

A novel prognostic biomarker *LCP2* correlates with metastatic melanoma-infiltrating CD8⁺ T cells

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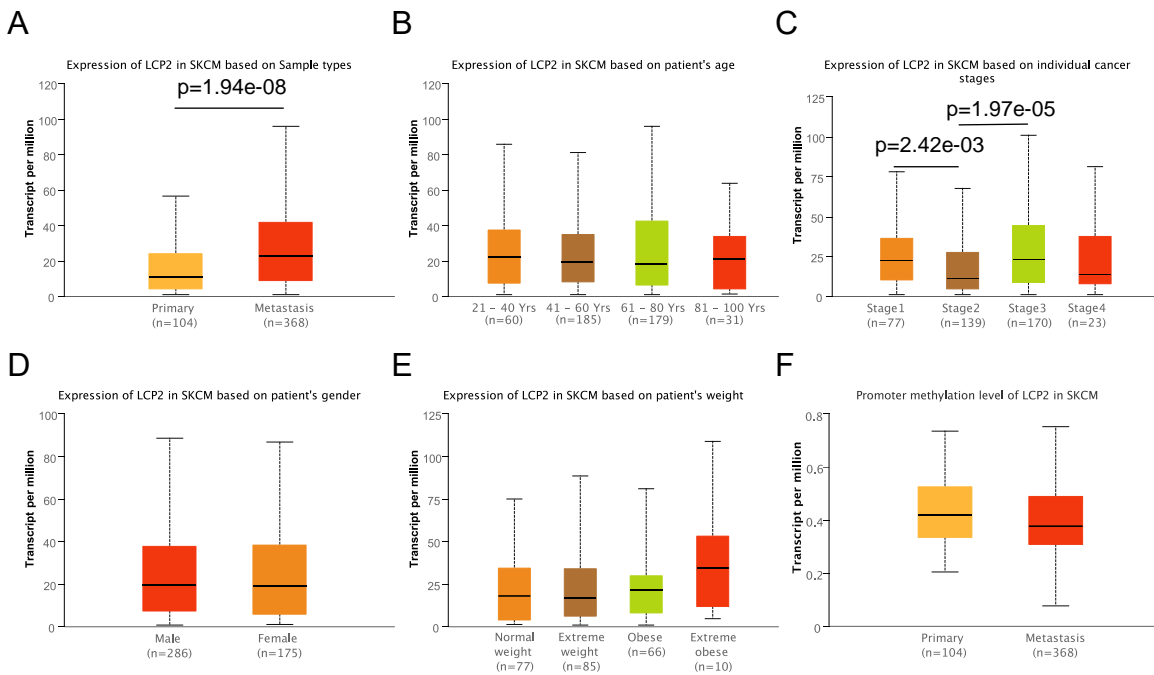
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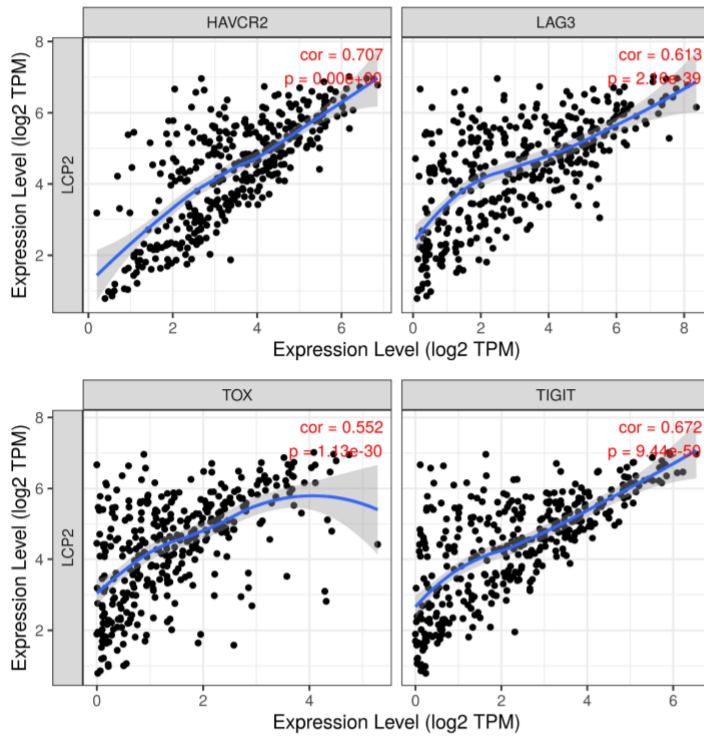
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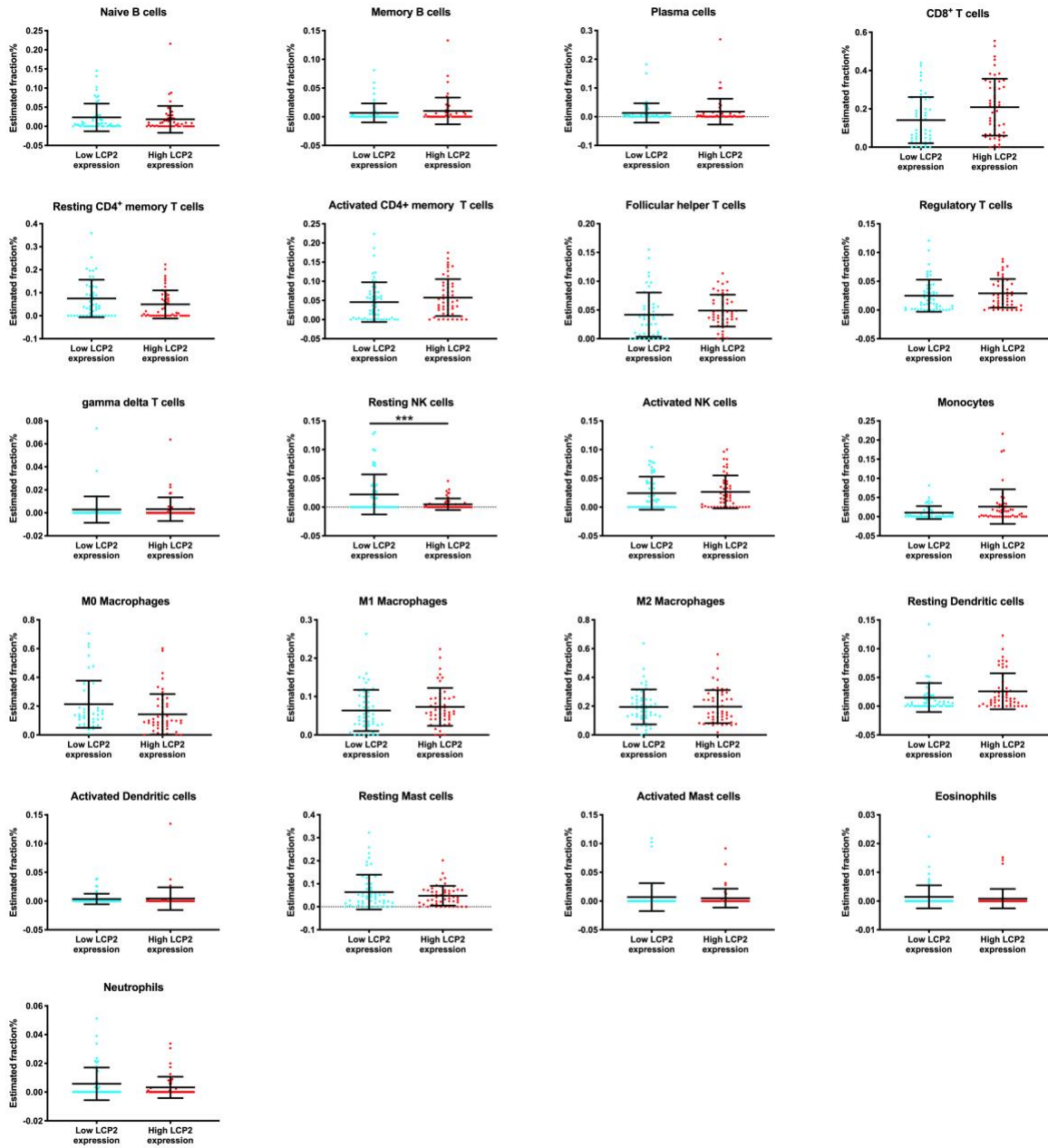
Supplementary Figure S1 The relationship between LCP2 expression with clinical characteristics of cutaneous melanoma. A. LCP2 was highly expressed in SKCM with metastasis compared to primary SKCM ($p=1.93E-08$). B. There were no significant differences in patient's age in SKCM. C. LCP2 was over-expressed in SKCM with stage 1 and stage 3 compared to stage 2, respectively (stage 1 vs stage 2: $P=2.422E-03$, stage 2 vs stage 3: $P=1.971E-05$). D&E&F. There were no significant differences in patient's gender (D), weight (E) and promoter methylation level of LCP2 in SKCM (F). SKCM: skin cutaneous melanoma.



