Supplemental Dataset 1 Pathway analysis of differential gene expression in CK

Summary of WikiPathways data-base analysis for CK uNK versus CK pNK. Frequency of significant differentially-expressed genes (p-value <0.05, Z-Score >1.96), based on Z score.

Criterion: ([LogFC CK uNK vs CK pNK] < -0.26 OR [LogFC CK uNK vs CK pNK] > 0.26) AND [P-value [LogFC CK uNK vs CK pNK] < 0.05

Pathway	positive	measured	total	%	Z Score	p-value
HIF1A and PPARG regulation of glycolysis	6	6	19	100.00%	3.64	0
TGF-beta Signaling Pathway	51	111	133	45.95%	3.38	0.003
Cori Cycle	8	10	53	80.00%	3.33	0
Gastric Cancer Network 1	14	22	30	63.64%	3.29	0.001
Retinoblastoma Gene in Cancer	38	80	98	47.50%	3.16	0.001
Extracellular vesicle-mediated signaling in recipient cells	12	19	31	63.16%	3.01	0
Regulation of sister chromatid separation at metaphase-anaphase transition	10	15	16	66.67%	2.96	0.004
Calcium Regulation in the Cardiac Cell	31	65	164	47.69%	2.88	0.003
Primary Focal Segmental Glomerulosclerosis FSGS	20	38	78	52.63%	2.86	0.003
Fluoropyrimidine Activity	13	22	58	59.09%	2.82	0.001
Integrin-mediated Cell Adhesion	30	64	102	46.88%	2.72	0.004
Focal Adhesion	46	108	201	42.59%	2.57	0.014
Chemokine signaling pathway	42	99	172	42.42%	2.42	0.024
Ebola Virus Pathway on Host	39	91	141	42.86%	2.41	0.018
B Cell Receptor Signaling Pathway	36	83	99	43.37%	2.4	0.009
Nanoparticle-mediated activation of receptor signaling	12	22	36	54.55%	2.36	0.016
Lamin A-processing pathway	4	5	8	80.00%	2.35	0.015
Signal Transduction of S1P Receptor	11	20	26	55.00%	2.3	0.022
MFAP5-mediated ovarian cancer cell motility and invasiveness	6	9	18	66.67%	2.29	0.026
Microglia Pathogen Phagocytosis Pathway	15	30	44	50.00%	2.22	0.027
Histone Modifications	27	61	68	44.26%	2.21	0.024
Association Between Physico-Chemical Features and Toxicity Associated Pathways	22	48	78	45.83%	2.19	0.026
Human Thyroid Stimulating Hormone (TSH) signaling pathway	24	54	67	44.44%	2.1	0.032
Mesodermal Commitment Pathway	35	84	154	41.67%	2.08	0.024
Apoptosis-related network due to altered Notch3 in ovarian cancer	20	44	54	45.45%	2.04	0.047
Regulation of Wnt/B-catenin Signaling by Small Molecule Compounds	7	12	33	58.33%	2.03	0.036
T-Cell antigen Receptor (TCR) Signaling Pathway	32	77	93	41.56%	1.97	0.047

Purine metabolism	6	10	75	60.00%	1.96	0.044
G Protein Signaling Pathways	25	58	97	43.10%	1.96	0.047
EDA Signalling in Hair Follicle Development	3	4	16	75.00%	1.89	0.045
miRNA targets in ECM and membrane receptors	3	4	46	75.00%	1.89	0.055
TCA Cycle Nutrient Utilization and Invasiveness of Ovarian Cancer	3	4	11	75.00%	1.89	0.04
Non-genomic actions of 1,25 dihydroxyvitamin D3	21	48	97	43.75%	1.88	0.062
ErbB Signaling Pathway	28	67	101	41.79%	1.88	0.063
Development and heterogeneity of the ILC family	8	15	33	53.33%	1.85	0.063
Hypothesized Pathways in Pathogenesis of Cardiovascular Disease	8	15	27	53.33%	1.85	0.045
Vitamin D Receptor Pathway	30	73	188	41.10%	1.83	0.07
Glycolysis and Gluconeogenesis	14	30	69	46.67%	1.83	0.067
Pancreatic adenocarcinoma pathway	31	76	97	40.79%	1.81	0.061
T-Cell antigen Receptor (TCR) pathway during Staphylococcus aureus infection	21	49	70	42.86%	1.76	0.08
Phosphodiesterases in neuronal function	9	18	66	50.00%	1.72	0.088
Genotoxicity pathway	23	55	65	41.82%	1.7	0.077
Regulation of Actin Cytoskeleton	34	86	159	39.53%	1.67	0.105
MAPK and NFkB Signalling Pathways Inhibited by Yersinia YopJ	6	11	13	54.55%	1.67	0.073
Inhibition of exosome biogenesis and secretion by Manumycin A in CRPC cells	8	16	19	50.00%	1.62	0.11
Non-small cell lung cancer	22	53	76	41.51%	1.62	0.12
Myometrial Relaxation and Contraction Pathways	33	84	161	39.29%	1.6	0.102
Signaling Pathways in Glioblastoma	28	70	88	40.00%	1.59	0.111
Epithelial to mesenchymal transition in colorectal cancer	29	73	161	39.73%	1.58	0.107
Disorders of Folate Metabolism and Transport	5	9	46	55.56%	1.58	0.108
Ethanol metabolism resulting in production of ROS by CYP2E1	5	9	28	55.56%	1.58	0.111
GPR40 Pathway	5	9	20	55.56%	1.58	0.114
Adipogenesis	30	76	132	39.47%	1.56	0.118
Factors and pathways affecting insulin-like growth factor (IGF1)-Akt signaling	11	24	34	45.83%	1.55	0.131
MAPK Cascade	11	24	33	45.83%	1.55	0.133
IL-3 Signaling Pathway	17	40	50	42.50%	1.54	0.133
Nucleotide Metabolism	9	19	37	47.37%	1.52	0.123
Hypertrophy Model	7	14	21	50.00%	1.52	0.127
TGF-beta Receptor Signaling	15	35	56	42.86%	1.49	0.154
Arrhythmogenic Right Ventricular Cardiomyopathy	12	27	81	44.44%	1.48	0.13

