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Gene Name	Coefficient	Location in genome
ACAT2	0.03	6q25.3
ADAM9	0.04	8p11.22
ADAMTS1	0.03	21q21.3
AGPAT5	0.09	8p23.1
B3GALNT2	0.23	1q42.3
COL11A1	0.02	1p21.1
CPT2	-0.52	1p32.3
DSC3	0.02	18q12.1
FAT1	0.12	4q35.2
FTSJD1	-0.01	16q22.2
KIAA1199	-0.02	15q25.1
MAP4K4	0.21	2q11.2
MCTP2	-0.27	15q26.2
METTL1	0.07	12q14.1
MR1	-0.27	1q25.3
NRIP1	0.2	21q11.2-q21.1
PANK4	-0.11	1p36.32
PLXND1	-0.02	3q22.1
PWP1	0.05	12q23.3
RAP1GDS1	0.65	4q23
RUVBL2	0.27	19q13.33
SH3TC1	0.5	4p16.1
SNX5	0.57	20p11.23
SPAG5	0.34	17q11.2
SPRY2	-0.24	13q31.1
SYS1	-0.11	20q13.12
TMEM183A	0.24	1q32.1
TSPAN3	0.15	15q24.3
UVRAG	-0.57	11q13.5

20 Supplementary Table 2 Univariable Cox Regression

	Univariable Cox Regression		
	TCGA-MESO	Bueno	Bott_GSE29354
PRACME	1.12(2.6e-16)	1.40 (4.6e-04)	1.61 (1.3e-02)
ORACLE	1.04 (1.0e-08)	1.63 (1.6e-09)	1.51 (6.2e-03)

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29 Supplementary Table 3 Multivariable Cox Regression

	Multivariable Cox Regression		
	TCGA-MESO	Bueno	Bott_GSE29354
PRACME	1.13(5.3e-13)	1.37 (4.60e-04)	1.61(1.3e-02)
ORACLE	1.04(4.0e-07)	1.61 (4.46e-06)	2.08(4.1e-03)

38 Supplementary Table 4 Bueno MPM stratification

<b>Validation Histology</b>	<b>HR</b>	<b>p-value</b>
Biphasic (n = 62)	1.03	0.88
Epithelioid (n = 141)	1.61	7.21e-07
All patients (n = 211)	1.43	2.63e-06
<b>Patient Stages</b>	<b>HR</b>	<b>p-value</b>
Early (stage I and II) (n=58)	1.49	0.02
Late (stage III and IV) (n=125)	1.45	4.04e-05
<b>Smoking History</b>	<b>HR</b>	<b>p-value</b>
Smoking history (n = 114)	1.48	3.64e-04
No smoking history (n = 96)	1.41	1.14e-09

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51 Supplementary Table 5 Correlation between PRACME score and Throsson-immunity table

Intratumor Heterogeneity	0.40
Proliferation	0.77
TGF beta Response	0.47

58 Supplementary Table 6. Correlation with GSVA pathways

Pathways	PRACME
REACTOME_PHASE1_FUNCTIONALIZATION_OF_COMPOUNDS	0.67
REACTOME_NUCLEAR_SIGNALING_BY_ERBB4	0.59
KEGG_LINOLEIC_ACID_METABOLISM	0.55
REACTOME_BIOLOGICAL_OXIDATIONS	0.58
REACTOME_COMPLEMENT_CASCADE	0.52

KEGG_DRUG_METABOLISM_CYTOCHROME_P450	0.52	59
REACTOME_BILE_ACID_AND_BILE_SALT_METABOLISM	0.48	61
KEGG_TYROSINE_METABOLISM	0.48	62
REACTOME_CYTOCHROME_P450_ARRANGED_BY_SUBSTRATE_TYPE	0.52	64
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68 Supplementary Table 7 Summary of Cox Regression of PRACME on all clinical variables

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70 Bueno Univariable analysis with PRACME