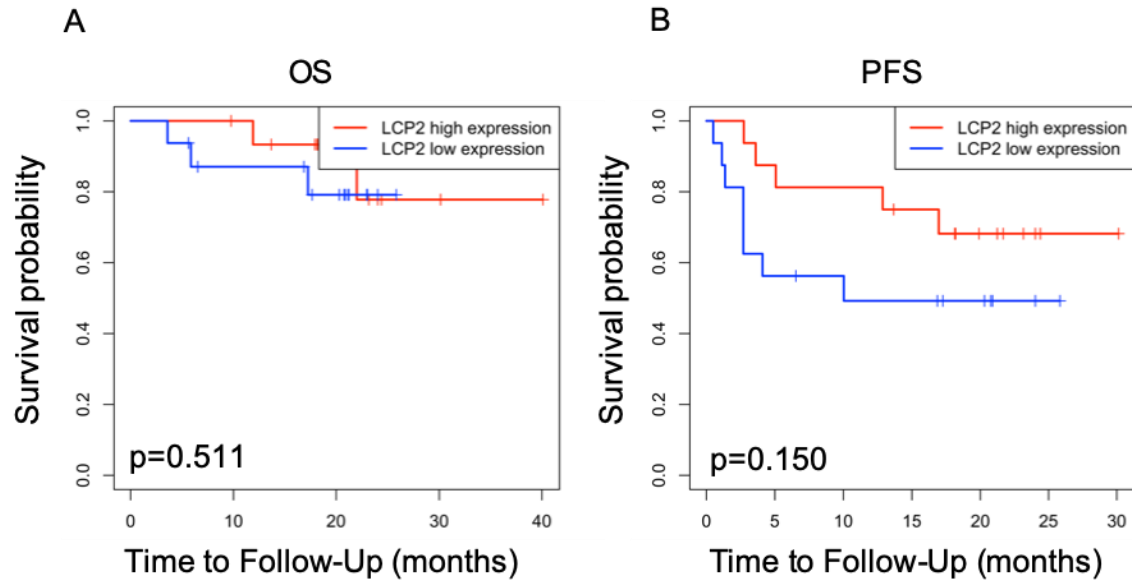
Supplementary Figure S2 The *LCP2* expression was positively correlated with *HAVCR2*, *LAG3*, *TOX* and *TIGIT* in metastatic cutaneous melanoma.



Supplementary Figure S3 CIBERSORT analysis of 22 immune cells based on *LCP2* expression level in primary melanoma cohort. Significantly lower estimated fractions of resting NK cells existed in the high-*LCP2* expression group.