Thyroxine (Thyroid Hormone) Production	1	1	12	100.00%	1.48	0.123
Tyrosine Metabolism	1	1	23	100.00%	1.48	0.137
Bone Morphogenic Protein (BMP) Signalling and Regulation	4	7	13	57.14%	1.48	0.13
NOTCH1 regulation of human endothelial cell calcification	4	7	18	57.14%	1.48	0.155
Heart Development	8	17	48	47.06%	1.41	0.16
ID signaling pathway	6	12	17	50.00%	1.4	0.197
Striated Muscle Contraction Pathway	6	12	39	50.00%	1.4	0.162
miR-517 relationship with ARCN1 and USP1	3	5	7	60.00%	1.39	0.109
Serotonin and anxiety-related events	3	5	16	60.00%	1.39	0.168
Focal Adhesion-PI3K-Akt-mTOR-signaling pathway	55	152	305	36.18%	1.33	0.185
Common Pathways Underlying Drug Addiction	9	20	50	45.00%	1.33	0.186
Rett syndrome causing genes	12	28	60	42.86%	1.33	0.2
EV release from cardiac cells and their functional effects	2	3	17	66.67%	1.32	0.221
Farnesoid X Receptor Pathway	2	3	21	66.67%	1.32	0.173
Osteoblast Signaling	2	3	18	66.67%	1.32	0.175
Oxytocin signaling	2	3	10	66.67%	1.32	0.22
Synthesis and Degradation of Ketone Bodies	2	3	13	66.67%	1.32	0.224
Vitamins A and D - action mechanisms	2	3	14	66.67%	1.32	0.239
RalA downstream regulated genes	5	10	13	50.00%	1.28	0.232
Transcriptional cascade regulating adipogenesis	5	10	14	50.00%	1.28	0.222
DNA Damage Response (only ATM dependent)	33	88	118	37.50%	1.28	0.201
T-Cell Receptor and Co-stimulatory Signaling	10	23	45	43.48%	1.27	0.187
Type 2 papillary renal cell carcinoma	10	23	41	43.48%	1.27	0.192
Sudden Infant Death Syndrome (SIDS) Susceptibility Pathways	28	74	182	37.84%	1.23	0.204
BDNF-TrkB Signaling	11	26	38	42.31%	1.22	0.213
Fatty Acid Biosynthesis	8	18	37	44.44%	1.21	0.223
Physiological and Pathological Hypertrophy of the Heart	8	18	27	44.44%	1.21	0.24
Hair Follicle Development: Cytodifferentiation (Part 3 of 3)	12	29	92	41.38%	1.18	0.189
Signaling of Hepatocyte Growth Factor Receptor	12	29	35	41.38%	1.18	0.265
TYROBP Causal Network	17	43	61	39.53%	1.18	0.252
Cell Cycle	38	104	124	36.54%	1.18	0.257
Canonical and Non-Canonical TGF-B signaling	6	13	18	46.15%	1.16	0.204
Melatonin metabolism and effects	9	21	64	42.86%	1.15	0.247

Sphingolipid pathway	9	21	64	42.86%	1.15	0.249
Osteoclast Signaling	4	8	21	50.00%	1.15	0.235
Serotonin and anxiety	4	8	22	50.00%	1.15	0.226
Pathways Affected in Adenoid Cystic Carcinoma	20	52	72	38.46%	1.13	0.251
Alzheimers Disease	21	55	166	38.18%	1.12	0.284
Metabolic reprogramming in colon cancer	15	38	81	39.47%	1.1	0.307
EGF/EGFR Signaling Pathway	49	138	163	35.51%	1.1	0.287
Canonical and Non-canonical Notch signaling	7	16	31	43.75%	1.08	0.294
Wnt Signaling Pathway	16	41	52	39.02%	1.08	0.318
Endochondral Ossification	11	27	69	40.74%	1.07	0.307
Endoderm Differentiation	33	91	147	36.26%	1.04	0.286
Bladder Cancer	12	30	47	40.00%	1.04	0.278
Prostaglandin Synthesis and Regulation	8	19	61	42.11%	1.02	0.274
Vitamin D in inflammatory diseases	8	19	25	42.11%	1.02	0.304
Osteopontin Signaling	5	11	14	45.45%	1.02	0.269
TGF-B Signaling in Thyroid Cells for Epithelial-Mesenchymal Transition	5	11	20	45.45%	1.02	0.283
Pathways in clear cell renal cell carcinoma	22	59	92	37.29%	1.01	0.308
Caloric restriction and aging	3	6	13	50.00%	0.99	0.297
Mammary gland development pathway - Embryonic development (Stage 1 of 4)	3	6	21	50.00%	0.99	0.299
Nicotine Activity on Dopaminergic Neurons	3	6	31	50.00%	0.99	0.308
Alpha 6 Beta 4 signaling pathway	9	22	34	40.91%	0.98	0.329
The effect of progerin on the involved genes in Hutchinson-Gilford Progeria Syndrome	10	25	29	40.00%	0.95	0.352
miRNAs involved in DNA damage response	6	14	70	42.86%	0.94	0.326
Serotonin Receptor 2 and ELK-SRF/GATA4 signaling	6	14	24	42.86%	0.94	0.359
ESC Pluripotency Pathways	19	51	123	37.25%	0.93	0.336
IL-4 Signaling Pathway	19	51	56	37.25%	0.93	0.356
G1 to S cell cycle control	20	54	66	37.04%	0.92	0.348
Corticotropin-releasing hormone signaling pathway	22	60	98	36.67%	0.91	0.347
Chromosomal and microsatellite instability in colorectal cancer	23	63	81	36.51%	0.91	0.346
Prolactin Signaling Pathway	25	69	79	36.23%	0.9	0.355
G13 Signaling Pathway	12	31	39	38.71%	0.9	0.37
Brain-Derived Neurotrophic Factor (BDNF) signaling pathway	36	102	150	35.29%	0.89	0.384
GPCRs, Other	7	17	118	41.18%	0.89	0.379

