## Supplementary

BTM Module	DIS	log(FDR)	MAST
type I interferon response (M127)	1.78	29.68	No
suppression of MAPK signaling (M56)	1.57	29.68	Yes
AP-1 transcription factor network (M20)	1.50	38.37	Yes
signaling in T cells (I) (M35.0)	1.26	29.68	No
complement activation (I) (M112.0)	1.07	29.68	No
enriched in B cells (V) (M47.4)	1.07	29.68	No
spliceosome (M250)	0.94	29.68	Yes
phosphatidylinositol signaling system (M101)	0.87	29.68	No
myeloid, dendritic cell activation via NFkB (II) (M43.1)	0.72	29.68	No
enriched for TF motif TNCATNTCCYR (M232)	0.71	29.68	No
enriched in T cells (II) (M223)	0.68	29.68	No
proteasome (M226)	0.63	29.68	Yes
cell cycle and growth arrest (M31)	0.62	29.68	Yes
leukocyte activation and migration (M45)	0.56	29.68	No
transcription elongation, RNA polymerase II (M234)	0.56	29.68	Yes
respiratory electron transport chain (mitochondrion) (M238)	0.54	29.68	Yes
myeloid, dendritic cell activation via NFkB (I) (M43.0)	0.54	29.68	No
translation initiation factor 3 complex (M245)	0.53	29.68	Yes
respiratory electron transport chain (mitochondrion) (M219)	0.52	29.68	Yes
respiratory electron transport chain (mitochondrion) (M216)	0.49	29.68	Yes
cell cycle, ATP binding (M144)	0.47	29.68	Yes
leukocyte differentiation (M160)	0.44	29.68	No
T cell differentiation (Th2) (M19)	0.43	38.37	No
mitotic cell cycle in stimulated CD4 T cells (M4.9)	0.42	38.37	No

BTM, Blood transcriptional modules; DIS, difference of IScore; FDR, false discovery rate.

GO Terms	Tu Mu	DIS	FDR
GO:0071456	cellular response to hypoxia	1.97	1.1E-144
GO:0043154	negative regulation of cysteine-type endopeptidase…	1.46	4.71E-74
GO:0019216	regulation of lipid metabolic process	1.30	3.36E-66
GO:0016310	phosphorylation	1.10	1.53E-35
GO:0043547	positive regulation of GTPase activity	1.05	2.88E-46
GO:0048146	positive regulation of fibroblast proliferation	0.97	3.53E-65
GO:0007173	epidermal growth factor receptor signaling pathway	0.93	6.43E-37
GO:0032092	positive regulation of protein binding	0.91	1.63E-87
GO:0045087	innate immune response	0.81	4.49E-48
GO:0007155	cell adhesion	0.80	1.24E-33
GO:0042127	regulation of cell proliferation	0.77	3.29E-42
GO:2001237	negative regulation of extrinsic apoptotic	0.72	3.8E-26
GO:0098869	cellular oxidant detoxification	0.70	5.26E-25
GO:0007584	response to nutrient	0.68	1.53E-22
GO:0072659	protein localization to plasma membrane	0.66	4.61E-29
GO:0050776	regulation of immune response	0.65	2.81E-27
GO:0002474	antigen processing and presentation of peptide…	0.62	1.93E-29
GO:0044267	cellular protein metabolic process	0.61	1.02E-29
GO:0070301	cellular response to hydrogen peroxide	0.61	5.74E-14
GO:0042493	response to drug	0.61	1.02E-25
GO:0010468	regulation of gene expression	0.57	9.4E-22
GO:0002479	antigen processing and presentation of exogenous	0.57	4E-20
GO:0001843	neural tube closure	0.56	8.46E-24
GO:0030855	epithelial cell differentiation	0.55	2E-19
GO:0032088	negative regulation of NF-kappaB transcription…	0.53	7.08E-19
GO:0051496	positive regulation of stress fiber assembly	0.51	2.27E-19
GO:1900026	positive regulation of substrate adhesion-dependent…	0.51	1.07E-22
GO:0001649	osteoblast differentiation	0.51	1.43E-14
GO:0006397	mRNA processing	0.49	8.42E-20
GO:0043044	ATP-dependent chromatin remodeling	0.49	1.63E-14
GO:0009267	cellular response to starvation	0.48	2.3E-12
GO:0007517	muscle organ development	0.48	1.07E-11
GO:0007160	cell-matrix adhesion	0.47	1.33E-13
GO:0001525	angiogenesis	0.47	4.78E-20
GO:0006303	double-strand break repair via nonhomologous end joinin	0.47	9.14E-09

**Figure S1** Heatmap shows IScore difference of GO BP category between Tumor and Normal mucosa. Furthermore, 28/386 (7.2%) BP GO terms were identified as DBMs by setting DIS threshold to 0.5. IScore, integrated scores; DBMs, differential biological modules; GO, Gene Ontology; BP, biological process; DIS, difference of IScore.



**Figure S2** The violin plot shows gene expression patterns in non-stimulated (Unstim) and cytokine-stimulated (Stim) MAST cell. The genes displayed in the graph are annotated in "type I interferon response (M127)", "suppression of MAPK signaling (M56)", "AP-1 transcription factor network (M20)" and "signaling in T cells (I) (M35.0)". The letter (E) indicates FPKM value.



**Figure S3** The venn diagram shows the number of DBMs overlap between scRNA-seq and Bulk RNA-seq data which were collected at different time points. DBMs identified by NonLoss between any pair of time points using bulk RNA-seq and single cell RNA-seq data respectively. (A) Calculated by cells of DM and cells collected 24h after serum switch. (B) Calculated by cells of DM and cells collected 72h after serum switch.