Supplementary Figure S4 Kaplan-Meier curves of OS and PFS for low- and high-*LCP2* expression patients after anti-PD1 immunotherapy from Gide2019_PD1+CTLA4 cohorts. OS: overall survival; PFS: progression-free survival.



Supplementary Table S1 The correlation between LCP2 and overall survival in pan-cancers

cancer	variable	p-value
SKCM	LCP2	1.192E-05
SKCM-Metastasis	LCP2	2.205E-05
UVM	LCP2	1.466E-04
LGG	LCP2	5.174E-03
UCEC	LCP2	9.151E-03
THYM	LCP2	9.737E-03
SARC	LCP2	0.013
GBM	LCP2	0.016
HNSC-HPVpos	LCP2	0.019
THCA	LCP2	0.069
ESCA	LCP2	0.081
TGCT	LCP2	0.085
STAD	LCP2	0.118
READ	LCP2	0.160
BRCA-Her2	LCP2	0.168
LUSC	LCP2	0.182
CECSC	LCP2	0.193
LUAD	LCP2	0.198
BRCA	LCP2	0.202
PCPG	LCP2	0.311
OV	LCP2	0.357
SKCM-Primary	LCP2	0.373
CHOL	LCP2	0.386
BRCA-Luminal	LCP2	0.400
PAAD	LCP2	0.413
KICH	LCP2	0.428
MESO	LCP2	0.505
HNSC	LCP2	0.552
DLBC	LCP2	0.637
KIRP	LCP2	0.665
BLCA	LCP2	0.719
COAD	LCP2	0.732
HNSC-HPVneg	LCP2	0.748
PRAD	LCP2	0.752
ACC	LCP2	0.812
UCS	LCP2	0.839
LIHC	LCP2	0.924
KIRC	LCP2	0.946
BRCA-Basal	LCP2	0.989

Supplementary Table S2 *LCP2* correlated T cell co-signaling pathway genes in metastatic melanoma.

<i>LCP2</i> correlated T cell co-signaling pathway genes	Correlation coefficient	p value
<i>HLA-DRA</i>	0.711	5.50E-58
<i>CD3E</i>	0.656	0
<i>CD80</i>	0.673	6.61E-50
<i>CD86</i>	0.726	0
<i>CD274</i>	0.595	1.29E-36
<i>HHLA2</i>	0.282	3.71E-08
<i>CD28</i>	0.630	0
<i>ICOS</i>	0.649	2.28E-45
<i>TMIGD2</i>	0.456	2.64E-20
<i>PDCDILG2</i>	0.680	0
<i>PDCD1</i>	0.628	0
<i>BTLA</i>	0.615	1.06E-39
<i>BTNL8</i>	0.532	2.70E-28
<i>BTN3A1</i>	0.513	0
<i>CD48</i>	0.687	0
<i>SLAMF1</i>	0.631	2.86E-42
<i>CD2</i>	0.689	0
<i>CD244</i>	0.572	2.64E-33
<i>TIMD4</i>	0.580	2.10E-34
<i>HAVCR1</i>	0.433	3.00E-18
<i>LGALS9</i>	0.603	0
<i>HAVCR2</i>	0.707	0
<i>CD226</i>	0.612	3.73E-39
<i>TIGIT</i>	0.672	9.44E-50
<i>LAIR1</i>	0.700	0
<i>CD40</i>	0.614	0
<i>TNFSF14</i>	0.643	2.77E-44
<i>CD40LG</i>	0.566	1.64E-32
<i>CD70</i>	0.555	4.08E-31
<i>TNFSF8</i>	0.667	1.03E-48
<i>TNFSF18</i>	0.333	5.61E-11
<i>TNFRSF9</i>	0.698	5.24E-55
<i>CD27</i>	0.638	1.76E-43
<i>TNFRSF8</i>	0.619	2.39E-40
<i>TNFRSF18</i>	0.586	0

