

GEO dataset	Sample Type	Cancer type	Met site	N	Microarray Platform	Normalization
GSE100534	Metastatic	Breast	Brain	3	HG 1.0 ST Array	Affymetrix
GSE101607	Metastatic	Prostate(88.9%), NSCLC (1.8%), kidney(5.6%), colorectal(3.7%)	Bone	54	Illumina Human HT-12 V4.0	GenomeStudio cubic spline
GSE10961	Metastatic	Colorectal	Liver	18	HG U133 Plus 2	MASS.0
GSE44660	Metastatic	Melanoma	Brain	7	Human Exon 1.0 ST	RMA
GSE11078	Metastatic	Breast	Lung	5	HG U133 Plus 2	RMA
GSE12630	Metastatic	Breast (13.6%), kidney (27.2%), colorectal (13.6%), prostate (4.5%), skin melanoma (40.9%)	Lung(72.7%), liver(27.3%)	22	HG U133A	Pathwork standardization
GSE14017	Metastatic	Breast	Lung(13.8%), brain(51.7%), bone(34.5%)	29	HG U133 Plus 2	RMA
GSE14018	Metastatic	Breast	Lung(44.4%), brain(19.44%), bone(22.2%), liver(13.9%)	36	HG U133A	RMA
GSE43837	Metastatic	Breast	Brain	19	HG U133 X3P	MASS.0
GSE46141	Metastatic	Breast	Lung(8.7%), liver(69.6%), bone(21.74%)	23	HuRSTA 2.0	QC-RMA
GSE14108.1	Metastatic	NSCLC	Brain	19	HG U133 Plus 2	RMA
GSE14108.2	Metastatic	NSCLC	Brain	9	HG U133A	RMA
GSE40367	Metastatic	Colorectal	Liver	7	HG U133 Plus 2	RMA
GSE41258	Metastatic	Colorectal	Lung(29.9%), liver(70.2%)	67	HG U133A	PLIER algorithm
GSE50496.1	Metastatic	Melanoma	Lung(15%), brain(72.5%), bone(7.5%), liver(5%)	40	HuRSTA 2.0	Quantile normalization
GSE85258	Metastatic	Kidney	Lung	16	HG U133 Plus 2	RMA
TOTAL	Metastatic	Breast(31.6%), colorectal(26%), Kidney(6.7%), NSCLC(7.8%), Prostate(13%), Skin(15%)	Bone(21.4%), Brain(28.9%), Liver(27%), Lung(22.7%)	374		

Supplementary Table 1. Public datasets containing gene expression data on metastatic human samples.

GEO dataset	Sample Type	Tissue site	-	N	Microarray Platform	Normalization
GSE7307	Normal	Brain(56.25%), Lung(18.75%), Liver(25%)		16	HG U133 Plus 2	RMA
GSE45878	Normal	Brain(73.3%), Lung(26.7%)		281	HuGene 11 stv1	RMA
GSE803	Normal	Bone(25%), Brain(25%), Liver(25%), Lung(25%)		8	HG U133 Plus 2	RMA
GSE3526	Normal	Bone(23.8%), Brain(42.9%), Liver(19%), Lung(14.3%)		21	HG U133 Plus 2	RMA
GSE1133	Normal	Bone(45.5%), Brain(36.3%), Liver(9%), Lung(9%)		22	HG U133A	MAS5.0
TOTAL	Normal	Bone(4.9%), Brain(67.2%), Liver(3.5%), Lung(24.4%)		348		

Supplementary Table 2. Public datasets containing gene expression data on normal tissues.

