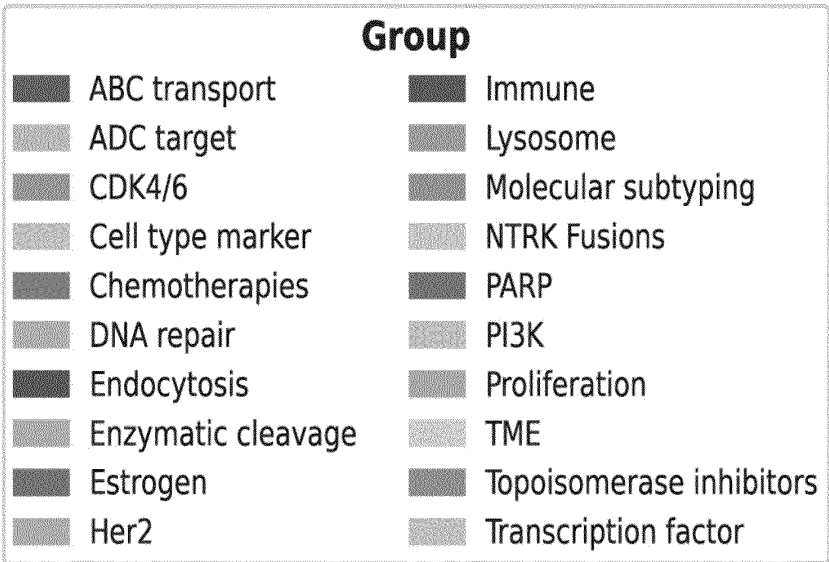
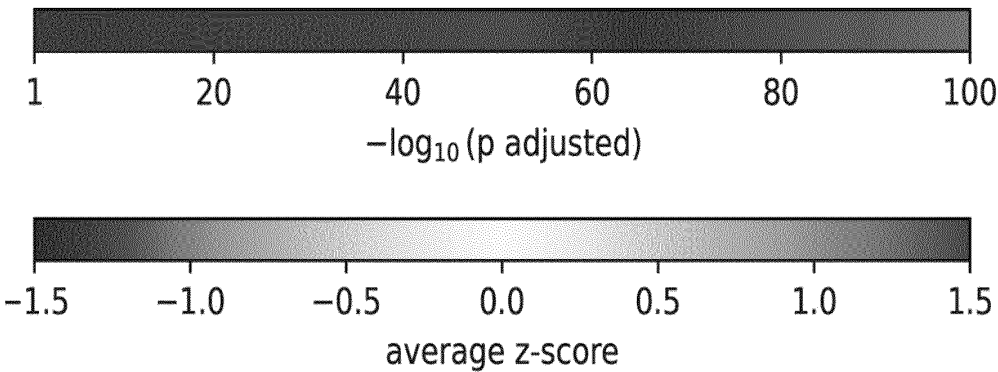
114 / 186
Figure 18 (cont.)

i (cont.)

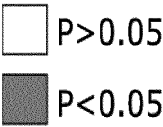


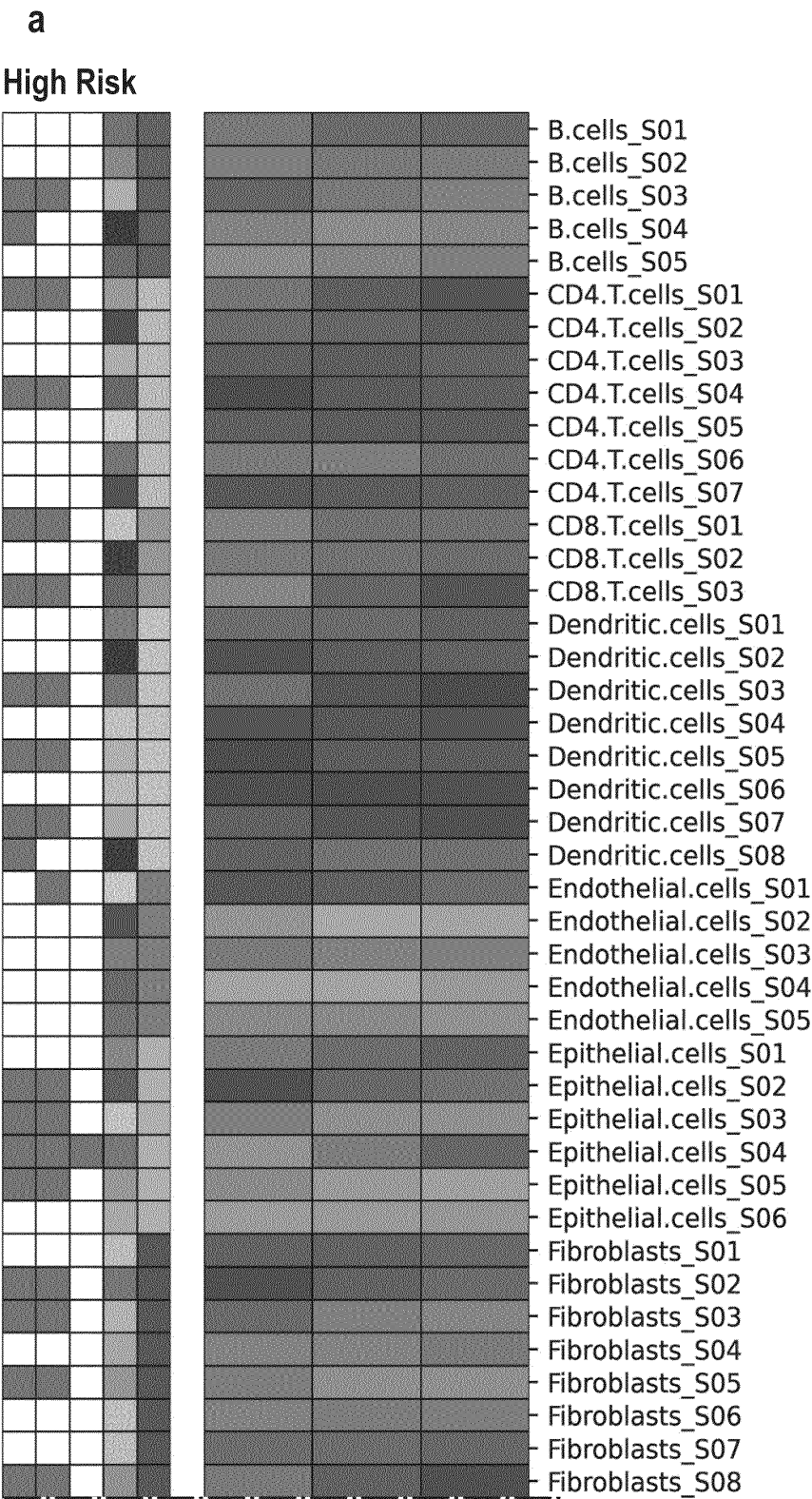
115 / 186
Figure 18 (cont.)

i (cont.)

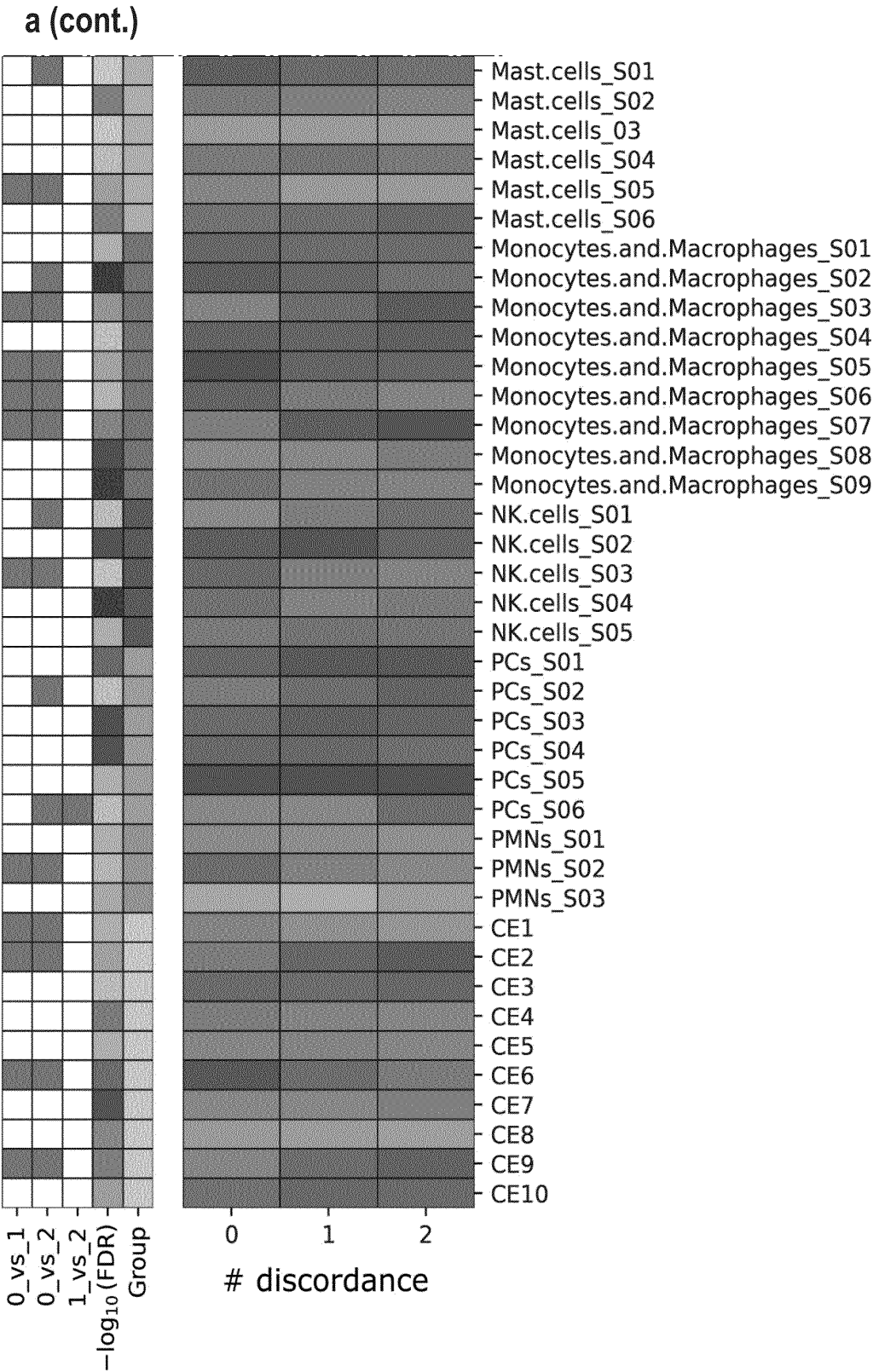


Dunn's test



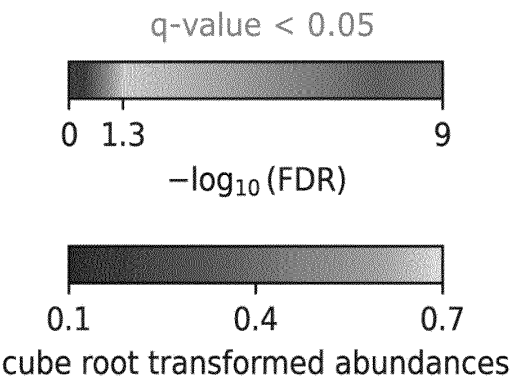


117 / 186
Figure 19 (cont.)



118 / 186
Figure 19 (cont.)

a (cont.)



Cell type	
B cells	Mast cells
CD4 T cells	Monocytes/Macrophages
CD8 T cells	Her2
Dendritic cells	NK cells
Endothelial cells	Plasma cells
Epithelial cells	Neutrophils
Fibroblasts	Carcinoma ecotype

Dunn's test

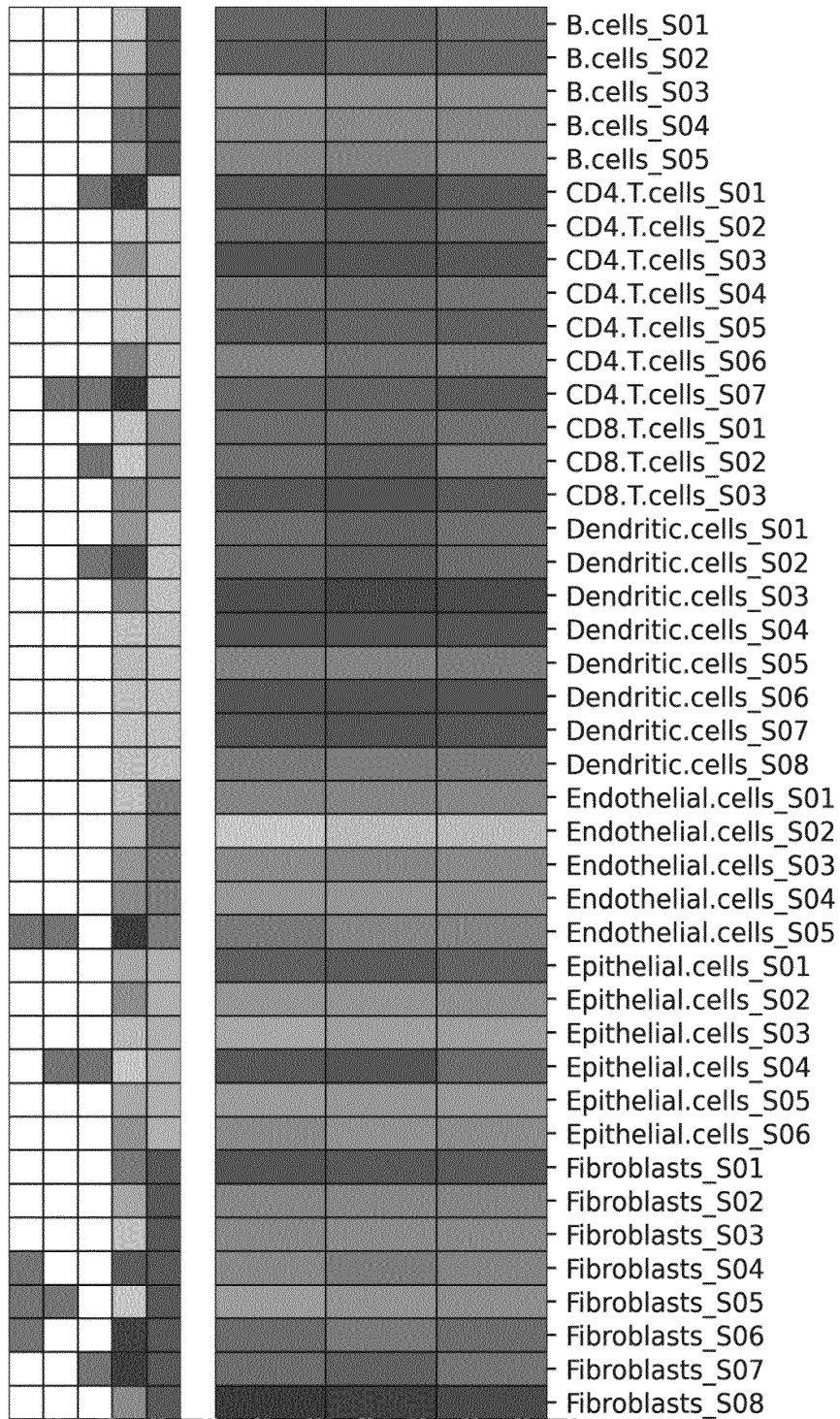
- p-value > 0.05
- p-value < 0.05

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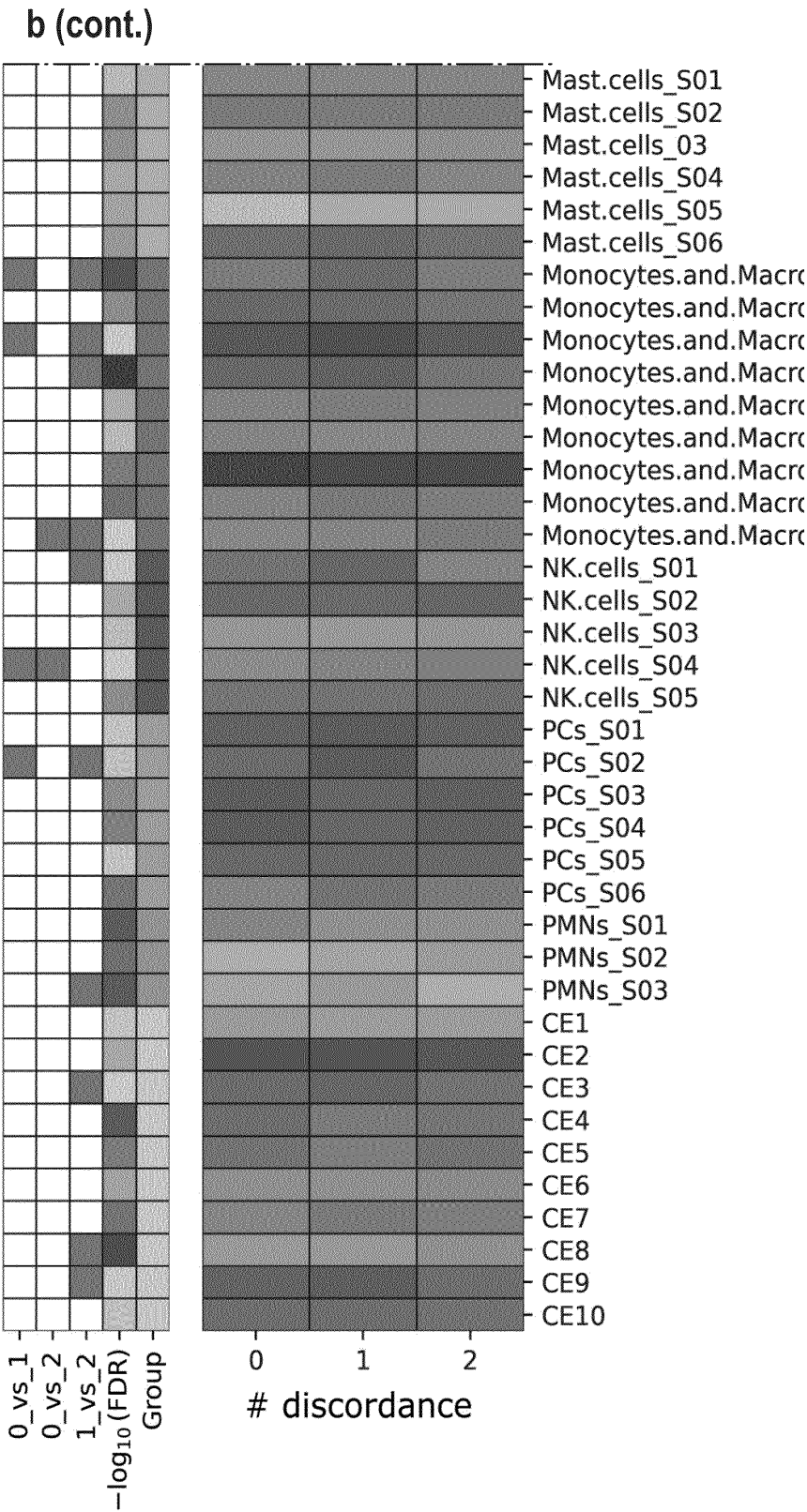
Figure 19 (cont.)

b

Low Risk

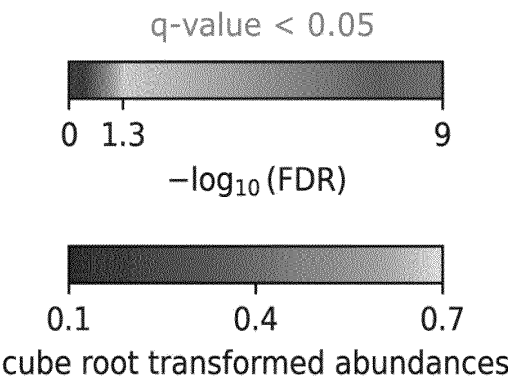


120 / 186
Figure 19 (cont.)



121 / 186
Figure 19 (cont.)

b (cont.)



Cell type	
B cells	Mast cells
CD4 T cells	Monocytes/Macrophages
CD8 T cells	Her2
Dendritic cells	NK cells
Endothelial cells	Plasma cells
Epithelial cells	Neutrophils
Fibroblasts	Carcinoma ecotype

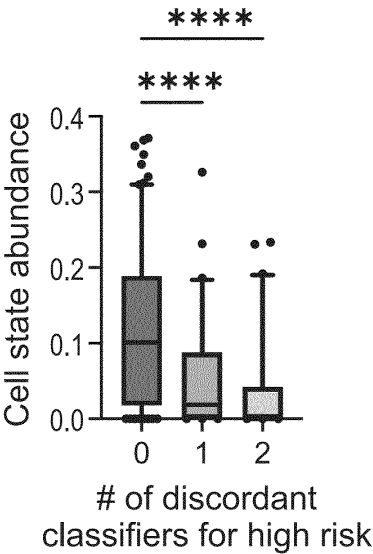
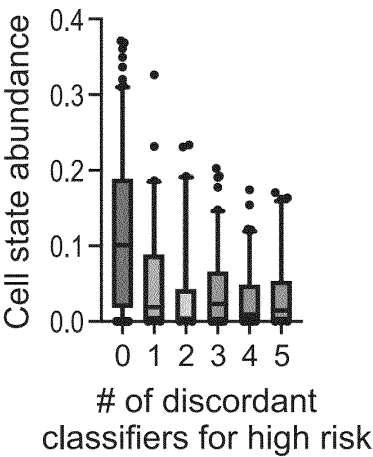
Dunn's test

- p-value > 0.05
- p-value < 0.05

122 / 186
Figure 19 (cont.)

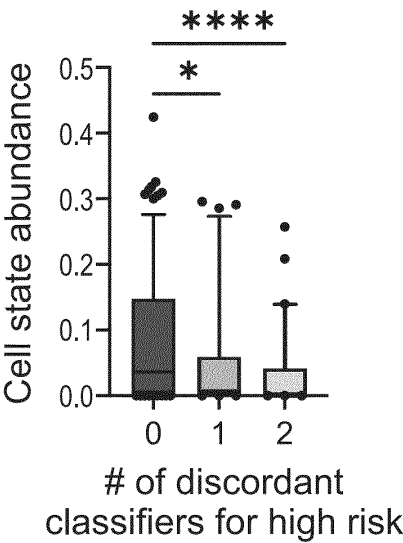
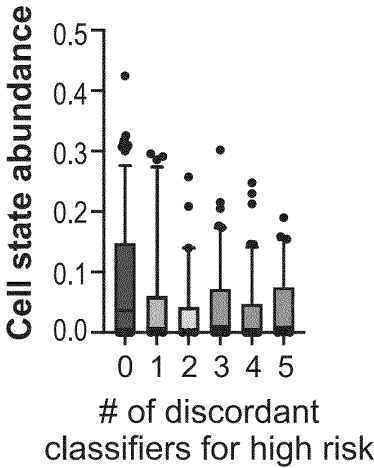
c

CD8 T cells - Exhausted /
effector memory (S03)



d

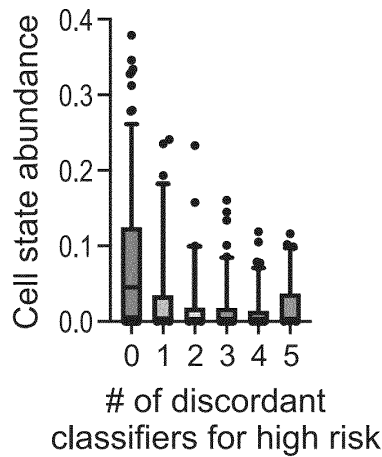
CD4 T cells - Exhausted /
effector memory/Treg (S01)



123 / 186
Figure 19 (cont.)