GPCRs, Class A Rhodopsin-like	14	37	272	37.84%	0.87	0.426
Vitamin A and Carotenoid Metabolism	4	9	65	44.44%	0.86	0.383
One Carbon Metabolism	8	20	57	40.00%	0.85	0.384
Tryptophan metabolism	8	20	133	40.00%	0.85	0.418
Endometrial cancer	18	49	75	36.73%	0.83	0.426
Kit receptor signaling pathway	18	49	60	36.73%	0.83	0.405
RAC1/PAK1/p38/MMP2 Pathway	18	49	74	36.73%	0.83	0.407
AMP-activated Protein Kinase (AMPK) Signaling	19	52	78	36.54%	0.83	0.382
DNA IR-damage and cellular response via ATR	25	70	90	35.71%	0.81	0.407
Cell-type Dependent Selectivity of CCK2R Signaling	2	4	26	50.00%	0.81	0.415
miR-222 in Exercise-Induced Cardiac Growth	2	4	5	50.00%	0.81	0.422
Phase I biotransformations, non P450	2	4	13	50.00%	0.81	0.409
Vitamin D Metabolism	2	4	21	50.00%	0.81	0.407
Angiogenesis	5	12	25	41.67%	0.78	0.403
Neovascularisation processes	5	12	25	41.67%	0.78	0.413
Initiation of transcription and translation elongation at the HIV-1 LTR	11	29	35	37.93%	0.78	0.447
PDGF Pathway	13	35	52	37.14%	0.76	0.447
Endothelin Pathways	6	15	48	40.00%	0.73	0.476
TP53 Network	6	15	23	40.00%	0.73	0.476
Nuclear Receptors	7	18	44	38.89%	0.7	0.471
The human immune response to tuberculosis	7	18	24	38.89%	0.7	0.512
miRs in Muscle Cell Differentiation	8	21	42	38.10%	0.68	0.511
Cell Differentiation - Index	3	7	56	42.86%	0.66	0.525
Differentiation of white and brown adipocyte	3	7	26	42.86%	0.66	0.52
Ganglio Sphingolipid Metabolism	3	7	39	42.86%	0.66	0.527
Hedgehog Signaling Pathway	3	7	17	42.86%	0.66	0.512
Valproic acid pathway	3	7	36	42.86%	0.66	0.503
Nucleotide-binding Oligomerization Domain (NOD) pathway	11	30	43	36.67%	0.64	0.554
Hepatitis C and Hepatocellular Carcinoma	13	36	63	36.11%	0.63	0.552
Exercise-induced Circadian Regulation	14	39	49	35.90%	0.63	0.525
Cardiac Progenitor Differentiation	4	10	56	40.00%	0.6	0.55
Eicosanoid Synthesis	4	10	57	40.00%	0.6	0.548
Aflatoxin B1 metabolism	1	2	16	50.00%	0.57	0.566

Blood Clotting Cascade	1	2	27	50.00%	0.57	0.588
Hypothetical Craniofacial Development Pathway	1	2	11	50.00%	0.57	0.562
Hypoxia-mediated EMT and Stemness	1	2	6	50.00%	0.57	0.612
miR-509-3p alteration of YAP1/ECM axis	1	2	19	50.00%	0.57	0.607
Ultraconserved region 339 modulation of tumor suppressor microRNAs in cancer	1	2	6	50.00%	0.57	0.618
TNF alpha Signaling Pathway	28	82	97	34.15%	0.57	0.571
Circadian rhythm related genes	41	122	210	33.61%	0.57	0.565
Simplified Interaction Map Between LOXL4 and Oxidative Stress Pathway	5	13	19	38.46%	0.56	0.591
Transcription factor regulation in adipogenesis	5	13	24	38.46%	0.56	0.595
Type II diabetes mellitus	5	13	28	38.46%	0.56	0.59
Wnt Signaling	22	64	121	34.38%	0.54	0.58
4-hydroxytamoxifen, Dexamethasone, and Retinoic Acids Regulation of p27 Expression	6	16	31	37.50%	0.54	0.602
Imatinib and Chronic Myeloid Leukemia	6	16	25	37.50%	0.54	0.62
Interactome of polycomb repressive complex 2 (PRC2)	6	16	17	37.50%	0.54	0.624
MicroRNAs in cardiomyocyte hypertrophy	20	58	109	34.48%	0.54	0.59
Ethanol effects on histone modifications	7	19	53	36.84%	0.53	0.579
Synaptic Vesicle Pathway	7	19	59	36.84%	0.53	0.603
Trans-sulfuration and one carbon metabolism	9	25	66	36.00%	0.51	0.59
Regulation of Microtubule Cytoskeleton	13	37	47	35.14%	0.51	0.655
PI3K-AKT-mTOR signaling pathway and therapeutic opportunities	10	28	33	35.71%	0.51	0.635
Ras Signaling	38	114	192	33.33%	0.49	0.604
GPCRs, Class B Secretin-like	2	5	24	40.00%	0.42	0.63
Liver X Receptor Pathway	2	5	12	40.00%	0.42	0.655
LncRNA-mediated mechanisms of therapeutic resistance	2	5	14	40.00%	0.42	0.667
Macrophage markers	2	5	10	40.00%	0.42	0.668
Role of Osx and miRNAs in tooth development	2	5	39	40.00%	0.42	0.67
RANKL/RANK (Receptor activator of NFKB (ligand)) Signaling Pathway	16	47	58	34.04%	0.42	0.673
Cardiac Hypertrophic Response	14	41	61	34.15%	0.4	0.642
IL-5 Signaling Pathway	12	35	41	34.29%	0.39	0.674
Neural Crest Differentiation	12	35	102	34.29%	0.39	0.697
Target Of Rapamycin (TOR) Signaling	11	32	40	34.38%	0.38	0.666
BMP Signaling Pathway in Eyelid Development	3	8	23	37.50%	0.38	0.697
DNA Mismatch Repair	3	8	10	37.50%	0.38	0.744

