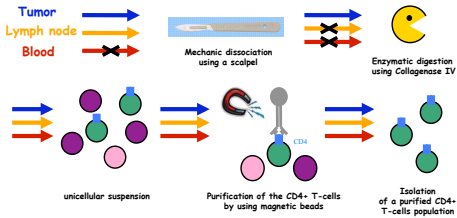


Study Aim

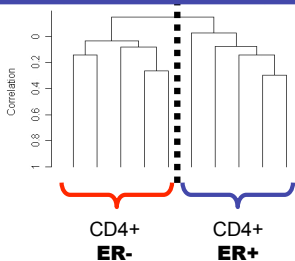
•Several studies have demonstrated the role of the adaptive immune response in controlling growth and recurrence of human tumors. However, its role in BC remains largely unknown.

•Here, we aim to gain further insight into the functional defects characterizing breast tumor-infiltrating T cells and to assess their relationship with BC subtypes and clinical outcome.

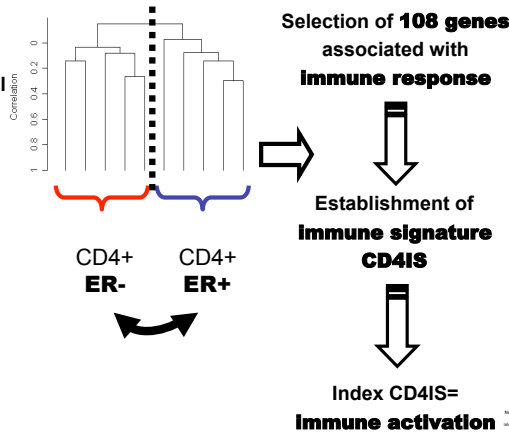
Isolation of CD4+ T-cells from different sites from the same breast cancer patient
N=10 patients (5 ER+; 5 ER-)



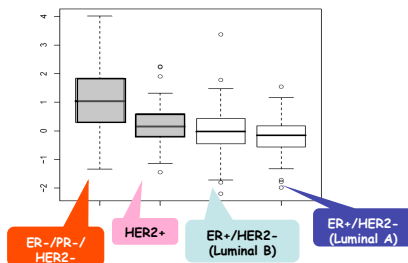
Global gene expression analysis of **tumor-infiltrating CD4+ cells** reveals **several gene differences** according to BC subtypes from which they derive



Defining CD4 IS from tumor CD4+ T-cells

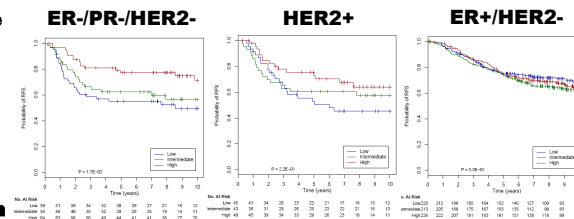
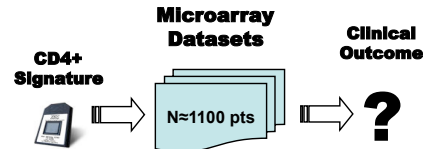


CD4 IS levels are higher in **ER-/PR-/HER2-** and **HER2+** tumors, suggesting several functional differences in immune response of CD4+ T cells according to BC subtypes



Clinical Relevance?

Publicly Available Datasets
 Systemically Untreated Pts (N≈1100)



Univariate and Multivariate Analysis (Triple negative)

	Univariate Analysis		Multivariate Analysis		
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	
UNTREATED	Age	0.978 (0.956-1.001)	0.063	0.976 (0.951-1.001)	0.059
	Size	1.276 (1.004-1.621)	0.046	1.288 (0.992-1.671)	0.058
	Node	0.959 (0.416-2.210)	0.921	0.838 (0.356-1.972)	0.686
	Grade	1.431 (0.811-2.527)	0.216	1.383 (0.772-2.480)	0.276
	CD4 index	0.792 (0.638-0.983)	0.034	0.750 (0.597-0.943)	0.014
TREATED	Age	1.317 (1.099-1.578)	0.003	1.001 (0.976-1.027)	0.924
	Size	1.317 (1.099-1.578)	0.003	1.229 (0.975-1.548)	0.080
	Node	1.214 (0.635-2.322)	0.558	0.923 (0.449-1.898)	0.828
	Grade	1.339 (0.731-2.451)	0.345	1.405 (0.723-2.729)	0.316
	CD4 index	0.673 (0.512-0.884)	0.004	0.596 (0.419-0.848)	0.004

CD4 IS is the signature having a strong prognostic information in triple negative subtype

Cox regression analysis		
Variables	Triple negative - Untreated	
	Hazard Ratio (95% CI)	P Value
Wound	0.93 (0.62-1.39)	0.74
IGS	1.02 (0.62-1.53)	0.92
Oncotype	1.02 (0.45-2.29)	0.95
Genomic grade	0.87 (0.52-1.46)	0.61
Gene70	1.12 (0.65-1.92)	0.67
Gene76	1.85 (0.79,3.42)	0.24
CD4 index	0.642 (0.478-0.862)	0.003

Conclusions

•There are differences in the **“immune function”** of tumor-infiltrating CD4+ cells according to **BC molecular subtypes**:

Higher **“immune response”** in **triple-negative** and **HER2+**

•triple-negative and HER2+ tumors may be suitable candidates for **adjuvant immunotherapy strategies**

Acknowledgments