



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν
Πανεπιστήμιον Ἀθηνῶν
— ΙΔΡΥΘΕΝ ΤΟ 1837 —



pMedGR

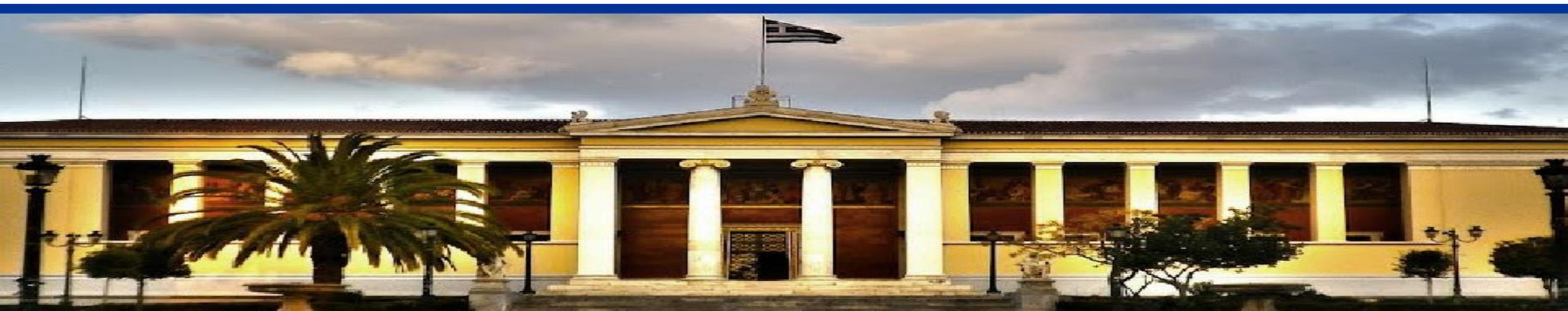
Revealing molecular mechanisms in NAFLD and its progression to cirrhosis and HCC

Antonios Chatzigeorgiou (MD, PhD)