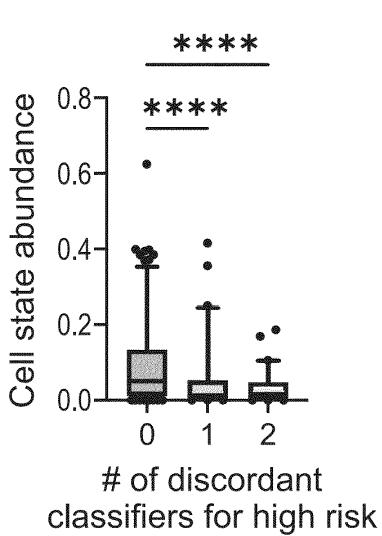
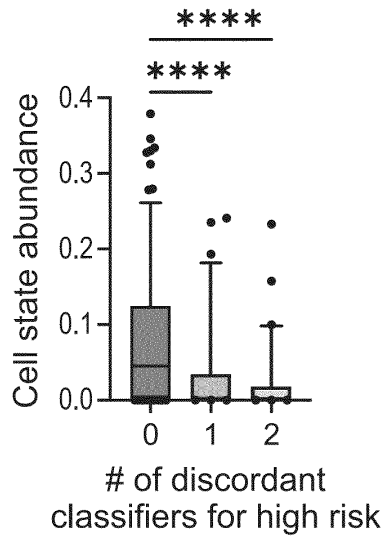
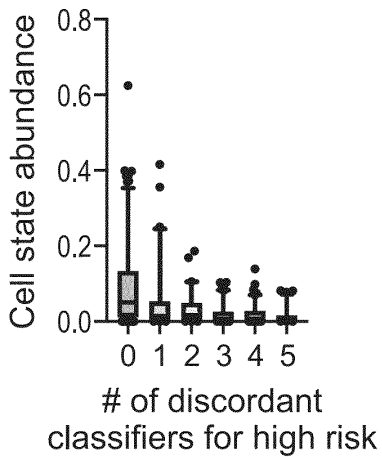
e

Dendritic cells -
Mature immunogenic (S03)



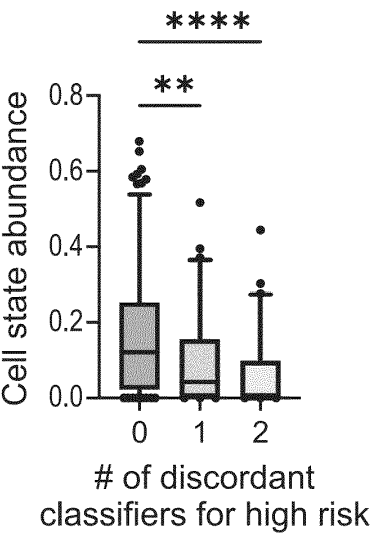
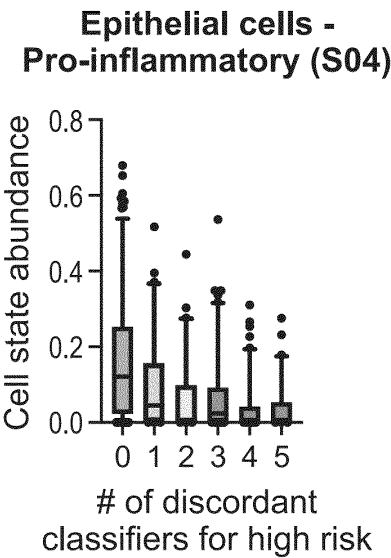
f

Monocytes/Macrophages -
M2-like proliferative (S07)

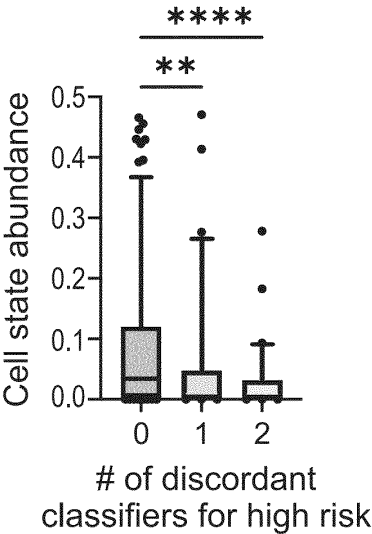
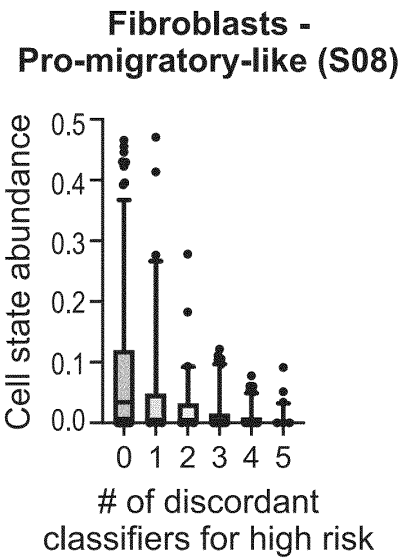


124 / 186
Figure 19 (cont.)

g



h



125 / 186
Figure 19 (cont.)

i

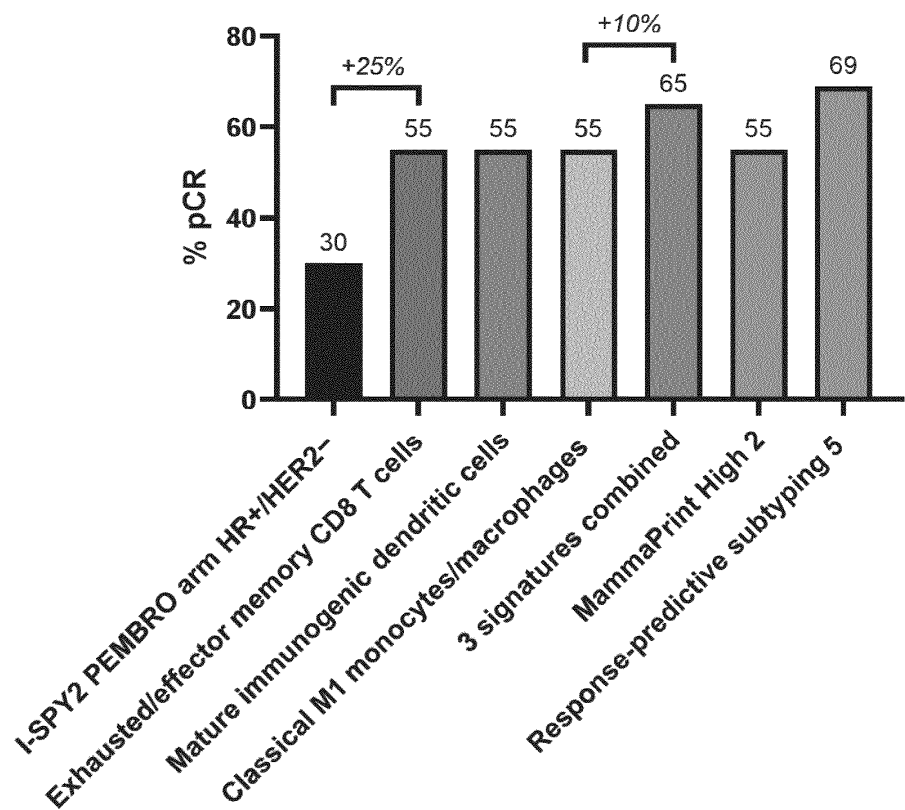
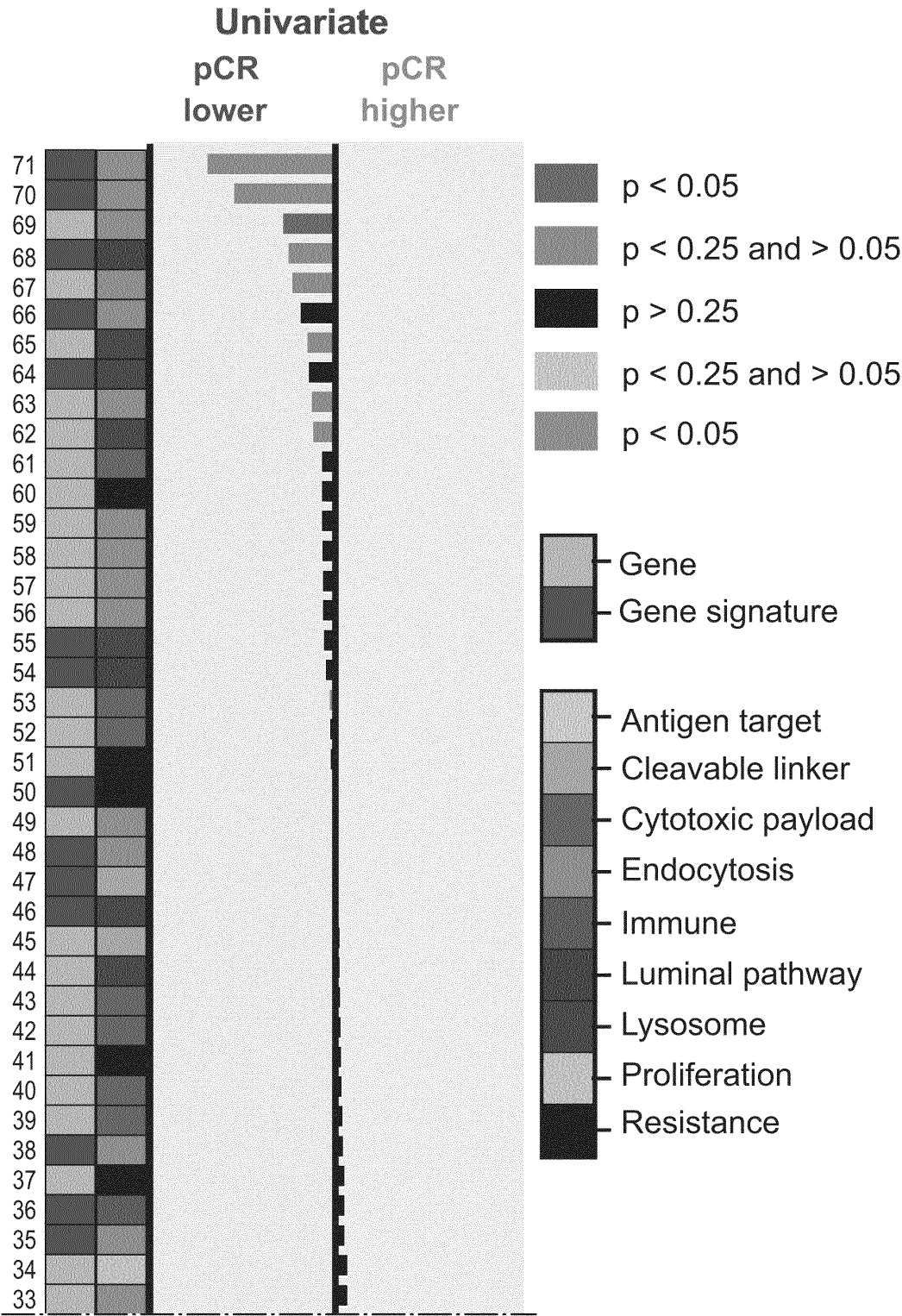
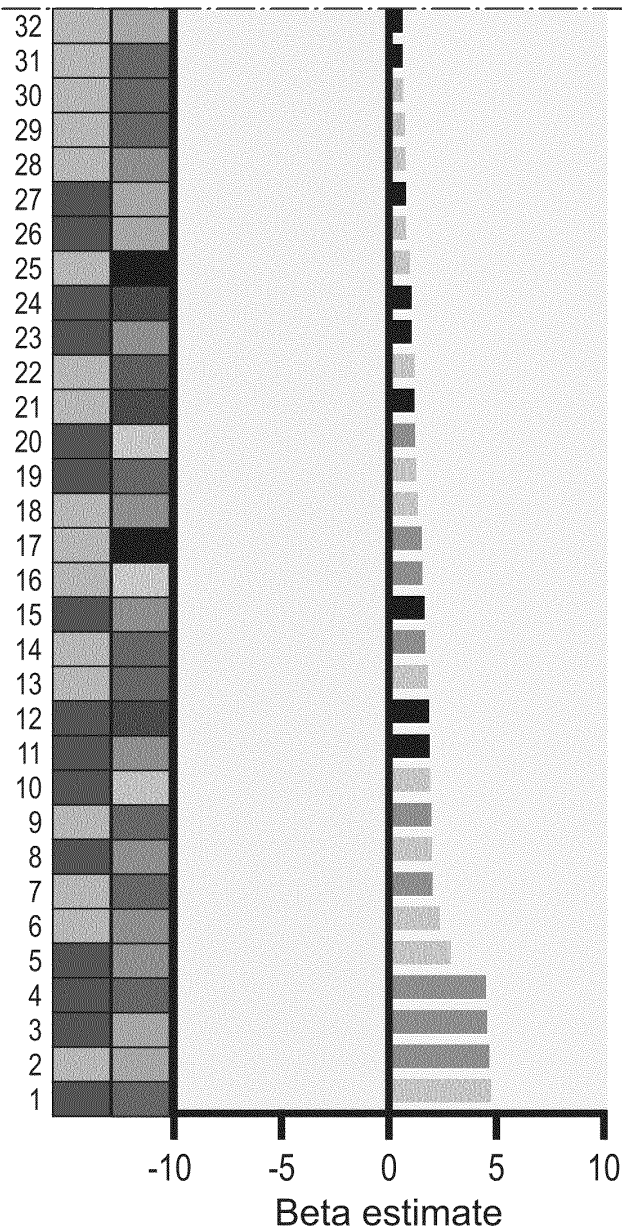


Figure 20

a

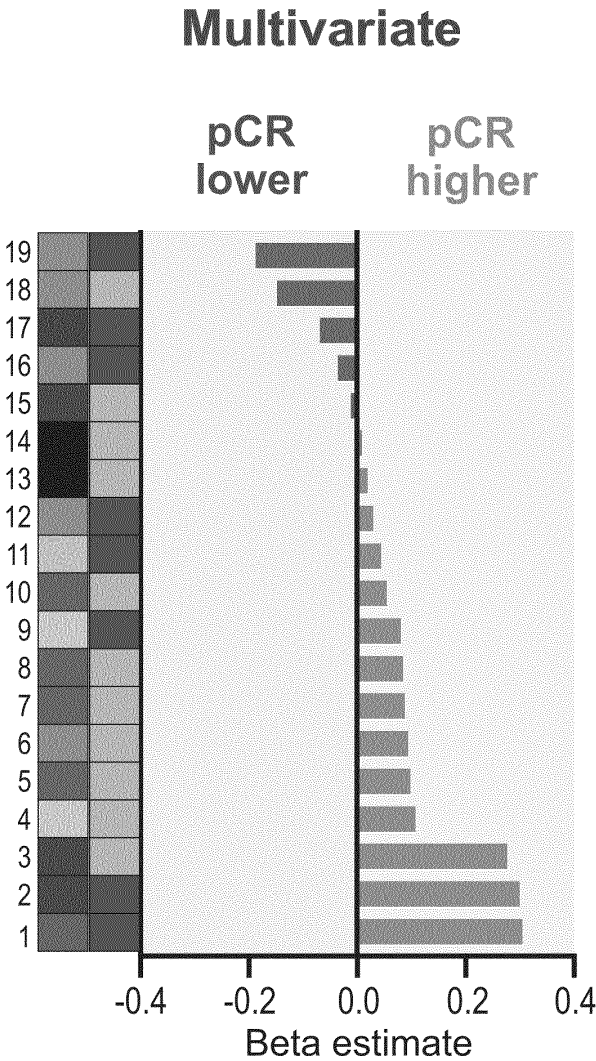


a (cont.)

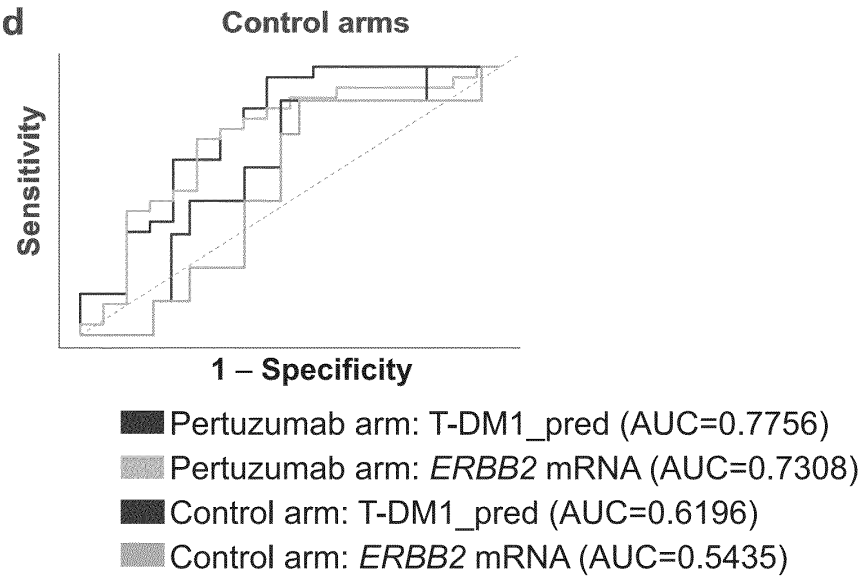
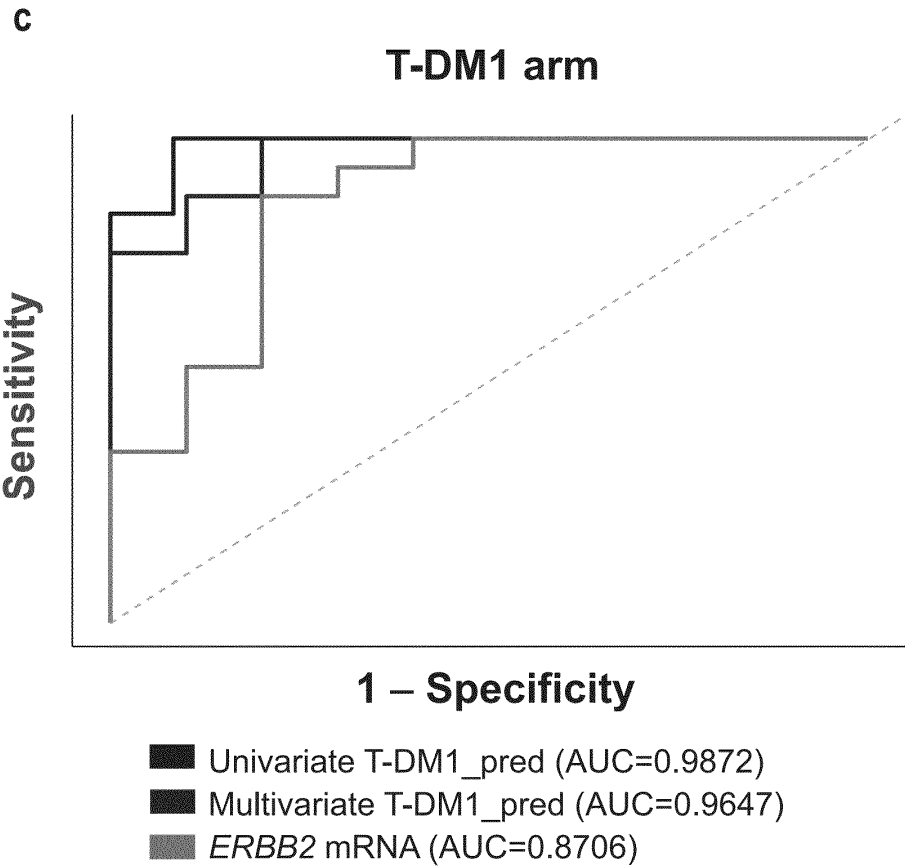


128 / 186
Figure 20 (cont.)

b

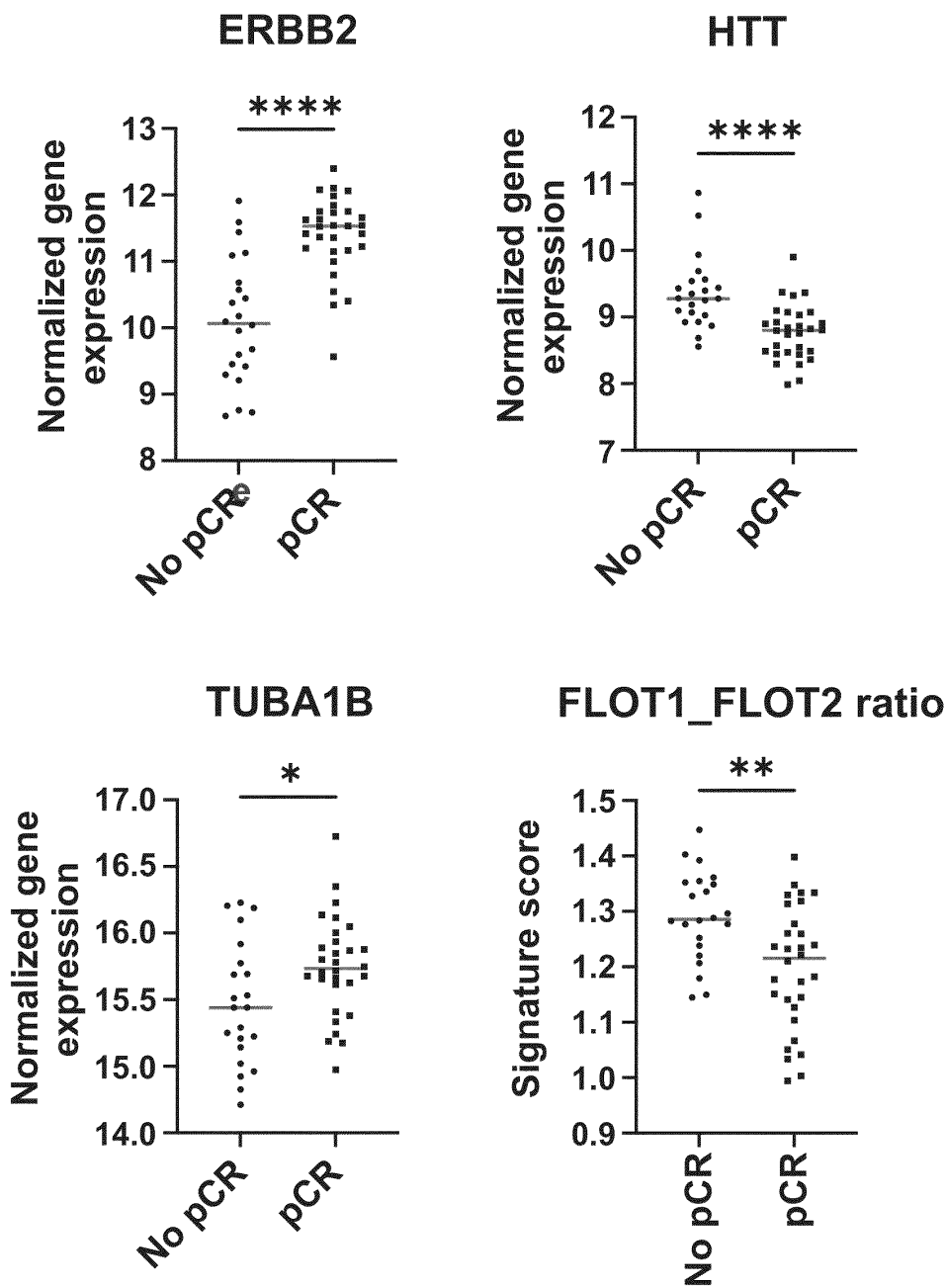


129 / 186
Figure 20 (cont.)



