

Supplemental Online Content

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Supplemental Table 1. Genes used in Inflammatory, EMT, and IPRES signatures

Inflammatory Genes	EMT Genes	IPRES Genes
CCL5	Epithelial	ANGPT2
CCR5	CDH1	AXL
CD274 (PDL1)	CDH3	CCL13
CD3D	CLDN4	CCL2
CD3E	EPCAM	CCL7
CD8A	ST14	CDH1
CIITA	MAL2	FAP
CTLA4		FLT1
CXCL10	Mesenchymal	1L10
CXCL11	VIM	LOXL2
CXCL13	SNAI2	RORS
CXCL9	ZEB2	TAGLN
GZMA	FN1	TWIST2
GZMB	MMP2	VEGFA
HLA-DRA	AGER	VEGFC
HKA.DRB1		WNT5A
HLA-E		
IDO1		
IL2RG		
ITGAL		
LAG3		
NKG7		
PDCD1		
PRF1		
PTPRC		
STAT1		
TAGAP		

Supplemental Table 2. EMT Gene Lists from the Literature

Genes	Ref 1 (lung)	Ref 2 (lung)	Ref 3 (lung)	Ref 4 (lung)	Ref 5 (lung)	Ref 6 (pan tumor)	Ref 7 EMT database	Ref 8 (breast)	Avg gene reads	Notes
Epithelial										
CDH1	X	X	X	X	X	x	X	X	45	
CDH3		X	X	X		x			136	
CLDN4				X			X	X	127	
EPCAM		X	X	X		x	X		158	
ST14		X	X	X		x			202	
MAL2			X			x			155	
Mesenchymal										
VIM	X	X	X	X		x	X	X	326	
SNAI2	X	X		X	X		X	X	39	
ZEB2		X		X	X		X	X	34	
FN1	X		X						71	
MMP2	X		X				X		265	
AGER				X			X		33	
SNAI1	X				X		X	X	9	1
TWIST1	X	X		X	X			X	9	1
ZEB1		X	X	X	X	x	X	X	8	1
FOXC1							X	X	5	1
TWIST2		X			X			X	2	1
CDH2	X			X	X			X	2	1

Notes.

1. Classic EMT gene, but expression level too low so not used

References:

Reference 1. Chae YK, Chang S, Ko T, et al: Epithelial-mesenchymal transition (EMT) signature is inversely associated with T-cell infiltration in non-small cell lung cancer (NSCLC). *Sci Rep* 8:2918, 2018

Reference 2. Schliekelman MJ, Tagiuchi A, Zhu J, et al. Molecular portraits of epithelial, mesenchymal and hybrid states in lung adenocarcinoma and their relevance to survival. *Cancer Res.* 75: 1789–1800, 2015.

Reference 3. Byers LA, Diao LX, Wang J, et al: An Epithelial-Mesenchymal Transition Gene Signature Predicts Resistance to EGFR and PI3K Inhibitors and Identifies Axl as a Therapeutic Target for Overcoming EGFR Inhibitor Resistance. *Clinical Cancer Research* 19:279-290, 2013

Reference 4. Tan ZT, Miow QH, Miki Y, et al. Epithelial-mesenchymal transition spectrum quantification and its efficacy in deciphering survival and drug responses of cancer patients. *EMBO Mol Med* 6: 1279–1293, 2014

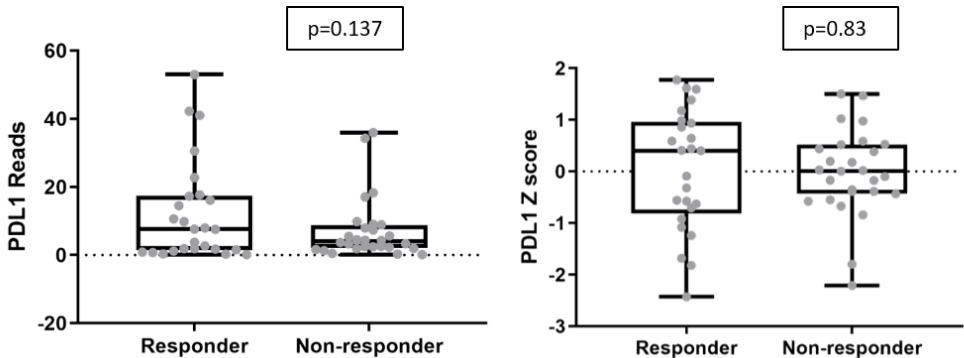
Reference 5. Kuner R, Muley T, Meister M, et al: Global gene expression analysis reveals specific patterns of cell junctions in non-small cell lung cancer subtypes. *Lung Cancer* 63:32-38, 2009

Reference 6. Huang RY-J, Wong MK, Tan TZ, et al. An EMT spectrum defines an anoikis-resistant and spheroidogenic intermediate mesenchymal state that is sensitive to e-cadherin restoration by a src-kinase inhibitor, saracatinib (AZD0530)/ Cell Death and Disease (2013) 4, e915; 2013

Reference 7. Zhao M., Kong L, Liu Y. Qu, H. dbEMT: a literature-based resource for Epithelial-Mesenchymal Transition genes. Sci Rep. 11459. 2015: <http://dbemt.bioinfo-minzhao.org/index.html>