Supplementary S3 Univariate and multivariate analysis for evaluating the prognostic factors of progression-free survival in the Gide2019_PD1 cohort

Characteristics	Hazard Ratio	univariate Cox analysis			multivariate Cox analysis		
			CI95	P. Value	Hazard Ratio	CI95	P. Value
B_cells_memory	0.01	0-2.08		0.088			
B_cells_naive	0.43	0.01-21.35		0.673			
Dendritic_cells_activated	0	0-116608.22		0.389			
Dendritic_cells_resting	616.56	0.09-4400411.87		0.156			
Eosinophils	0.84	0-242.86		0.953			
Macrophages_M0	0.23	0-35.89		0.571			
Macrophages_M1	0.02	0-28.22		0.297			
Macrophages_M2	5.38	0.19-150.69		0.323			
Mast_cells_activated	2.07	0.01-659.52		0.804			
Mast_cells_resting	48.83	2-1190.13		0.017	5.25	0.16-177.53	0.356
Monocytes	0.15	0-1905.58		0.696			
Neutrophils	0.28	0.01-13.45		0.52			
NK_cells_activated	2640.27	0.25-28153691.89		0.096			
NK_cells_resting	0	0-7.98		0.148			
Plasma_cells	0.23	0-20.91		0.52			
T_cells_CD4_memory_activated	0	0-0.77		0.04	0	0-2.07	0.081
T_cells_CD4_memory_resting	14.99	0.22-1001.97		0.207			
T_cells_CD4_naive	34.6	0.93-1281.24		0.054			
T_cells_CD8	0.01	0-0.73		0.035	1.07	0.01-92.45	0.977
T_cells_follicular_helper	0	0-0.07		0.016	0	0-1.12	0.052
T_cells_gamma_delta	0	0-6.71		0.098			
Tregs	0.2	0-227.46		0.657			
LCP2	0.7	0.53-0.92		0.01	0.98	0.68-1.41	0.923

Supplementary Table S4 Univariate and multivariate analysis for evaluating the prognostic factors of overall survival in the Gide2019_PD1 cohort

Characteristics	univariate Cox analysis			multivariate Cox analysis		
	Hazard Ratio	CI95	P. Value	Hazard Ratio	CI95	P. Value
B_cells_memory	0.09	0-21.91	0.391			
B_cells_naive	0.55	0.01-38.91	0.783			
Dendritic_cells_activated	0	0-220752.49	0.326			
Dendritic_cells_resting	0.2	0-11006.91	0.775			
Eosinophils	6.8	0.02-2303.2	0.519			
Macrophages_M0	0.37	0-108.18	0.729			
Macrophages_M1	0	0-2.36	0.066			
Macrophages_M2	5.84	0.15-229.55	0.346			
Mast_cells_activated	0.78	0-249.34	0.933			
Mast_cells_resting	52.33	1.72-1589.3	0.023	14.94	0.4-551.87	0.142
Monocytes	0.01	0-5233.32	0.492			
Neutrophils	0.41	0.01-24.41	0.67			
NK_cells_activated	3257.01	0.11-100517288.52	0.125			
NK_cells_resting	0	0-6.7	0.118			
Plasma_cells	0.37	0-50.11	0.691			
T_cells_CD4_memory_activated	0	0-1.69	0.072			
T_cells_CD4_memory_resting	28.34	0.22-3587.84	0.176			
T_cells_CD4_naive	10.35	0.2-527.33	0.244			
T_cells_CD8	0.02	0-1.45	0.072			
T_cells_follicular_helper	0	0-0.41	0.037	0	0-2.17	0.064
T_cells_gamma_delta	0	0-2.84	0.068			
Tregs	0.09	0-506.65	0.58			
LCP2	0.76	0.56-1.03	0.072			