

Supplementary Table S7 All 163 statistically significant pathway maps, in which the 265 genes showing non-alcoholic steatohepatitis-specific DNA methylation alterations were significantly ($P < 0.05$) accumulated, revealed by MetaCore software analysis.

Pathway maps	<i>P</i> value
Development_NOTCH-induced EMT	1.408 x 10 ⁻⁷
Development_Notch Signaling Pathway	1.027 x 10 ⁻⁵
Development_NOTCH1-mediated pathway for NF-KB activity modulation	2.699 x 10 ⁻⁵
Development_Gastrin in cell growth and proliferation	6.243 x 10 ⁻⁵
Oxidative stress_ROS-mediated activation of MAPK via inhibition of phosphatases	8.034 x 10 ⁻⁴
Development_EGFR signaling pathway	1.198 x 10 ⁻⁴
Development_Thromboxane A2 signaling pathway	3.674 x 10 ⁻⁴
Development_Oligodendrocyte differentiation from adult stem cells	3.967 x 10 ⁻⁴
Immune response_T regulatory cell-mediated modulation of effector T cell and NK cell functions	4.600 x 10 ⁻⁴
Development_Mu-type opioid receptor signaling via Beta-arrestin	5.635 x 10 ⁻⁴
G-protein signaling_M-RAS regulation pathway	5.635 x 10 ⁻⁴
Development_Keratinocyte differentiation	5.682 x 10 ⁻⁴
G-protein signaling_TC21 regulation pathway	6.372 x 10 ⁻⁴
G-protein signaling_R-RAS regulation pathway	6.372 x 10 ⁻⁴
Neurogenesis_NGF/ TrkA MAPK-mediated signaling	7.426 x 10 ⁻⁴
Development_Mu-type opioid receptor regulation of proliferation	8.944 x 10 ⁻⁴
Immune response_Sublytic effects of membrane attack complex	1.185 x 10 ⁻³
Development_Positive regulation of STK3/4 (Hippo) pathway and negative regulation of YAP/TAZ function	1.320 x 10 ⁻³
Signal transduction_ERK1/2 signaling pathway	1.328 x 10 ⁻³
Reproduction_Gonadotropin-releasing hormone (GnRH) signaling	1.466 x 10 ⁻³
Development_Epigenetic and transcriptional regulation of oligodendrocyte precursor cell differentiation and myelination	1.586 x 10 ⁻³
Signal transduction_Erk Interactions: Inhibition of Erk	1.586 x 10 ⁻³
Development_SIP1 receptor signaling via beta-arrestin	1.586 x 10 ⁻³
Development_Transcriptional regulation of megakaryopoiesis	1.727 x 10 ⁻³
Role of growth factor receptors transactivation by Hyaluronic acid / CD44 signaling in tumor progression	1.727 x 10 ⁻³
Nociception_Nociceptin receptor signaling	1.791 x 10 ⁻³
HBV signaling via protein kinases leading to HCC	1.875 x 10 ⁻³
Role of red blood cell adhesion to endothelium in vaso-occlusion in Sickle cell disease	2.030 x 10 ⁻³
Development_Beta-adrenergic receptors transactivation of EGFR	2.030 x 10 ⁻³
Immune response_Role of integrins in NK cells cytotoxicity	2.193 x 10 ⁻³
Development_Gastrin in differentiation of the gastric mucosa	2.193 x 10 ⁻³
Translation_Regulation of EIF2 activity	2.364 x 10 ⁻³
Apoptosis and survival_BAD phosphorylation	2.927 x 10 ⁻³
Development_ACM2 and ACM4 activation of ERK	3.131 x 10 ⁻³
Regulation of Tissue factor signaling in cancer	3.131 x 10 ⁻³
K-RAS signaling in pancreatic cancer	3.344 x 10 ⁻³
