

Sample parameters affecting the clinical relevance of RNA biomarkers in translational breast cancer research

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ESM_5:

EFFECT OF TCC% AND SAMPLE SITE ON THE PROGNOSTIC SIGNIFICANCE OF INDIVIDUAL AND CLUSTERED RNA MARKERS

ESM_5_1: Cluster discrimination efficacy for DFS and OS.

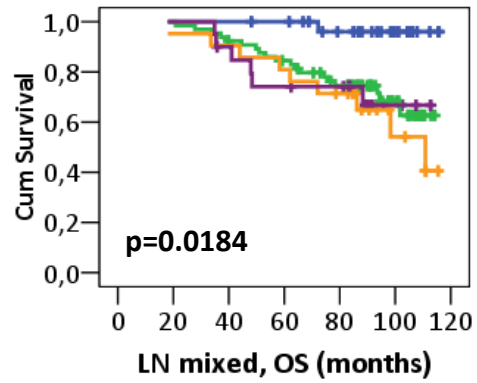
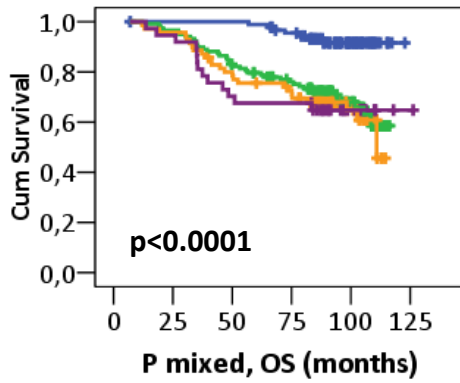
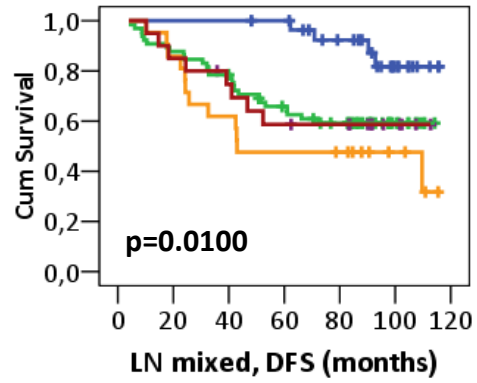
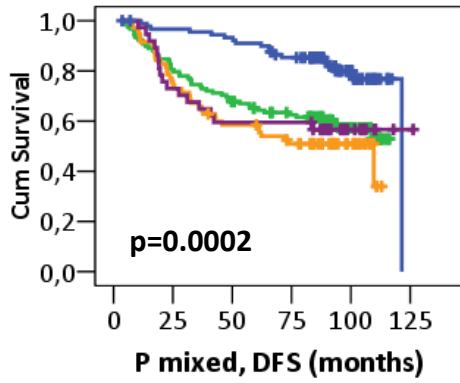
Note that the C-index is similar for the same end-point between paired sample groups.

	<i>C-Index</i>	<i>Lower 95%CL</i>	<i>Upper 95%CL</i>
P, MD DFS	0,72	0,37	0,99
P, MD OS	0,66	0,24	1,01
P, NMD DFS	0,79	0,46	1,02
P, NMD OS	0,67	0,25	1,01
LN, MD DFS	0,72	0,30	1,03
LN, MD OS	0,75	0,23	1,12
LN, NMD DFS	0,67	0,26	1,00
LN, NMD OS	0,67	0,14	1,08
matched P DFS	0,88	0,58	1,06
matched P OS	0,86	0,46	1,08
matched LN DFS	0,80	0,48	1,02
matched LN OS	0,73	0,30	1,04

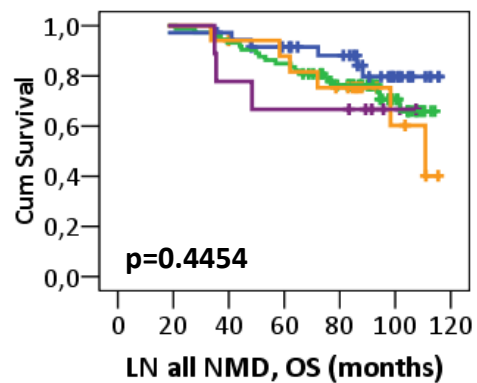
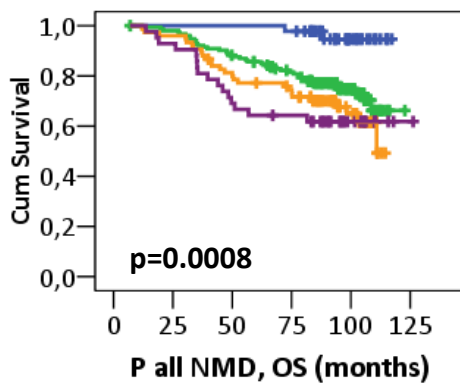
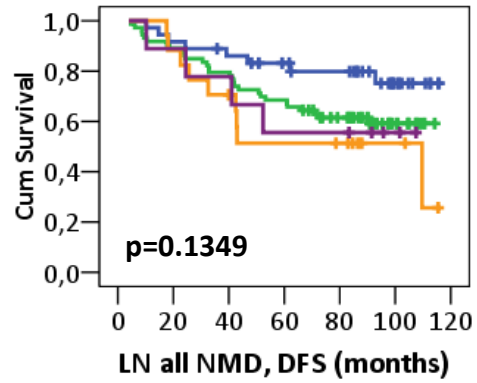
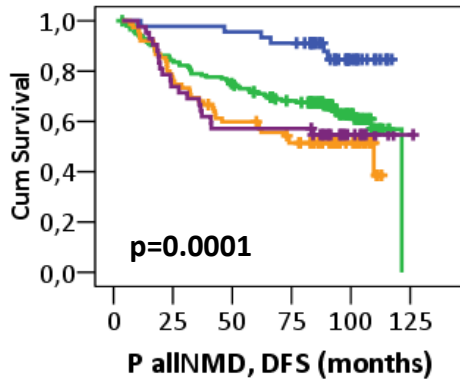
DFS = disease-free survival; OS = overall survival