		HR	p-value	71
Age	Age	1.0	0.008	72
Stage	Stage I	reference	reference	74
	Stage II	1.8	0.2	75
	Stage III	2.1	0.1	76
	Stage IV	2.5	0.06	77
Sex	Female	reference	reference	78
	Male	1.3	0.2	79
Histology	Epithelioid	reference	reference	80
	Biphasic	1.5	0.01	81
	Sacomatoid	2.1	0.07	82
Asbestos exposure	No	reference	reference	83
	Yes	1.9	0.001	84
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88 Bott Univariable Analysis with PRACME

		HR	p-value	89
Age	Age	1.0	0.04	90
Stage	Stage I	reference	reference	92
	Stage II	1.5	0.5	93
	Stage III	3.7	0.03	94
	Stage IV	4.8	0.01	94
Sex	Female	reference	reference	95
	Male	1.1	0.8	96
Histology	Epithelioid	reference	reference	96
	Biphasic	1.2	0.002	97
	Sacomatoid	1.5	0.007	98
Asbestos exposure	No	reference	reference	99
	Yes	1.0	0.9	99

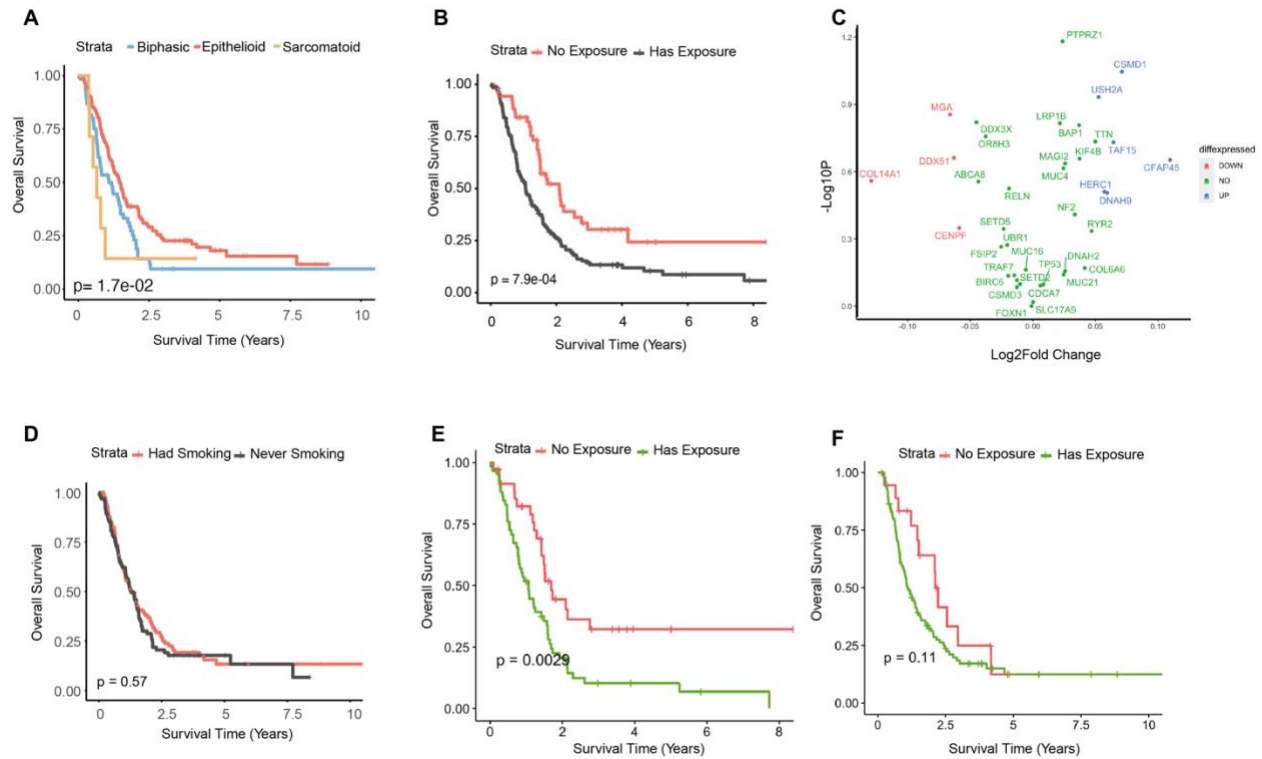
100 Supplementary Table 8 Mutation status in MPM data  
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<b>Mutation</b>	<b>Mutated Size</b>	<b>T-score</b>	<b>T-test p-value</b>	<b>Wilcox Test p-value</b>	<b>Mutated Mean</b>	<b>WO Mut Mean</b>
NF2	37	2.80	0.007	0.002	0.66	0.65
BAP1	46	0.94	0.35	0.35	0.67	0.65
SETD2	17	-1.40	0.18	0.18	0.64	0.66
TP53	16	0.24	0.81	0.94	0.66	0.65

