



**Figure S1.** General views of M5-T1 tumors from the group of untreated rats (HPS staining, scale bars at the bottom left corner of each photograph). Samples **1** and **2** were selected for the study according to criteria described in sections 4.2 and 4.3 (Materials and methods). The dashed black circles (arrows) represent areas of interest, used both for histological (morphology of tumor infiltrating lymphocytes) and proteomic analyses. T = tumor.

**Table S1.**

**Supplementary Table S1: Complete list of proteins exhibiting common abundance changes under curcumin treatment.** ↑ and ↓ symbolize significant ( $p < 0.05$ ) common increase or decrease relative to tumors from untreated rats.

Gene	Full name	G2/G1, G3/G1
<i>Impdh1</i>	Inosine-5'-monophosphate dehydrogenase 1	↑
<i>Pld3</i>	5'-3' exonuclease PLD3	↑
<i>F3</i>	Tissue factor	↑
<i>Rbp4</i>	Retinol-binding protein 4	↑
<i>Tf</i>	Serotransferin	↑
<i>Cav1</i>	Caveolin-1	↑
<i>Ankh</i>	Progressive ankylosis protein homolog	↑
<i>Cacna2d1</i>	Voltage-dependent calcium channel subunit alpha-2/delta-1	↑
<i>Cpne1</i>	Copine-1	↑
<i>Tmem231</i>	Transmembrane protein 231	↑
<i>Ctsl</i>	Procathepsin L	↑
<i>Rasgrf1</i>	Ras-specific guanine nucleotide-releasing factor 1	↑
<i>Rraga</i>	Ras-related GTP-binding protein A	↑

<i>Fkbp6</i>	Inactive peptidyl-prolyl cis-trans isomerase FKBP6	↑
<i>Mmgt1</i>	ER membrane protein complex subunit 5	↑
<i>Arl6ip6</i>	ADP-ribosylation factor-like protein 6-interacting protein 6	↑
<i>Dab2</i>	Disabled homolog 2	↑
<i>Map2k2</i>	Dual specificity mitogen-activated protein kinase kinase 2	↑
<i>Pip4k2c</i>	Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma	↑
<i>Cdh2</i>	Cadherin-2	↑
<i>Epdr1</i>	Mammalian ependymin-related protein 1	↑
<i>Nptn</i>	Neuroplastin	↑
<i>Emd</i>	Emerin	↑
<i>Aprt</i>	Adenine phosphoribosyltransferase	↑
<i>Akr1b7</i>	Aldo-keto reductase family 1 member B7	↑
<i>Dhcr24</i>	Delta(24)-sterol reductase	↑
<i>Enpp1</i>	Ectonucleotide pyrophosphatase/phosphodiesterase family member 1	↑
<i>Spr</i>	Sepiapterin reductase	↑
<i>Slc27a1</i>	Long-chain fatty acid transport protein 1	↑
<i>Acad10</i>	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	↑
<i>Ech1</i>	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	↑
<i>D2hgdh</i>	D-2-hydroxyglutarate dehydrogenase, mitochondrial	↑
<i>Gpd2</i>	Glycerol-3-phosphate dehydrogenase, mitochondrial	↑
<i>Ndufs1</i>	NADH-ubiquinone oxidoreductase 75 kDa subunits, mitochondrial	↑
<i>Pdk1</i>	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isoenzyme 1, mitochondrial	↑
<i>Plgrkt</i>	Plasminogen receptor	↑
<i>Prdx5</i>	Peroxisomal oxidoreductin-5, mitochondrial	↑
<i>Sardh</i>	Sarcosine dehydrogenase, mitochondrial	↑
<i>Mrppl23</i>	39S ribosomal protein L23, mitochondrial	↑
<i>Mrps25</i>	28S ribosomal protein S25, mitochondrial	↑
<i>Igf2bp1</i>	Insulin-like growth factor 2 mRNA-binding protein 1	↑
<i>Lsg1</i>	Large subunit GTPase 1 homolog	↑
<i>Rpl13a</i>	60S ribosomal protein L13a	↑
<i>Rpl18</i>	60S ribosomal protein L18	↑
<i>Rpl19</i>	60S ribosomal protein L19	↑
<i>Rps4x</i>	40S ribosomal protein S4, X isoform	↑
<i>Mphosph8</i>	M-phase phosphoprotein 8	↑
<i>Psmb5</i>	Proteasome subunit beta type-5	↑
<i>Psmb6</i>	Proteasome subunit beta type-6	↑
<i>Flnc</i>	Filamin-C	↑
<i>Apaf1</i>	Apoptotic protease-activating factor 1	↓
<i>Casp1</i>	Caspase-1	↓
<i>Cd74</i>	H-2 class II histocompatibility antigen gamma chain	↓
<i>Erap1</i>	Endoplasmic reticulum aminopeptidase 1	↓
<i>Fcer1g</i>	High affinity immunoglobulin epsilon receptor subunit gamma	↓
<i>Fcgr3a</i>	Low affinity immunoglobulin gamma Fc region receptor subunit gamma	↓
<i>Fcn2</i>	Ficolin-2	↓
<i>Gbp2</i>	Guanylate-binding protein 1	↓
<i>Gimap4</i>	GTPase IMAP family member 4	↓
<i>Irgm</i>	Immunity-related GTPase family M protein	↓
<i>Nampt</i>	N-acylethanolamine-hydrolyzing acidamidase	↓