Gene set	MsigDB/Reference	Genes (in expression matrix)
IFN Gamma	REACTOME_INTERFERON_GAMMA_SIGNALING	38
Antigen processing and presentation	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	46
CTLA4 Signalling	BIOCARTA_CTLA4_PATHWAY	17
PDL1 Signalling	REACTOME_PD1_SIGNALING	10
Inflammatory response Up	GO_POSITIVE_REGULATION_OF_INFLAMMATORY_RESPONSE	68
Leukocyte migration	GO_LEUKOCYTE_MIGRATION_INVOLVED_IN_INFLAMMATORY_RESPONSE	10
Acute inflammatory response Up	GO_POSITIVE_REGULATION_OF_ACUTE_INFLAMMATORY_RESPONSE	19
Chronic inflammatory response Up	GO_REGULATION_OF_CHRONIC_INFLAMMATORY_RESPONSE	6
Regulation of cytokine production	GO_REGULATION_OF_CYTOKINE_PRODUCTION_INVOLVED_IN_INFLAMMATORY	9
JAK/STAT signalling	HALLMARK_IL6_JAK_STAT3_SIGNALING	70
IFN Alpha	HALLMARK_INTERFERON_ALPHA_RESPONSE	65
Adaptive immune response	GO_ADAPTIVE_IMMUNE_RESPONSE	140
Cytokine production	GO_CYTOKINE_PRODUCTION_INVOLVED_IN_IMMUNE_RESPONSE	11
Macrophage activation	GO_MACROPHAGE_ACTIVATION_INVOLVED_IN_IMMUNE_RESPONSE	9
Mastocytes activation	GO_MAST_CELL_MEDIATED_IMMUNITY	14
Myeloid cells activation	GO_MYELOID_CELL_ACTIVATION_INVOLVED_IN_IMMUNE_RESPONSE	32
Natural killers mediated immunity	GO_NATURAL_KILLER_CELL_MEDIATED_IMMUNITY	13
Cytokines production Immune response	GO_POSITIVE_REGULATION_OF_CYTOKINE_PRODUCTION_INVOLVED_IN_IMMUNE_RESPONSE	18
Myeloid leukocyte cytokines Immune	GO_POSITIVE_REGULATION_OF_MYELOID_LEUKOCYTE_CYTOKINE_PRODUCTION_INVOLVED_IN_IMMUNE_RESPONSE	6
Regulation of Thelp 1 Immune respons	GO_POSITIVE_REGULATION_OF_T_HELPER_1_TYPE_IMMUNE_RESPONSE	10
"Regulation of Type 2 Immune Response	GO_POSITIVE_REGULATION_OF_TYPE_2_IMMUNE_RESPONSE	10
T cell medidated Immunity	GO_T_CELL_MEDIATED_IMMUNITY	16
Tolerance Induction	GO_TOLERANCE_INDUCTION	5
Immunoscore signature	Galon J et al., 2013 Jul 25;39(1):11-26. doi: 10.1016/j.immuni.2013.07.008.	11
MHC class II	Manually selected genes	4

Supplementary Table 3. Gene sets used to make the cluster analysis.

Cell type	Subtype	MCPcounter (RELATIVE)	xCell (RELATIVE)	QuanTiseq (ABSOLUTE)	Total
T regulatory cells		-	0.89	0.77	0
T cells		0.04(Bo)	-	-	1
CD4+ T cells	T CD4 memory	-	0.12	0.23	0
	T CD4 naive		0.31		0
	T CD4 non regulatory		0.57		0
CD8+ T cells		0.001(Bo,Br,Lv)	0.27	0.0003(Bo, Lv)	2
B cells		<0.001(Bo,Br,Lv)	0.55	0.006(Lv)	2
NK cells		0.69	0.21	0.43	0
Macrophages	Macrophages M1	0.32	0.08(Br)	0.11	0
	Macrophages M2		0.16	0.28	
Monocytes		0.32	0.21	0.008(Lv)	1
Dendritic cells		0.004(Bo,Br,Lv)	<0.001(Br,Bo,Lv)	0.42	2
Neutrophils		0.47	0.47	0.45	0
Endothelial cells		0.006(Lv)	<0.001(Br,Bo,Lv)	-	2
Cancer Associated Fibroblasts (CAFs)		<0.001(Br,Lv)	0.12	-	1

Kruskal-Wallis rank sum test p-val (Lung Step-wise test p-val < 0.05).

Supplementary Table 4. Immune cell infiltration validation. Values indicate the Kruskal-Wallis rank sum test p-value between the four metastatic sites. Sites in parentheses indicate Lung vs Site Step-wise test p-val <0.05. Bo:bone, Br:brain, Lv:liver, Lu:lung.