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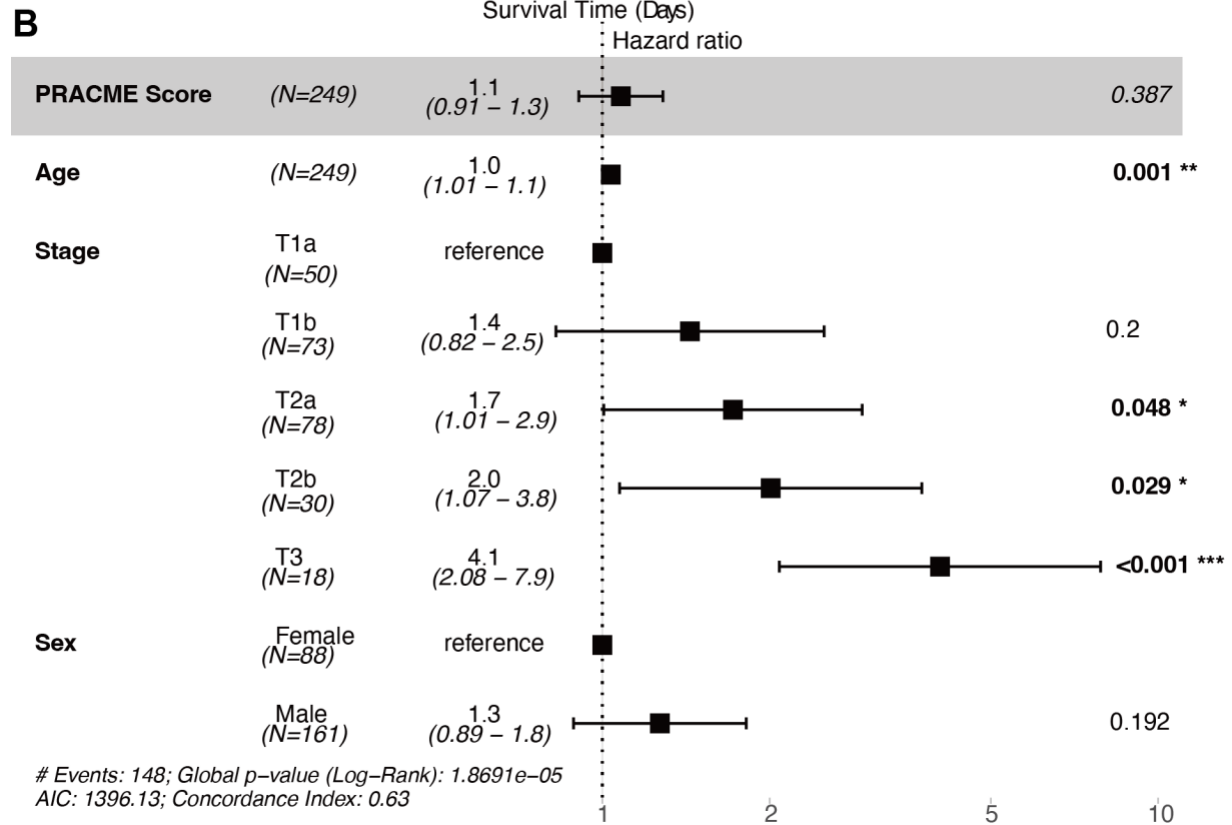
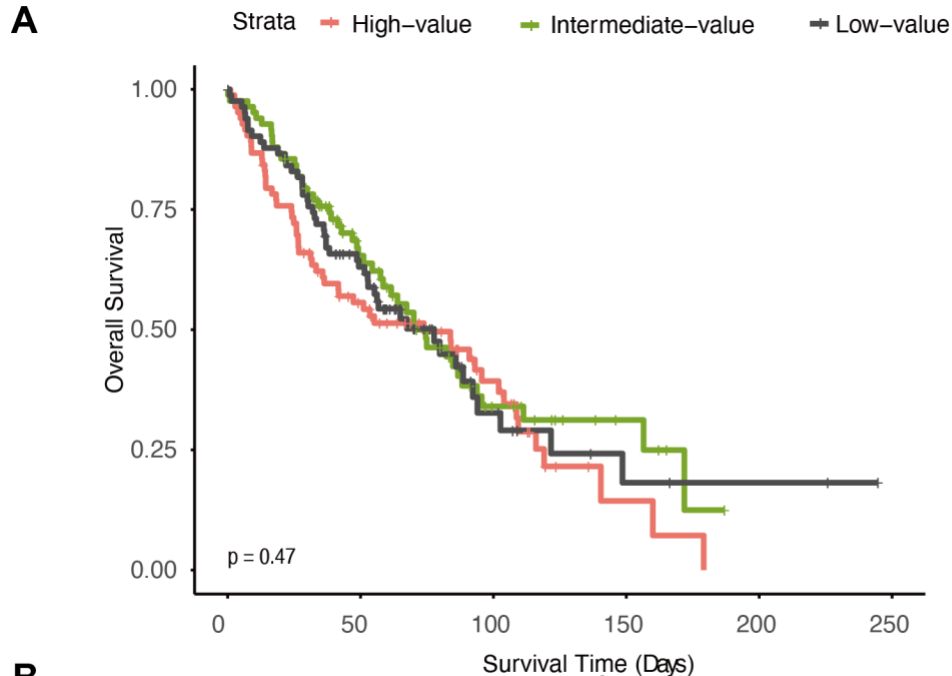
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Supplementary Figure 1 Association of PRACME signature score with additional clinical features

