Table 1S Identification of EMT hallmark gene sets. Tumor cell genes (top) and non-tumor cell genes (bottom) by Gene Set Enrichment Analysis-Molecular Signatures Database (GSEA-MSigDB)

12 tumor cell genes overlapped in EMT hallmark gene set

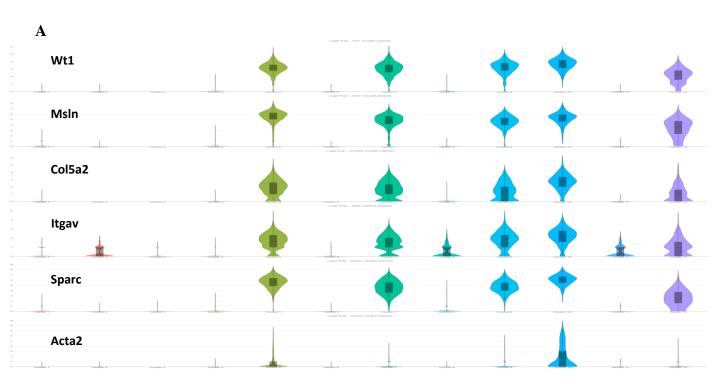
Symbol	Gene Description	
GJA1	gap junction protein alpha 1 [Source:HGNC Symbol;Acc:HGNC:4274]	
IGFBP4	insulin like growth factor binding protein 4 [Source:HGNC Symbol;Acc:HGNC:5473]	
ITGAV	integrin subunit alpha V [Source:HGNC Symbol;Acc:HGNC:6150]	
APLP1	amyloid beta precursor like protein 1 [Source:HGNC Symbol;Acc:HGNC:597]	
VCAM1	vascular cell adhesion molecule 1 [Source:HGNC Symbol;Acc:HGNC:12663]	
COL5A2	collagen type V alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2210]	
TIMP3	TIMP metallopeptidase inhibitor 3 [Source:HGNC Symbol;Acc:HGNC:11822]	
SDC4	syndecan 4 [Source:HGNC Symbol;Acc:HGNC:10661]	
SERPINH1	serpin family H member 1 [Source:HGNC Symbol;Acc:HGNC:1546]	
GAS1	growth arrest specific 1 [Source:HGNC Symbol;Acc:HGNC:4165]	
FBLN2	fibulin 2 [Source:HGNC Symbol;Acc:HGNC:3601]	
CALD1	caldesmon 1 [Source:HGNC Symbol;Acc:HGNC:1441]	

11 non-tumor cell genes overlapped in EMT hallmark gene set

Symbol	Gene Description	
Symbol	·	
SPARC	secreted protein acidic and cysteine rich [Source:HGNC Symbol;Acc:HGNC:11219]	
HTRA1	HtrA serine peptidase 1 [Source:HGNC Symbol;Acc:HGNC:9476]	
DCN	decorin [Source:HGNC Symbol;Acc:HGNC:2705]	
BGN	biglycan [Source:HGNC Symbol;Acc:HGNC:1044]	
TNFRSF12A	TNF receptor superfamily member 12A [Source:HGNC Symbol;Acc:HGNC:18152]	
TPM2	tropomyosin 2 [Source:HGNC Symbol;Acc:HGNC:12011]	
TGM2	transglutaminase 2 [Source:HGNC Symbol;Acc:HGNC:11778]	
FBLN1	fibulin 1 [Source:HGNC Symbol;Acc:HGNC:3600]	
PCOLCE	procollagen C-endopeptidase enhancer [Source:HGNC Symbol;Acc:HGNC:8738]	
ACTA2	"actin alpha 2, smooth muscle [Source:HGNC Symbol;Acc:HGNC:130]"	
TPM1	tropomyosin 1 [Source:HGNC Symbol;Acc:HGNC:12010]	

Figure 1S EMT genes expressed predominantly on tumor cells

- A. Mouse data: scRNA-Seq. EMT genes expressed in tumor cell clusters.
- B. Patient data: scRNA-Seq. EMT genes expressed in tumor cell clusters (MSLN+WT1+).