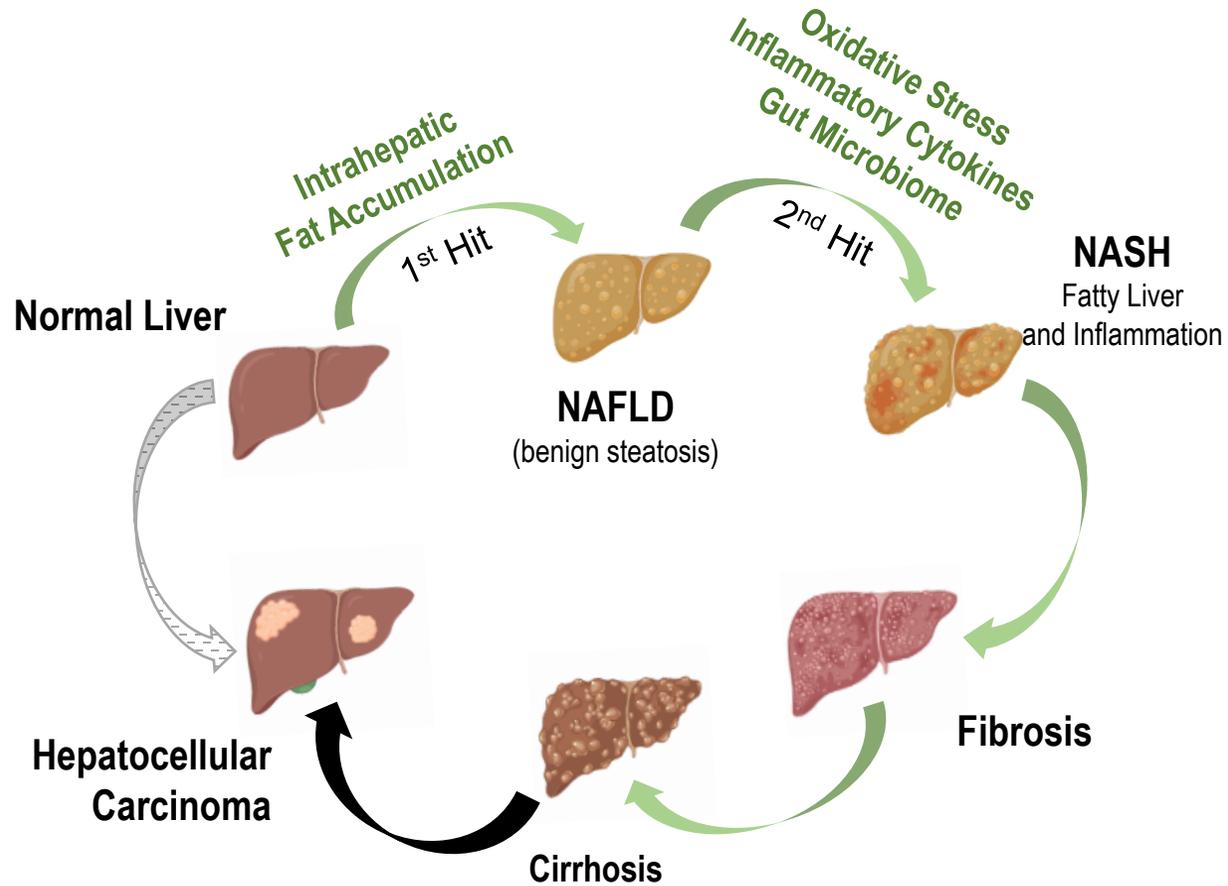
Associate Professor

Department of Physiology - Medical School

National and Kapodistrian University of Athens, Greece

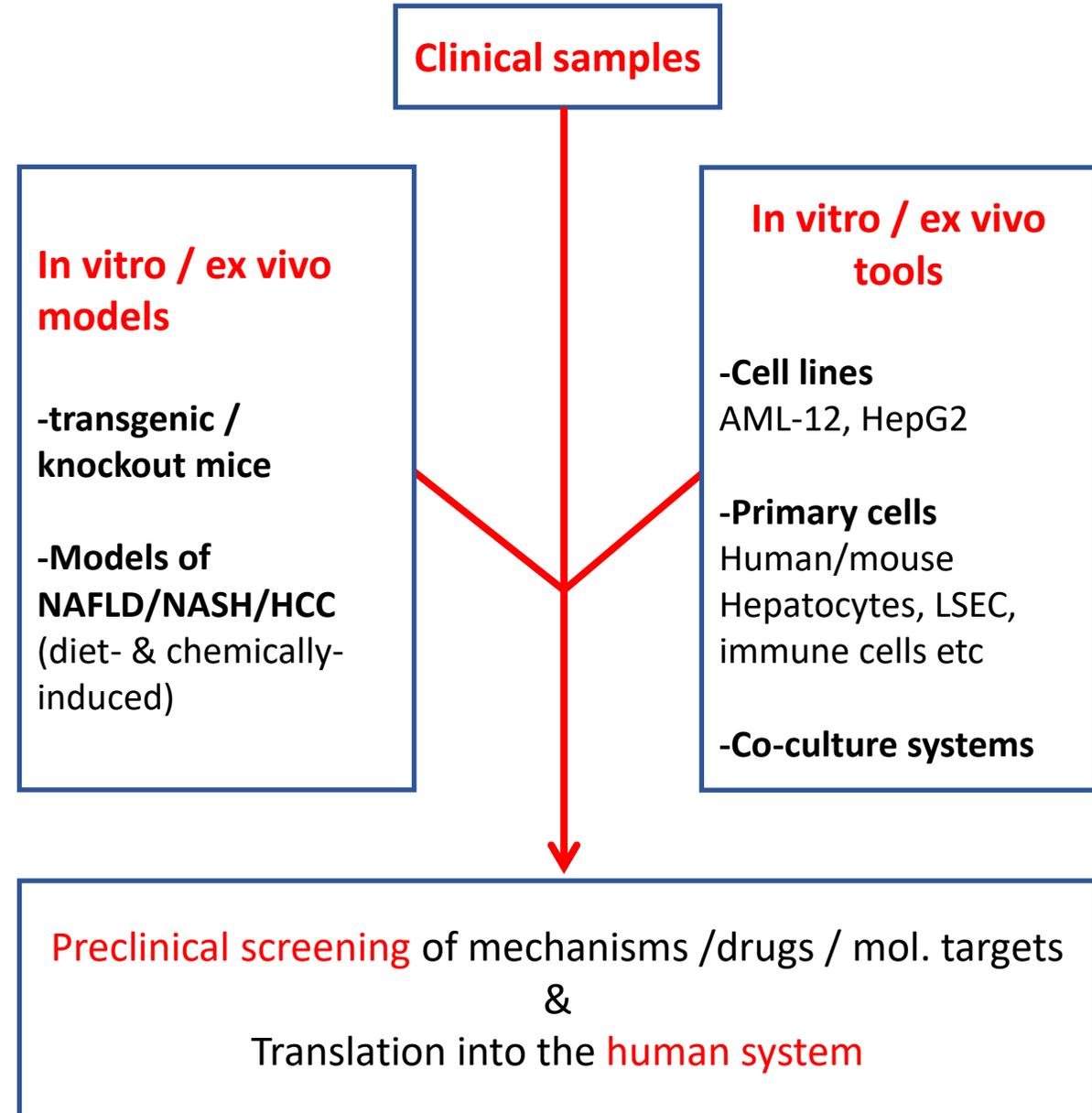


Our research topic