<i>Rassf2</i>	Ras association domain-containing protein 2	↓
<i>Rgs19</i>	Regulator of G-protein signaling 19	↓
<i>RT1-Aw2</i>	Class I histocompatibility antigen, Non-RT1.A alpha-1 chain	↓
<i>RT1-Bb</i>	Rano class II histocompatibility antigen, B-1 beta chain	↓
<i>RT1-Db1</i>	Rano class II histocompatibility antigen, D-1 beta chain	↓
<i>Serpinb1a</i>	Leukocyte elastase inhibitor A	↓
<i>Sh3bp1</i>	SH3 domain-containing protein 1	↓
<i>Sting1</i>	Stimulator of interferon genes protein	↓
<i>Stk17b</i>	Serine/threonine-protein kinase 17B	↓
<i>Tap1</i>	Antigen peptide transporter 1	↓
<i>Tap2</i>	Antigen peptide transporter 2	↓
<i>Traf1</i>	TRAF-type zinc finger domain-containing protein 1	↓
<i>Vcam1</i>	Vascular cell adhesion protein 1	↓
<i>Wars1</i>	Tryptophan t-RNA ligase, cytoplasmic	↓
<i>A1bg</i>	Alpha-1B-glycoprotein	↓
<i>B2m</i>	Beta-2-microglobulin	↓
<i>Hp</i>	Haptoglobin	↓
<i>Lifr</i>	Leukemia inhibitory factor receptor	↓
<i>Rab27a</i>	Ras-related protein Rab-27A	↓
<i>Bst2</i>	Bone marrow stromal antigen 2	↓
<i>Pak1</i>	Serine/threonine-protein kinase PAK1	↓
<i>Mcf2</i>	Multiple coagulation factor deficiency protein 2 homolog	↓
<i>Ssr3</i>	Translocon-associated protein subunit gamma	↓
<i>GLTP</i>	Glycolipid transfer protein	↓
<i>Mob4</i>	MOB-like protein phocein	↓
<i>Rbp1</i>	Retinol-binding protein 1	↓
<i>Lap3</i>	Cytosol aminopeptidase	↓
<i>Dock9</i>	Dedicator of cytokinesis protein 9	↓
<i>Ltbp1</i>	Latent-transforming growth factor beta-binding protein 1	↓
<i>Wdr91</i>	WD repeat-containing protein 91	↓
<i>Numb</i>	Protein numb homolog	↓
<i>Hagh</i>	Hydroxyacyl glutathione hydrolase, mitochondrial	↓
<i>Naaa</i>	N-acyl ethanolamine-hydrolyzing acidamidase	↓
<i>Pgd</i>	6-phosphogluconate dehydrogenase, decarboxylating	↓
<i>Rnpep</i>	Aminopeptidase B	↓
<i>Uggf1</i>	UDP-glucose: glycoprotein glucosyltransferase 1	↓
<i>Xdh</i>	Xanthine dehydrogenase/oxidase	↓
<i>Acsf2</i>	Medium-chain acyl-CoA ligase ACSF2, mitochondrial	↓
<i>Bdh1</i>	D-beta-hydroxybutyrate dehydrogenase, mitochondrial	↓
<i>Mfn1</i>	Mitofusin-1	↓
<i>Nmes1</i>	Normal mucosa of esophagus-specific gene 1 protein	↓
<i>Celf2</i>	CUGBP Elav-like family member 2	↓
<i>Dnajc8</i>	Dnaj homolog subfamily C member 8	↓
<i>Iah1</i>	Isoamyl acetate-hydrolyzing esterase 1 homolog	↓
<i>Ptbp3</i>	Polypyrimidine tract-binding protein 3	↓
<i>Sub1</i>	Activated RNA polymerase II transcriptional coactivator p15	↓
<i>Psm10</i>	Proteasome subunit beta type-10	↓
<i>Psme1</i>	Proteasome activator complex subunit 1	↓
<i>Psme2</i>	Proteasome activator complex subunit 2	↓
<i>Add3</i>	Gamma-adducin	↓

<i>Cotl1</i>	Coactosin-like protein	↓
<i>Entpd1</i>	Ectonucleoside triphosphate diphosphohydrolase I	↓
<i>Evl</i>	Ena/VASP-like protein	↓
<i>Fnbp1</i>	Formin-binding protein 1	↓
<i>Mapre2</i>	Microtubule-associated protein RP/EB family member 2	↓

**Table S2.**

**Supplementary Table S2: Complete list of proteins exhibiting specific abundance changes in G3 rats (multiple early curcumin treatment).** ↑ and ↓ symbolize significant common significant ( $p < 0.05$ ) increase or decrease in G3 vs G1 (untreated rats) and G3 vs G2 (rats receiving two late curcumin injections), but not in G2 vs G1.