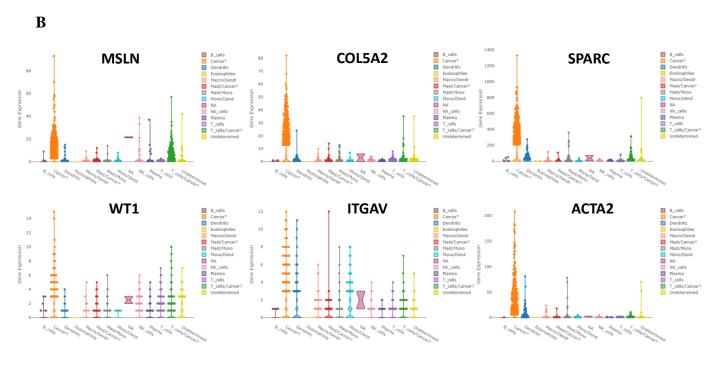


Figure 2S Co-expression of EMT genes in MESO cohort of TCGA analysed by Timer2.0. Gene expression of COL5A2, ITGAV, SPARC and ACTA2 was observed positively correlated between each other.

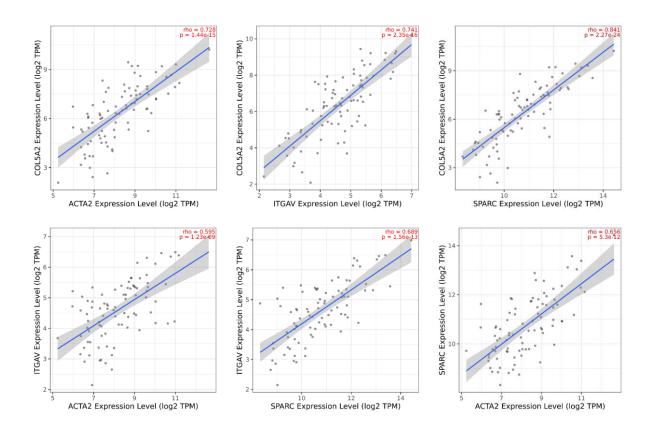


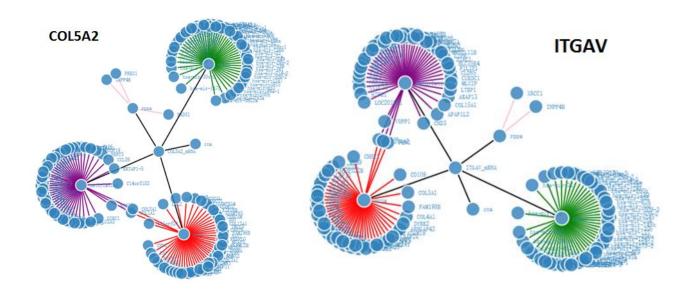
Table 2S Identification of EMT hallmark gene sets. Among the list, 12/72 tumor cell genes are involved in EMT pathway.