Revealing molecular mechanisms in NAFLD and its progression to cirrhosis and HCC

Our team and tools

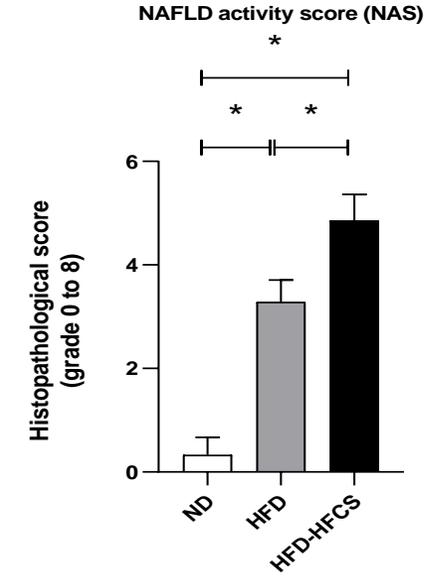
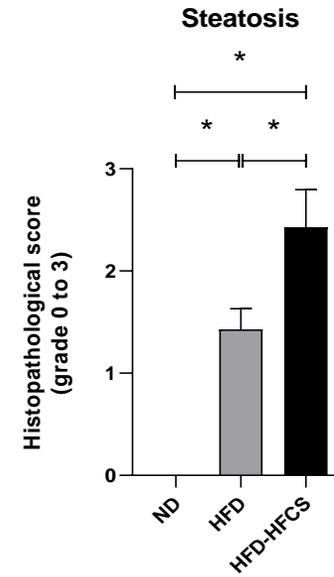
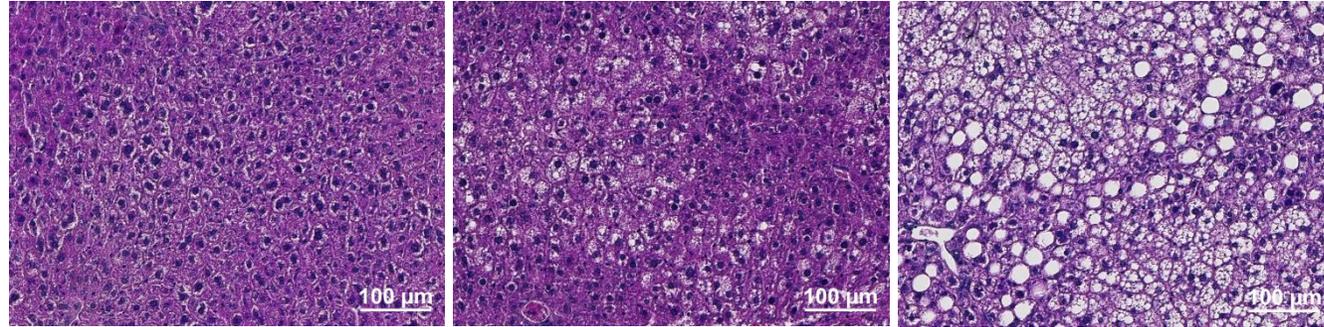