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX
HALLMARK_IL2_STAT5_SIGNALING	145	0.65	1.82	0.00	0.15	0.07	1575
HALLMARK_APOPTOSIS	141	0.62	1.81	0.00	0.09	0.07	1708
HALLMARK_INFLAMMATORY_RESPONSE	158	0.76	1.79	0.00	0.06	0.08	1363
HALLMARK_ALLOGRAFT_REJECTION	151	0.82	1.78	0.00	0.05	0.09	948
HALLMARK_COMPLEMENT	150	0.70	1.77	0.00	0.05	0.09	1351
HALLMARK_INTERFERON_GAMMA_RESPONSE	147	0.80	1.75	0.00	0.05	0.11	1330
HALLMARK_TNFA_SIGNALING_VIA_NFKB	164	0.71	1.73	0.00	0.05	0.13	1584
HALLMARK_IL6_JAK_STAT3_SIGNALING	70	0.76	1.72	0.00	0.04	0.13	1343
HALLMARK_KRAS_SIGNALING_UP	158	0.69	1.72	0.00	0.04	0.14	1331
HALLMARK_INTERFERON_ALPHA_RESPONSE	65	0.80	1.69	0.00	0.05	0.18	1288
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	174	0.75	1.62	0.01	0.07	0.27	1575
HALLMARK_COAGULATION	109	0.67	1.61	0.01	0.07	0.30	1489
HALLMARK_HYPOXIA	158	0.54	1.60	0.02	0.07	0.31	1741
HALLMARK_UV_RESPONSE_UP	132	0.44	1.59	0.01	0.07	0.33	1627
HALLMARK_APICAL_JUNCTION	145	0.50	1.55	0.03	0.09	0.42	1368
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	39	0.47	1.52	0.05	0.11	0.48	2089
HALLMARK_ANGIOGENESIS	27	0.70	1.51	0.03	0.10	0.49	1716
HALLMARK_ADIPOGENESIS	153	0.39	1.49	0.04	0.11	0.52	1319
HALLMARK_MYOGENESIS	150	0.47	1.47	0.03	0.12	0.55	1949
HALLMARK_P53_PATHWAY	166	0.39	1.46	0.03	0.12	0.57	2018
HALLMARK_APICAL_SURFACE	28	0.56	1.44	0.05	0.13	0.60	1414
HALLMARK_UV_RESPONSE_DN	112	0.47	1.43	0.05	0.13	0.63	1799
HALLMARK_TGF_BETA_SIGNALING	42	0.45	1.33	0.12	0.23	0.81	2060
HALLMARK_XENOBIOTIC_METABOLISM	155	0.50	1.30	0.19	0.25	0.84	1929
HALLMARK_NOTCH_SIGNALING	23	0.47	1.30	0.17	0.24	0.85	2423
HALLMARK_HEME_METABOLISM	153	0.32	1.28	0.13	0.25	0.86	1875
HALLMARK_MTORC1_SIGNALING	171	0.29	1.05	0.39	0.54	0.99	652
HALLMARK_KRAS_SIGNALING_DN	103	0.33	1.04	0.37	0.54	0.99	1561
HALLMARK_FATTY_ACID_METABOLISM	127	0.29	1.01	0.44	0.57	0.99	1439
HALLMARK_BILE_ACID_METABOLISM	83	0.36	1.00	0.47	0.56	0.99	2125
HALLMARK_PI3K_AKT_MTOR_SIGNALING	81	0.23	1.00	0.46	0.55	0.99	2239
HALLMARK_ESTROGEN_RESPONSE_EARLY	165	0.30	0.93	0.57	0.63	1.00	1933
HALLMARK_HEDGEHOG_SIGNALING	27	0.34	0.92	0.59	0.64	1.00	2091
HALLMARK_ESTROGEN_RESPONSE_LATE	172	0.28	0.90	0.64	0.64	1.00	1885
HALLMARK_GLYCOLYSIS	153	0.25	0.90	0.61	0.63	1.00	2270
HALLMARK_ANDROGEN_RESPONSE	91	0.25	0.84	0.68	0.70	1.00	1504
HALLMARK_WNT_BETA_CATENIN_SIGNALING	32	0.24	0.72	0.87	0.86	1.00	1770
HALLMARK_PROTEIN_SECRETION	85	0.15	0.61	0.95	0.95	1.00	1878
HALLMARK_CHOLESTEROL_HOMEOSTASIS	52	0.19	0.60	0.97	0.93	1.00	2122

Supplementary Table 5. Functional enrichment in HIC metastases (GSEA Hallmarks).