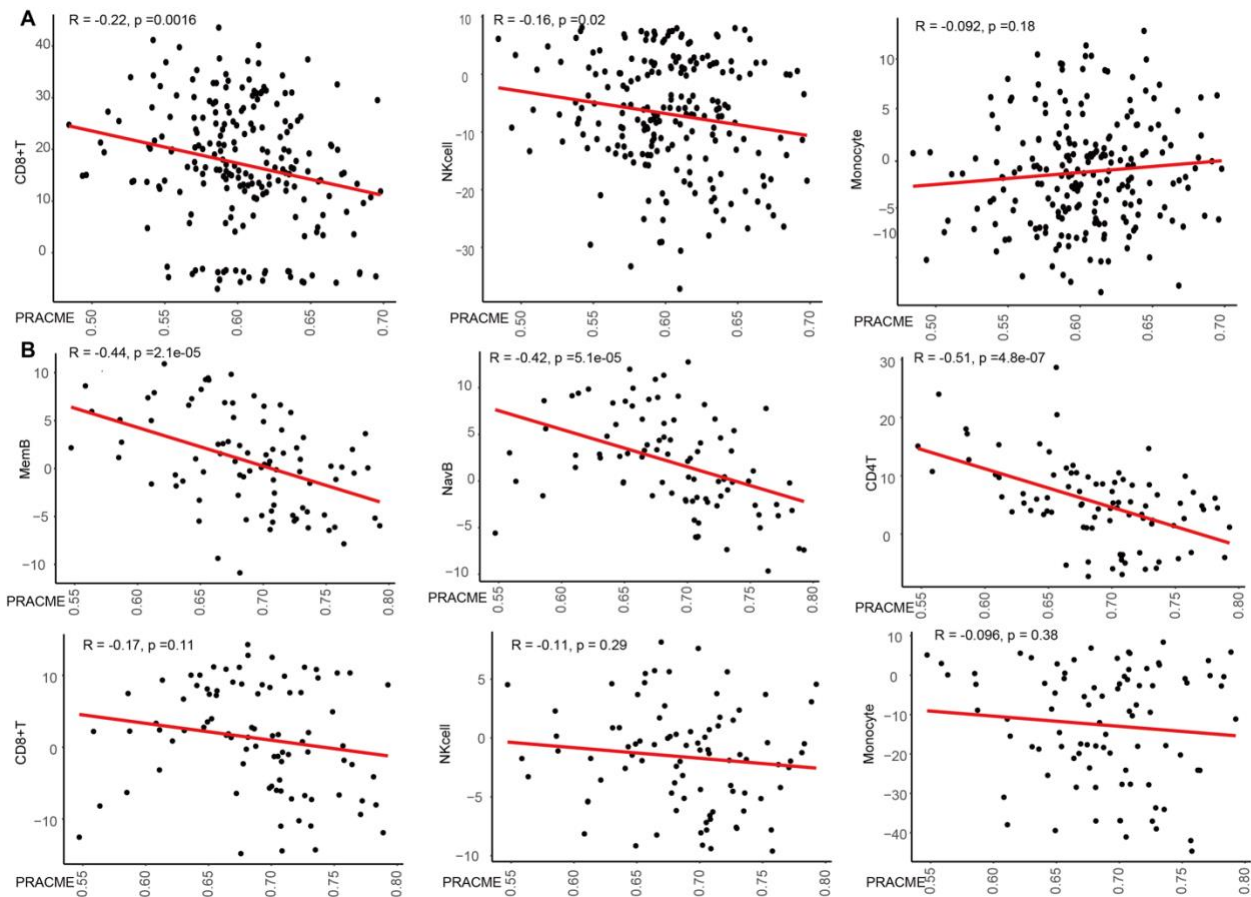
In Bueno MPM dataset, A) PRACME score for three histology; B) PRACME for asbestos exposure; C) Targeted mutation volcano plot; D) PRACME score for patients smoking history. We separated patients with never smokers and ever smokers; E) PRACME score for asbestos exposure in never-smokers; F) PRACME score for asbestos exposure in ever-smokers.