Globo Sphingolipid Metabolism	3	8	29	37.50%	0.38	0.664
Cell Differentiation - Index expanded	4	11	69	36.36%	0.37	0.738
H19 action Rb-E2F1 signaling and CDK-Beta-catenin activity	4	11	17	36.36%	0.37	0.784
Cannabinoid receptor signaling	6	17	54	35.29%	0.36	0.712
Pyrimidine metabolism	24	73	140	32.88%	0.3	0.745
Resistin as a regulator of inflammation	8	24	34	33.33%	0.22	0.8
Follicle Stimulating Hormone (FSH) signaling pathway	7	21	28	33.33%	0.21	0.846
IL17 signaling pathway	7	21	32	33.33%	0.21	0.823
Splicing factor NOVA regulated synaptic proteins	7	21	44	33.33%	0.21	0.813
Leptin signaling pathway	21	65	77	32.31%	0.19	0.855
IL-9 Signaling Pathway	5	15	18	33.33%	0.18	0.806
Ovarian Infertility Genes	5	15	33	33.33%	0.18	0.825
Wnt Signaling in Kidney Disease	5	15	39	33.33%	0.18	0.846
VEGFA-VEGFR2 Signaling Pathway	56	176	238	31.82%	0.17	0.879
Pathogenic Escherichia coli infection	12	37	79	32.43%	0.16	0.875
Amplification and Expansion of Oncogenic Pathways as Metastatic Traits	4	12	18	33.33%	0.16	0.849
Development of pulmonary dendritic cells and macrophage subsets	4	12	14	33.33%	0.16	0.825
Androgen receptor signaling pathway	25	78	90	32.05%	0.16	0.882
Extracellular vesicles in the crosstalk of cardiac cells	3	9	30	33.33%	0.14	0.903
NAD metabolism, sirtuins and aging	3	9	16	33.33%	0.14	0.884
SRF and miRs in Smooth Muscle Differentiation and Proliferation	3	9	18	33.33%	0.14	0.886
PI3K-Akt Signaling Pathway	51	161	359	31.68%	0.12	0.879
Alanine and aspartate metabolism	2	6	66	33.33%	0.11	0.902
Cytokines and Inflammatory Response	2	6	32	33.33%	0.11	0.922
Degradation pathway of sphingolipids, including diseases	2	6	38	33.33%	0.11	0.938
exRNA mechanism of action and biogenesis	2	6	8	33.33%	0.11	0.848
Glucuronidation	2	6	41	33.33%	0.11	0.925
Insulin signalling in human adipocytes (diabetic condition)	2	6	12	33.33%	0.11	0.873
Insulin signalling in human adipocytes (normal condition)	2	6	16	33.33%	0.11	0.902
Methionine metabolism leading to Sulphur Amino Acids and related disorders	2	6	41	33.33%	0.11	0.911
miRNA Biogenesis	2	6	7	33.33%	0.11	0.828
Pyrimidine metabolism and related diseases	2	6	51	33.33%	0.11	0.919
Somatroph axis (GH) and its relationship to dietary restriction and aging	2	6	12	33.33%	0.11	0.889