130 / 186
Figure 20 (cont.)

e



131 / 186
Figure 20 (cont.)

e (cont.)

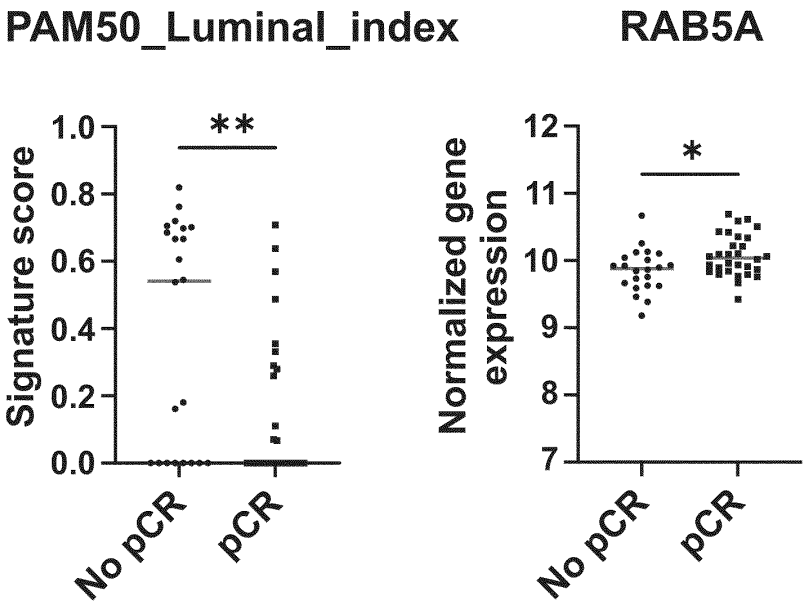


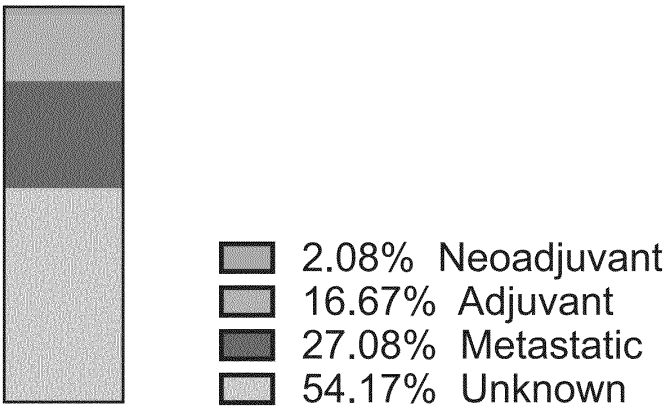
Figure 21

a

Drug type / pathway	Genes	Gene signatures
Prognosis	1	3
Proliferation	2	2
Luminal	2	4
Her2	3	3
Chemotherapy	9	8
Immunotherapy	3	5
CDK4/6 inhibitors	5	0
PI3K inhibitors	0	1
DNA damage and repair	2	1
Angiogenesis / Hypoxia	1	1
Antibody drug-conjugates	20	0
Total	40	28

b

Treatment setting



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Figure 21 (cont.)

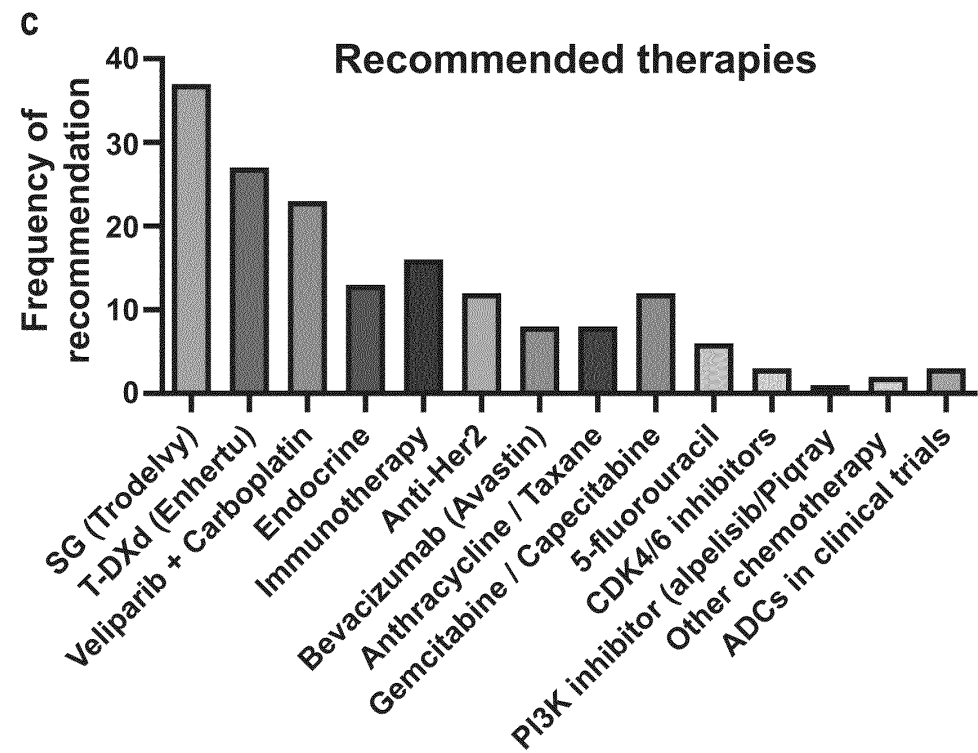
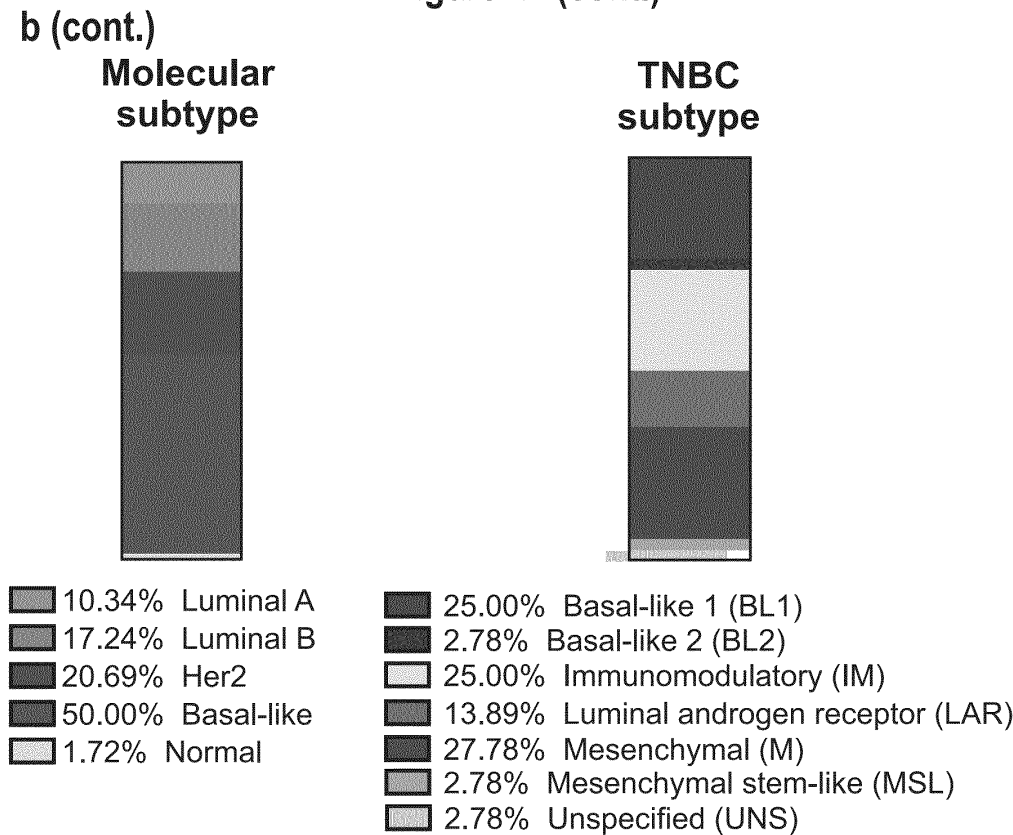
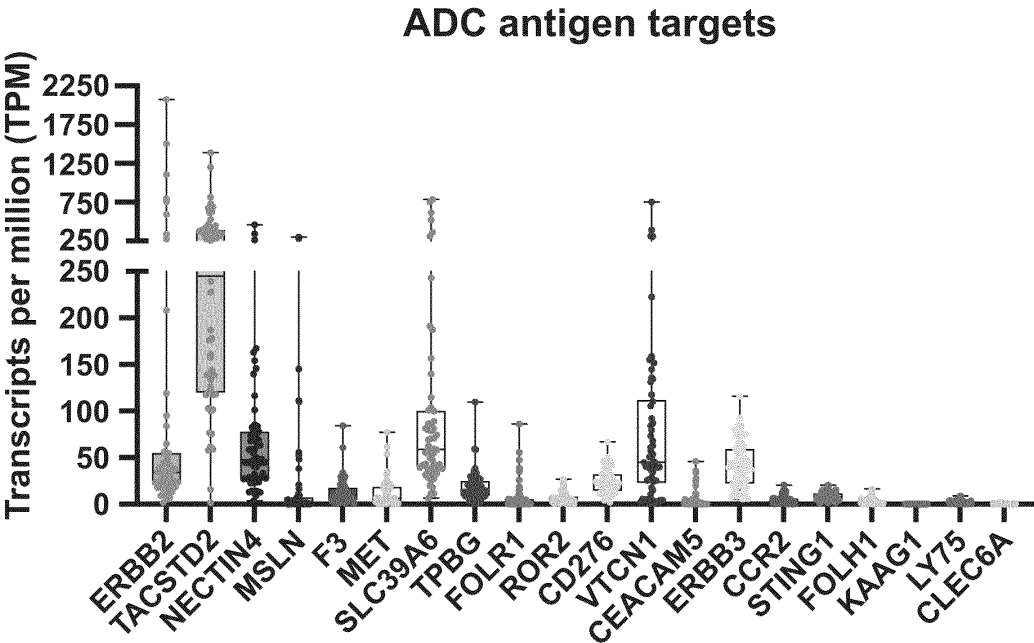


Figure 21 (cont.)

d



e

ADC payload targets

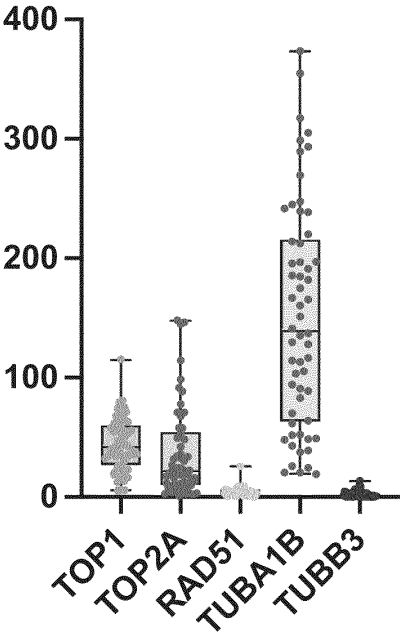
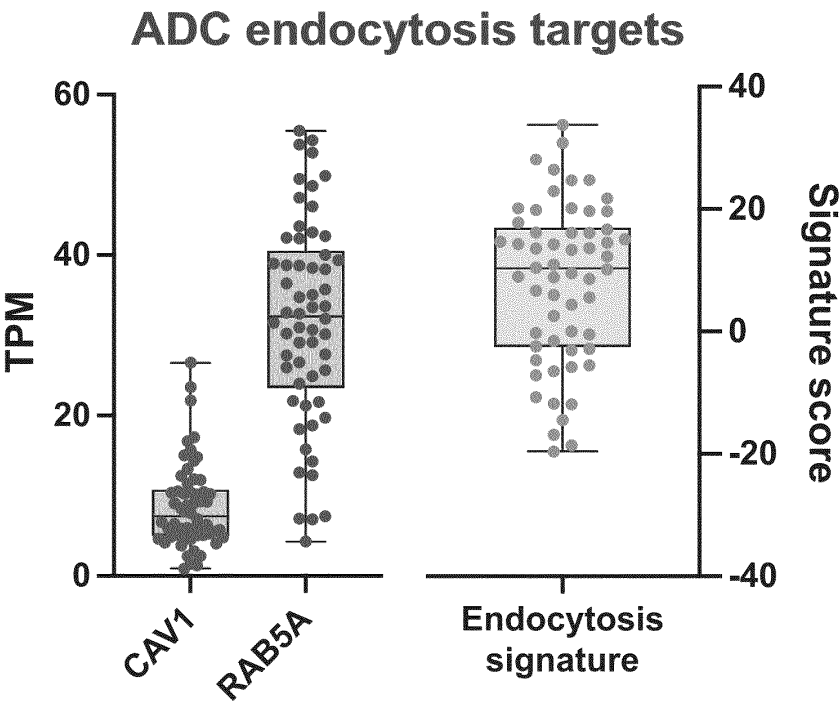


Figure 21 (cont.)

f



g

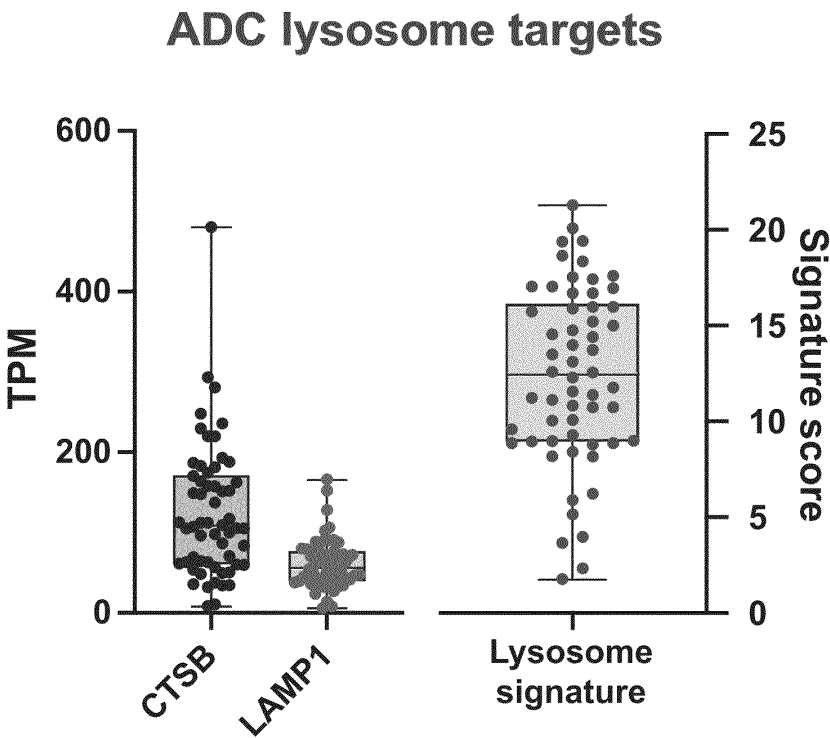
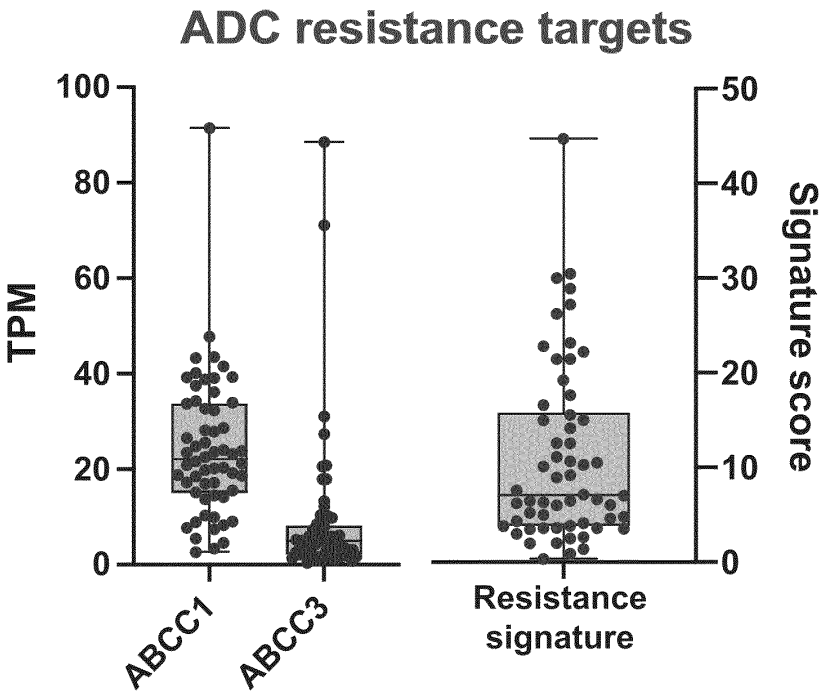
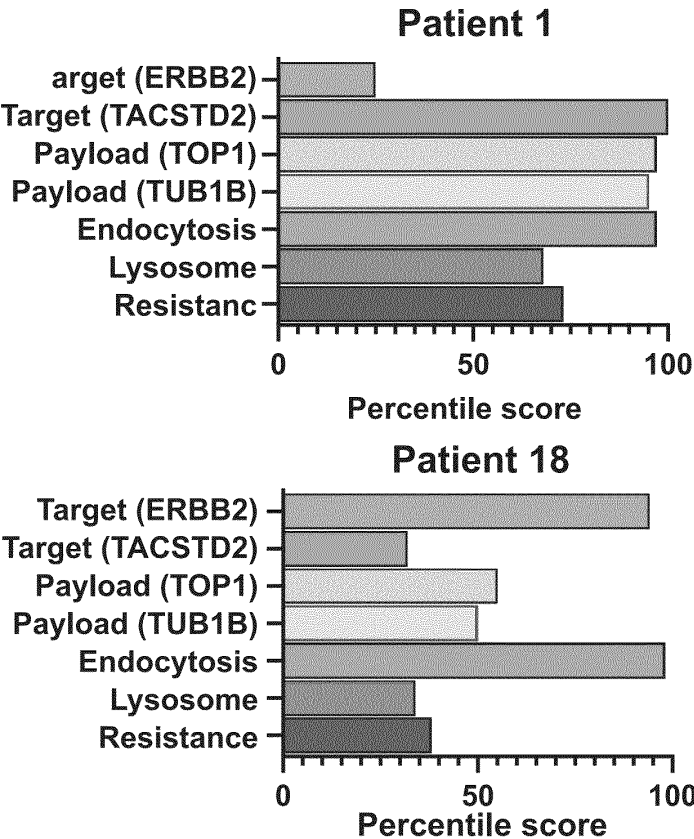


Figure 21 (cont.)

h

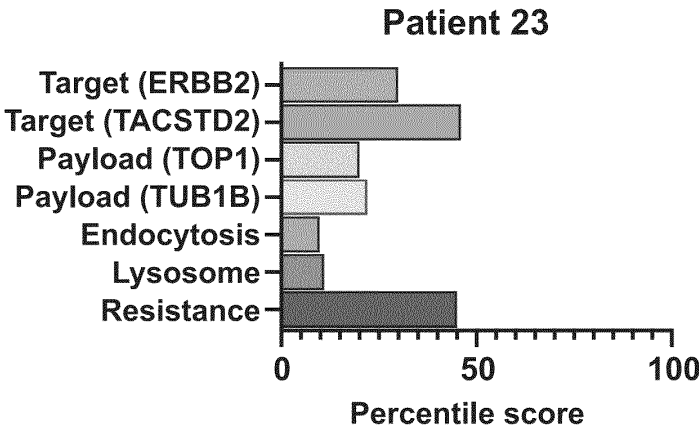
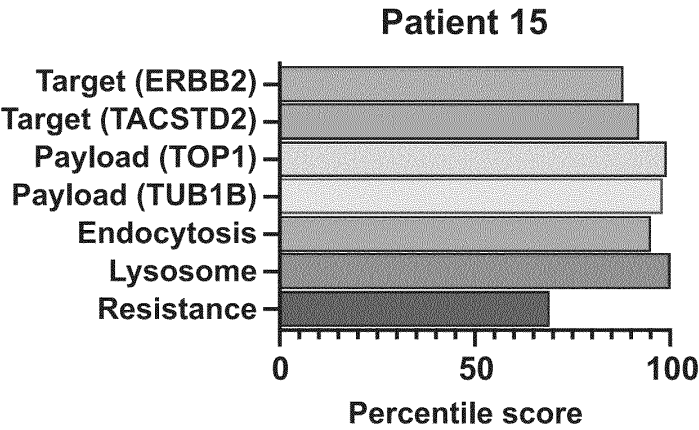


i



137 / 186
Figure 21 (cont.)

i (cont.)