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Supplementary Figure 2 PRACME signature is not predictive of prognosis in lung squamous carcinoma

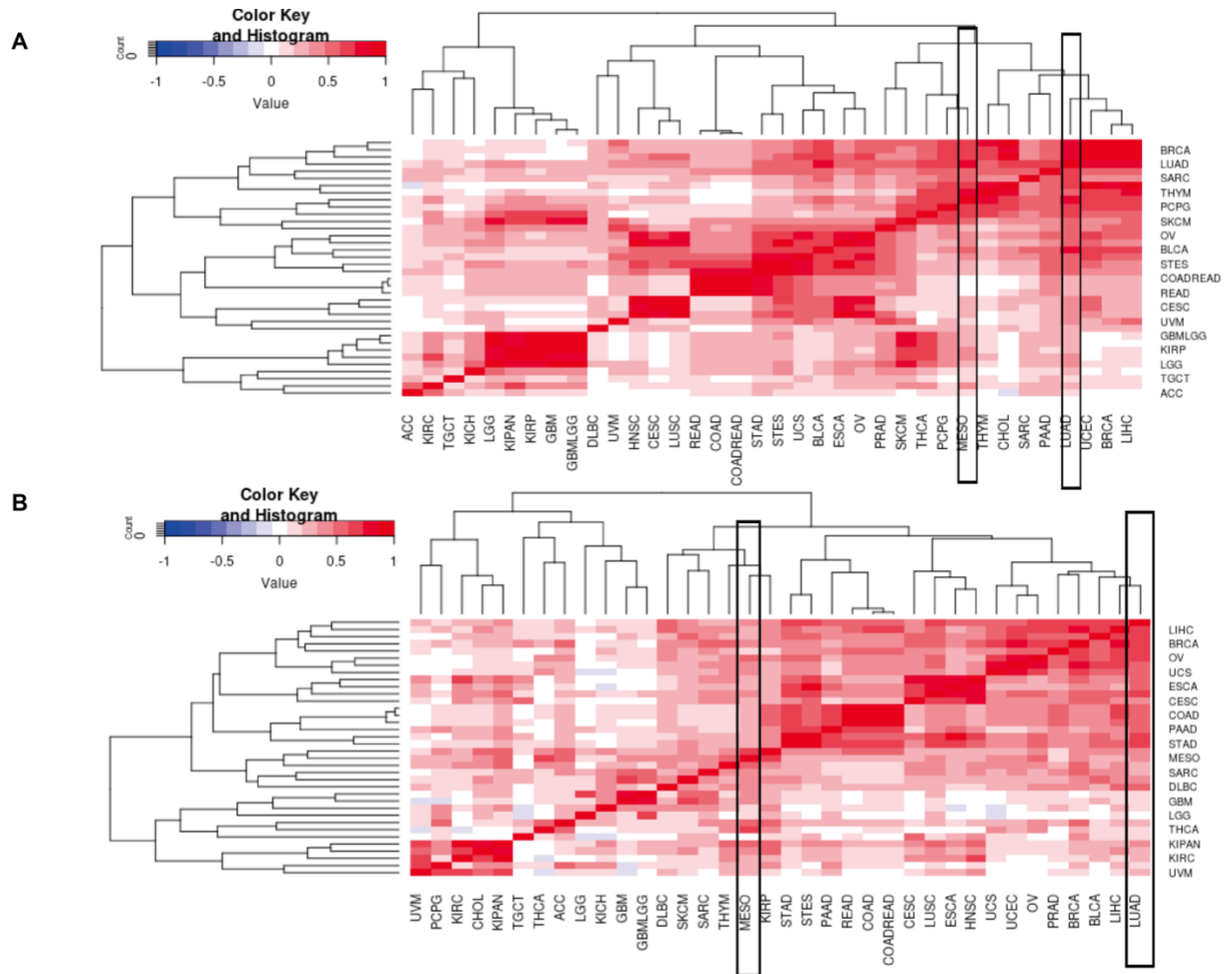
In Bueno GSE157011 LUSC patients, A) PRACME score for high-, intermediate-, and low-group patients; B) PRACME score adjusted for age, stage, and sex.