Type III interferon signaling	2	6	11	33.33%	0.11	0.881
Breast cancer pathway	27	85	167	31.76%	0.11	0.92
Fatty Acid Beta Oxidation	9	28	71	32.14%	0.1	0.909
Arachidonate Epoxygenase / Epoxide Hydrolase	1	3	18	33.33%	0.08	0.987
FTO Obesity Variant Mechanism	1	3	11	33.33%	0.08	0.913
Hfe effect on hepcidin production	1	3	8	33.33%	0.08	0.856
Irinotecan Pathway	1	3	18	33.33%	0.08	0.992
let-7 inhibition of ES cell reprogramming	1	3	17	33.33%	0.08	0.986
Monoamine GPCRs	1	3	43	33.33%	0.08	0.925
Nucleotide GPCRs	1	3	15	33.33%	0.08	0.974
Serotonin Receptor 2 and STAT3 Signaling	1	3	6	33.33%	0.08	0.856
Tgif disruption of Shh signaling	1	3	10	33.33%	0.08	0.905
Vitamin B6-dependent and responsive disorders	1	3	28	33.33%	0.08	0.955
EPO Receptor Signaling	7	22	27	31.82%	0.06	0.974
Hematopoietic Stem Cell Gene Regulation by GABP alpha/beta Complex	6	19	26	31.58%	0.03	0.995
IL-1 signaling pathway	16	51	57	31.37%	0.02	0.994
DNA IR-Double Strand Breaks (DSBs) and cellular response via ATM	15	48	65	31.25%	0	0.993
Notch Signaling Pathway	14	45	62	31.11%	-0.02	0.993
PPAR signaling pathway	9	29	76	31.03%	-0.02	0.964
Prader-Willi and Angelman Syndrome	9	29	90	31.03%	-0.02	0.986
Prion disease pathway	9	29	36	31.03%	-0.02	0.981
IL-2 Signaling Pathway	12	39	43	30.77%	-0.06	0.938
IL-7 Signaling Pathway	7	23	26	30.43%	-0.08	0.965
Tumor suppressor activity of SMARCB1	7	23	35	30.43%	-0.08	0.938
Cysteine and methionine catabolism	3	10	55	30.00%	-0.08	0.894
Glutathione metabolism	3	10	57	30.00%	-0.08	0.92
Nanoparticle triggered regulated necrosis	3	10	25	30.00%	-0.08	0.931
ncRNAs involved in STAT3 signaling in hepatocellular carcinoma	3	10	19	30.00%	-0.08	0.955
Overview of nanoparticle effects	3	10	41	30.00%	-0.08	0.926
Peptide GPCRs	3	10	79	30.00%	-0.08	0.938
Urea cycle and metabolism of amino groups	3	10	71	30.00%	-0.08	0.915
Wnt Signaling Pathway and Pluripotency	19	62	106	30.65%	-0.1	0.909
EBV LMP1 signaling	6	20	25	30.00%	-0.12	0.915

Disorders of the Krebs cycle	2	7	35	28.57%	-0.15	0.926
Matrix Metalloproteinases	2	7	31	28.57%	-0.15	0.906
Supression of HMGB1 mediated inflammation by THBD	2	7	10	28.57%	-0.15	0.859
Integrated Cancer Pathway	12	40	50	30.00%	-0.17	0.852
Interleukin-11 Signaling Pathway	11	37	45	29.73%	-0.2	0.853
MECP2 and Associated Rett Syndrome	11	37	101	29.73%	-0.2	0.828
TNF related weak inducer of apoptosis (TWEAK) Signaling Pathway	11	37	45	29.73%	-0.2	0.841
Gastric Cancer Network 2	7	24	33	29.17%	-0.22	0.799
One carbon metabolism and related pathways	9	31	94	29.03%	-0.27	0.791
Acetylcholine Synthesis	1	4	18	25.00%	-0.27	0.781
BMP2-WNT4-FOXO1 Pathway in Human Primary Endometrial Stromal Cell Differentiation	1	4	16	25.00%	-0.27	0.79
Drug Induction of Bile Acid Pathway	1	4	45	25.00%	-0.27	0.773
Methylation Pathways	1	4	15	25.00%	-0.27	0.782
MicroRNA for Targeting Cancer Growth and Vascularization in Glioblastoma	1	4	10	25.00%	-0.27	0.736
Molybdenum cofactor (Moco) biosynthesis	1	4	20	25.00%	-0.27	0.776
Oligodendrocyte Specification and differentiation(including remyelination), leading to Myelin C	1	4	46	25.00%	-0.27	0.788
PTF1A related regulatory pathway	1	4	12	25.00%	-0.27	0.783
Energy Metabolism	12	41	49	29.27%	-0.27	0.763
Thymic Stromal LymphoPoietin (TSLP) Signaling Pathway	12	41	49	29.27%	-0.27	0.764
Differentiation Pathway	3	11	64	27.27%	-0.28	0.76
Monoamine Transport	3	11	47	27.27%	-0.28	0.796
miRNA Regulation of DNA Damage Response	18	61	106	29.51%	-0.29	0.797
NRF2 pathway	18	61	145	29.51%	-0.29	0.768
DNA Damage Response	17	58	76	29.31%	-0.32	0.734
Aryl Hydrocarbon Receptor	10	35	57	28.57%	-0.34	0.761
Ectoderm Differentiation	22	75	145	29.33%	-0.36	0.688
ERK Pathway in Huntington's Disease	2	8	16	25.00%	-0.38	0.713
Iron metabolism in placenta	2	8	15	25.00%	-0.38	0.75
NLR Proteins	2	8	11	25.00%	-0.38	0.723
Small Ligand GPCRs	2	8	25	25.00%	-0.38	0.688
Notch Signaling	9	32	48	28.13%	-0.38	0.668
Methionine De Novo and Salvage Pathway	4	15	74	26.67%	-0.38	0.709
TCA Cycle and Deficiency of Pyruvate Dehydrogenase complex (PDHc)	4	15	37	26.67%	-0.38	0.686