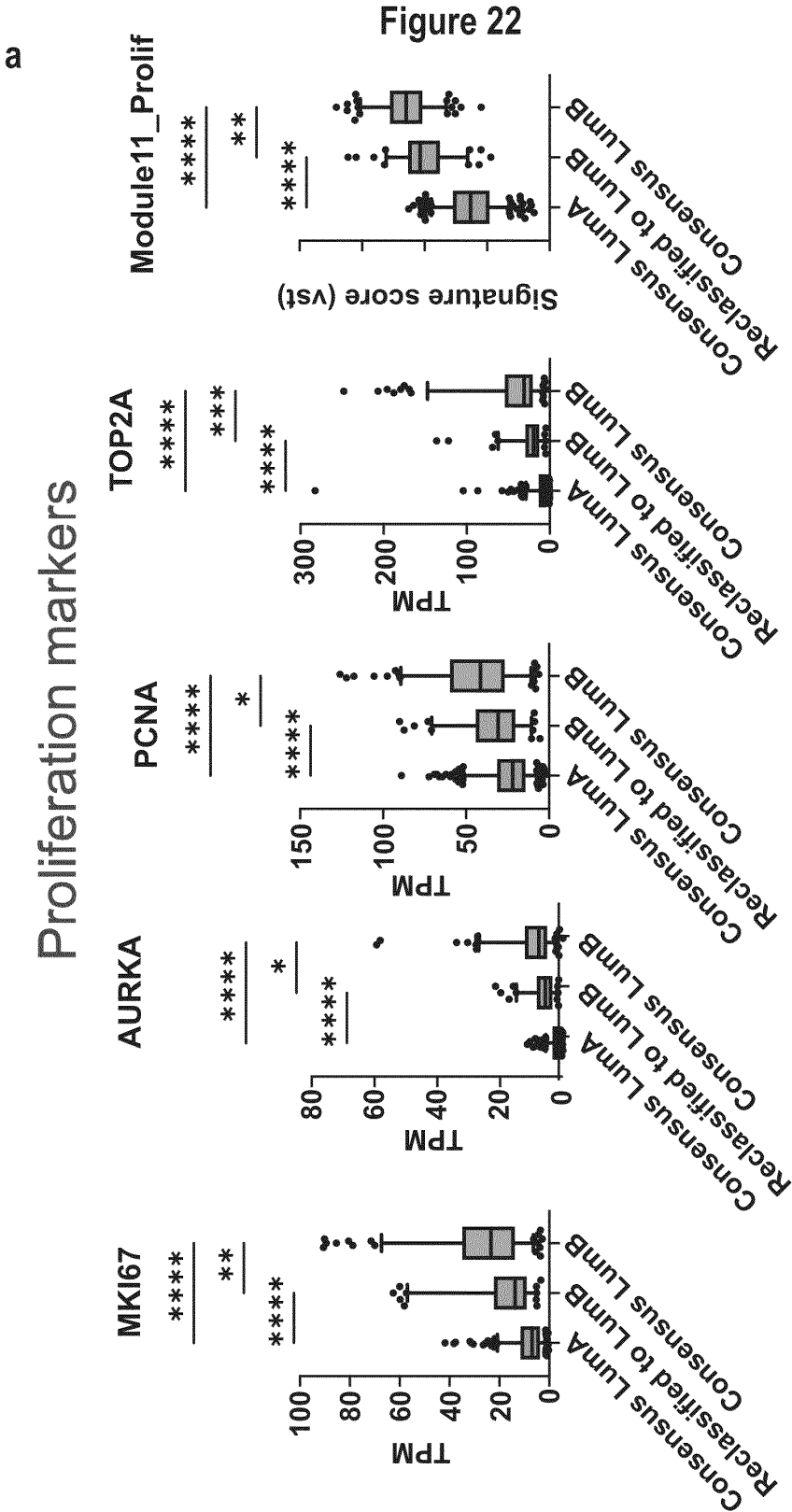


Figure 22 (cont.)

a (cont.)

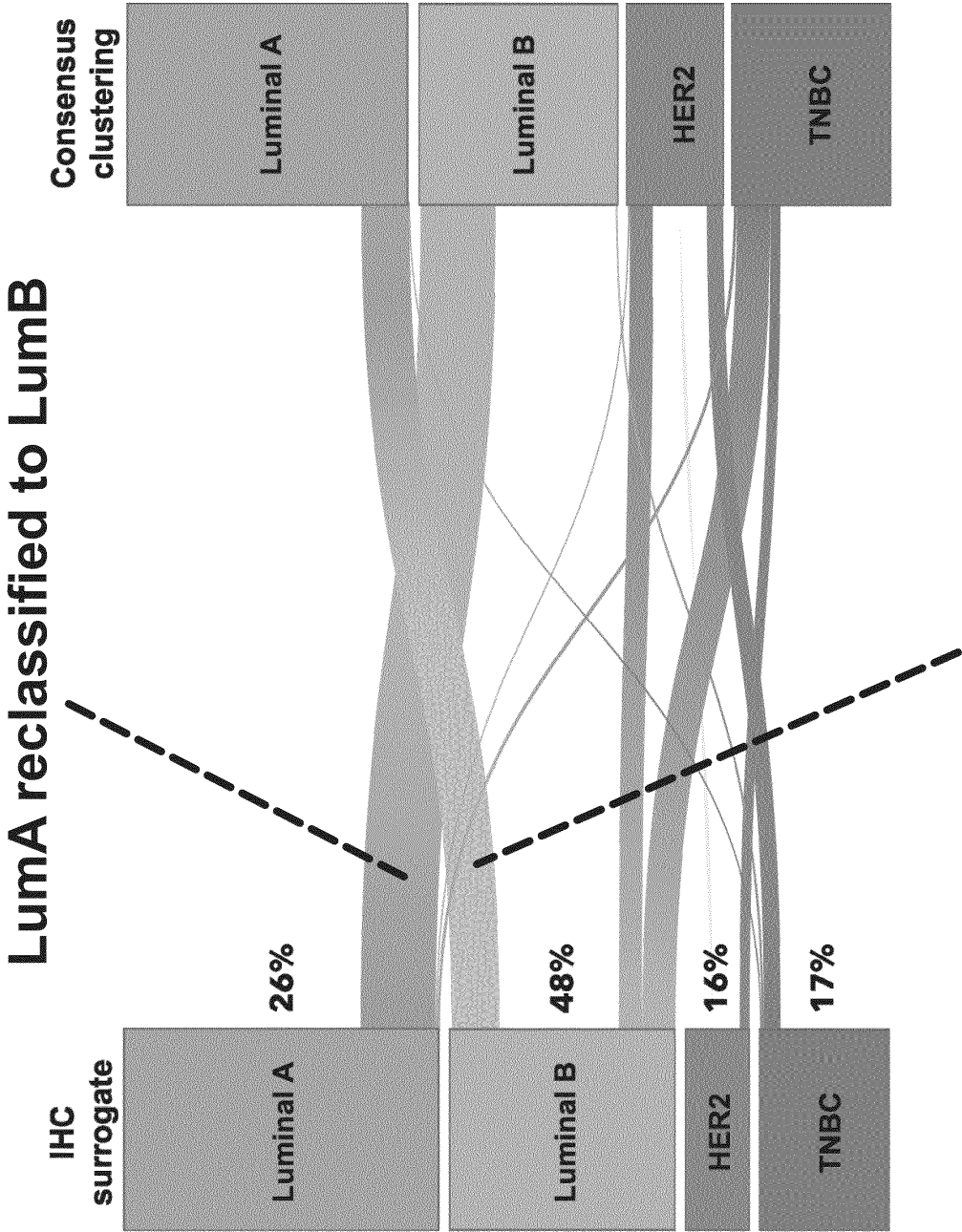


Figure 22 (cont.)

b

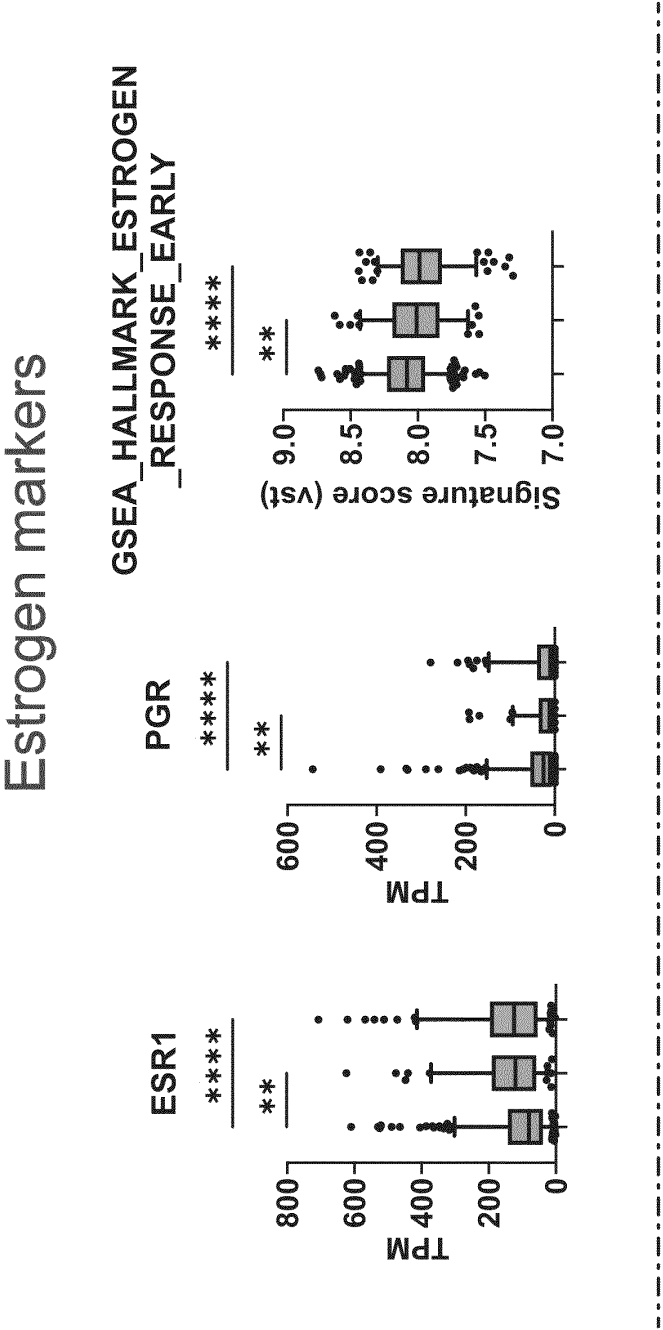


Figure 22 (cont.)

b (cont.)

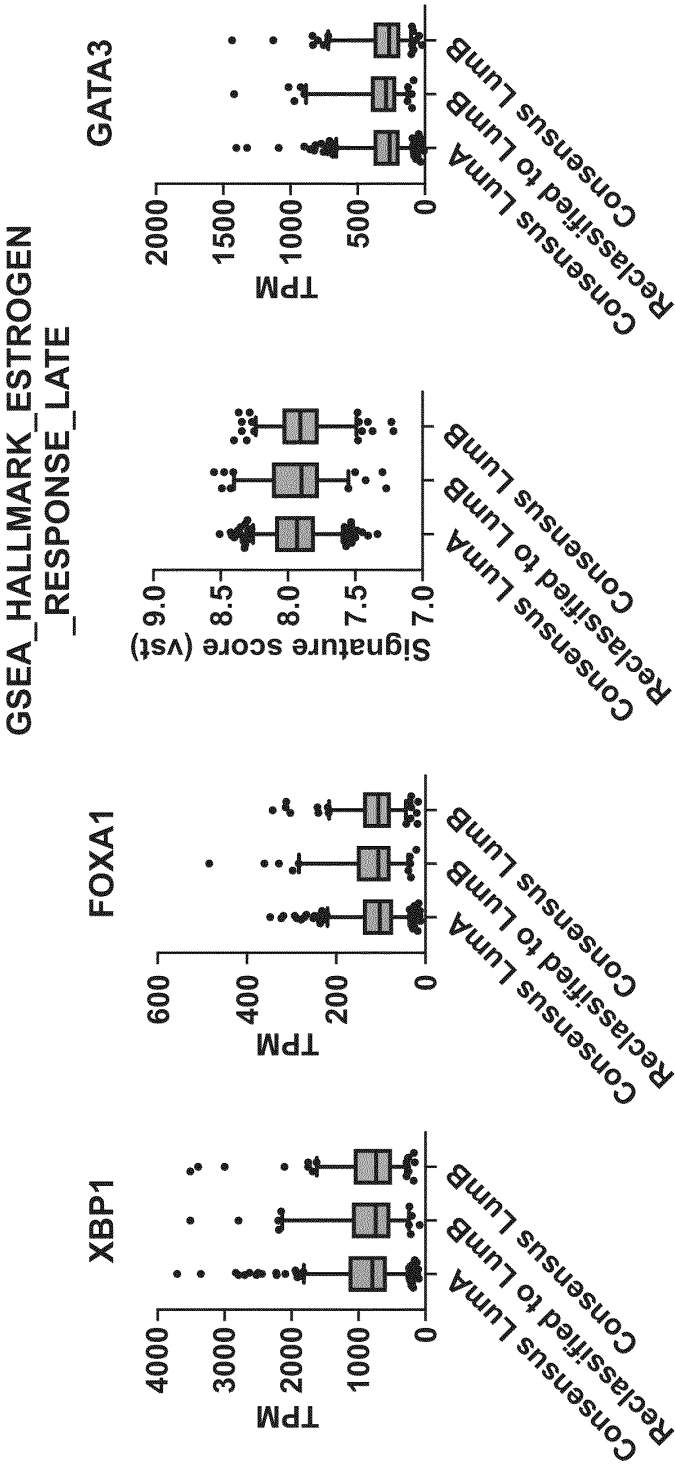
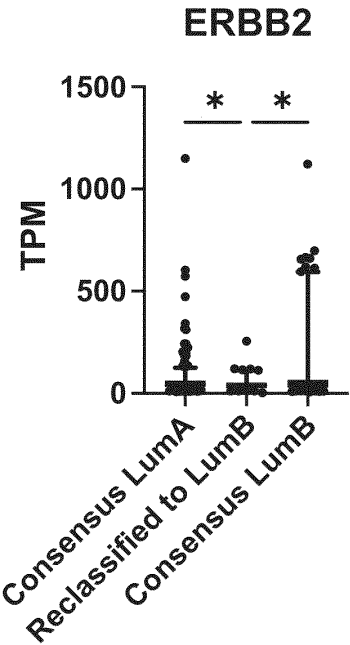


Figure 22 (cont.)

C

Her2 markers



d

LumB reclassified to LumA
Proliferation markers

Figure 22 (cont.)

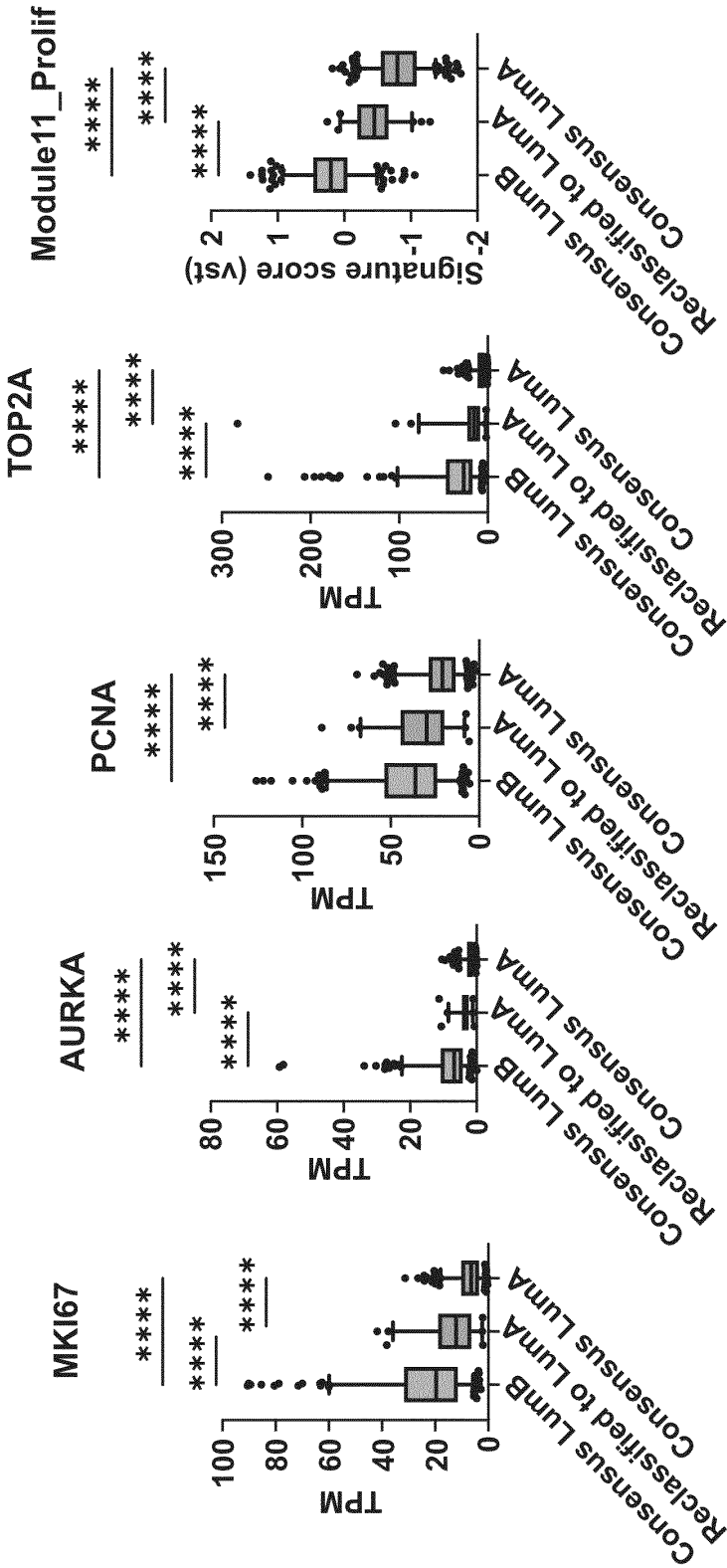


Figure 22 (cont.)

e

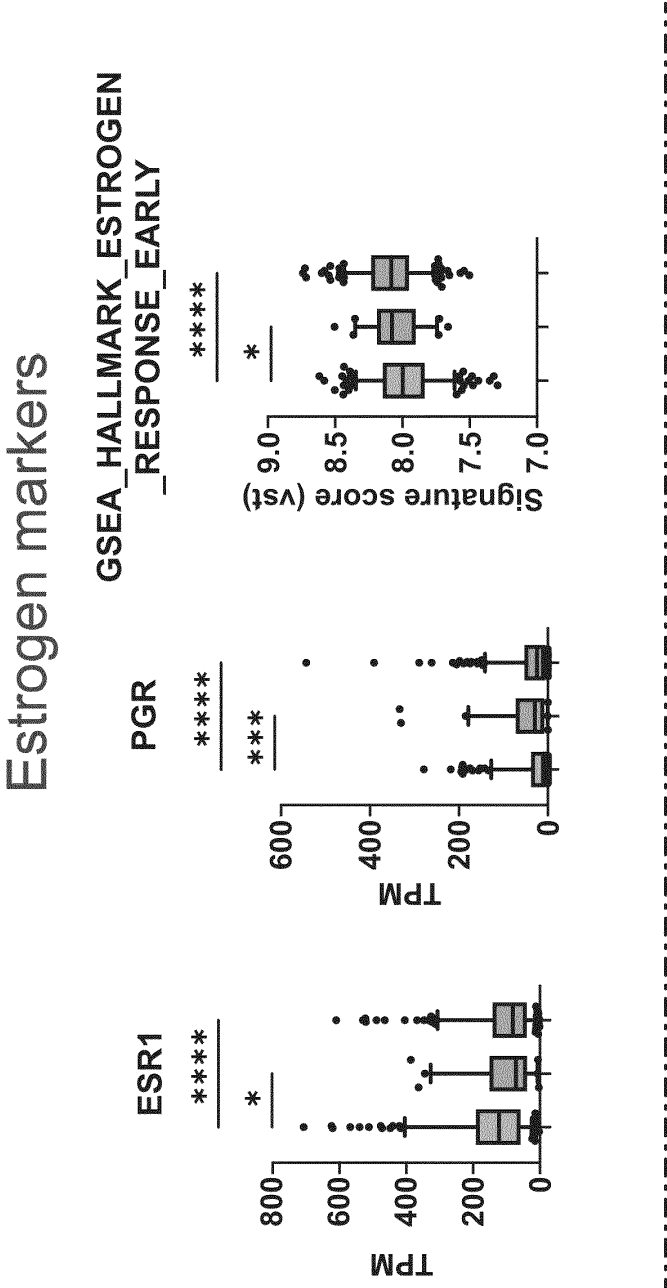


Figure 22 (cont.)

e (cont.)