Gene Description (EMT genes are highlighted) Gene Symbol Gene Description (EMT genes are highlighted) Gene GJA1 gap junction protein al [Source:HGNC Symbol;Acc:HGNC:4274] insulin like growth factor binding protein 4 [Source:HGNC Symbol;Acc:HGNC:5473] integrin subunit alpha V [Source:HGNC Symbol;Acc:HGNC:597] 7412 VCAM1 vascular cell adhesion molecule 1 [Source:HGNC Symbol;Acc:HGNC:12663] 1290 COLSA2 collagen type V alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2210] 7078 TiMP3 TiMP metallopeptidase inhibitor 3 [Source:HGNC Symbol;Acc:HGNC:11822] 831 SERPINH1 serpin family H member 1 [Source:HGNC Symbol;Acc:HGNC:1546] 832 SPC4 syndecan 4 [Source:HGNC Symbol;Acc:HGNC:1546] 833 growth arrest specific 1 [Source:HGNC Symbol;Acc:HGNC:4165] 831 SERPINH1 serpin family H member 1 [Source:HGNC Symbol;Acc:HGNC:1546] 832 growth arrest specific 1 [Source:HGNC Symbol;Acc:HGNC:4165] 833 [Bblul 2 [Source:HGNC Symbol;Acc:HGNC:6430]] 800 CALD1 caldesmon 1 [Source:HGNC Symbol;Acc:HGNC:6436] 802 CLIC3 chloride intracellular channel 3 [Source:HGNC:5ymbol;Acc:HGNC:6436] 8022 CLIC3 shoride intracellular channel 3 [Source:HGNC:5ymbol;Acc:HGNC:6430] 8420 PODXL podocalyxin like [Source:HGNC Symbol;Acc:HGNC:9171] 8420 PODXL podocalyxin like [Source:HGNC Symbol;Acc:HGNC:9171] 8420 PODXL podocalyxin like [Source:HGNC Symbol;Acc:HGNC:9179] 85269 SERPINB6 serpin family B member 6 [Source:HGNC Symbol;Acc:HGNC:30238] 87 ACTN1 actinin alpha 1 [Source:HGNC Symbol;Acc:HGNC:630] 87971 WLS Wnt ligand secretion mediator [Source:HGNC Symbol;Acc:HGNC:630] 875742 PARVA parvin alpha [Source:HGNC Symbol;Acc:HGNC:630] 87675 ITGA3 integrin subunit alpha 3 [Source:HGNC Symbol;Acc:HGNC:630] 8776 ITGA3 integrin subunit alpha 3 [Source:HGNC Symbol;Acc:HGNC:630] 87971 WLS Wnt ligand secretion mediator [Source:HGNC Symbol;Acc:HGNC:630] 87972 PARVA parvin alpha [Source:HGNC Symbol;Acc:HGNC:1651] 87985 CVP251 Cytochrome PA50 Fource:HGNC Symbol;Acc:HGNC:1652] 87986 CRSP1 cytochrome PA50 Fource:HGNC Symbol;Acc:HGNC:1654] 87986 CRSP1 cytoc	
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22808 MRAS muscle RAS oncogene homolog [Source:HGNC Symbol;Acc:HGNC:7227] 10232 MSLN mesothelin [Source:HGNC Symbol;Acc:HGNC:7371] 10417 SPON2 spondin 2 [Source:HGNC Symbol;Acc:HGNC:11253]	
10232 MSLN mesothelin [Source:HGNC Symbol;Acc::HGNC:7371] 10417 SPON2 spondin 2 [Source:HGNC Symbol;Acc::HGNC:11253]	