Revealing the role of High-Fructose Corn Syrup in the progression of NAFLD

ND

HFD

HFD-HFCS



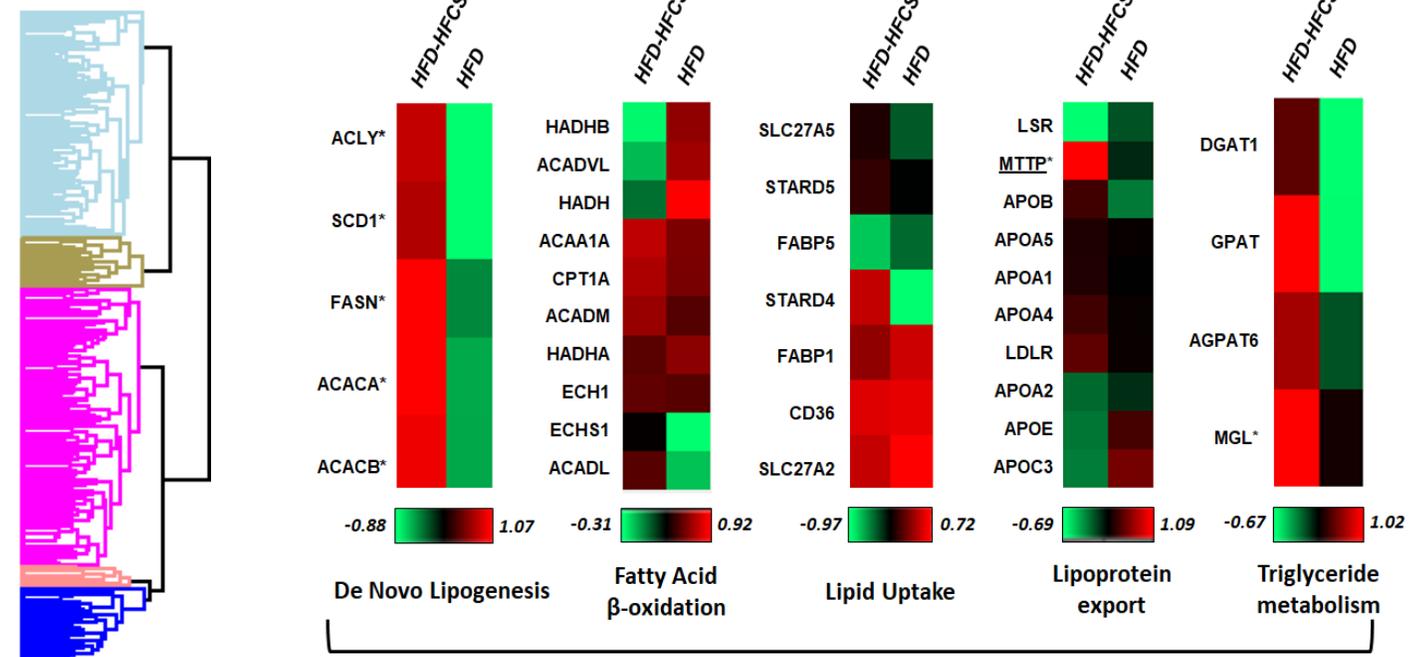
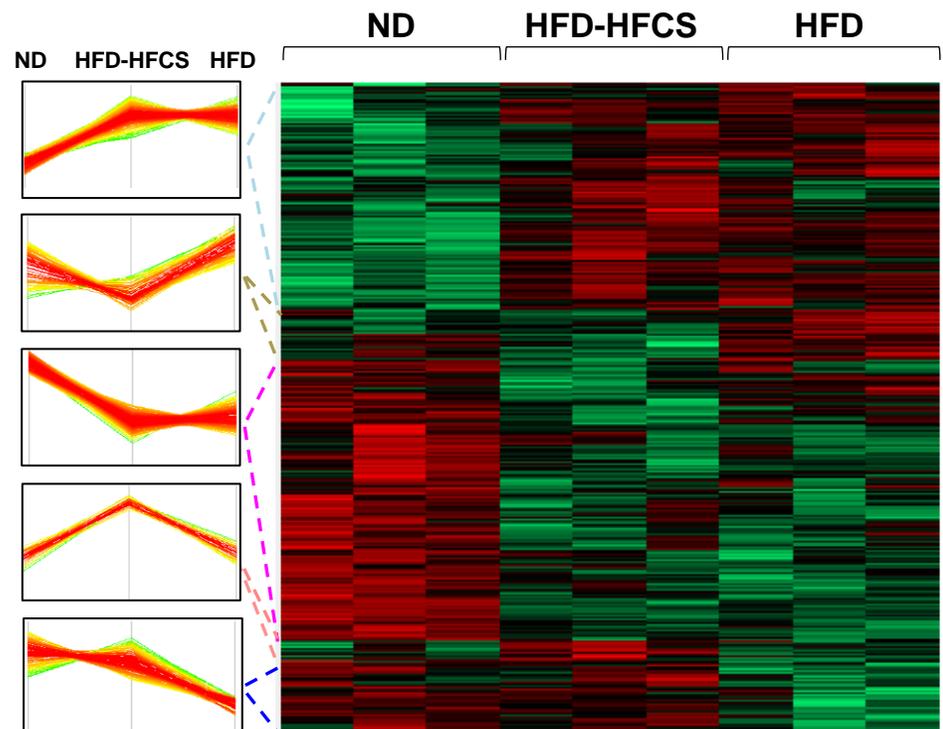
