Abstract ID# 3133: The genomic, transcriptomic, and immunologic landscape in solid tumors expressing leukocyte immunoglobulin-like receptor B2 (*LILRB2*).

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Background

- Leukocyte immunoglobulin-like receptor B2 (*LILRB2)* is primarily expressed on myeloid cells and provides negative feedback during inflammatory responses.
- A blocking antibody targeting *LILRB2* in myeloid cells is in clinical trials.
- Various solid tumors are also enriched with these receptors.
- Here we investigate differences between *LILRB2* expression in the local versus metastatic setting, influences on the tumor microenvironment, and effects on clinical outcomes for a group of solid tumors.

Methods

- Hepatocellular carcinoma(HCC, N = 532), urothelial carcinoma (UC, N = 4125), pancreatic cancer (PDAC, N = 5488), prostate adenocarcinoma (PA, N = 5500) and non-small cell lung cancer (NSCLC, N = 21604) tumors were tested at Caris Life Sciences (Phoenix, AZ) with NextGen sequencing of DNA (592-gene or whole exome) and RNA (whole transcriptome).
- Primary and metastatic sites were defined based on the biopsy site relative to known primary site. *LILRB2*-High (H) and -Low (L) expression was defined as top and bottom quartile of *LILRB2* transcripts/million (TPM), respectively.
- PD-L1 (SP142; Positive (+): ≥2, ≥%5) expression was tested by IHC.
- Gene expression profiles were analyzed for transcriptomic signatures predictive of response to immunotherapy (T-cell inflamed score).
- Immune cell fractions were estimated with RNA deconvolution using quanTIseq.
- Mann-Whitney U and χ^2 tests were applied as appropriate with P-values adjusted for multiple comparisons.
- Overall survival data was obtained from insurance claims, and Kaplan-Meier estimates were calculated for molecularly defined subpopulations of patients.

Results

1. Expression in primary vs metastatic sites

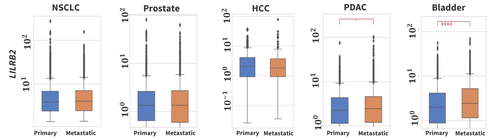


Figure 1 – *LILRB2* expression (TPM) for primary and metastatic sites across investigated cancers (asterisk indicates significance, $p < 0.05$).

2. Genomic landscape

	NSCLC	Prostate	HCC	PDAC	Bladder
CNA-FGF3	-1.90	1.78	3.33	0.15	-0.08
CNA-MDM2	-0.30	-0.15	-0.78	-0.07	**-4.04**
CNA-MNX1	-0.32	3.19	1.82	-0.14	0.46
CNA-TRAF7	-0.17	3.09	0.00	-0.81	0.34
Fusion-FGFR3	-0.11	0.00	0.00	0.07	**-2.62**
NGS-APC	-1.06	1.24	3.79	-0.27	-0.11
NGS-CTNNB1	-1.50	-1.84	**-21.47**	-0.69	0.26
NGS-FGFR3	-0.43	0.00	0.00	0.00	**-14.33**
NGS-JAK1	-0.03	2.65	0.00	0.33	0.05
NGS-KDM6A	0.05	0.08	-1.60	-0.79	-3.59
NGS-KRAS	3.00	0.44	-0.75	-0.17	2.20
NGS-NFE2L2	-1.58	0.00	-5.65	-0.19	1.14
NGS-RASA1	3.44	-2.25	0.00	0.00	-5.22
NGS-RB1	-3.00	1.99	-3.97	-1.25	2.48
NGS-STK11	-2.85	0.17	0.00	-0.12	-0.06
NGS-TERT*	2.09	-0.19	**12.38**	0.46	2.93
NGS-TP53	4.34	6.98	**30.42**	3.21	**11.08**
NGS-TSC1	-0.22	0.42	4.59	0.08	-0.85
NGS-XRCC1	0.21	-0.33	6.90	0.00	0.01

% prevalence in *LILRB2* Q4-Q1
≥ 10
0
≤ −10

Figure 2 - : Difference in prevalence of genomic alterations between *LILRB2*-High and –Low tumors . An alteration is included in the heatmap if it has an absolute difference in prevalence of >2% in one of the investigated cancer types. Bolded numbers in heat map indicate statistical significance ($q < 0.05$)