spondin 2 [Source:HGNC Symbol;Acc:HGNC:11253]	
128414 NKAIN4 sodium/potassium transporting ATPase interacting 4 [Source:HGNC:16191]	
CXADR Ig-like cell adhesion molecule [Source:HGNC Symbol;Acc:HGNC:2559]	
LRRN4 leucine rich repeat neuronal 4 [Source:HGNC Symbol;Acc:HGNC:16208]	
TMEM98 transmembrane protein 98 [Source:HGNC Symbol;Acc:HGNC:24529]	
glycoprotein M6A [Source:HGNC Symbol;Acc:HGNC:4460]	
RSPO1 R-spondin 1 [Source:HGNC Symbol;Acc:HGNC:21679]	
glutathione S-transferase alpha 1 [Source:HGNC Symbol;Acc:HGNC:4626]	
KRT7 keratin 7 [Source:HGNC Symbol;Acc:HGNC:6445]	
KRT14 keratin 14 [Source:HGNC Symbol;Acc:HGNC:6416]	
RAS like family 11 member A [Source:HGNC Symbol;Acc:HGNC:23802]	
387597 ILDR2 immunoglobulin like domain containing receptor 2 [Source:HGNC:18131]	
FAM180A family with sequence similarity 180 member A [Source:HGNC:33773]	
3911 LAMA5 laminin subunit alpha 5 [Source:HGNC Symbol;Acc:HGNC:6485]	
3957 LGALS2 galectin 2 [Source:HGNC Symbol;Acc:HGNC:6562]	
3995 FADS3 fatty acid desaturase 3 [Source:HGNC Symbol;Acc:HGNC:3576]	
MYO1D myosin ID [Source:HGNC Symbol;Acc:HGNC:7598]	
51196 PLCE1 phospholipase C epsilon 1 [Source:HGNC Symbol;Acc:HGNC:17175]	
51232 CRIM1 cysteine rich transmembrane BMP regulator 1 [Source:HGNC:2359]	
FXYD3 FXYD4 domain containing ion transport regulator 3 [Source:HGNC:4027]	
55512 SMPD3 sphingomyelin phosphodiesterase 3 [Source:HGNC Symbol;Acc:HGNC:14240]	
57493 HEG1 heart development protein with EGF like domains 1 [Source:HGNC:29227]	
PTPRF protein tyrosine phosphatase receptor type F [Source:HGNC:9670]	
64759 TNS3 tensin 3 [Source:HGNC Symbol;Acc:HGNC:21616]	
TMEM108 transmembrane protein 108 [Source:HGNC Symbol;Acc:HGNC:28451]	
SOX4 SRY-box transcription factor 4 [Source:HGNC Symbol;Acc:HGNC:11200]	
728113 ANXA8L1 annexin A8 like 1 [Source:HGNC Symbol;Acc:HGNC:23334]	
7348 UPK1B uroplakin 1B [Source:HGNC Symbol;Acc:HGNC:12578]	
745 MYRF myelin regulatory factor [Source:HGNC Symbol;Acc:HGNC:1181]	
7490 WT1 WT1 transcription factor [Source:HGNC Symbol;Acc:HGNC:12796]	
DDR1 discoidin domain receptor tyrosine kinase 1 [Source:HGNC Symbol;Acc:HGNC:2730]	
BICC1 BicC family RNA binding protein 1 [Source:HGNC Symbol;Acc:HGNC:19351]	
9032 TM4SF5 transmembrane 4 L six family member 5 [Source:HGNC Symbol;Acc:HGNC:11857]	
91584 PLXNA4 plexin A4 [Source:HGNC Symbol;Acc:HGNC:9102]	
PKHD1L1 PKHD1 like 1 [Source:HGNC Symbol;Acc:HGNC:20313]	