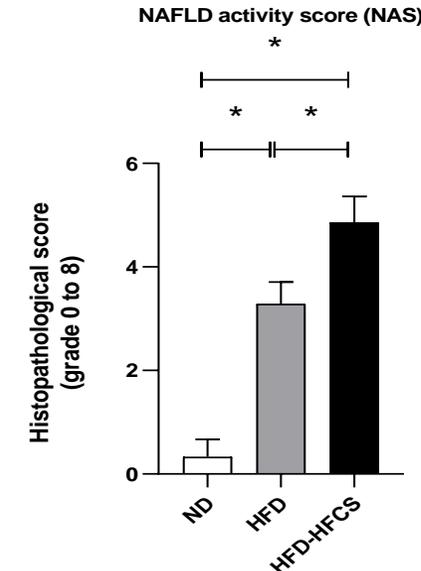
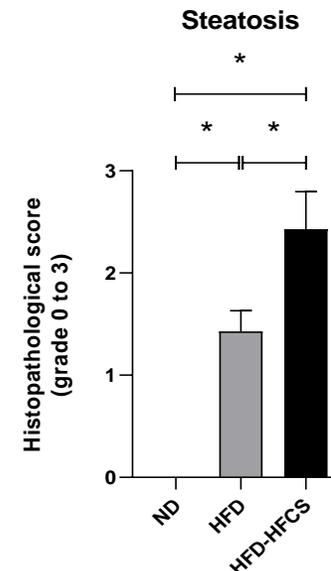
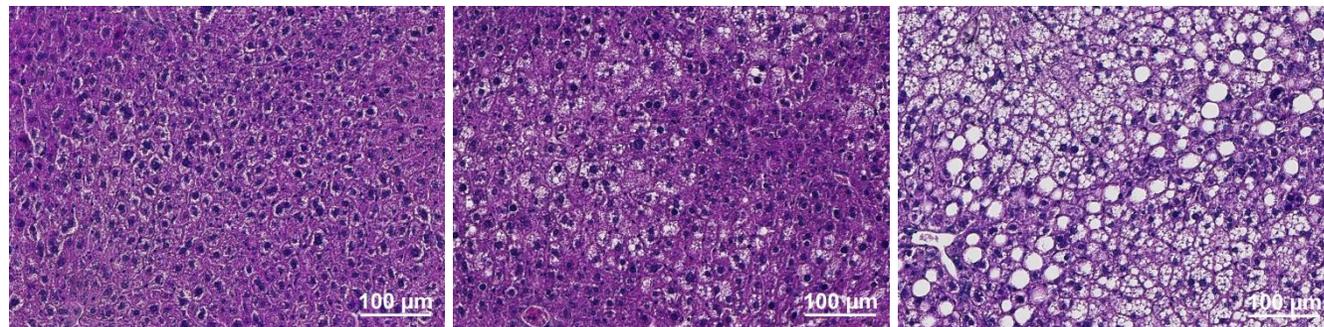
Revealing the role of High-Fructose Corn Syrup in the progression of NAFLD