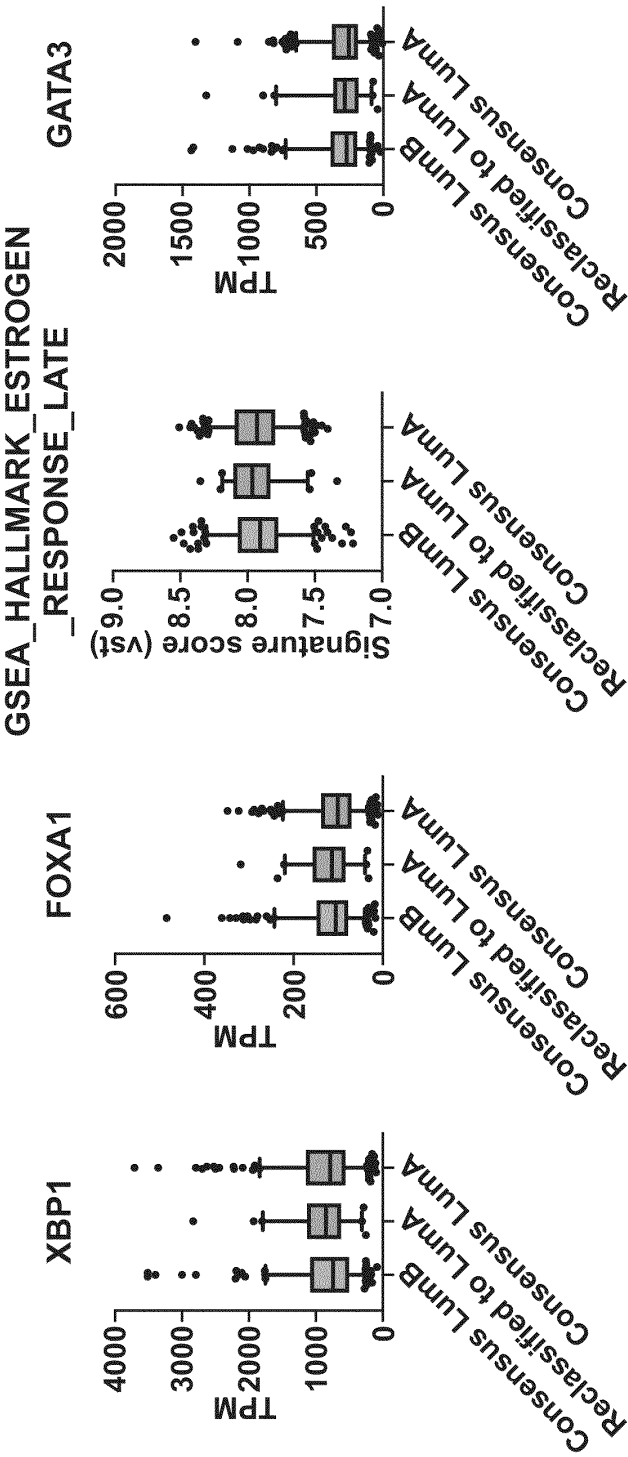


Figure 22 (cont.)

f

Her2 markers

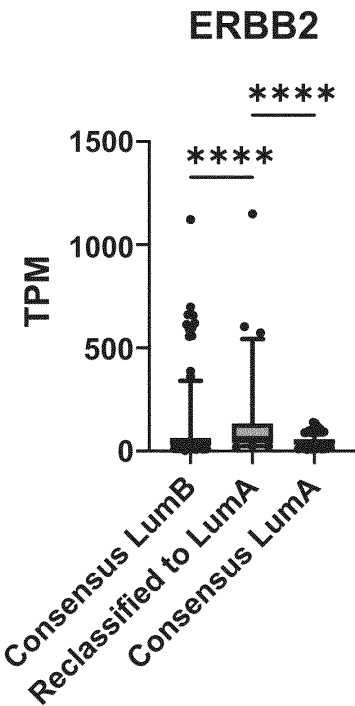


Figure 23

a

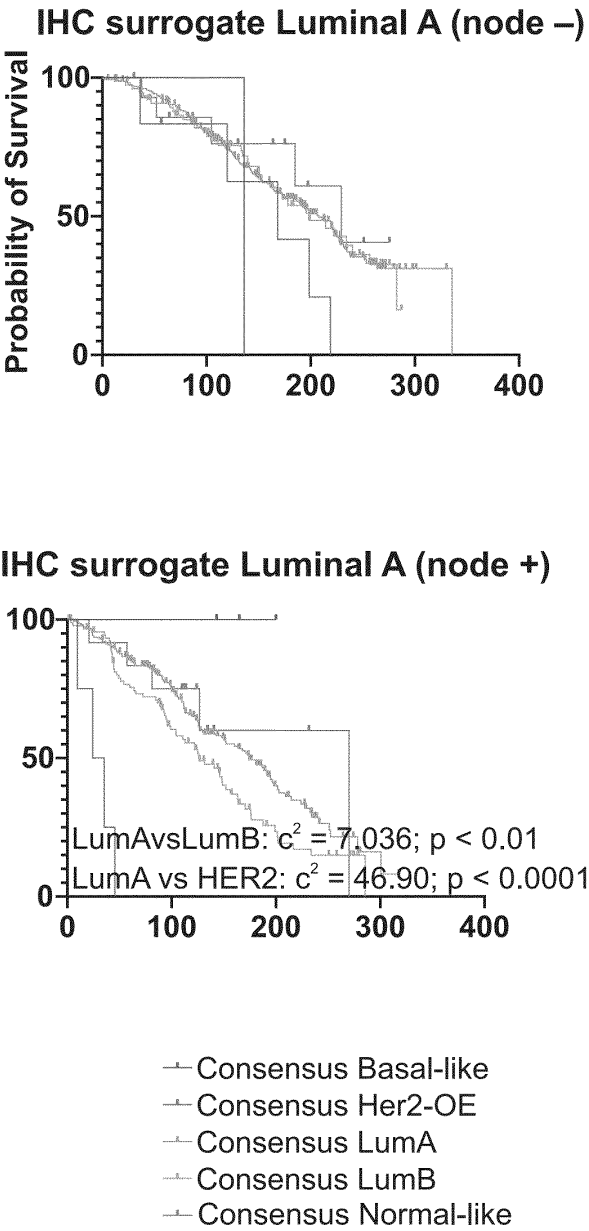


Figure 23 (cont.)

b

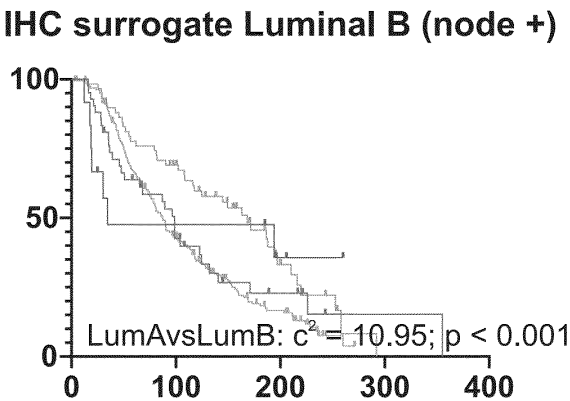
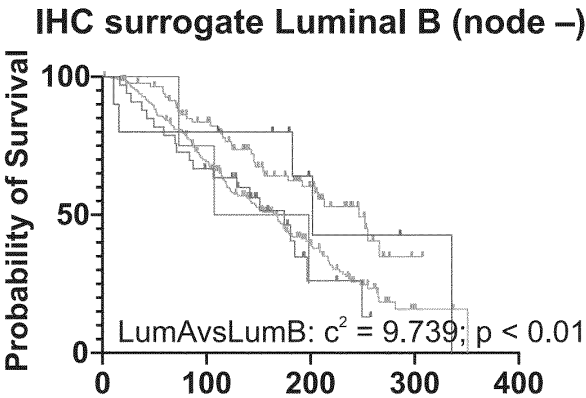


Figure 23 (cont.)

C

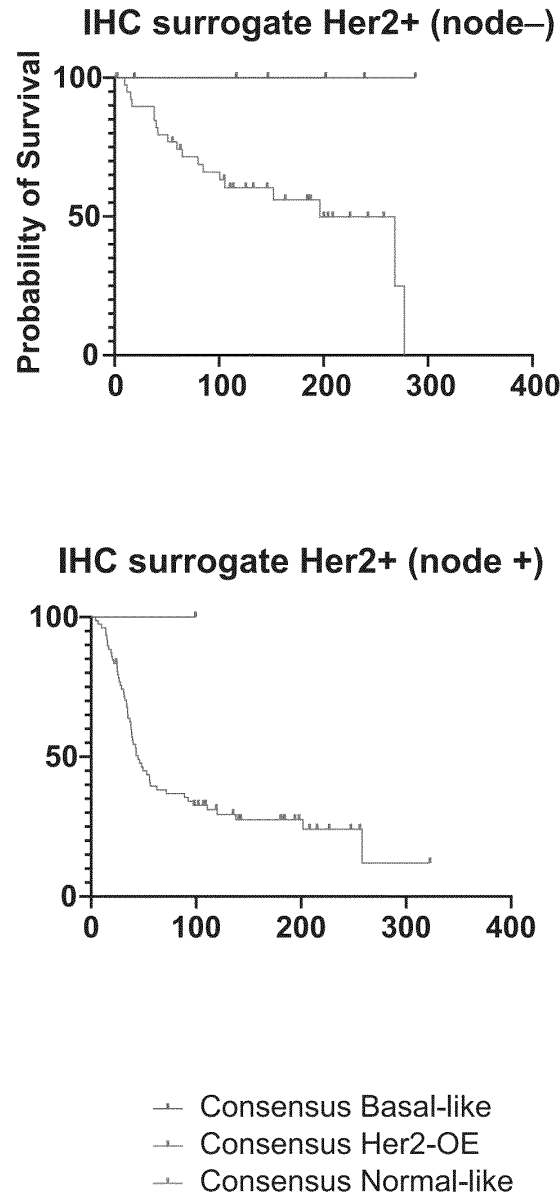
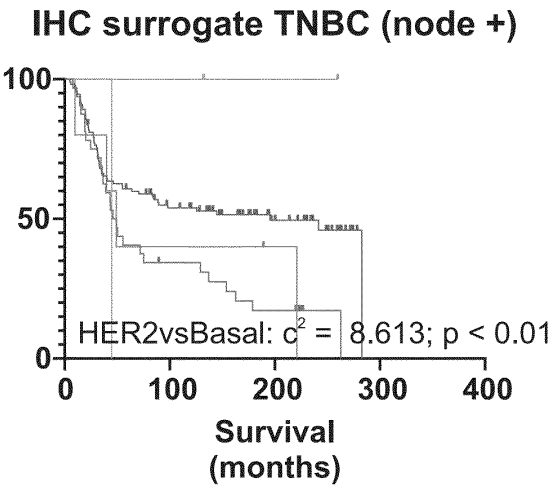
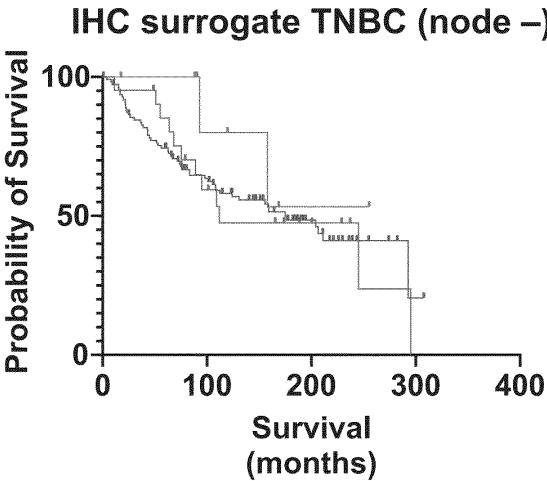


Figure 23 (cont.)

d



- Consensus Basal-like
- Consensus Her2-OE
- Consensus LumA
- Consensus LumB
- Consensus Normal-like

Figure 23 (cont.)

e

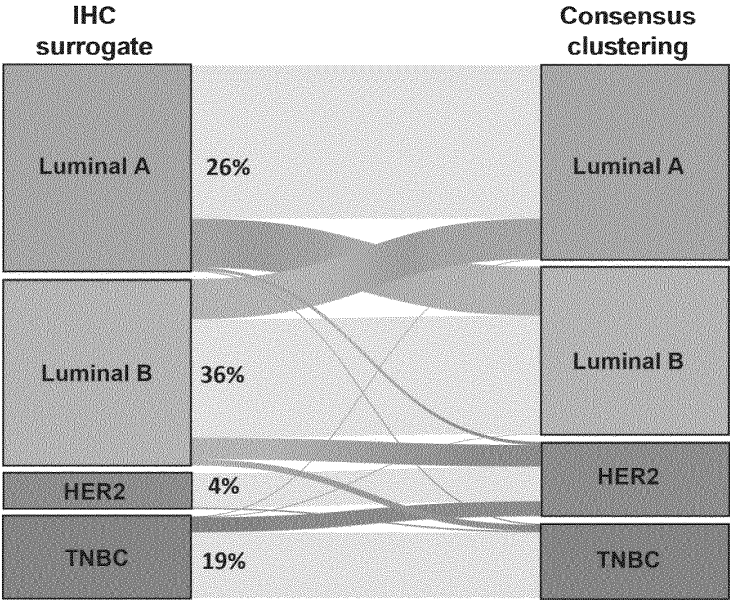
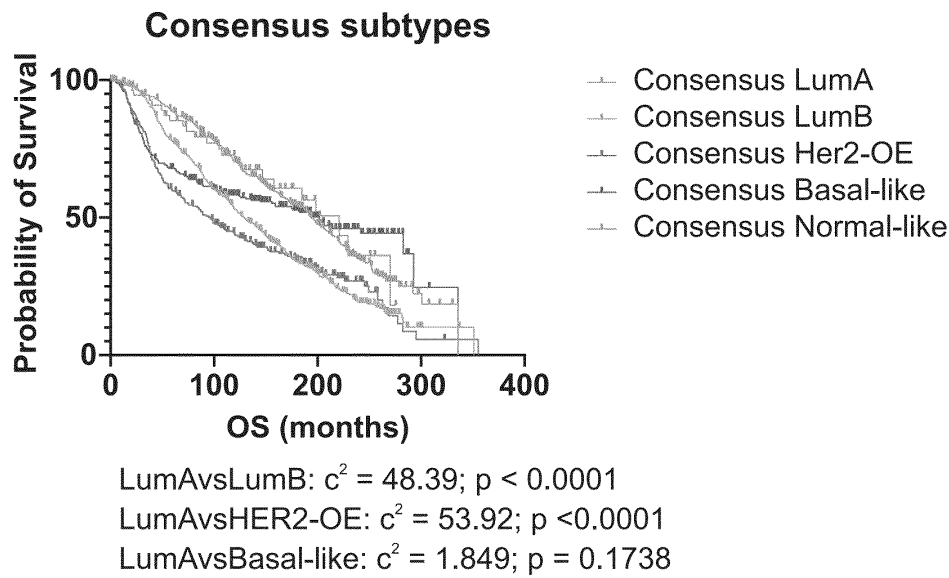


Figure 23 (cont.)

f



g

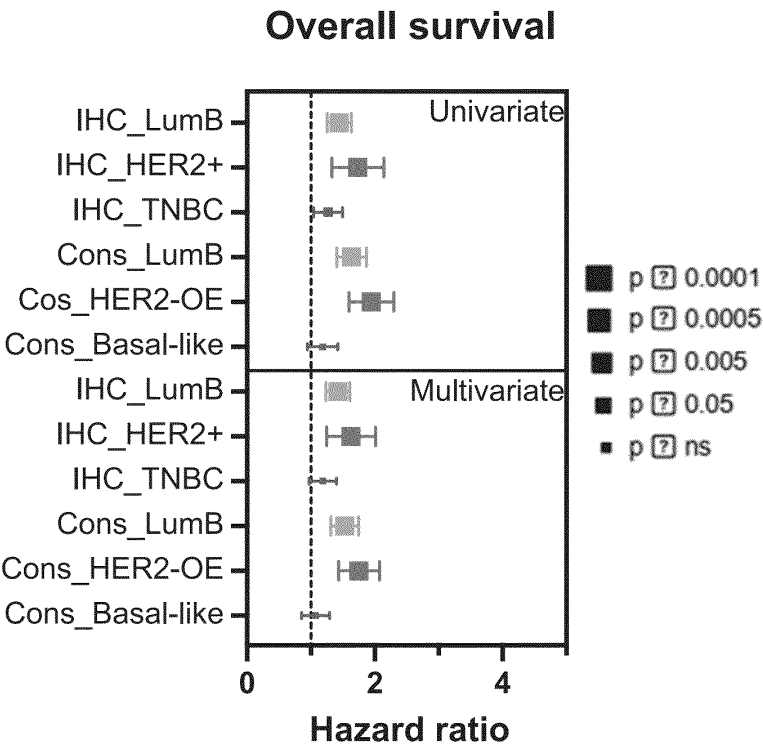
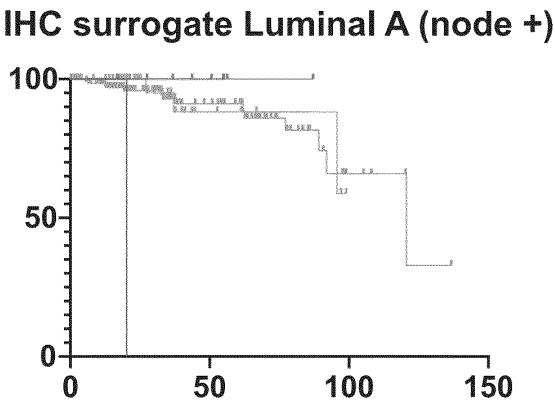
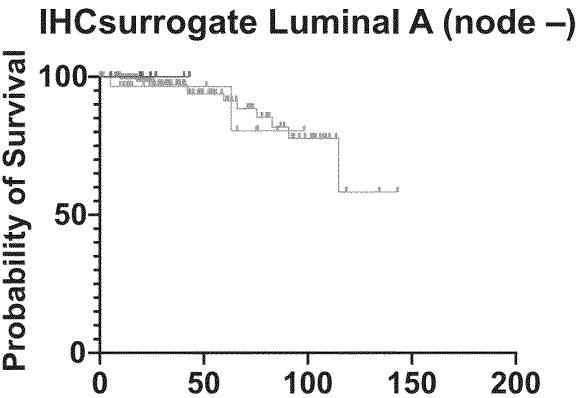


Figure 24

a

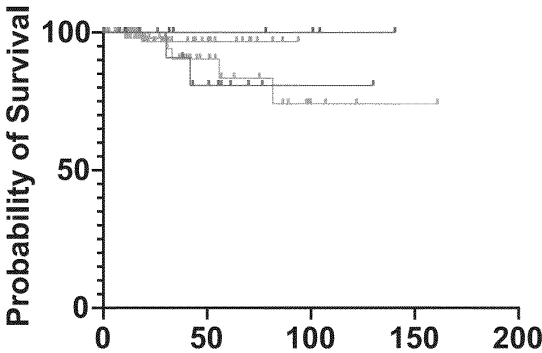


- Consensus Basal-like
- - Consensus Her2-OE
- ... Consensus LumA
- . Consensus LumB
- - - Consensus Normal-like

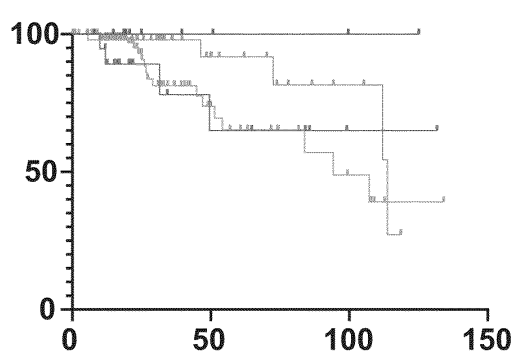
Figure 24 (cont.)

b

IHC surrogate Luminal B (node -)



IHC surrogate Luminal B (node +)



- Consensus Basal-like
- - Consensus Her2-OE
- ... Consensus LumA
- . Consensus LumB

Figure 24 (cont.)

C

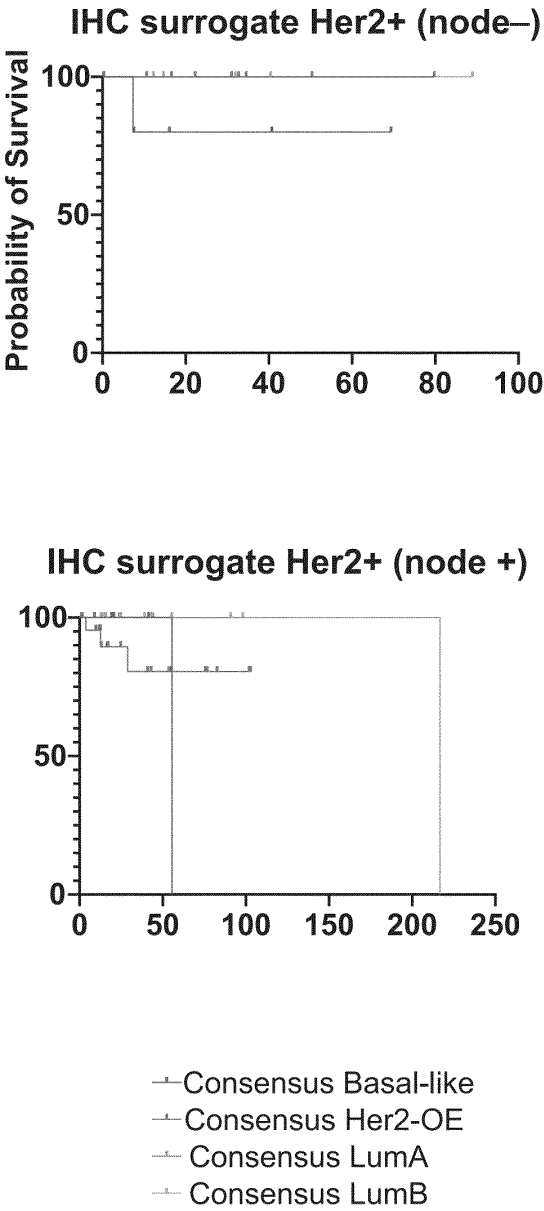
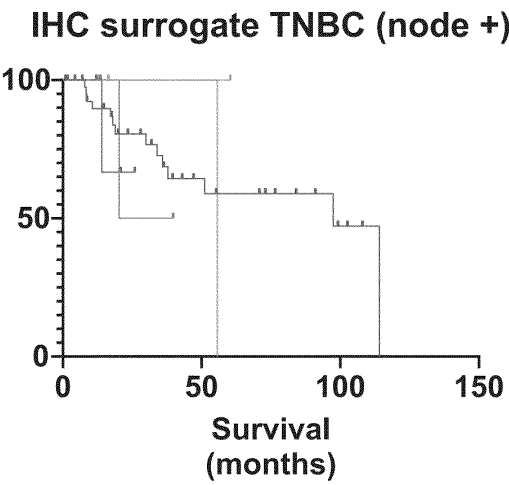
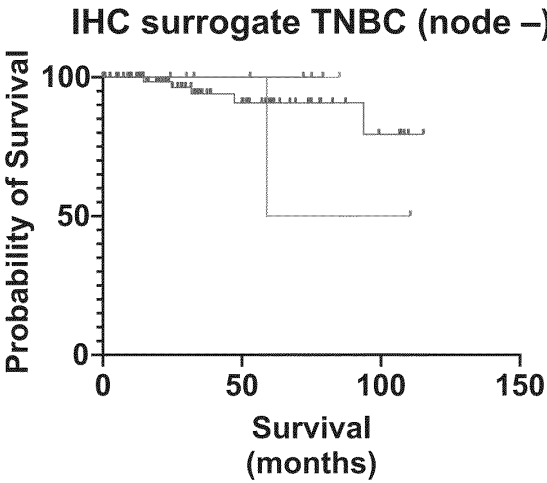


Figure 24 (cont.)

d



- +— Consensus Basal-like
- +— Consensus Her2-OE
- +— Consensus LumA
- +— Consensus LumB
- +— Consensus Normal-like

Figure 24 (cont.)