Development_Activation of Erk by ACM1, ACM3 and ACM5	3.344 x 10 ⁻³
Influence of smoking on activation of EGFR signaling in lung cancer cells	3.344 x 10 ⁻³
Cytoskeleton remodeling_RalB regulation pathway	3.445 x 10 ⁻³
Development_Ligand-independent activation of ESR1 and ESR2	3.565 x 10 ⁻³
Development_G-protein-mediated regulation of MAPK-ERK signaling	3.796 x 10 ⁻³
Signal transduction_PTMs in IL-17-induced CIKS-independent signaling pathways	3.796 x 10 ⁻³
Development_PEDF signaling	4.540 x 10 ⁻³

Pathway maps	<i>P</i> value
Role and regulation of Prostaglandin E2 in gastric cancer	4.540 x 10 ⁻³
Development_EDNRB signaling	4.806 x 10 ⁻³
Immune response_C5a signaling	4.806 x 10 ⁻³
Development_TGF-beta receptor signaling	4.806 x 10 ⁻³
Immune response_IL-13 signaling via PI3K-ERK pathway	4.806 x 10 ⁻³
Development_IGF-1 receptor signaling	5.367 x 10 ⁻³
Immune response_Role of DAP12 receptors in NK cells	6.279 x 10 ⁻³
Aberrant B-Raf signaling in melanoma progression	6.279 x 10 ⁻³
Aberrant production of IL-2 and IL-17 in SLE T cells	7.278 x 10 ⁻³
Oxidative stress_Activation of NADPH oxidase	7.631 x 10 ⁻³
IGF family signaling in colorectal cancer	7.993 x 10 ⁻³
Development_Thyroliberin signaling	7.993 x 10 ⁻³
Glucocorticoid-induced elevation of intraocular pressure as glaucoma risk factor	8.749 x 10 ⁻³
Muscle contraction_Oxytocin signaling in uterus and mammary gland	8.749 x 10 ⁻³
Development_Alpha-2 adrenergic receptor activation of ERK	8.749 x 10 ⁻³
Development_Negative regulation of STK3/4 (Hippo) pathway and positive regulation of YAP/TAZ function	8.749 x 10 ⁻³
Immune response_IL-15 signaling	9.142 x 10 ⁻³
Transport_Macropinocytosis regulation by growth factors	9.142 x 10 ⁻³
Transcription_Sirtuin6 regulation and functions	9.545 x 10 ⁻³
Role of Tissue factor-induced Thrombin signaling in cancerogenesis	1.038 x 10 ⁻²
Development_EGFR signaling via PIP3	1.069 x 10 ⁻²
Development_Growth factors in regulation of oligodendrocyte precursor cell proliferation	1.082 x 10 ⁻²
Ligand-independent activation of Androgen receptor in Prostate Cancer	1.082 x 10 ⁻²
Development_Dopamine D2 receptor transactivation of EGFR	1.161 x 10 ⁻²
Development_GDNF signaling	1.161 x 10 ⁻²
Mucin expression in CF airways	1.172 x 10 ⁻²
Immune response_Gastrin in inflammatory response	1.172 x 10 ⁻²
G-protein signaling_K-RAS regulation pathway	1.257 x 10 ⁻²
Apoptosis and survival_Apoptotic Activin A signaling	1.257 x 10 ⁻²
Transcription_Transcription regulation of aminoacid metabolism	1.257 x 10 ⁻²
Signal transduction_mTORC1 upstream signaling	1.266 x 10 ⁻²
Neurophysiological process_Dopamine D2 receptor transactivation of PDGFR in CNS	1.356 x 10 ⁻²
Cell adhesion_Endothelial cell contacts by junctional mechanisms	1.356 x 10 ⁻²
HCV-dependent regulation of membrane receptors signaling in HCC	1.458 x 10 ⁻²
Platelet activation during ADAM-TS13-deficient thrombotic microangiopathy development	1.563 x 10 ⁻²