Gene	logFC	AveExpr	t	P.Value	adj.P.Val	B
HLA-DMA	2.02	8.39	19.77	1.85E-42	1.45E-38	86.07
GZMA	2.10	6.04	19.71	2.62E-42	2.06E-38	85.73
HLA-DPA1	2.61	8.37	19.47	9.31E-42	7.31E-38	84.47
ITGB2	2.17	8.45	18.70	5.47E-40	4.29E-36	80.44
CD74	2.38	9.63	18.55	1.25E-39	9.80E-36	79.62
CCL5	2.43	6.94	18.44	2.29E-39	1.80E-35	79.02
LAPTM5	2.21	8.82	17.81	7.15E-38	5.61E-34	75.61
HLA-DPB1	2.25	7.87	17.75	9.74E-38	7.64E-34	75.30
EVI2B	2.06	6.55	17.14	2.92E-36	2.29E-32	71.93
TYROBP	2.12	8.24	17.09	3.85E-36	3.02E-32	71.66
HLA-DRA	3.03	9.18	17.06	4.57E-36	3.59E-32	71.49
IL7R	2.41	6.53	17.03	5.41E-36	4.25E-32	71.32
FCER1G	2.01	8.04	16.58	6.76E-35	5.31E-31	68.82
AIF1	2.42	7.28	16.55	7.72E-35	6.06E-31	68.69
C1QA	2.04	7.70	16.54	8.19E-35	6.43E-31	68.63
GZMK	2.01	6.28	16.37	2.14E-34	1.68E-30	67.67
CD69	2.32	5.64	16.37	2.16E-34	1.69E-30	67.66
SLAMF8	2.04	5.88	16.26	4.06E-34	3.18E-30	67.04
MS4A6A	2.29	7.68	16.13	8.25E-34	6.48E-30	66.33
FGL2	2.36	6.76	16.09	1.06E-33	8.36E-30	66.08
C1QB	2.31	8.34	16.02	1.58E-33	1.24E-29	65.69
PTPRC	2.22	6.47	15.61	1.63E-32	1.28E-28	63.37
CD14	2.19	8.41	15.43	4.63E-32	3.64E-28	62.34
SAMSN1	2.06	5.85	15.14	2.50E-31	1.96E-27	60.67
TRIM22	2.06	7.59	15.03	4.75E-31	3.73E-27	60.03
SRGN	2.17	8.83	14.70	3.15E-30	2.48E-26	58.15
HLA-DRB1	2.32	8.81	14.44	1.44E-29	1.13E-25	56.64
MS4A4A	2.08	6.20	13.89	3.58E-28	2.81E-24	53.45
GBP1	2.35	6.96	13.36	8.36E-27	6.56E-23	50.32
CXCL9	2.25	6.66	13.11	3.72E-26	2.92E-22	48.84
CD52	2.03	6.75	13.08	4.28E-26	3.36E-22	48.70
CXCL10	2.36	7.20	12.83	1.99E-25	1.56E-21	47.18
SERPING1	2.01	8.41	12.26	5.89E-24	4.62E-20	43.82
LYZ	2.61	7.70	11.97	3.29E-23	2.58E-19	42.11
RARRES3	2.14	8.08	11.79	9.43E-23	7.40E-19	41.06
CD163	2.16	7.66	11.66	2.03E-22	1.59E-18	40.30
IGJ	2.71	6.11	10.66	8.02E-20	6.29E-16	34.37
C1S	2.31	8.17	10.15	1.62E-18	1.27E-14	31.39
S100A8	2.38	7.91	9.86	9.45E-18	7.42E-14	29.65
MXRA5	2.09	8.14	9.34	1.96E-16	1.54E-12	26.64
S100A9	2.07	7.58	9.22	3.97E-16	3.12E-12	25.94
CXCL13	2.24	5.86	8.44	3.54E-14	2.77E-10	21.51
MMP1	2.10	5.53	7.52	5.83E-12	4.57E-08	16.47

Supplementary Table 6. List of 43 differentially expressed genes (DEG) between HIC and LIC that passed filters $\log_2FC > \text{abs}(2)$ and $p\text{-val} < 0.01$.