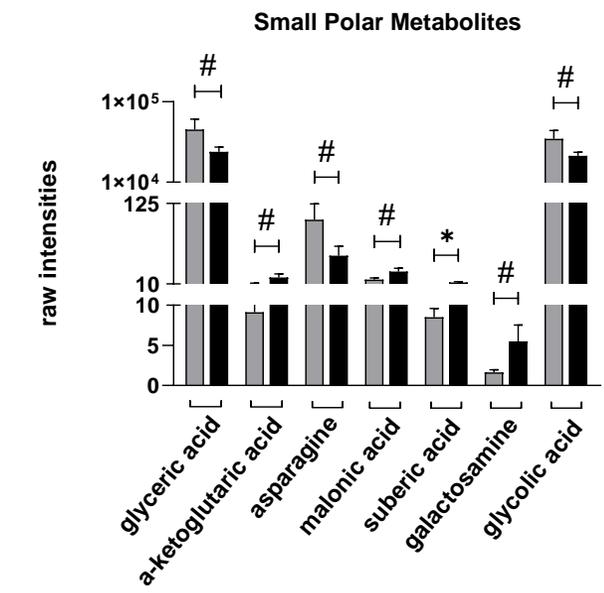
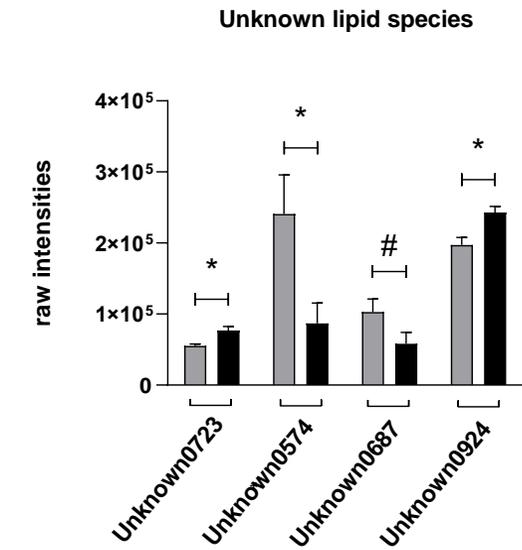
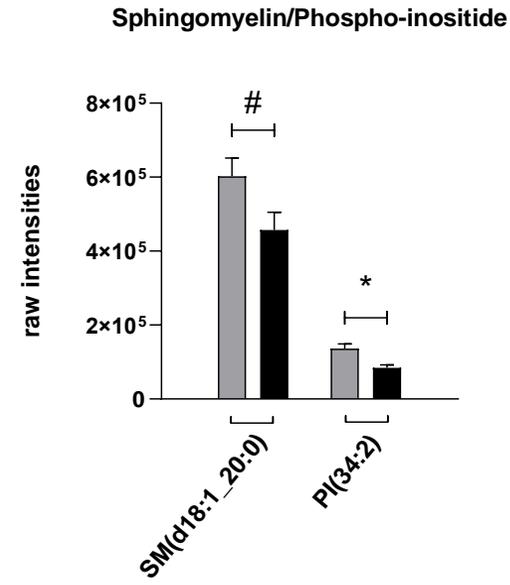
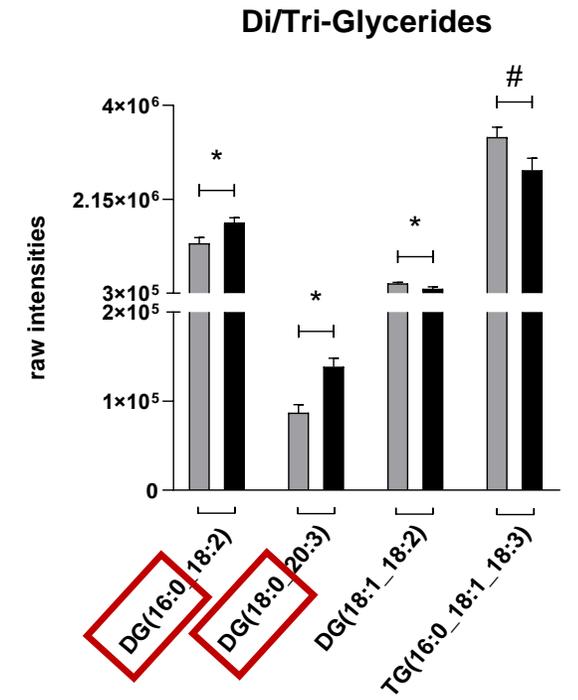
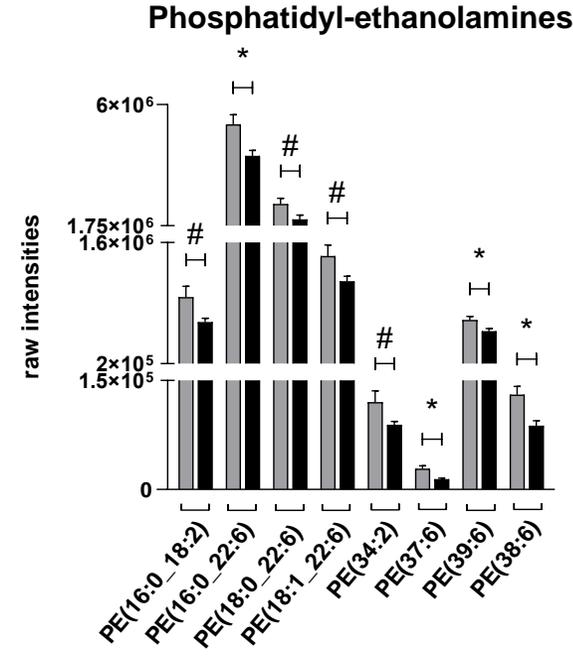
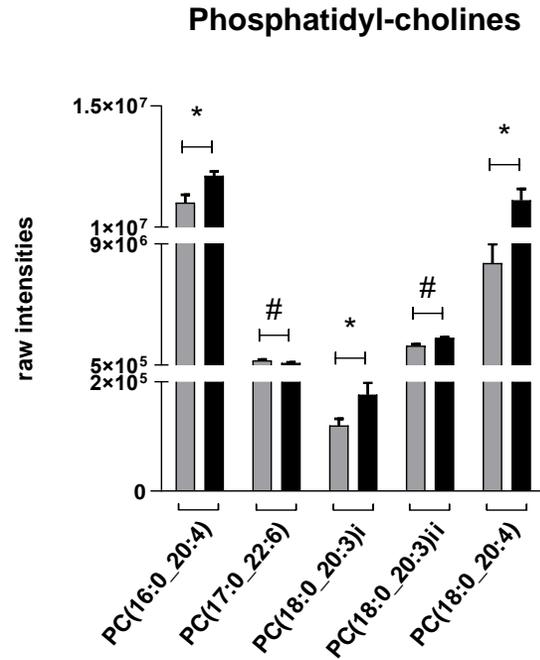
ND