Lung fibrosis	6	22	85	27.27%	-0.4	0.675
White fat cell differentiation	6	22	35	27.27%	-0.4	0.68
Metapathway biotransformation Phase I and II	14	49	191	28.57%	-0.4	0.694
Triacylglyceride Synthesis	3	12	37	25.00%	-0.47	0.63
Type II interferon signaling (IFNG)	7	26	38	26.92%	-0.48	0.633
Glycogen Synthesis and Degradation	9	33	54	27.27%	-0.49	0.66
Interferon type I signaling pathways	14	50	57	28.00%	-0.5	0.632
Mammary gland development pathway - Pregnancy and lactation (Stage 3 of 4)	4	16	42	25.00%	-0.54	0.598
MTHFR deficiency	4	16	54	25.00%	-0.54	0.569
Serotonin Receptor 4/6/7 and NR3C Signaling	4	16	22	25.00%	-0.54	0.611
Wnt/beta-catenin Signaling Pathway in Leukemia	4	16	29	25.00%	-0.54	0.635
Benzo(a)pyrene metabolism	1	5	17	20.00%	-0.54	0.628
Genes targeted by miRNAs in adipocytes	1	5	19	20.00%	-0.54	0.587
Metabolism of Spingolipids in ER and Golgi apparatus	1	5	69	20.00%	-0.54	0.564
mir-124 predicted interactions with cell cycle and differentiation	1	5	8	20.00%	-0.54	0.641
Oncostatin M Signaling Pathway	15	54	66	27.78%	-0.55	0.581
Angiopoietin Like Protein 8 Regulatory Pathway	29	101	156	28.71%	-0.55	0.574
Structural Pathway of Interleukin 1 (IL-1)	12	44	52	27.27%	-0.57	0.546
Mammary gland development pathway - Puberty (Stage 2 of 4)	2	9	15	22.22%	-0.58	0.554
Trans-sulfuration pathway	2	9	25	22.22%	-0.58	0.548
Insulin Signaling	39	135	162	28.89%	-0.6	0.536
Oxidative Damage	7	27	44	25.93%	-0.6	0.575
MAPK Signaling Pathway	45	155	259	29.03%	-0.6	0.571
Phytochemical activity on NRF2 transcriptional activation	3	13	20	23.08%	-0.64	0.539
PI3K/AKT/mTOR - VitD3 Signalling	3	13	34	23.08%	-0.64	0.532
IL-6 signaling pathway	10	38	45	26.32%	-0.66	0.526
Aryl Hydrocarbon Receptor Pathway	6	24	49	25.00%	-0.66	0.53
Arylamine metabolism	0	1	13	0.00%	-0.67	0.519
Biogenic Amine Synthesis	0	1	33	0.00%	-0.67	0.482
Composition of Lipid Particles	0	1	21	0.00%	-0.67	0.52
Evolocumab Mechanism	0	1	5	0.00%	-0.67	0.476
Fatty Acid Omega Oxidation	0	1	20	0.00%	-0.67	0.493
Heroin metabolism	0	1	8	0.00%	-0.67	0.513

Hormonal control of Pubertal Growth Spurt	0	1	8	0.00%	-0.67	0.492
Influenza A virus infection	0	1	16	0.00%	-0.67	0.506
mir34a and TGIF2 in osteoclastogenesis	0	1	5	0.00%	-0.67	0.457
Model for regulation of MSMP expression in cancer cells and its proangiogenic role in ovariar	0	1	6	0.00%	-0.67	0.493
Proprotein convertase subtilisin/kexin type 9 (PCSK9) mediated LDL receptor degradation	0	1	3	0.00%	-0.67	0.336
SCFA and skeletal muscle substrate metabolism	0	1	17	0.00%	-0.67	0.508
Mitochondrial Gene Expression	4	17	23	23.53%	-0.69	0.488
NAD+ biosynthetic pathways	4	17	37	23.53%	-0.69	0.516
miRNA regulation of p53 pathway in prostate cancer	5	21	37	23.81%	-0.74	0.448
NRF2-ARE regulation	5	21	24	23.81%	-0.74	0.51
ATM Signaling Network in Development and Disease	10	39	49	25.64%	-0.76	0.431
Statin Pathway	2	10	50	20.00%	-0.77	0.463
DDX1 as a regulatory component of the Drosha microprocessor	1	6	8	16.67%	-0.77	0.479
Dual hijack model of Vif in HIV infection	1	6	10	16.67%	-0.77	0.457
Role Altered Glycolysation of MUC1 in Tumour Microenvironment	1	6	10	16.67%	-0.77	0.461
Photodynamic therapy-induced HIF-1 survival signaling	6	25	38	24.00%	-0.78	0.423
Inflammatory Response Pathway	3	14	34	21.43%	-0.79	0.426
Oxidation by Cytochrome P450	3	14	75	21.43%	-0.79	0.444
ncRNAs involved in Wnt signaling in hepatocellular carcinoma	11	43	89	25.58%	-0.8	0.427
TCA Cycle (aka Krebs or citric acid cycle)	4	18	49	22.22%	-0.83	0.411
Fibrin Complement Receptor 3 Signaling Pathway	5	22	44	22.73%	-0.86	0.347
ATM Signaling Pathway	8	33	50	24.24%	-0.87	0.338
Photodynamic therapy-induced unfolded protein response	6	26	28	23.08%	-0.9	0.396
Nuclear Receptors Meta-Pathway	42	151	339	27.81%	-0.92	0.34
Complement and Coagulation Cascades	2	11	63	18.18%	-0.94	0.358
Homologous recombination	2	11	14	18.18%	-0.94	0.402
NAD+ metabolism	2	11	34	18.18%	-0.94	0.372
Mitochondrial LC-Fatty Acid Beta-Oxidation	3	15	24	20.00%	-0.94	0.35
SREBF and miR33 in cholesterol and lipid homeostasis	3	15	19	20.00%	-0.94	0.364
Integrated Breast Cancer Pathway	38	138	201	27.54%	-0.95	0.358
ACE Inhibitor Pathway	0	2	29	0.00%	-0.95	0.347
Benzene metabolism	0	2	17	0.00%	-0.95	0.372
Butyrate-induced histone acetylation	0	2	11	0.00%	-0.95	0.367