e

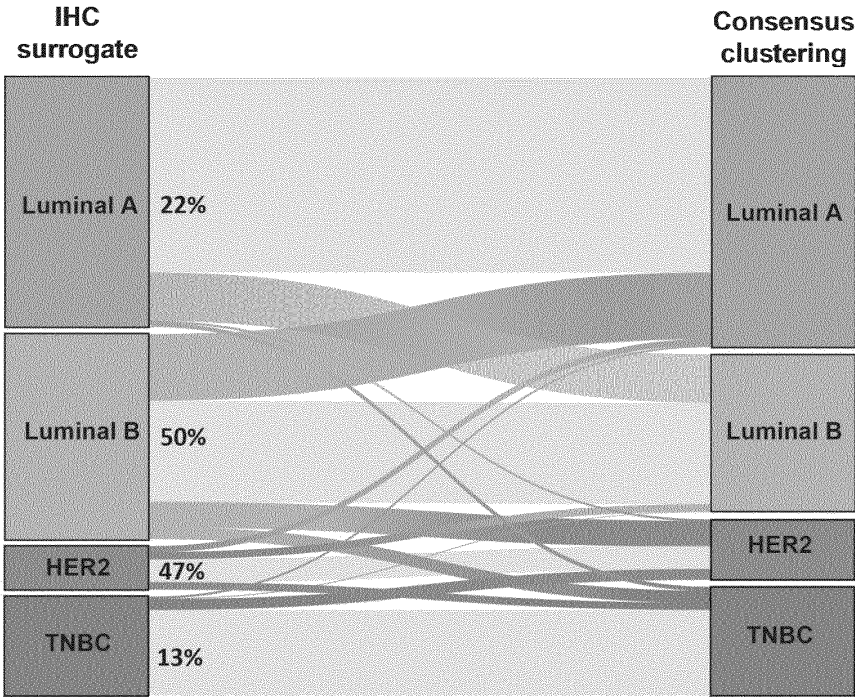
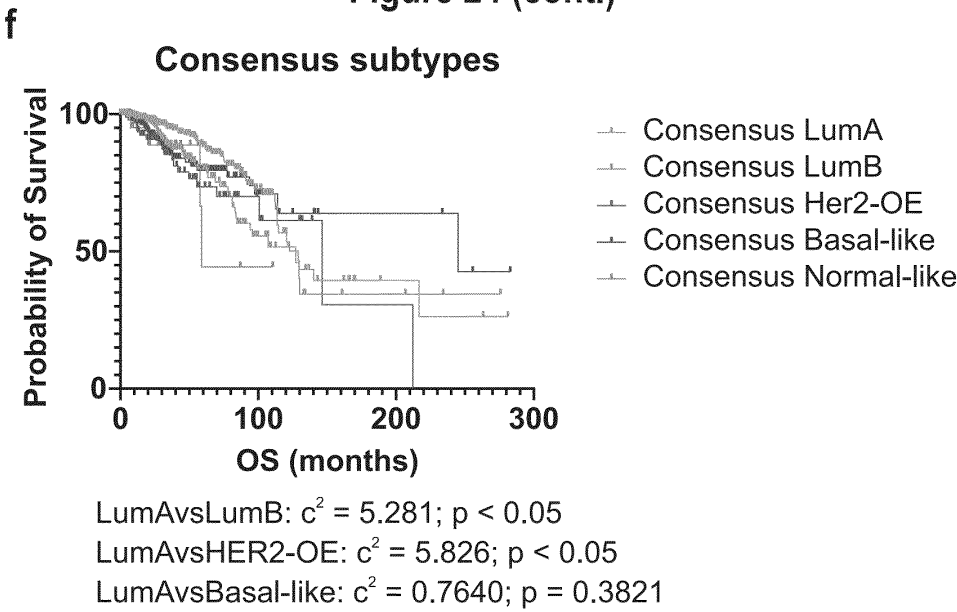


Figure 24 (cont.)



g

Overall survival

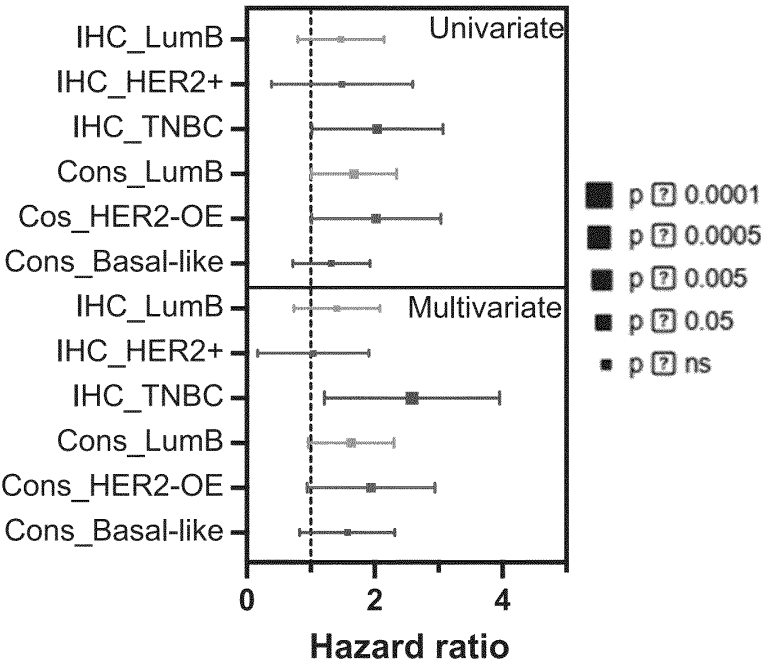


Figure 25

a

METABRIC

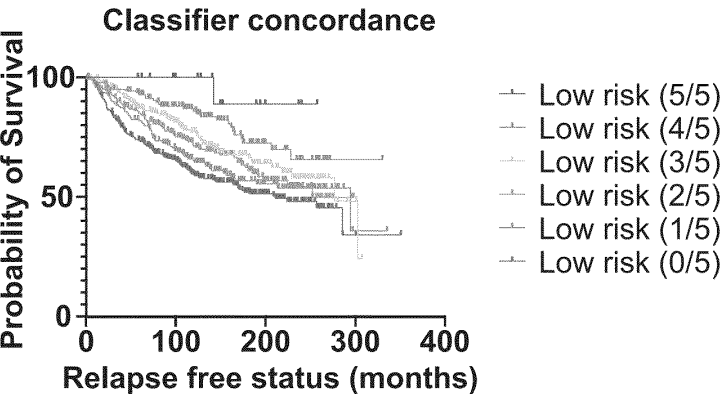
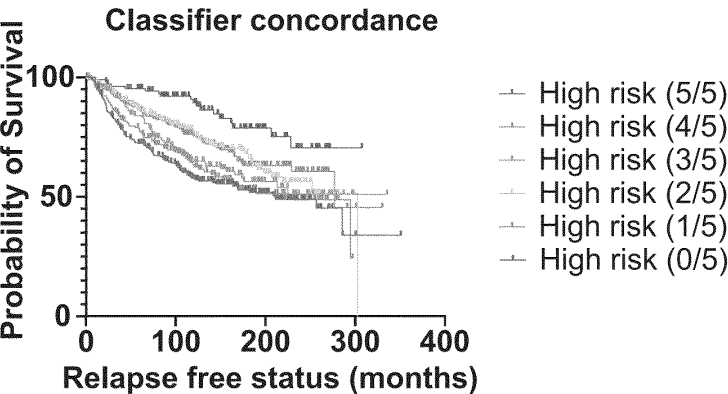


Figure 25 (cont.)

b

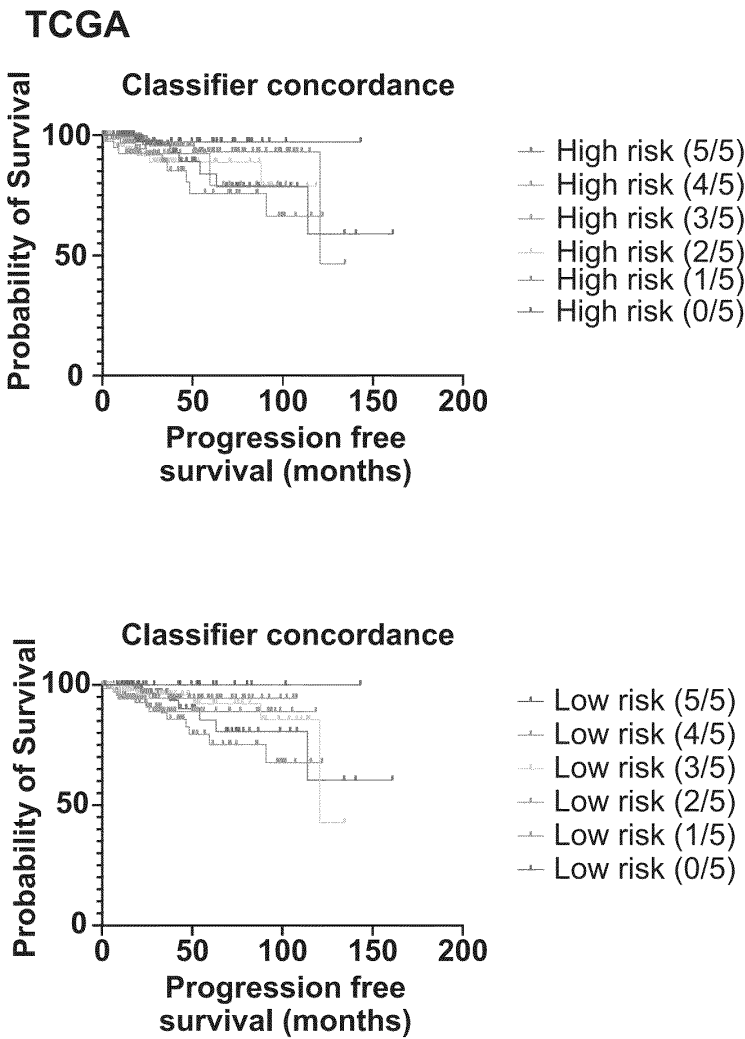


Figure 25 (cont.)

C

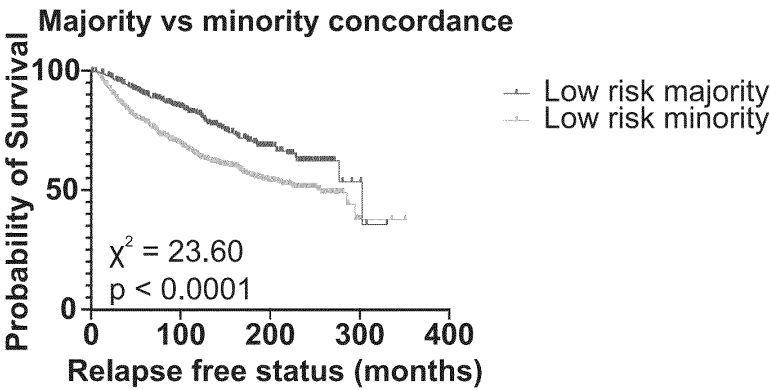
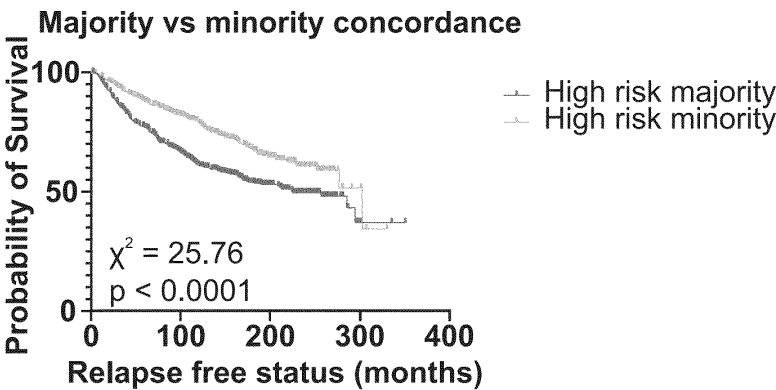


Figure 25 (cont.)

d

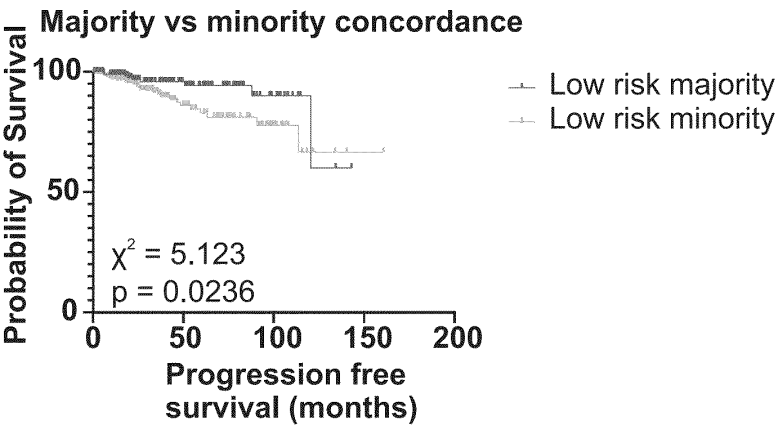
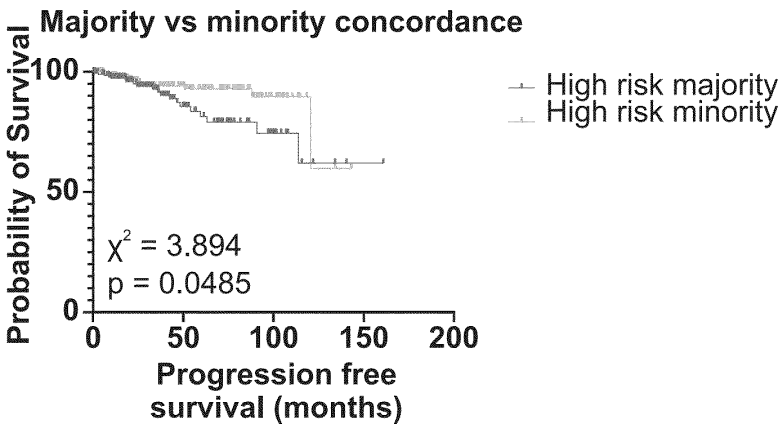


Figure 25 (cont.)

e

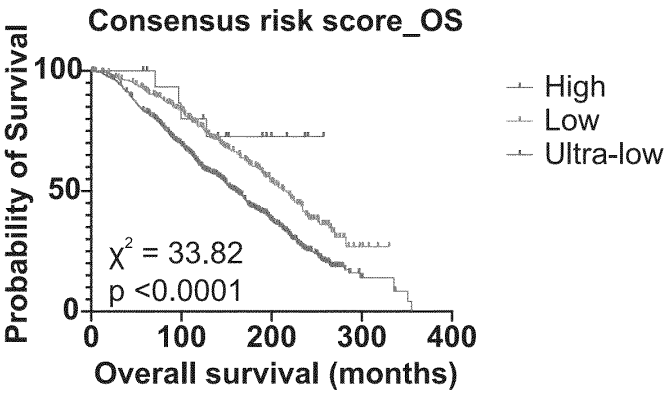
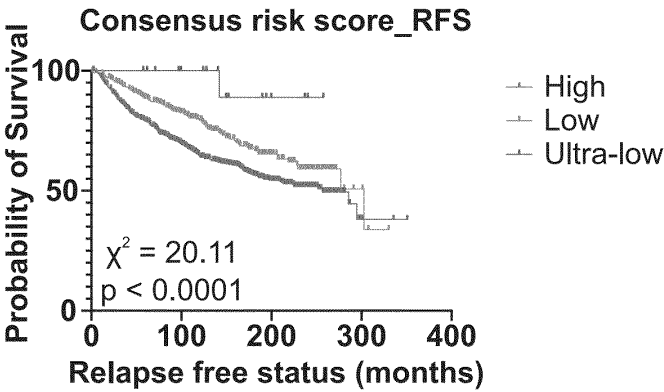


Figure 25 (cont.)

f

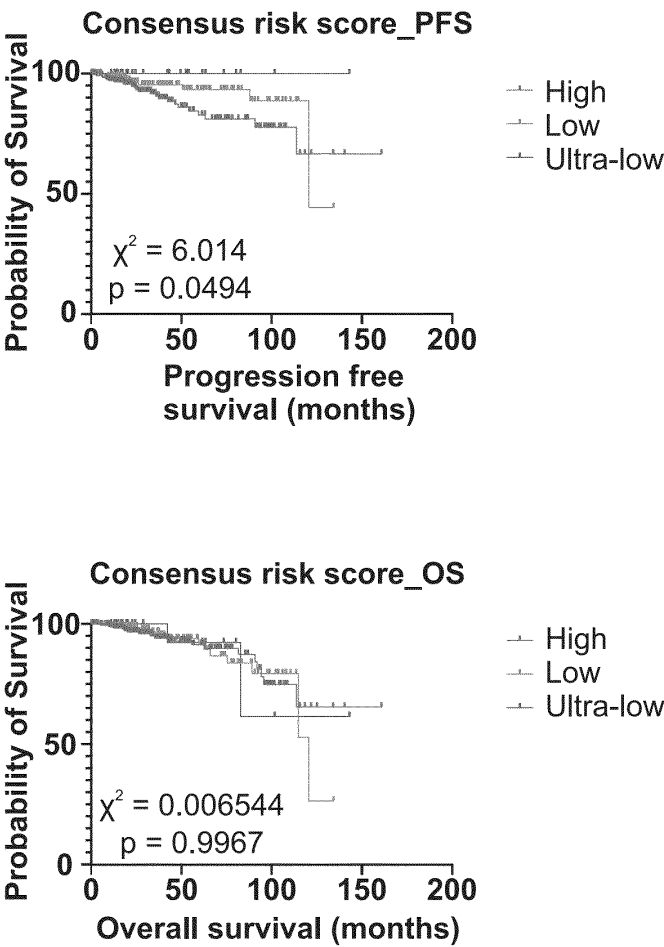
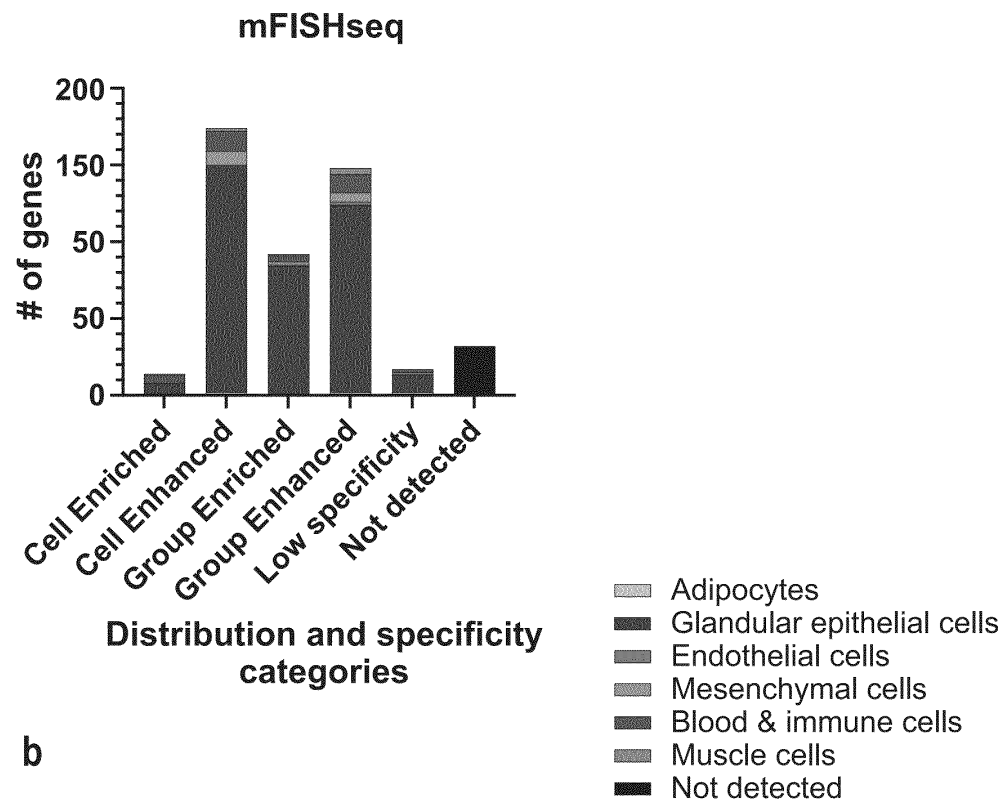


Figure 26

a



b

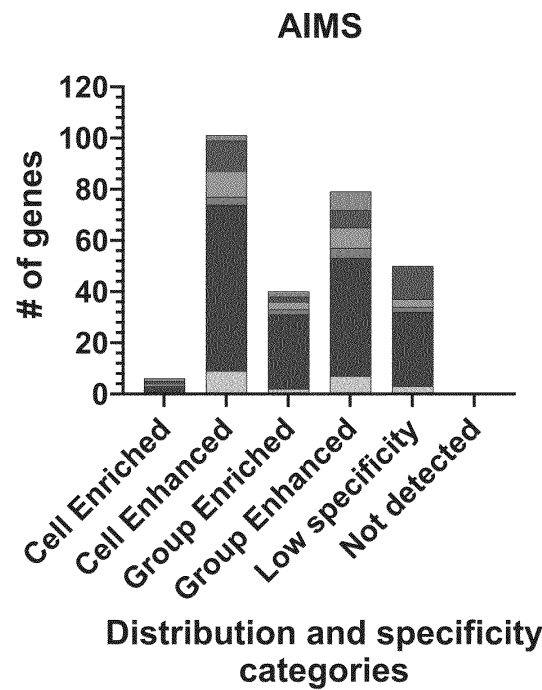
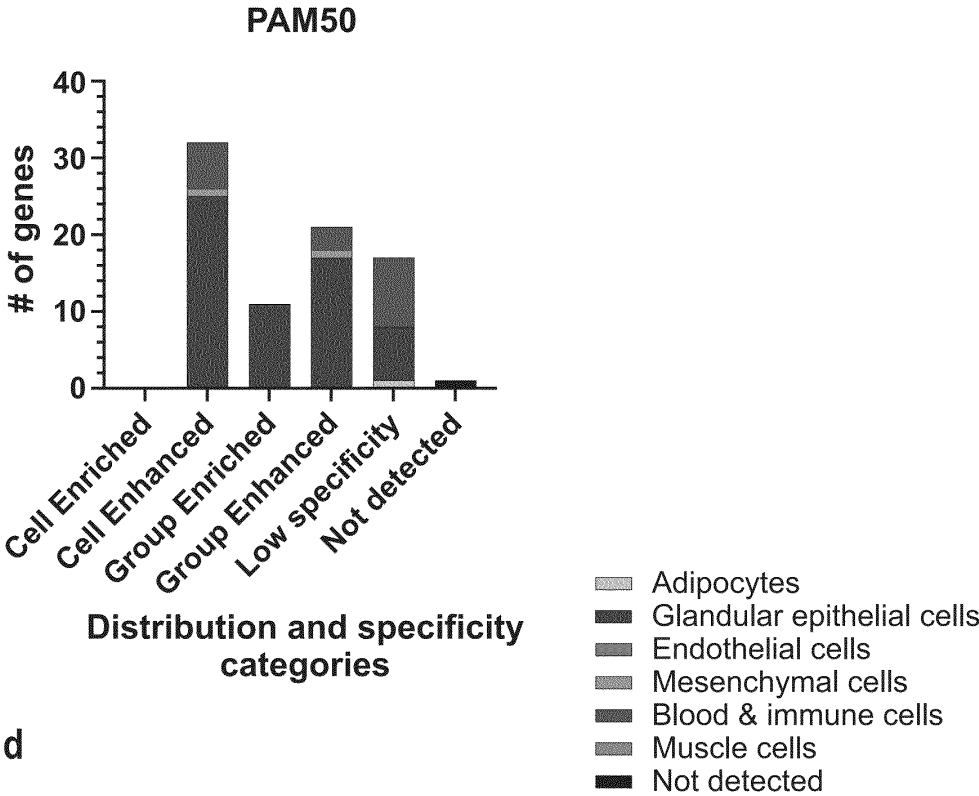