ESM_5_2

A



B



ESM_5_2: Performance of the 4-cluster model in the entire primary (n=307) and lymph node (n=135) series from the HE10/97 project. In **A**, clusters were analyzed in primary tumour (P) and metastatic lymph node (LN) samples containing the highest possible TCC% (>28%). In **B**, P and LN samples from whole sections only were analyzed. The difference in cluster performance is obvious for the LN group, according to the detailed results presented. By contrast, cluster performance was not influenced by TCC% in primary tumours. **Blue: LumA; Green: LumB; Purple: HER2; Orange: TN.**

ESM_5_3: Multivariate COX regression analysis in paired sample groups.

sample group	Label	disease free survival			overall survival		
		Hazard Ratio	95% CI	Pr > ChiSq	Hazard Ratio	95% CI	Pr > ChiSq
P-MD	cluster, Lum B vs. LumA	6.135	2.40-15.70	0.0002	14.854	4.17-52.92	<.0001
	hormonal therapy, yes vs. no	0.166	0.05-0.56	0.0036	0.069	0.02-0.29	0.0003
	tumor size >5cm vs. ≤2cm*	6.746	1.86-24.50	0.0037	26.764	5.84-122.6	<.0001
	HER2 status, positive vs. negative^	4.399#	1.56-12.41	0.0051	5.324#	1.39-20.46	0.0149
	post- vs. pre-menopausal	n.a.	n.a.	n.a.	4.004	1.47-10.94	0.0068
	E-CMF vs. E-T-CMF	n.a.	n.a.	n.a.	3.415	1.23-9.50	0.0187
P-NMD	cluster, Lum B vs. LumA	2.564	0.91-7.19	0.0734	15.61	1.95-125.1	0.0097
	hormonal therapy, yes vs. no	0.137	0.04-0.42	0.0005	0.111	0.03-0.42	0.0013
	tumor size, >5cm vs. ≤2cm*	5.447	1.65-18.02	0.0055	13.315	3.22-55.06	0.0004
	HER2 status, positive vs. negative^	2.688#	1.02-7.11	0.0463	n.a.	n.a.	n.a.
	cluster, triple negative vs. Lum A	n.a.	n.a.	n.a.	21.547	2.01-230.8	0.0112
	E-CMF vs. E-T-CMF	n.a.	n.a.	n.a.	2.935	1.14-7.54	0.0254
LN-MD	lymph node status, ≥4 vs. 0-3 positive	5.151	1.20-22.13	0.0276	n.a.	n.a.	n.a.
	cluster, Lum B vs. LumA	n.a.	n.a.	n.a.	6.993	1.63-30.07	0.009
	cluster, HER2 enriched vs. LumA	n.a.	n.a.	n.a.	9.225&	1.88-45.24	0.0062
	HER2 status, positive vs. negative^	n.a.	n.a.	n.a.	0.231#	0.06-0.95	0.0418
LN-NMD	cluster, HER2 enriched vs. LumA	3.412&	1.22-9.54	0.0194	18.594&	3.40-101.6	0.0007
	lymph node status, ≥4 vs. 0-3 positive	4.477	1.02-19.57	0.0464	n.a.	n.a.	n.a.
	cluster, triple negative vs. Lum A	n.a.	n.a.	n.a.	10.083	2.15-47.21	0.0033
	HER2 status, positive vs. negative^	n.a.	n.a.	n.a.	0.205#	0.05-0.81	0.0238
matched P	lymph node status, ≥4 vs. 0-3 positive	3.956	1.21-12.97	0.0233	3.855	0.89-16.72	0.0714
matched LN	lymph node status, ≥4 vs. 0-3 positive	3.956	1.21-12.97	0.0233	n.a.	n.a.	n.a.
	cluster, Lum B vs. Lum A	n.a.	n.a.	n.a.	13.937	1.79-108.6	0.0119
	cluster, HER2 enriched vs. Lum A	n.a.	n.a.	n.a.	9.734&	1.13-83.68	0.0381
	cluster, triple negative vs. Lum A	n.a.	n.a.	n.a.	15.734	1.59-155.7	0.0184
total P	lymph node status, ≥4 vs. 0-3 positive	3.191	1.74-5.84	0.0002	3.062	1.46-6.40	0.0029
	hormonal therapy, yes vs. no	0.553	0.31-0.99	0.0461	0.487	0.26-0.92	0.027
	HER2 status, positive vs. negative^	2.069	1.18-3.64	0.0117	2.057	1.08-3.93	0.0292
total LN	lymph node status, ≥4 vs. 0-3 positive	2.91	1.15-7.39	0.0247	3.09	0.93-10.21	0.0645

*: comparisons for tumor size >5cm vs. >2-5cm were insignificant; ^: HER2 status was always determined in primary tumors; #: HER2 status was an unfavorable prognosticator in primary tumours but a favorable one in the LN MD/NMD sample cohort; &: by contrast, the HER2-enriched cluster was an unfavourable prognostic factor in the LN MD/NMD group