Table 2S Identification of EMT hallmark gene sets. Among the list, 11/55 non-tumor cell genes are involved in EMT pathway.

Gene Id	Gene Symbol	Gene Description (EMT genes are highlighted)
6678	SPARC	secreted protein acidic and cysteine rich [Source:HGNC Symbol;Acc:HGNC:11219]
5654	HTRA1	HtrA serine peptidase 1 [Source:HGNC Symbol;Acc:HGNC:9476]
1634	DCN	decorin [Source:HGNC Symbol;Acc:HGNC:2705]
633	BGN	biglycan [Source:HGNC Symbol;Acc:HGNC:1044]
51330	TNFRSF12A	TNF receptor superfamily member 12A [Source:HGNC Symbol;Acc:HGNC:18152]
7169	TPM2	tropomyosin 2 [Source:HGNC Symbol;Acc:HGNC:12011]
7052	TGM2	transglutaminase 2 [Source:HGNC Symbol;Acc:HGNC:11778]
2192	FBLN1	fibulin 1 [Source:HGNC Symbol;Acc:HGNC:3600]
5118	PCOLCE	procollagen C-endopeptidase enhancer [Source:HGNC Symbol;Acc:HGNC:8738]
59	ACTA2	"actin alpha 2, smooth muscle [Source:HGNC Symbol;Acc:HGNC:130]"
7168	TPM1	tropomyosin 1 [Source:HGNC Symbol;Acc:HGNC:12010]
1191	CLU	clusterin [Source:HGNC Symbol;Acc:HGNC:2095]
2934	GSN	gelsolin [Source:HGNC Symbol;Acc:HGNC:4620]
718	C3	complement C3 [Source:HGNC Symbol;Acc:HGNC:1318]
716	C1S	complement C1s [Source:HGNC Symbol;Acc:HGNC:1247]
710	SERPING1	serpin family G member 1 [Source:HGNC Symbol;Acc:HGNC:1228]
11098	PRSS23	serine protease 23 [Source:HGNC Symbol;Acc:HGNC:14370]
857	CAV1	caveolin 1 [Source:HGNC Symbol;Acc:HGNC:1527]
3005	H1-0	H1.0 linker histone [Source:HGNC Symbol;Acc:HGNC:4714]
3489	IGFBP6	insulin like growth factor binding protein 6 [Source:HGNC Symbol;Acc:HGNC:5475]
1410	CRYAB	crystallin alpha B [Source:HGNC Symbol;Acc:HGNC:2389]
165	AEBP1	AE binding protein 1 [Source:HGNC Symbol;Acc:HGNC:303]
3490	IGFBP7	insulin like growth factor binding protein 7 [Source:HGNC Symbol;Acc:HGNC:5476]
9806	SPOCK2	"SPARC (osteonectin), cwcv and kazal like domains proteoglycan 2 [Source:HGNC:13564]"
7167	TPI1	triosephosphate isomerase 1 [Source:HGNC Symbol;Acc:HGNC:12009]
6566	SLC16A1	solute carrier family 16 member 1 [Source:HGNC Symbol;Acc:HGNC:10922]
1363	CPE	carboxypeptidase E [Source:HGNC Symbol;Acc:HGNC:2303]
8611	PLPP1	phospholipid phosphatase 1 [Source:HGNC Symbol;Acc:HGNC:9228]
8848	TSC22D1	TSC22 domain family member 1 [Source:HGNC Symbol;Acc:HGNC:16826]
2202	EFEMP1	EGF containing fibulin extracellular matrix protein 1 [Source:HGNC:3218]
4781	NFIB	nuclear factor I B [Source:HGNC Symbol;Acc:HGNC:7785]
23710	GABARAPL1	GABA type A receptor associated protein like 1 [Source:HGNC Symbol;Acc:HGNC:4068]
9411	ARHGAP29	Rho GTPase activating protein 29 [Source:HGNC Symbol;Acc:HGNC:30207]
977	CD151	CD151 molecule (Raph blood group) [Source:HGNC Symbol;Acc:HGNC:1630]
55107	ANO1	anoctamin 1 [Source:HGNC Symbol;Acc:HGNC:21625]
481	ATP1B1	ATPase Na+/K+ transporting subunit beta 1 [Source:HGNC Symbol;Acc:HGNC:804]
4734	NEDD4	NEDD4 E3 ubiquitin protein ligase [Source:HGNC Symbol;Acc:HGNC:7727]
7103	TSPAN8	tetraspanin 8 [Source:HGNC Symbol;Acc:HGNC:11855]
100532736	MICOS10-NBL1	MICOS10-NBL1 readthrough [Source:HGNC Symbol;Acc:HGNC:48338]
10079	АТР9А	ATPase phospholipid transporting 9A (putative) [Source:HGNC:13540]
10787	NCKAP1	NCK associated protein 1 [Source:HGNC Symbol;Acc:HGNC:7666]
151887	CCDC80	coiled-coil domain containing 80 [Source:HGNC Symbol;Acc:HGNC:30649]
23164	MPRIP	myosin phosphatase Rho interacting protein [Source:HGNC Symbol;Acc:HGNC:30321]
23213	SULF1	sulfatase 1 [Source:HGNC Symbol;Acc:HGNC:20391]
3281	HSBP1	heat shock factor binding protein 1 [Source:HGNC Symbol;Acc:HGNC:5203]
379	ARL4D	ADP ribosylation factor like GTPase 4D [Source:HGNC Symbol;Acc:HGNC:656]
3791 4054	KDR	kinase insert domain receptor [Source:HGNC Symbol;Acc:HGNC:6307]
4054	LTBP3	latent transforming growth factor beta binding protein 3 [Source:HGNC:6716]
51765	STK26	serine/threonine kinase 26 [Source:HGNC Symbol;Acc:HGNC:18174]
55353	LAPTM4B	lysosomal protein transmembrane 4 beta [Source:HGNC Symbol;Acc:HGNC:13646]
58189	WFDC1	WAP four-disulfide core domain 1 [Source:HGNC Symbol;Acc:HGNC:15466]
58480	RHOU	ras homolog family member U [Source:HGNC Symbol;Acc:HGNC:17794]
30400		
6038	RNASE4	ribonuclease A family member 4 [Source:HGNC Symbol;Acc:HGNC:10047] matrix metallopeptidase 23B [Source:HGNC Symbol;Acc:HGNC:7171]

Figure 3S Network of OMICS profile of interest. Significant correlation between gene of interest (RNA expression) in TCGA cohort MESO with OMICS profile with FDR < 0.05. OMICS includes mRNA, miRNA, copy number alteration (CNA), methylation, and reverse phase protein analysis (RPPA) correlation was also analyzed. Only the most significantly correlated genes (*COL5A2, ITGAV, SPARC* and *ACTA2*) were presented.