Development_Delta-type opioid receptor signaling via G-protein alpha-14	1.563 x 10 ⁻²
Neurophysiological process_NMDA-dependent postsynaptic long-term potentiation in CA1 hippocampal neurons	1.742 x 10 ⁻²
Colorectal cancer (general schema)	1.783 x 10 ⁻²
Cytoskeleton remodeling_RalA regulation pathway	1.783 x 10 ⁻²
NETosis in SLE	1.897 x 10 ⁻²
Development_Transactivation of PDGFR in non-neuronal cells by Dopamine D2 receptor	1.897 x 10 ⁻²
Development_VEGF signaling via VEGFR2 - generic cascades	1.982 x 10 ⁻²
Development_Angiotensin activation of ERK	2.136 x 10 ⁻²
Development_EGFR signaling via small GTPases	2.136 x 10 ⁻²
G-protein signaling_N-RAS regulation pathway	2.136 x 10 ⁻²
Signal transduction_Activin A signaling regulation	2.136 x 10 ⁻²
Development_HGF-dependent inhibition of TGF-beta-induced EMT	2.259 x 10 ⁻²

Pathway maps	<i>P</i> value
Role of Tissue factor in cancer independent of coagulation protease signaling	2.386 x 10 ⁻²
Immune response_Oncostatin M signaling via MAPK in mouse cells	2.386 x 10 ⁻²
Development_TGF-beta-dependent induction of EMT via SMADs	2.386 x 10 ⁻²
Immune response_IL-9 signaling pathway	2.515 x 10 ⁻²
G-protein signaling_G-Protein alpha-12 signaling pathway	2.647 x 10 ⁻²
Immune response_Oncostatin M signaling via MAPK in human cells	2.647 x 10 ⁻²
Transcription_CoREST complex-mediated epigenetic gene silencing	2.647 x 10 ⁻²
G-protein signaling_H-RAS regulation pathway	2.647 x 10 ⁻²
Development_Delta-type opioid receptor mediated cardioprotection	2.647 x 10 ⁻²
Immune response_IL-4 signaling pathway	2.657 x 10 ⁻²
Transcription_Role of AP-1 in regulation of cellular metabolism	2.782 x 10 ⁻²
Cell cycle_Regulation of G1/S transition (part 1)	2.782 x 10 ⁻²
Apoptosis and survival_Anti-apoptotic action of membrane-bound ESR1	2.782 x 10 ⁻²
Development_ERBB-family signaling	2.920 x 10 ⁻²
Transcription_Receptor-mediated HIF regulation	2.920 x 10 ⁻²
Complement pathway disruption in thrombotic microangiopathy	2.920 x 10 ⁻²
Cell adhesion_PLAU signaling	2.920 x 10 ⁻²
G-protein signaling_Rap1A regulation pathway	3.060 x 10 ⁻²
Main growth factor signaling cascades in multiple myeloma cells	3.203 x 10 ⁻²
Neurophysiological process_Netrin-1 in regulation of axon guidance	3.203 x 10 ⁻²
Development_Regulation of lung epithelial progenitor cell differentiation	3.203 x 10 ⁻²
Androstenedione and testosterone biosynthesis and metabolism p.3	3.203 x 10 ⁻²
Breast cancer (general schema)	3.203 x 10 ⁻²
Immune response_IL-3 signaling via ERK and PI3K	3.275 x 10 ⁻²
Cytoskeleton remodeling_Cytoskeleton remodeling	3.275 x 10 ⁻²
Translation_Insulin regulation of translation	3.348 x 10 ⁻²
Development_Angiotensin signaling via PYK2	3.496 x 10 ⁻²
Immune response_Substance P-stimulated expression of proinflammatory cytokines via MAPKs	3.496 x 10 ⁻²
Apoptosis and survival_TNF-alpha-induced Caspase-8 signaling	3.496 x 10 ⁻²