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Supplementary Figure 3 PRACME signature is negatively correlated to immune infiltration levels In Buco MPM dataset, A) PRACME correlation with CD8+T cells, NK cells and Monocyte infiltration. In TCGA-MESO, B) PRACME correlation with Memory B cells, Naïve B cells, CD4+T cells, CD8+T cells, NK cells and Monocyte infiltration.



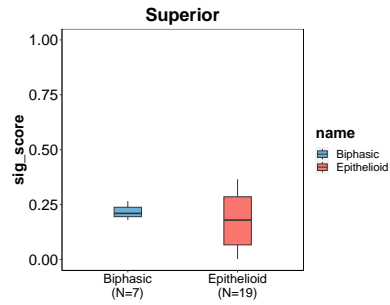
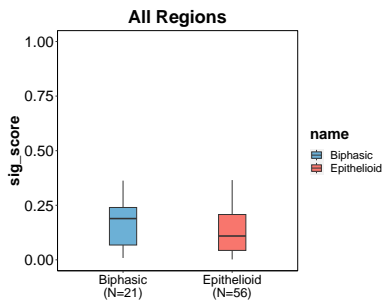


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In TCGA-MESO, A) Gene-level amplification frequency correlation between 37 other common cancer types; B) Gene-level deletion frequency correlation between 37 other common cancer types

131 Supplementary Figure 4 Wilcox Test Between signature score and histology in multiregional  
132 data

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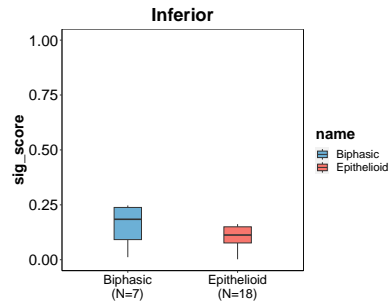
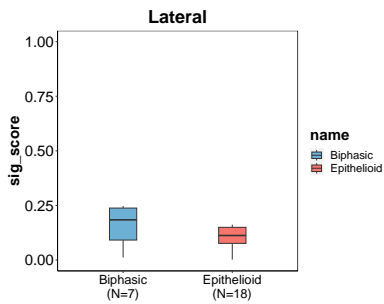


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135 p-value = 0.22

p-value = 0.9

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138 p-value = 0.7

p-value = 0.06

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