HFD

HFD-HFCS

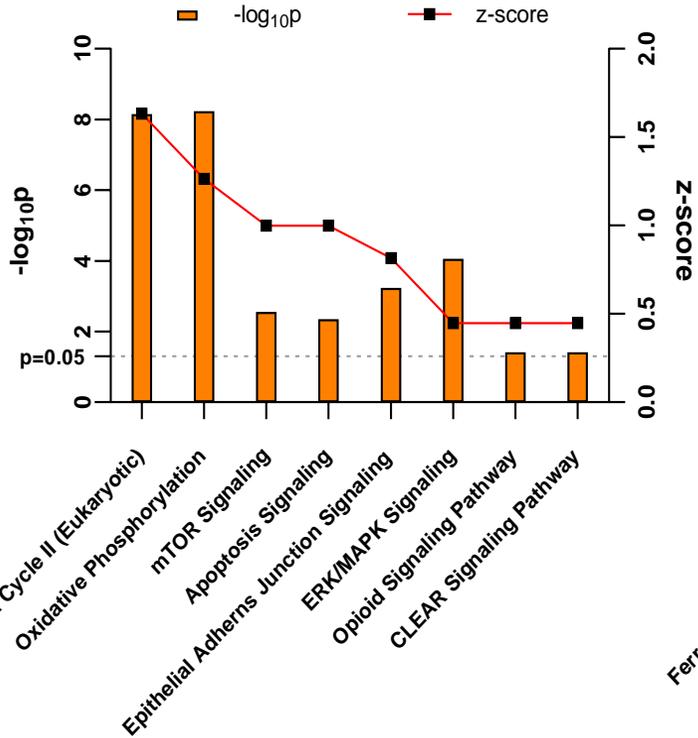


Lipidomic Analysis

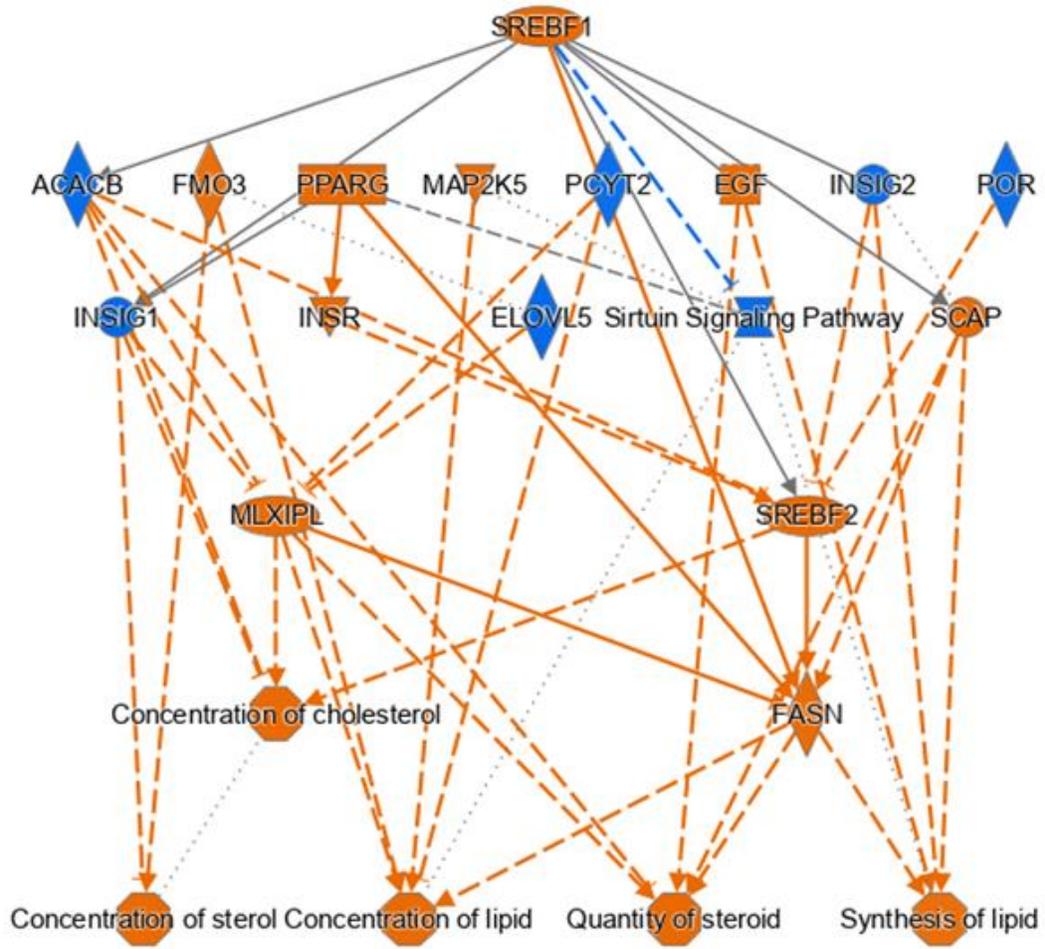
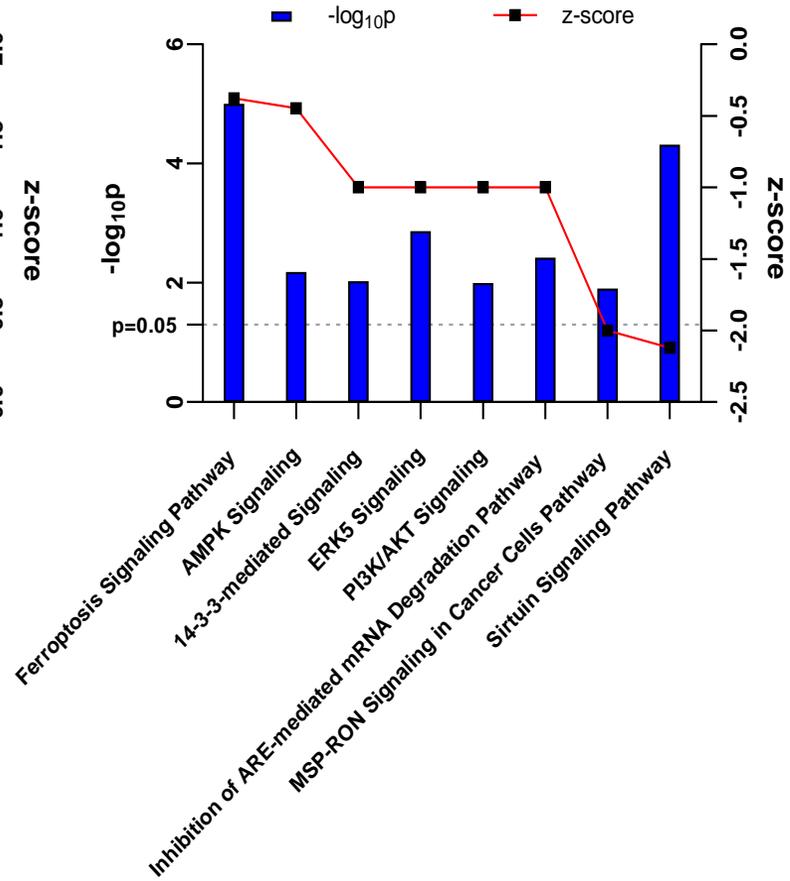