3. Immune Landscape

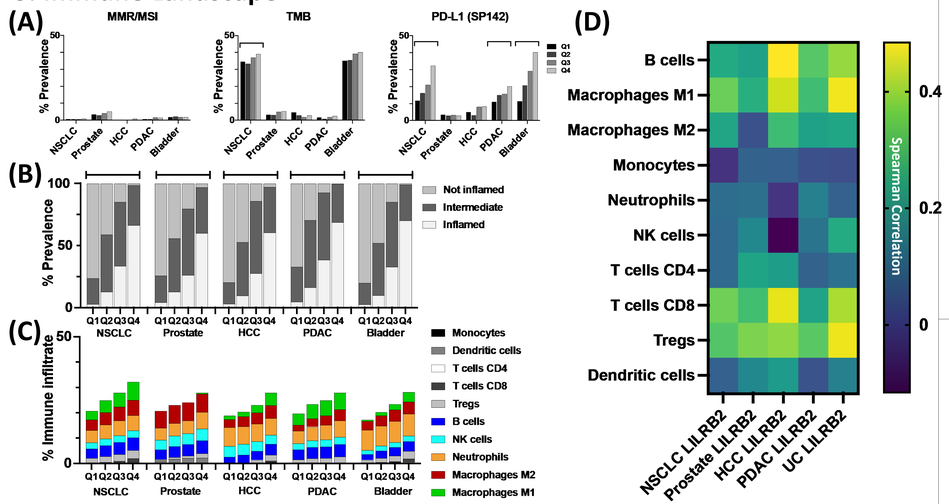


Figure 3 – (A) prevalence of immune biomarkers and **(B)** prevalence of T cell-inflamed tumors (suggestive of responsiveness to immune check point inhibitors) across *LILRB2* expression quartiles and investigated cancer types (asterisk indicates significance, $p < 0.05$). **(C)** Prevalence of different immune cell populations across *LILRB2* expression quartiles and **(D)** Spearman correlation between *LILRB2* expression and immune population prevalence.

4. Survival data

(A)

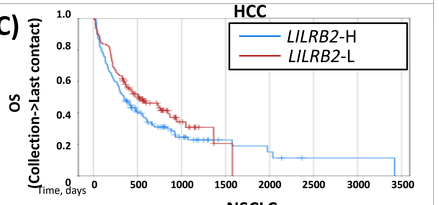
	Collection-> Last contact						Pembro> Last contact						First Pembro-> Last Pembro					
	HR	Low CI	Upper CI	p-value	Q1	Q4	HR	Low CI	Upper CI	p-value	Q1	Q4	HR	Low CI	Upper CI	p-value	Q1	Q4
HCC	1.28	0.933	1.755	0.124	110	112	2.75	0.488	15.52	0.233	4	4	1.099	0.22	5.57	0.909	4	3
NSCLC	0.94	0.89	0.99	**0.017**	4270	4251	1.064	0.93	1.21	0.354	701	850	0.865	0.78	0.97	**0.009**	592	714
PDAC	1.109	1.01	1.22	**0.029**	1123	1150	0.451	0.13	1.55	0.203	12	10	0.906	0.33	2.51	0.86	10	7
Prostate	0.94	0.82	1.08	0.412	851	839	0.853	0.35	2.09	0.738	14	24	0.698	0.32	1.51	0.36	12	18
UC	0.93	0.81	1.06	0.246	706	711	0.971	0.69	1.38	0.868	109	130	1.005	0.76	1.34	0.952	89	111

(B)

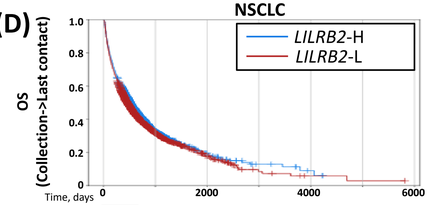
	Collection-> Last contact						First Pembro -> Last contact						First Pembro -> Last Pembro					
	HR	Low CI	Upper CI	p-value	Q1	Q4	HR	Low CI	Upper CI	p-value	Q1	Q4	HR	Low CI	Upper CI	p-value	Q1	Q4
NSCLC	0.94	0.89	0.99	**0.017**	4270	4251	1.064	0.93	1.21	0.354	701	850	0.865	0.78	0.97	**0.009**	592	714
NSCLC PDL1+	0.85	0.78	0.93	**0.001**	1091	2789	0.894	0.72	1.10	0.298	204	577	0.822	0.69	0.98	**0.03**	169	485
NSCLC PDL1-	1.007	0.92	1.11	0.891	1507	1270	1.059	0.83	1.35	0.641	204	227	1.126	0.91	1.39	0.269	169	185
Adenocarcinoma	0.979	0.91	1.05	0.564	2260	2439	0.979	0.82	1.17	0.82	377	518	0.894	0.77	1.03	0.127	323	442
Squamous	0.855	0.76	0.96	**0.007**	1090	726	0.914	0.70	1.20	0.516	192	145	0.85	0.67	1.08	0.181	159	122
Driver +	1.035	0.95	1.13	0.436	1815	1861	0.921	0.74	1.14	0.445	381	249	0.759	0.64	0.91	**0.002**	210	314
Driver -	0.885	0.80	0.98	**0.019**	965	1042	0.938	0.74	1.20	0.608	171	221	0.78	0.63	0.97	**0.026**	145	190

Figure 4 : (A,B) Table of survival data for different NSCLC subpopulations segmented by *SLC5A2*-H vs *SLC5A2*-L. Kaplan-Meier curves representing for HCC **(C)** and **(D)** NSCLC.

(C)



(D)



Higher hazard 2
1
Lower hazard 0
of death for LILRB2 high tumors

Study Highlights

- The genomic landscape of high versus low *LILRB2* expressors varied widely by cancer type.
- *LILRB2* expression was associated with biomarkers of response to immunotherapy such as PD-L1+ and an increased proportion of T cell-inflamed tumors.
- High expression of LILRB2 was associated with improved time on treatment with pembrolizumab in NSCLC.

Conclusions

- These data suggest that PDAC, NSCLC and UC tumors could potentially benefit from a combination of immune checkpoint inhibitors and *LILRB2*-blocking antibodies.

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