Figure 26 (cont.)

c



d

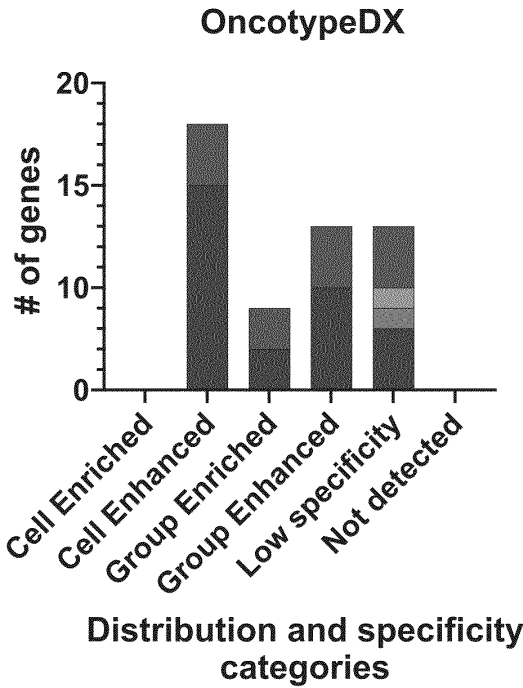
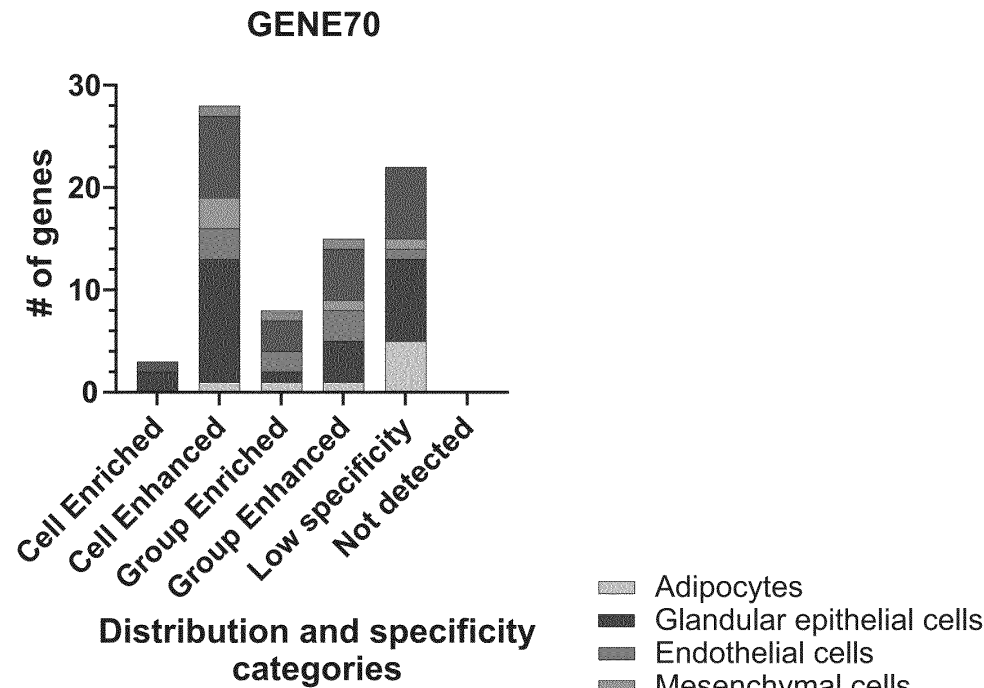


Figure 26 (cont.)

e



f

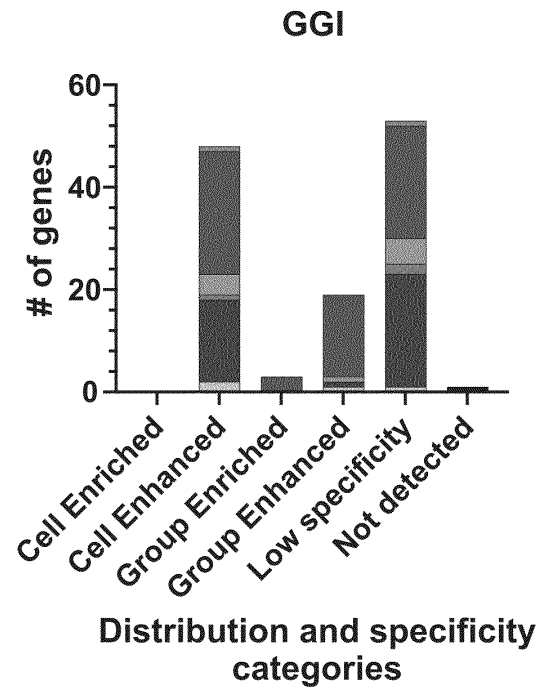


Figure 27

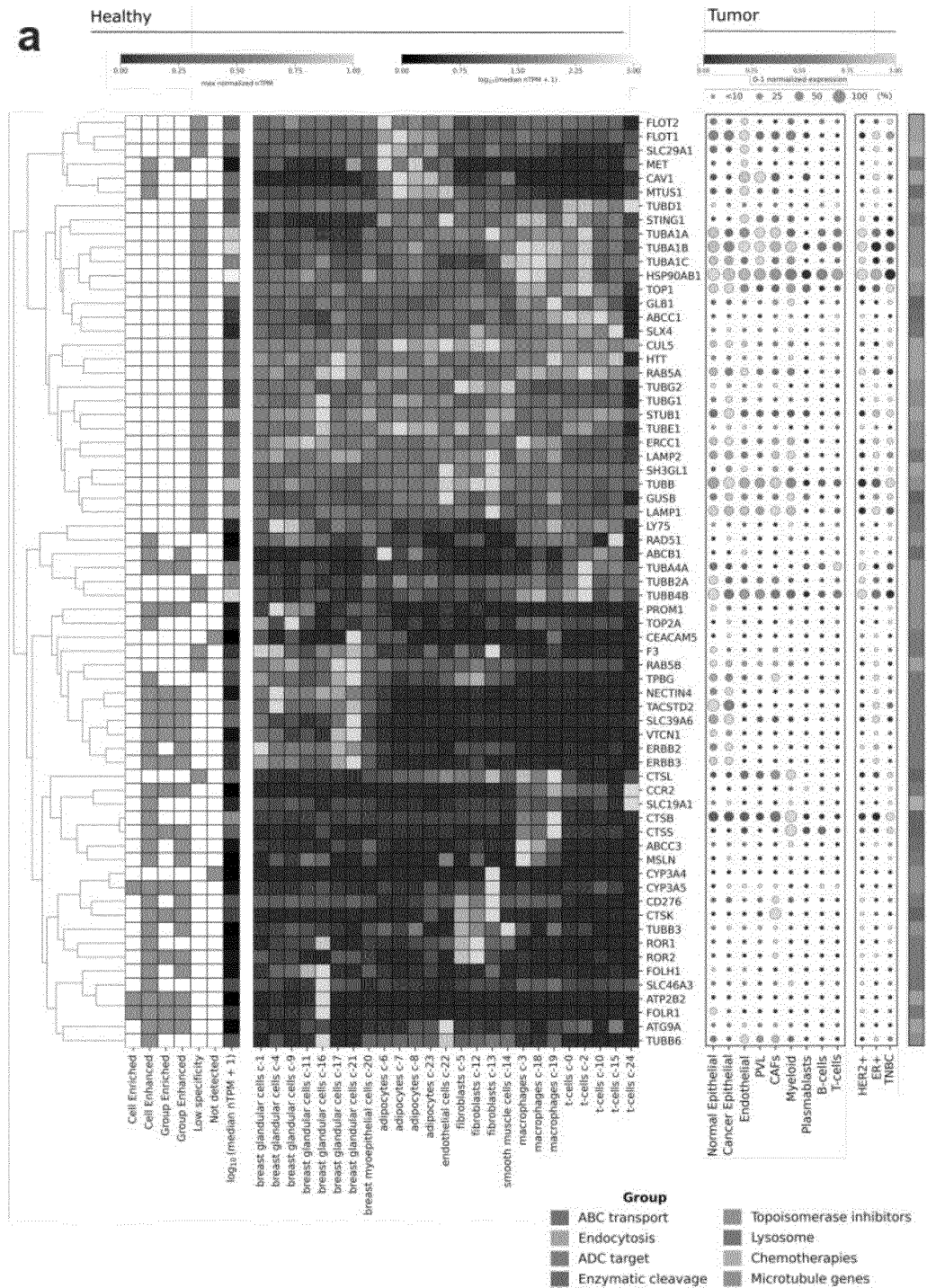


Figure 27 (cont.)

b

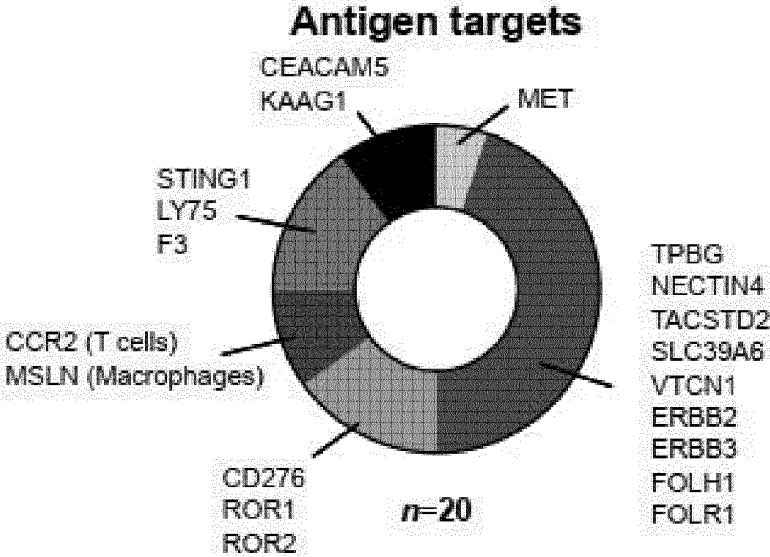
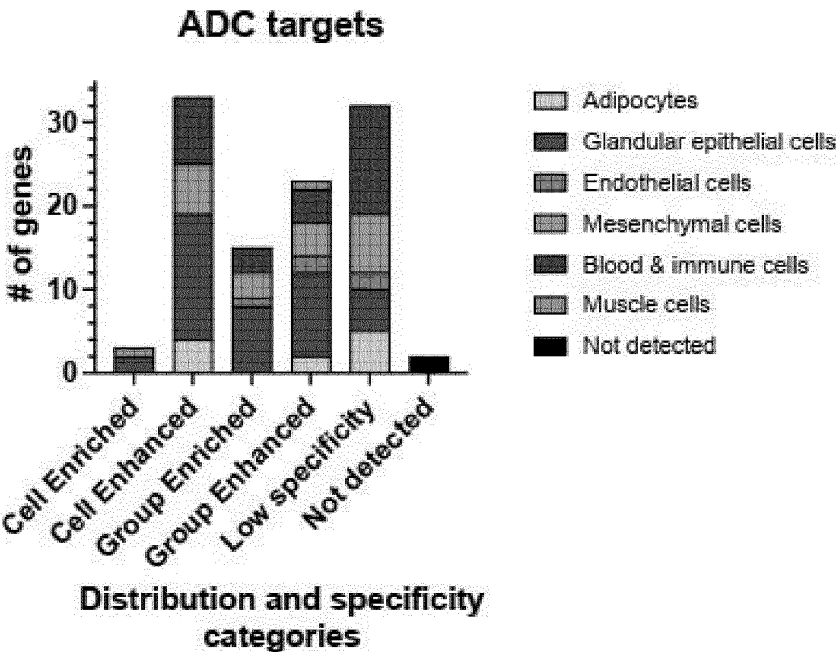


Figure 27 (cont.)

b (cont.)

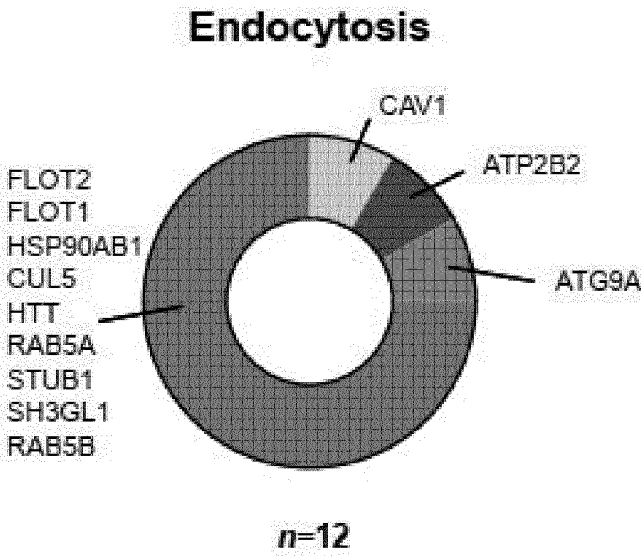
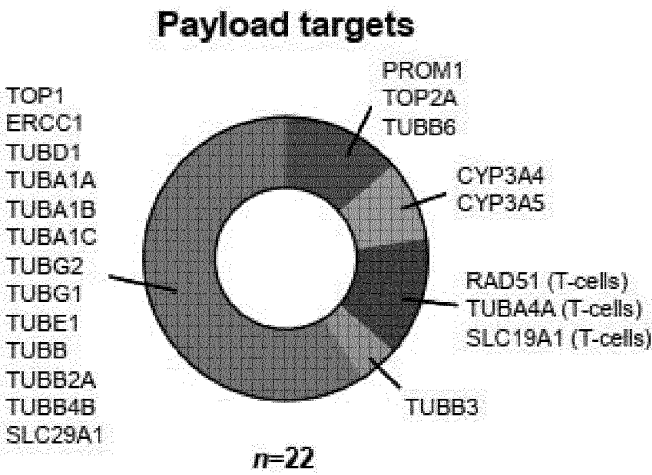


Figure 27 (cont.)

b (cont.)

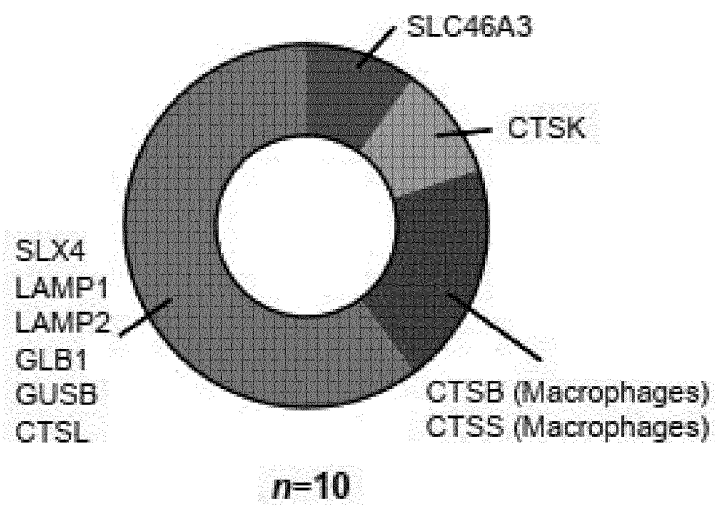
Lysosome/Enzymatic cleavage

Figure 27 (cont.)

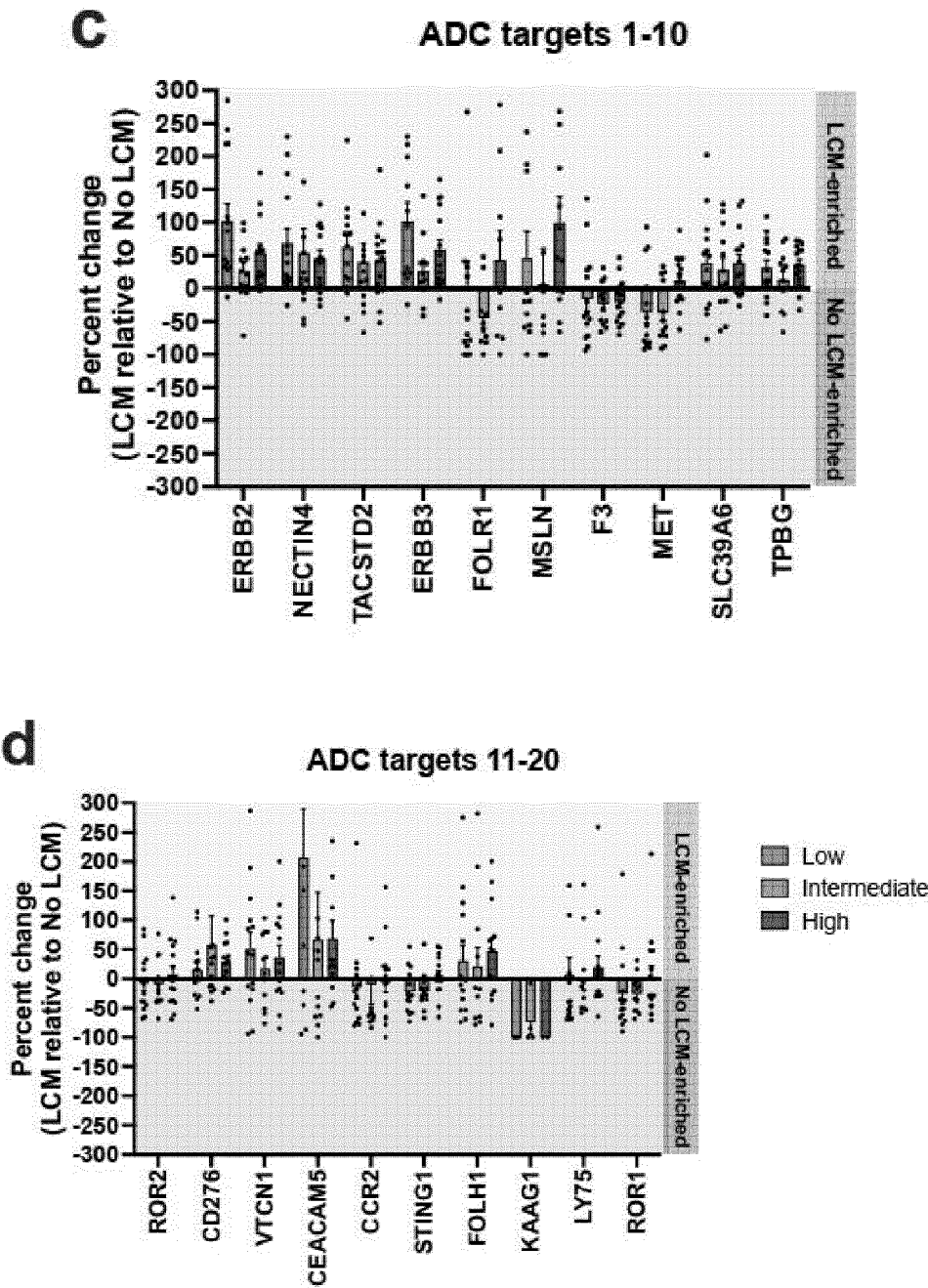


Figure 27 (cont.)

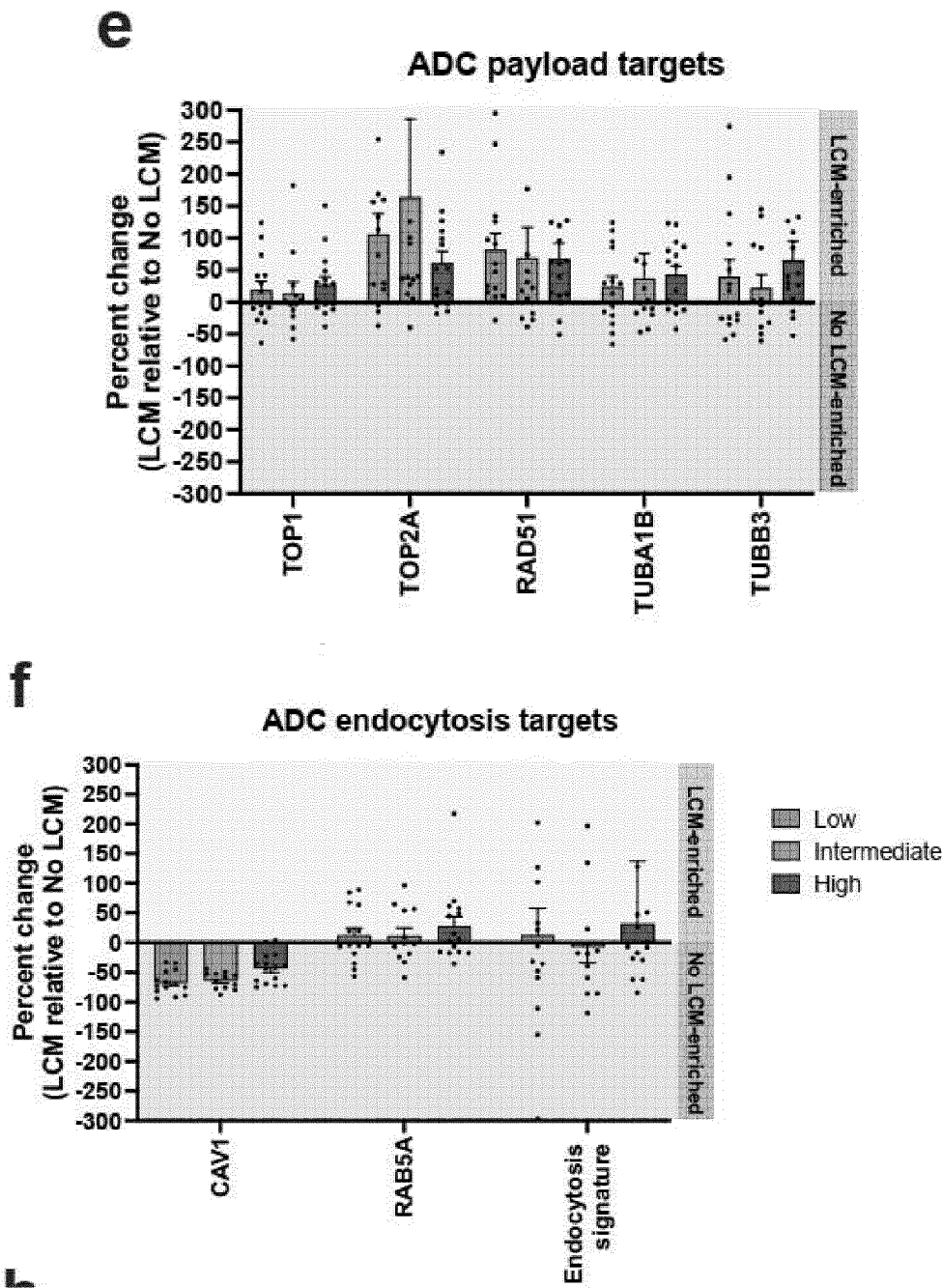


Figure 27 (cont.)