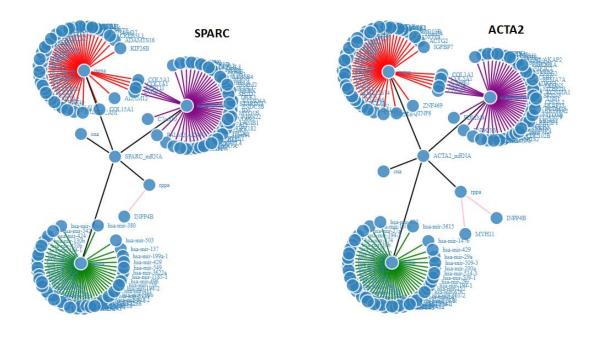


Fig. 4S Gene expression *COL5A2*, *ITGAV*, *SPARC* and *ACTA2* in Epithelioid *vs* non-Epithelioid subtype in MESO patients. A) Dotplot of 4 gene expression in scRNA-Seq was shown in five naïve MPM patients, and CDH1 and VIM were included as controls. B) Histology of HE staining of biphasic (SMTR02T0) and epithelioid (SMTR03T0) subtype.



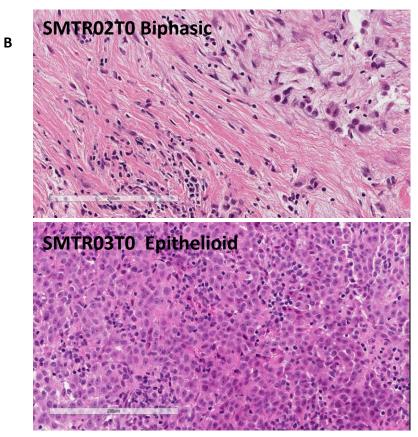
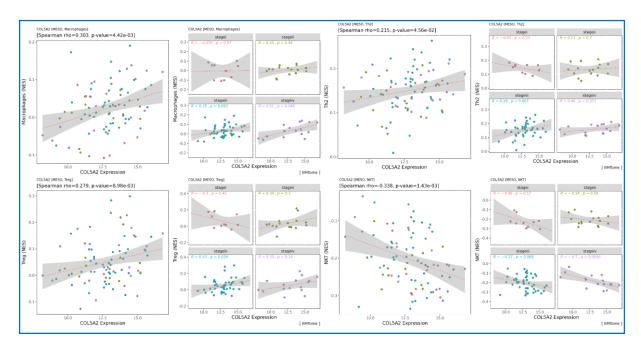


Figure 5S *COL5A2* and *SPARC* gene expression correlated with immune enrichment in MESO cohort of TCGA database. COL5A2 (top panel) and SPARC (bottom panel) gene expression correlated with immune enrichment: Macrophage, Th2, Treg and NKT in TCGA.



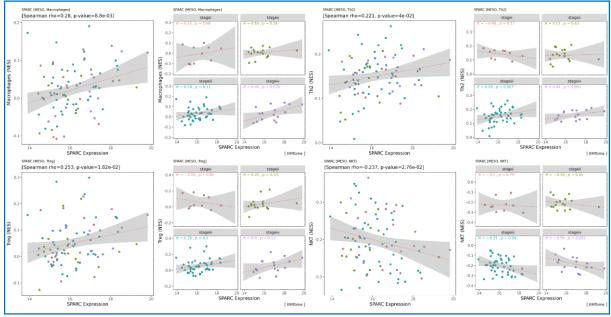
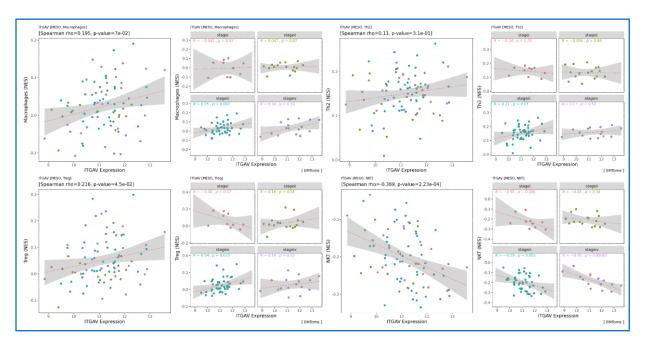