Codeine and Morphine Metabolism	0	2	26	0.00%	-0.95	0.346
Complement Activation	0	2	24	0.00%	-0.95	0.362
Mevalonate arm of cholesterol biosynthesis pathway with inhibitors	0	2	60	0.00%	-0.95	0.349
Polyol Pathway	0	2	17	0.00%	-0.95	0.405
Sulindac Metabolic Pathway	0	2	11	0.00%	-0.95	0.368
Tamoxifen metabolism	0	2	36	0.00%	-0.95	0.357
Non-homologous end joining	1	7	9	14.29%	-0.97	0.336
Thiamine metabolic pathways	1	7	34	14.29%	-0.97	0.322
Amino Acid metabolism	15	59	205	25.42%	-0.97	0.323
Senescence and Autophagy in Cancer	21	80	112	26.25%	-0.97	0.307
Hedgehog Signaling Pathway	5	23	44	21.74%	-0.99	0.326
Toll-like Receptor Signaling	5	23	32	21.74%	-0.99	0.318
Thermogenesis	19	74	140	25.68%	-1.04	0.291
AGE/RAGE pathway	13	53	67	24.53%	-1.06	0.292
Lipid Metabolism Pathway	4	20	43	20.00%	-1.09	0.265
Nanoparticle triggered autophagic cell death	4	20	30	20.00%	-1.09	0.276
Oxidative Stress	4	20	35	20.00%	-1.09	0.274
Leptin Insulin Overlap	2	12	20	16.67%	-1.09	0.278
LncRNA involvement in canonical Wnt signaling and colorectal cancer	12	50	102	24.00%	-1.11	0.245
ATR Signaling	1	8	10	12.50%	-1.14	0.317
GABA receptor Signaling	1	8	57	12.50%	-1.14	0.25
Heme Biosynthesis	1	8	28	12.50%	-1.14	0.272
Mammary gland development pathway - Involution (Stage 4 of 4)	1	8	13	12.50%	-1.14	0.277
Apoptosis Modulation and Signaling	18	72	97	25.00%	-1.15	0.269
Dopaminergic Neurogenesis	0	3	32	0.00%	-1.17	0.231
eIF5A regulation in response to inhibition of the nuclear export system	0	3	6	0.00%	-1.17	0.212
Glial Cell Differentiation	0	3	9	0.00%	-1.17	0.231
Glycine Metabolism	0	3	19	0.00%	-1.17	0.247
Robo4 and VEGF Signaling Pathways Crosstalk	0	3	7	0.00%	-1.17	0.233
Steroid Biosynthesis	0	3	25	0.00%	-1.17	0.226
Spinal Cord Injury	12	51	127	23.53%	-1.19	0.215
DNA Replication	9	40	50	22.50%	-1.2	0.224
miRNAs involvement in the immune response in sepsis	5	25	69	20.00%	-1.22	0.233

Human Complement System	7	33	143	21.21%	-1.25	0.199
Interleukin-1 Induced Activation of NF-kappa-B	1	9	13	11.11%	-1.3	0.247
Photodynamic therapy-induced NF-kB survival signaling	4	22	36	18.18%	-1.32	0.175
Glycerophospholipid Biosynthetic Pathway	3	18	94	16.67%	-1.34	0.175
Photodynamic therapy-induced NFE2L2 (NRF2) survival signaling	3	18	24	16.67%	-1.34	0.205
Zinc homeostasis	3	18	39	16.67%	-1.34	0.18
Ferroptosis	7	34	70	20.59%	-1.34	0.162
Gene regulatory network modelling somitogenesis	0	4	13	0.00%	-1.35	0.18
MicroRNA network associated with chronic lymphocytic leukemia	0	4	10	0.00%	-1.35	0.147
NAD Biosynthesis II (from tryptophan)	0	4	34	0.00%	-1.35	0.219
Peroxisomal beta-oxidation of tetracosanoyl-CoA	0	4	17	0.00%	-1.35	0.186
Toll-like Receptor Signaling Pathway	14	61	110	22.95%	-1.41	0.168
Eukaryotic Transcription Initiation	7	35	42	20.00%	-1.44	0.14
Deregulation of Rab and Rab Effector Genes in Bladder Cancer	1	10	17	10.00%	-1.45	0.15
Kennedy pathway from Sphingolipids	1	10	35	10.00%	-1.45	0.134
Simplified Depiction of MYD88 Distinct Input-Output Pathway	1	10	20	10.00%	-1.45	0.146
Regulation of toll-like receptor signaling pathway	22	91	153	24.18%	-1.47	0.15
IL1 and megakaryocytes in obesity	2	15	26	13.33%	-1.5	0.122
ApoE and miR-146 in inflammation and atherosclerosis	0	5	11	0.00%	-1.51	0.078
Folate-Alcohol and Cancer Pathway Hypotheses	0	5	24	0.00%	-1.51	0.124
Serotonin Transporter Activity	0	5	15	0.00%	-1.51	0.087
Sulfation Biotransformation Reaction	0	5	29	0.00%	-1.51	0.134
Sterol Regulatory Element-Binding Proteins (SREBP) signalling	13	59	77	22.03%	-1.53	0.109
TLR4 Signaling and Tolerance	4	24	30	16.67%	-1.54	0.123
Estrogen signaling pathway	3	20	26	15.00%	-1.57	0.11
NO/cGMP/PKG mediated Neuroprotection	3	20	64	15.00%	-1.57	0.127
Oxidative phosphorylation	10	49	68	20.41%	-1.64	0.104
RIG-I-like Receptor Signaling	10	49	64	20.41%	-1.64	0.1
Estrogen metabolism	0	6	45	0.00%	-1.65	0.128
Leptin and adiponectin	0	6	14	0.00%	-1.65	0.082
Metastatic brain tumor	0	6	28	0.00%	-1.65	0.09
Preimplantation Embryo	3	21	60	14.29%	-1.68	0.081
Fas Ligand (FasL) pathway and Stress induction of Heat Shock Proteins (HSP) regulation	7	38	48	18.42%	-1.71	0.093