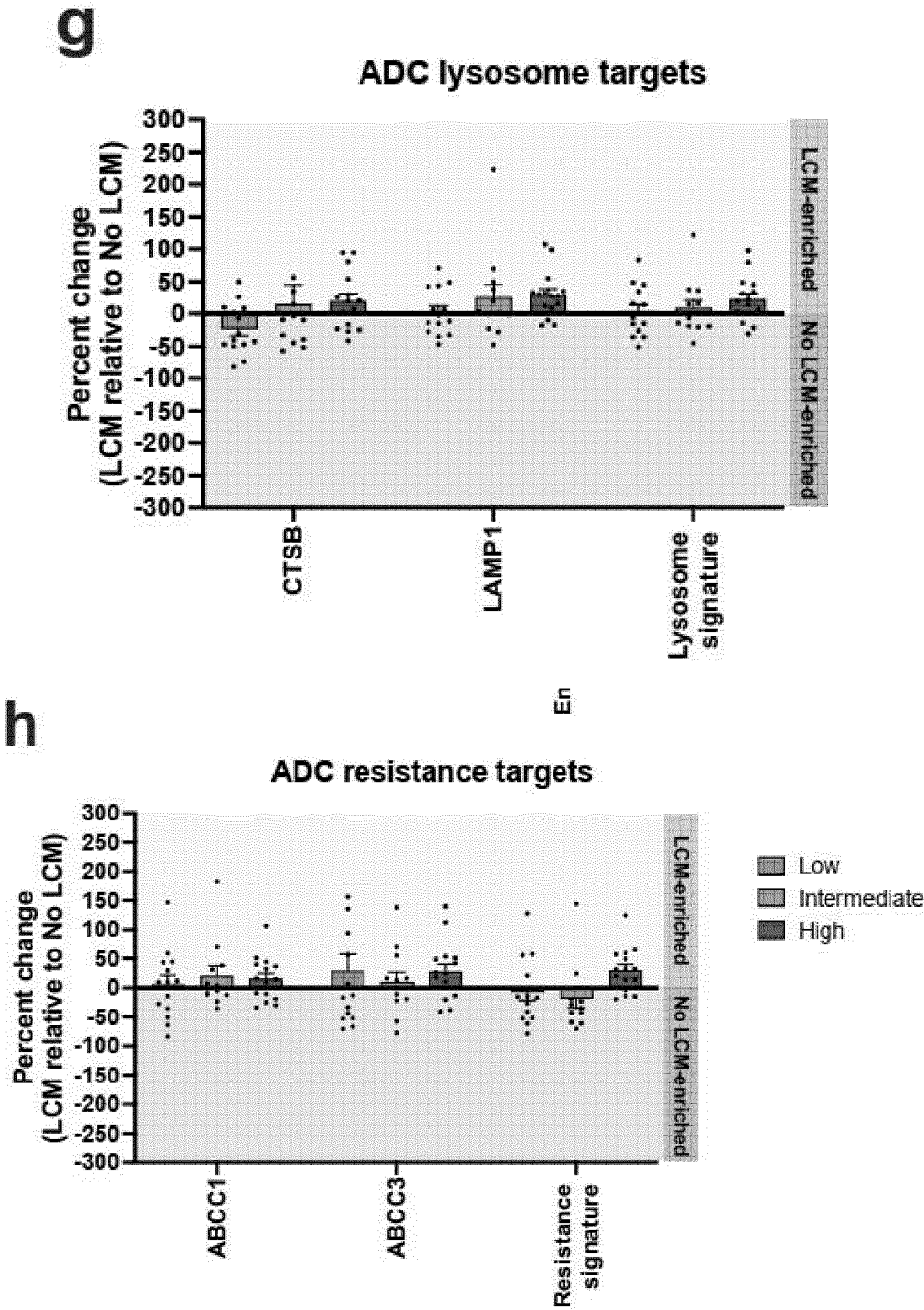


Figure 28

a

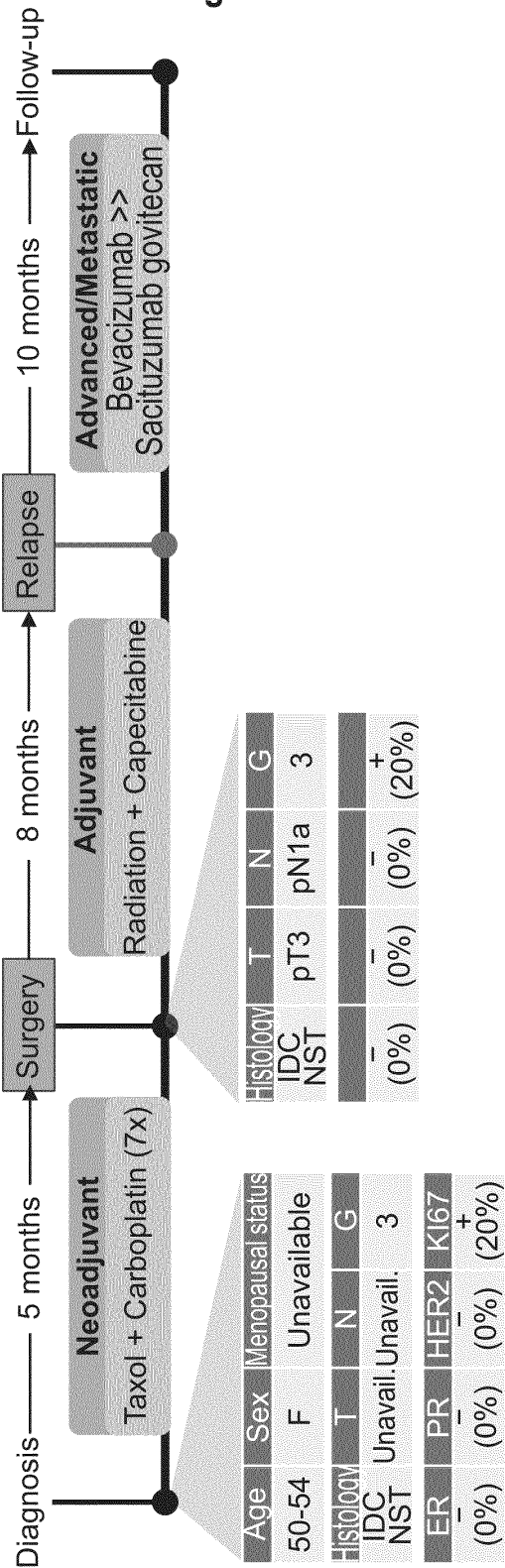


Figure 28 (cont.)

b

LASER CAPTURE MICRODISSECTION

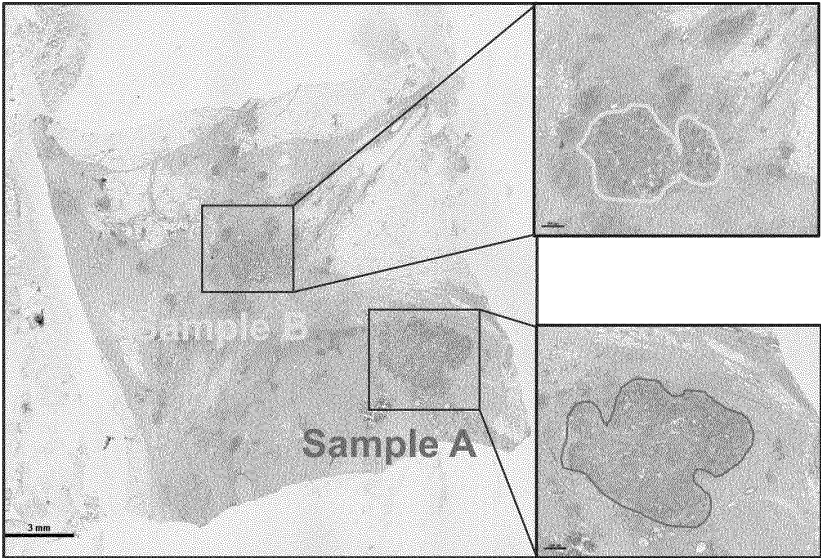
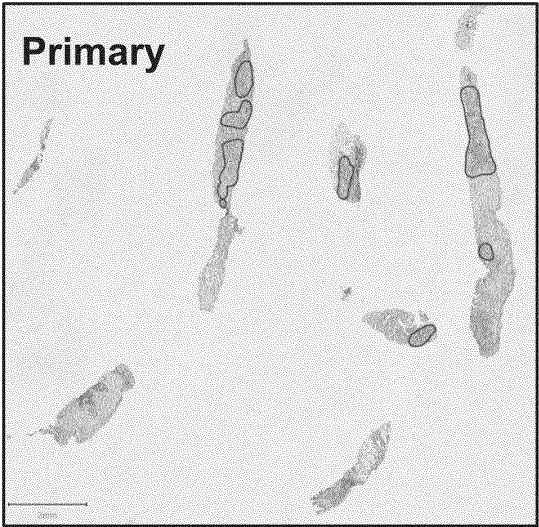


Figure 28 (cont.)

C

RECEPTOR STATUS

Sample	ESR1	PGR	ERBB2	MKI67
Primary	-	-	-	-
A	-	-	- low	+
B	-	-	- low	+

CONSENSUS MOLECULAR SUBTYPE

Sample	Intrinsic subtype	TNBC subtype
Primary	Basal-like	Mesenchymal (M)
A	Basal-like	Mesenchymal (M)
B	Basal-like	Immuno-modulatory (IM)

d

TREATMENT RESPONSE PREDICTION

Treatment / Pathway	Gene or gene signature	Primary Percentile	Sample A Percentile	Sample B Percentile
Chemo-therapy	MAPs_Mitotic_kinases_neoadj_chemo17	Low (32%)	High (100%)	High (98%)
	Early_Relapse_ER.Neg	Medium (33%)	High (97%)	High (92%)
	Residual_disease_ER.Neg	Medium (53%)	High (99%)	High (94%)
DNA damage and repair	VCpred_TN	Low (19%)	Low (14%)	Medium (48%)
Angiogenesis /hypoxia	VEGFA	Medium (64%)	High (75%)	Low (32%)
	Hypoxia / Angiogenesis / Inflammatory_MDX	Medium (64%)	High (84%)	High (81%)
ADC (antibody-drug conjugate) targets	TACSTD2	High (96%)	High (100%)	High (100%)
	TOP1	Medium (51%)	High (100%)	High (100%)

Figure 29

a

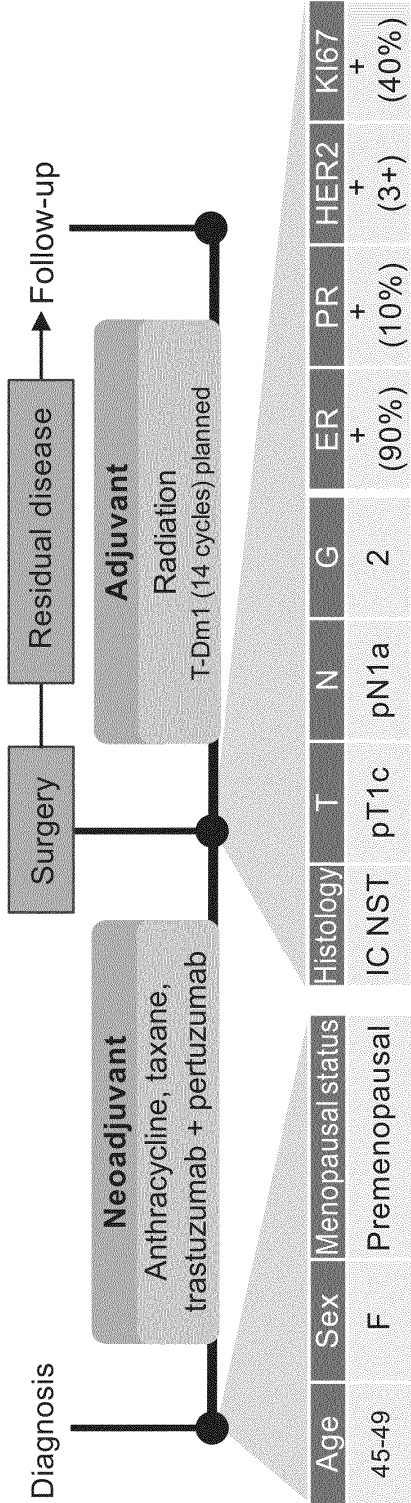
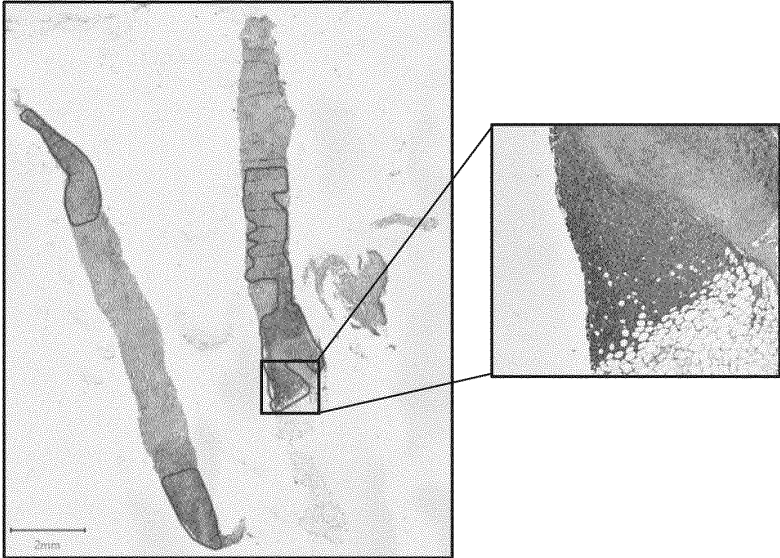


Figure 29 (cont.)

b

LASER CAPTURE MICRODISSECTION



c

RECEPTOR STATUS

Sample	<i>ESR1</i>	<i>PGR</i>	<i>ERBB2</i>	<i>MKI67</i>
A	+	+	+	+

CONSENSUS MOLECULAR SUBTYPE

Intrinsic subtype	TNBC subtype
Luminal B	N/A

CONSENSUS PROGNOSTIC RISK

ODX	ROR-S	GENE 70	GGI	CR
N/A	N/A	N/A	N/A	N/A

Figure 29 (cont.)

d

TREATMENT RESPONSE PREDICTION		
Treatment / Pathway	Gene or gene signature	Sample A Percentile
Her2	ERBB2	High (87%)
	NRG1	Medium (43%)
	pSTAT3-GS	Low (9%)
	Her2 amplicon_MDX	High (91%)
Chemo therapy	TOP1	High (97%)
	MAPs_Mitotic_kinases_neoadj_chemo118	High (88%)
	MAPs_Mitotic_kinases_neoadj_chemo17	High (78%)
	Residual_disease_ER.Pos	High (90%)
ADC targets	TACSTD2	High (92%)

a

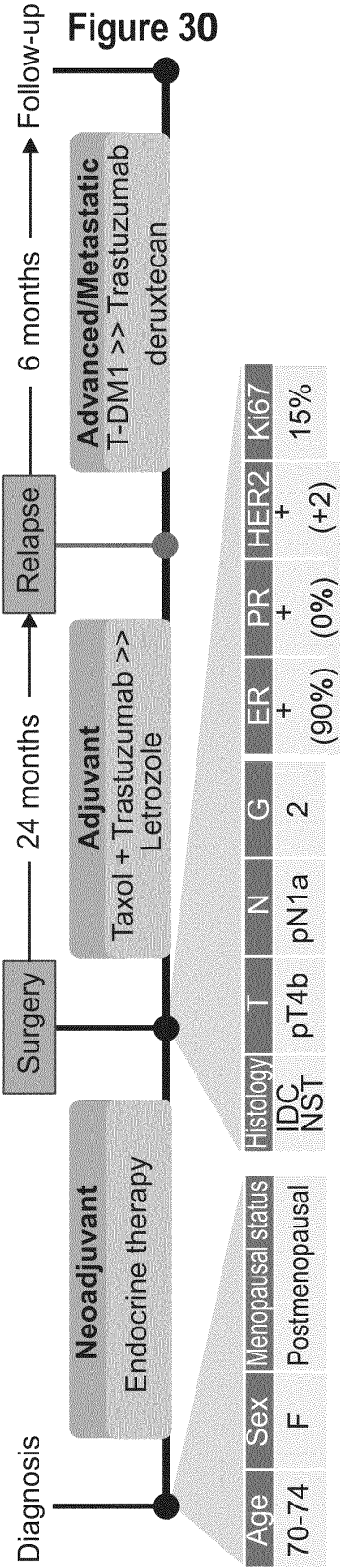
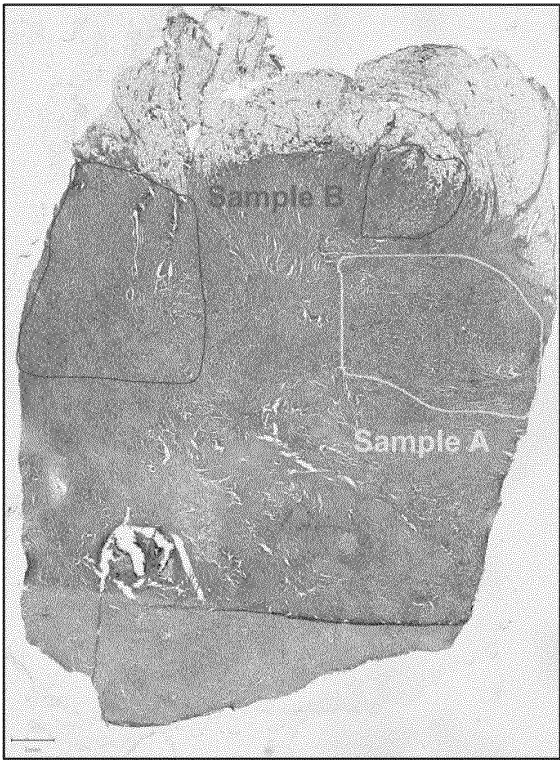


Figure 30 (cont.)

b

LASER CAPTURE MICRODISSECTION



c

RECEPTOR STATUS

Sample	<i>ESR1</i>	<i>PGR</i>	<i>ERBB2</i>	<i>MKI67</i>
A	+	−	+	+
B	+	−	− low	+

CONSENSUS MOLECULAR SUBTYPE

Sample	Intrinsic subtype	TNBC subtype
A	Luminal B	−
B	Luminal B	−

Figure 30 (cont.)

d

TREATMENT RESPONSE PREDICTION

Treatment / Pathway	Gene or gene signature	Sample A Percentile	Sample B Percentile
Her2	ERBB2	High (89%)	High (73%)
	Her2 amplicon_MDX	High (91%)	High (75%)
	Module7_ERBB2	High (86%)	Medium (65%)
ADC (antibody-drug conjugate) targets	TACSTD2	High (76%)	High (98%)
Chemotherapy	TOP1	High (98%)	High (99%)

Figure 31

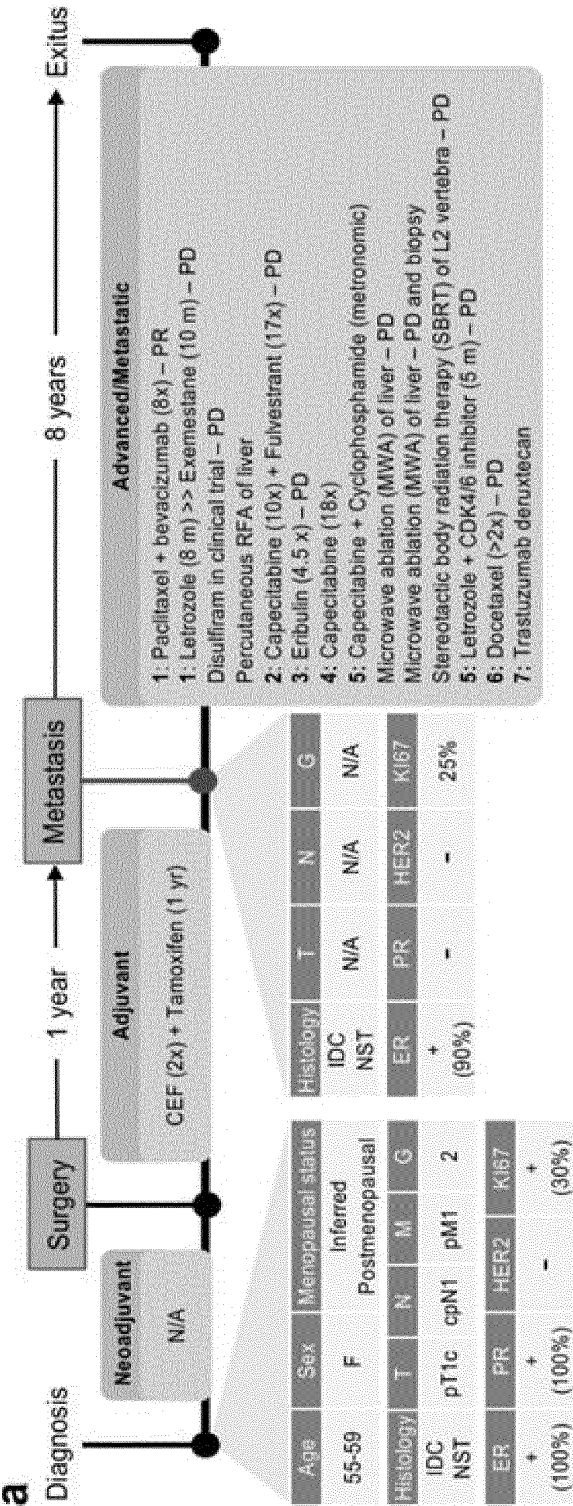


Figure 31 (cont.)

b LASER CAPTURE MICRODISSECTION



c RECEPTOR STATUS

Sample	<i>ESR1</i>	<i>PGR</i>	<i>ERBB2</i>	<i>MKI67</i>
A	+	-	- low	-

CONSENSUS MOLECULAR SUBTYPE

Intrinsic subtype	TNBC subtype
Luminal B	N/A

Figure 31 (cont.)

d TREATMENT RESPONSE PREDICTION

Treatment / Pathway	Gene or gene signature	Sample A Percentile
Luminal signatures	ESR1	Medium (36%)
	PGR	Low (10%)
	E2F4_score	Low (27%)
Her2	ERBB2	Low (27%)
	Her2 amplicon_MDX	Low (8%)
	Module7_ERBB2	Low (31%)
ADC (antibody-drug conjugate)	TACSTD2	High (95%)
	Cathepsins	Low (9%)
	CTSB	Low (3%)
	KEGG_LYSOSOME	Low (31%)
	CAV1	Low (18%)
	KEGG_ENDOCYTOSIS	Low (1%)
Chemotherapy	TOP1	High (93%)