Development_Adenosine A2A receptor signaling	3.496 x 10 ⁻²
Development_VEGF signaling and activation	3.496 x 10 ⁻²
Development_Flt3 signaling	3.647 x 10 ⁻²
Androstenedione and testosterone biosynthesis and metabolism p.3/ Rodent version	3.647 x 10 ⁻²
Role of alpha-6/beta-4 integrins in carcinoma progression	3.800 x 10 ⁻²
Development_EPO-induced MAPK pathway	3.800 x 10 ⁻²
Transcription_Androgen Receptor nuclear signaling	3.800 x 10 ⁻²
Development_Thrombopoietin-regulated cell processes	3.800 x 10 ⁻²
Development_Activation of ERK by Alpha-1 adrenergic receptors	3.800 x 10 ⁻²
High shear stress-induced platelet activation	3.955 x 10 ⁻²
Immune response_MIF-induced cell adhesion, migration and angiogenesis	3.955 x 10 ⁻²
Development_GDNF family signaling	3.955 x 10 ⁻²
Development_Endothelin-1/EDNRA transactivation of EGFR	3.955 x 10 ⁻²
Immune response_MIF - the neuroendocrine-macrophage connector	3.955 x 10 ⁻²
Regulation of GSK3 beta in bipolar disorder	3.955 x 10 ⁻²
Signal transduction_PTEN pathway	3.955 x 10 ⁻²
FGF signaling in pancreatic cancer	3.955 x 10 ⁻²
Androgen receptor activation and downstream signaling in Prostate cancer	3.955 x 10 ⁻²

Pathway maps	<i>P</i> value
Cytoskeleton remodeling_TGF, WNT and cytoskeletal remodeling	4.052 x 10 ⁻²
8Neurophysiological process_Circadian rhythm	4.113 x 10 ⁻²
Development_Leptin signaling via PI3K-dependent pathway	4.113 x 10 ⁻²
Immune response_PGE2 common pathways	4.113 x 10 ⁻²
Regulation of lipid metabolism_Insulin signaling: generic cascades	4.113 x 10 ⁻²
Development_PDGF signaling via MAPK cascades	4.113 x 10 ⁻²
Stimulation of TGF-beta signaling in lung cancer	4.273 x 10 ⁻²
Muscle contraction_Relaxin signaling pathway	4.273 x 10 ⁻²
Immune response_TLR5, TLR7, TLR8 and TLR9 signaling pathways	4.273 x 10 ⁻²
Oxidative stress_Role of IL-8 signaling pathway in respiratory burst	4.273 x 10 ⁻²
Transcription_CREB signaling pathway	4.436 x 10 ⁻²
Immune response_IL-2 activation and signaling pathway	4.436 x 10 ⁻²
Development_Adenosine A3 receptor signaling	4.436 x 10 ⁻²
Signal transduction_IP3 signaling	4.436 x 10 ⁻²
Cytoskeleton remodeling_Integrin outside-in signaling	4.436 x 10 ⁻²
Tissue Factor signaling in cancer via PAR1 and PAR2	4.436 x 10 ⁻²
Apoptosis and survival_HTR1A signaling	4.601 x 10 ⁻²
Development_Adenosine A2B receptor signaling	4.601 x 10 ⁻²
Signal transduction_PKA signaling	4.768 x 10 ⁻²
Cortisone biosynthesis and metabolism	4.768 x 10 ⁻²
Signal transduction_PTMs in BAFF-induced signaling	4.768 x 10 ⁻²
Development_Insulin, IGF-1 and TNF-alpha in brown adipocyte differentiation	4.937 x 10 ⁻²
Signal transduction_Activation of PKC via G-Protein coupled receptor	4.937 x 10 ⁻²
G-protein signaling_Proinsulin C-peptide signaling	4.937 x 10 ⁻²
Development_FGF-family signaling	4.937 x 10 ⁻²
Immune response_Antiviral actions of Interferons	4.937 x 10 ⁻²