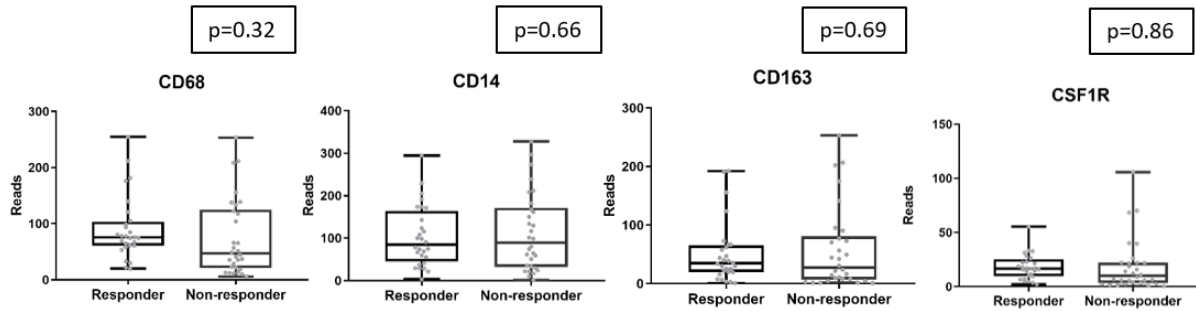
Reference 8. Taube JH, Herschkowitz JI, Komurov K, et al. Core epithelial-to-mesenchymal transition interactome gene-expression signature is associated with claudin-low and metaplastic breast cancer subtypes. Proc. Nat. Acad. Sci. 107:15449-15454, 2010.

Supplemental Figure 1: PD-L1 gene expression and response. (A) Number of counts of PD-L1 gene expression levels in responders and PD patients. (B) log₂ z-scores of PD-L1 gene expression levels in responders and PD patients.

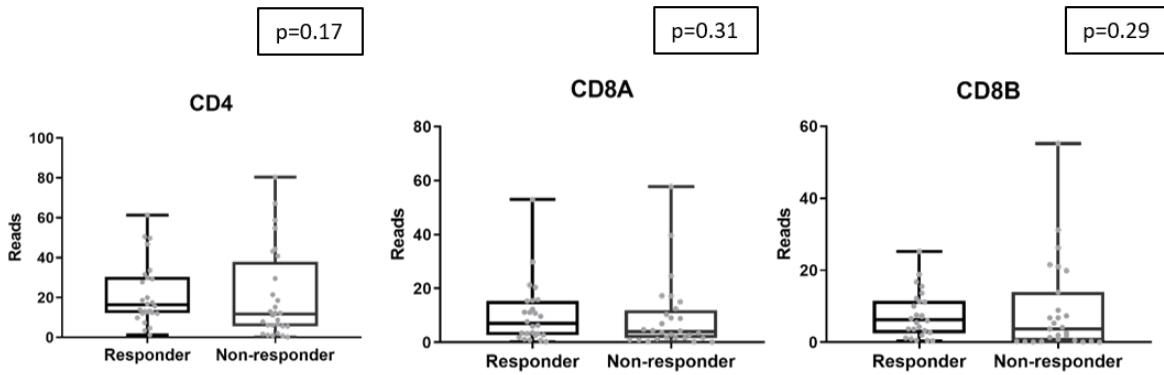


Supplemental Figure 2: Comparison of markers of T cells and Macrophages with response. (A) Expression levels (number of reads) of established macrophage associated genes (CD68, CD14, CD163, CSF1R) in responders and PD patients. (B) Expression levels of established T cell associated genes (CD4, CD8A, CD8B) in responders and PD patients.

A. Macrophage Genes



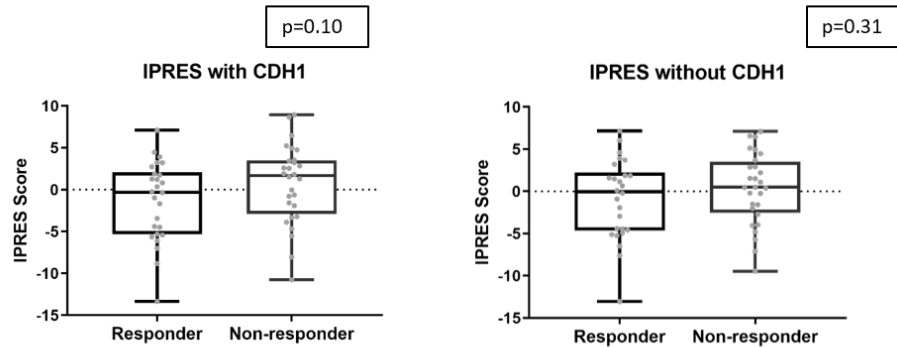
B. T Cell Genes



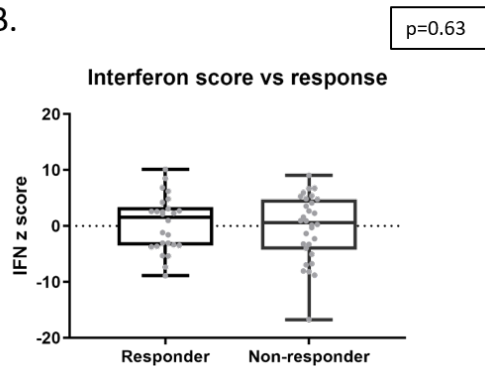
Supplemental Figure 3: Innate PD-1 resistance score (IPRES) and chronic IFN activation score and response.

(A) Comparison of the log₂ z-scores of the IPRES signature in responders and non-responders. The IPRES score was calculated with and without expression levels of CH1 (E-cadherin). (B) Comparison of a chronic interferon activation score in responders and non-responders. This score included 9 established genes involved in chronic interferon activation (STAT1, IFI44, IFIT1, IFIT3, OAS1, OAS2, MX1, IRF7, and ISG15).

A.



B.



Supplemental Figure 4. Markers of TGF β signaling and response. Expression levels (reads) of 5 established genes involved in TGF β signaling (TGFB1, TGFBR2, ACTA2, COL4A2, and TAGLN) in responders and non-responders.

