



C

Canonical Pathway	HCC vs LC	HCC vs HD	LC vs HD
CD28 Signaling in T Helper Cells	9.15	3.14	1.98
iCOS-iCOSL Signaling in T Helper Cells	8.01	2.82	1.19
Calcium-induced T Lymphocyte Apoptosis	7.83	1.79	0.43
PKCθ Signaling in T Lymphocytes	6.10	2.54	0.65
Role of NFAT in Regulation of the Immune Response	6.08	1.99	1.49
Integrin Signaling	5.87	1.77	3.93
Epithelial Adherens Junction Signaling	5.62	0.49	1.98
Nur77 Signaling in T Lymphocytes	5.55	0.76	0.00
B Cell Receptor Signaling	5.46	3.30	2.30
Natural Killer Cell Signaling	5.42	3.32	3.49
OX40 Signaling Pathway	5.32	1.48	0.00
Type I Diabetes Mellitus Signaling	5.26	2.04	0.51
B Cell Development	5.16	2.02	0.00
Cdc42 Signaling	4.96	1.70	1.92
NRF2-mediated Oxidative Stress Response	4.93	1.14	1.96
Fcy Receptor-mediated Phagocytosis in Macrophages and Monocytes	4.84	1.80	1.90
Actin Cytoskeleton Signaling	4.77	0.88	2.57
T Helper Cell Differentiation	4.63	1.49	0.31
Germ Cell-Sertoli Cell Junction Signaling	4.61	0.60	1.79
T Cell Receptor Signaling	4.61	2.29	2.12

-log p value

D

Categories	Diseases or Functions Annotation	p-Value	z-score
Cellular Movement	Cell movement	1,58E-10	-2,906
Cellular Movement	Migration of cells	1,25E-08	-2,605
Infectious Diseases	Viral Infection	1,30E-08	-3,244
Cellular Movement	Cell movement of tumor cell lines	4,74E-07	-2,191
Gene Expression	Transcription	1,44E-06	-2,055
Gene Expression	Expression of RNA	9,71E-06	-2,120
Cell Death and Survival	Cell death of lymphoma cell lines	1,14E-05	2,919
Cell Death and Survival	Cell viability of tumor cell lines	1,36E-05	-2,580
Cellular Movement	Cell movement of breast cancer cell lines	1,82E-05	-2,074
Cell-To-Cell Signaling and Interaction	Adhesion of tumor cell lines	2,68E-05	-2,262

Supplementary Figure 1

Gene expression pattern and IPA (ingenuity pathway analysis) of circulating NK-cells from patients with HCV-related liver cirrhosis (LC) or HCC and healthy donors (HD)

A. Representative fluorescence flow-cytometry cell sorting of CD56⁺CD3⁻ NK-cells. Left, pre-sorting illustrating the frequency of NK-cells within the overall lymphocyte cell population; right, post-sorting documenting the level of purity of sorted NK-cells. **B.** Heat-map representation of the 1435 differentially expressed genes in NK-cells from HCC and LC patients by Moderated T-test and Benjamini-Hochberg correction ($p \leq 0.05$, Fold Change threshold 1.5). Upregulated and downregulated genes are shown in red and green, respectively.

C. IPA canonical pathways (CPs) associated with genes differentially expressed in PBNK. Top 20 IPA CPs based on significance. Color intensity is proportional to increasing significance. -log p values are shown.

D. Top 10 IPA Diseases and Functions associated with DE genes in the comparison HCC vs LC. Orange: predicted upregulation. Light blue: predicted downregulation.