Constitutive Androstane Receptor Pathway	1	12	34	8.33%	-1.71	0.084
Nuclear Receptors in Lipid Metabolism and Toxicity	1	12	48	8.33%	-1.71	0.099
PPAR Alpha Pathway	1	12	28	8.33%	-1.71	0.083
Copper homeostasis	6	34	58	17.65%	-1.72	0.071
Translation Factors	9	46	51	19.57%	-1.72	0.095
Regulation of Apoptosis by Parathyroid Hormone-related Protein	2	17	24	11.76%	-1.74	0.071
Dopamine metabolism	0	7	48	0.00%	-1.78	0.068
Pentose Phosphate Metabolism	0	7	21	0.00%	-1.78	0.064
TFs Regulate miRNAs related to cardiac hypertrophy	0	7	16	0.00%	-1.78	0.056
Folate Metabolism	5	31	139	16.13%	-1.82	0.062
Pregnane X Receptor pathway	1	13	35	7.69%	-1.83	0.079
Viral Acute Myocarditis	11	56	109	19.64%	-1.88	0.066
Estrogen Receptor Pathway	0	8	16	0.00%	-1.91	0.044
p38 MAPK Signaling Pathway	4	28	36	14.29%	-1.94	0.048
Parkinsons Disease Pathway	4	28	84	14.29%	-1.94	0.061
Cholesterol Biosynthesis Pathway	1	14	32	7.14%	-1.95	0.04
Vitamin B12 Disorders	0	9	35	0.00%	-2.02	0.038
Amyotrophic lateral sclerosis (ALS)	4	29	56	13.79%	-2.03	0.042
Mitochondrial complex I assembly model OXPHOS system	8	46	61	17.39%	-2.04	0.042
Nanomaterial induced apoptosis	2	20	30	10.00%	-2.05	0.039
Nonalcoholic fatty liver disease	28	124	170	22.58%	-2.11	0.035
Apoptosis	14	71	88	19.72%	-2.11	0.041
Apoptosis Modulation by HSP70	1	17	22	5.88%	-2.26	0.023
Proteasome Degradation	8	53	67	15.09%	-2.55	0.01
Selenium Metabolism and Selenoproteins	3	31	56	9.68%	-2.6	0.008
Electron Transport Chain (OXPHOS system in mitochondria)	15	83	119	18.07%	-2.61	0.006
Vitamin B12 Metabolism	1	21	118	4.76%	-2.62	0.008
Selenium Micronutrient Network	5	41	195	12.20%	-2.64	0.008
Parkin-Ubiquitin Proteasomal System pathway	8	55	75	14.55%	-2.69	0.005
Allograft Rejection	2	32	113	6.25%	-3.06	0.002
Ciliary landscape	38	185	215	20.54%	-3.2	0.003
mRNA Processing	15	118	130	12.71%	-4.39	0
Cytoplasmic Ribosomal Proteins	3	80	89	3.75%	-5.35	0

Acrylamide Biotransformation and Exposure Biomarkers	0	0	10	NaN%	NaN	0
Amino acid conjugation of benzoic acid	0	0	14	NaN%	NaN	0
Amino acid conjugation	0	0	7	NaN%	NaN	0
Aripiprazole Metabolic Pathway	0	0	7	NaN%	NaN	0
Biochemical Pathways Part I	0	0	471	NaN%	NaN	0
Biosynthesis and regeneration of tetrahydrobiopterin (BH4) and catabolism of phenylalanine,	0	0	31	NaN%	NaN	0
Caffeine and Theobromine metabolism	0	0	17	NaN%	NaN	0
Carnosine's role in mucle contraction	0	0	14	NaN%	NaN	0
Catalytic cycle of mammalian Flavin-containing MonoOxygenases (FMOs)	0	0	14	NaN%	NaN	0
Colchicine Metabolic Pathway	0	0	5	NaN%	NaN	0
Diclofenac Metabolic Pathway	0	0	12	NaN%	NaN	0
Effects of Nitric Oxide	0	0	16	NaN%	NaN	0
FABP4 in ovarian cancer	0	0	3	NaN%	NaN	0
Felbamate Metabolism	0	0	12	NaN%	NaN	0
Gastric acid production	0	0	22	NaN%	NaN	0
GHB metabolic pathway	0	0	25	NaN%	NaN	0
Glucocorticoid and Mineralcorticoid Metabolism	0	0	26	NaN%	NaN	0
Glucose Homeostasis	0	0	24	NaN%	NaN	0
GPCRs, Class C Metabotropic glutamate, pheromone	0	0	15	NaN%	NaN	0
Human metabolism overview	0	0	115	NaN%	NaN	0
Lidocaine metabolism	0	0	11	NaN%	NaN	0
Metabolism of Dichloroethylene by CYP450	0	0	13	NaN%	NaN	0
Metabolism of Tetrahydrocannabinol (THC)	0	0	11	NaN%	NaN	0
Mevalonate arm of cholesterol biosynthesis pathway	0	0	29	NaN%	NaN	0
Modified nucleosides derived from t-RNA as urinary cancer markers	0	0	21	NaN%	NaN	0
Neurotransmitter Disorders	0	0	23	NaN%	NaN	0
Nicotine Activity on Chromaffin Cells	0	0	10	NaN%	NaN	0
Nicotine Metabolism	0	0	18	NaN%	NaN	0
Ophthalmate biosynthesis in hepatocytes	0	0	10	NaN%	NaN	0
Phosphatidylcholine catabolism	0	0	32	NaN%	NaN	0
Secretion of Hydrochloric Acid in Parietal Cells	0	0	15	NaN%	NaN	0

uNK versus CK pNK

total genes measured as a proportion of the total frequency of pathway enriched genes were ranked