Figure 6S *ITGAV* and *ACTA2* gene expression correlated with immune enrichment in MESO cohort of TCGA database. *ITGAV* (top panel) and *ACTA2* (bottom) gene expression in correlation with Macrophage, Th2, Treg and NKT in TCGA.



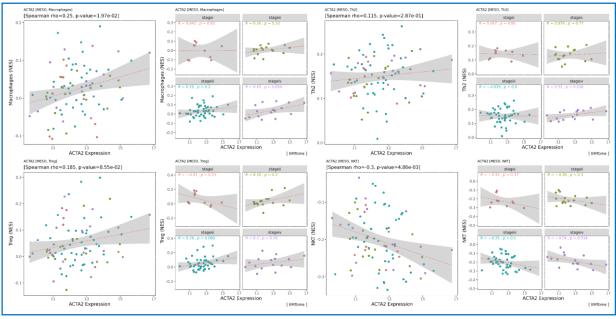


Figure 7S Gene expression correlated with immune enrichment in MESO cohort of TCGA database. $ITGAV\left(A\right)$ and $ACTA2\left(B\right)$

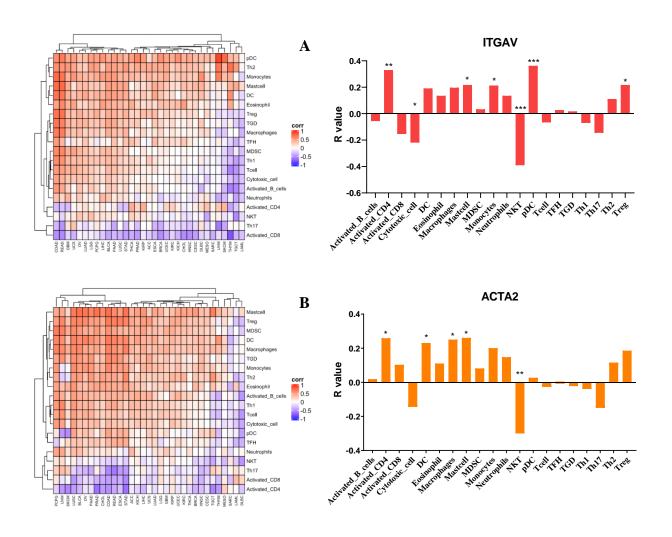


Figure 8S The immune infiltration associated with gene expression and clinical outcome in MESO of TCGA.

Gene module performed the correlation of gene expression with cancer associated fibroblasts (CAF) and immune cell infiltrates MDSC, Th2 cells in MESO.

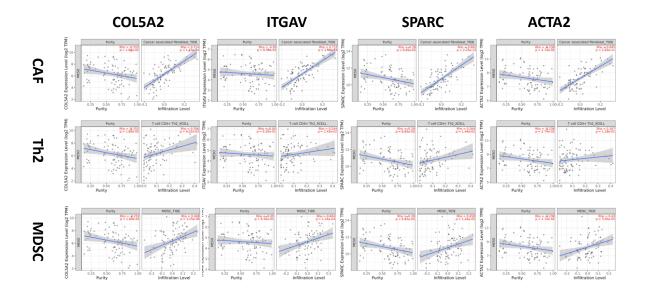


Figure 9S The immune infiltration associated with gene expression and clinical outcome in MESO of TCGA.

Gene module performed the correlation of gene expression with immune cell infiltration level in MESO. EMT gene expression and immune infiltrates of M2 macrophage and Treg cells in correlation with clinical outcome in MESO cohort.