Gene	Full name	Change
<i>Cd276</i>	CD276 antigen	↑
<i>Il33</i>	Interleukin-33	↑
<i>Mif</i>	Macrophage migration inhibitory factor	↑
<i>Lrp1</i>	Prolow-density lipoprotein receptor-related protein 1	↑
<i>Lrrfip1</i>	Leucine-rich repeat flightless-interacting protein 1	↑
<i>Ptms</i>	Parathymosin	↑
<i>Col5a1</i>	Collagen alpha-1(V) chain	↑
<i>Gpc1</i>	Glypican-1	↑
<i>Mrc2</i>	C-type mannose receptor 2	↑
<i>Ecm1</i>	Extracellular matrix protein 1	↑
<i>Gtf2i</i>	General transcription factor II-I	↑
<i>Hrg</i>	Histidine-rich glycoprotein	↑
<i>Ptpn11</i>	Tyrosine-protein phosphatase non-receptor type 11	↑
<i>Mapk3</i>	Mitogen-activated protein kinase 3	↑
<i>Grip1</i>	Glutamate receptor-interacting protein 1	↑
<i>Mxra8</i>	Matrix remodeling-associated protein 8	↑
<i>Adcy3</i>	Adenylate cyclase type 3	↑
<i>Pdcl</i>	Phosducin-like protein	↑
<i>Rin1</i>	Ras and Rab interactor 1	↑
<i>S100a10</i>	Protein S100-A10	↑
<i>Pdlim3</i>	PDZ and LIM domain protein 3	↑
<i>Fabp5</i>	Fatty acid-binding protein 5	↑
<i>Cavin1</i>	Caveolae-associated protein 1	↑
<i>Map1lc3b</i>	Microtubule-associated proteins 1A/1B light chain 3B	↑
<i>Os9</i>	Protein OS-9	↑
<i>Adamtsl4</i>	ADAMTS-like protein 4	↑
<i>Aga</i>	N(4)-beta-N-acetylglucosaminyl)-L-asparaginase	↑
<i>Oga</i>	Protein O-GlcNAcase	↑
<i>Gpi</i>	Glucose-6-phosphate isomerase	↑
<i>Pgm1</i>	Phosphoglucomutase-1	↑
<i>Irf2bpl</i>	Interferon regulatory factor 2 binding protein like	↑
<i>Niban2</i>	Protein Niban 2	↑
<i>Ahr</i>	Aryl hydrocarbon receptor	↑

<i>Abhd14b</i>	Putative protein-lysine deacylase ABHD14B	↑
<i>Psmc3ip</i>	Homologous-pairing protein 2 homolog	↑
<i>Nab1</i>	NGFI-A-binding protein 1	↑
<i>Sorbs2</i>	Sorbin and SH3 domain-containing protein 2	↑
<i>Synpo2</i>	Synaptopodin-2	↑
<i>Dnm3</i>	Dynamin-3	↑
<i>Gsn</i>	Gelsolin	↑
<i>Dpysl3</i>	Dihydropyrimidinase-related protein 3	↑
<i>Phldb1</i>	Pleckstrin homology-like domain family B member 1	↑
<i>Pcmt1</i>	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	↑
<i>Dnm1</i>	Dynamin-1	↑
<i>Jup</i>	Junction plakoglobin	↑
<i>Cd47</i>	Leukocyte surface antigen CD47	↓
<i>Il18</i>	Interleukin-18	↓
<i>Il1rn</i>	Interleukin-1 receptor antagonist protein	↓
<i>Coro1a</i>	Coronin-1A	↓
<i>Lyz1</i>	Lysozyme C-1	↓
<i>Icam1</i>	Intercellular adhesion molecule 1	↓
<i>Ptprc</i>	Receptor-type tyrosine-protein phosphatase C	↓
<i>Ifitm3</i>	Interferon-induced transmembrane protein 3	↓
<i>Arrb2</i>	Beta-arrestin-2	↓
<i>Gnai2</i>	Guanine nucleotide-binding protein G(i) subunit alpha-2	↓
<i>Hk3</i>	Hexokinase-3	↓
<i>Tmed5</i>	Transmembrane emp24 domain-containing protein 5	↓
<i>Gclm</i>	Glutamate – cysteine ligase regulatory subunit	↓
<i>Atp5mg</i>	ATP synthase subunit g, mitochondrial	↓
<i>Atp5pf</i>	ATP synthase-coupling factor 6, mitochondrial	↓
<i>Cox7a2</i>	Cytochrome c oxidase subunit 7A2, mitochondrial	↓
<i>Idh2</i>	Isocitrate dehydrogenase [NADP], mitochondrial	↓
<i>Sdhb</i>	Succinate dehydrogenase [ubiquinone] cytochrome b small subunit, mitochondrial	↓
<i>Thy1</i>	Thy-1 membrane glycoprotein	↓
<i>Stat3</i>	Signal transducer and activator of transcription 3	↓