Omics Integration

ACTIVATED Canonical Processes in HFD-HFCS

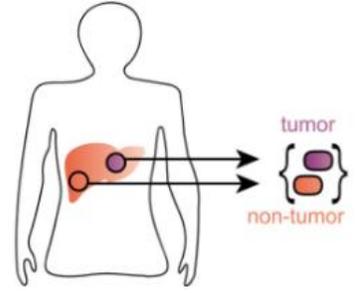
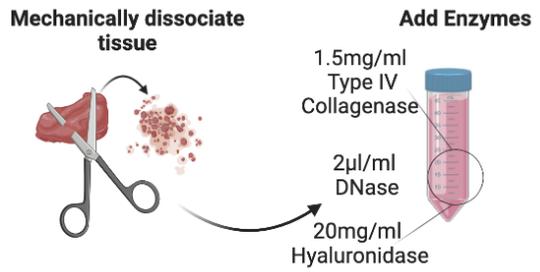
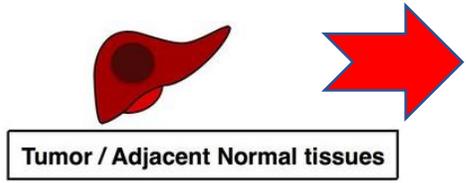


INACTIVATED Canonical Processes in HFD-HFCS



- Predicted to be activated
- Predicted to be inactivated
- predicted direct activation
- predicted direct inhibition
- - - predicted indirect activation
- - - predicted indirect inhibition
- ⋯ Not described before in IPA

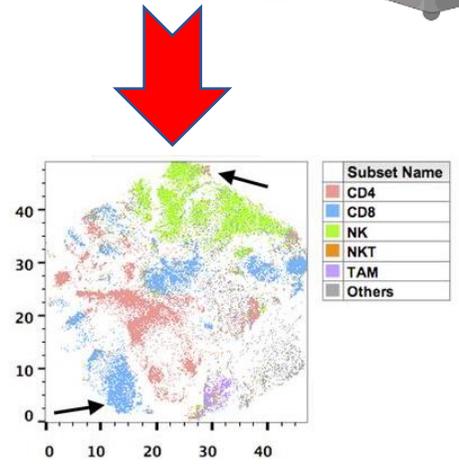
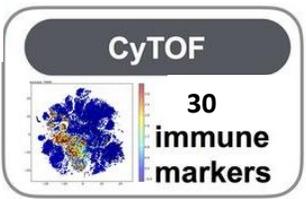
Revealing the immune microenvironment of NASH-associated HCC



Mechanic and enzymatic dissociation

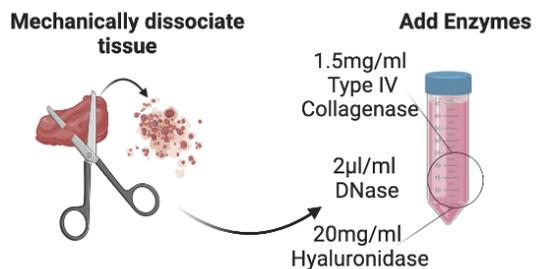
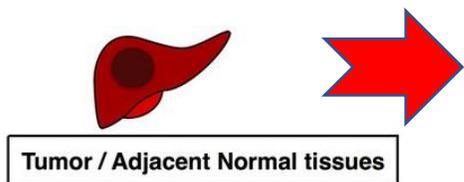
Tumor and adjacent non-tumor samples from patients with HCC

CyTOF Analysis

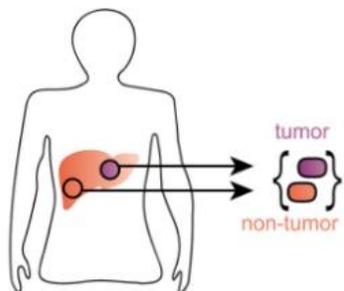


Identification of unique subsets

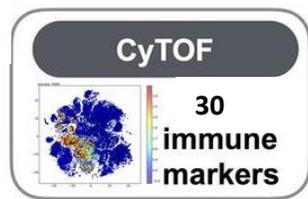
Revealing the immune microenvironment of NASH-associated HCC



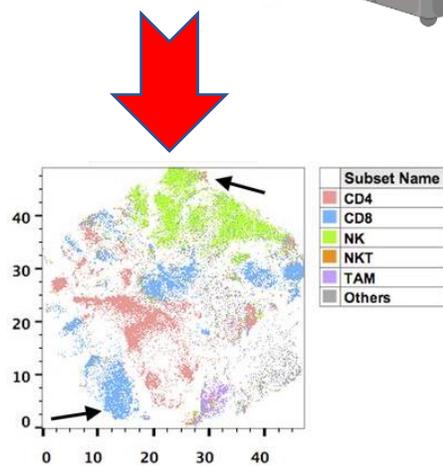
Mechanic and enzymatic dissociation



Tumor and adjacent non-tumor samples from patients with HCC



CyTOF Analysis



Identification of unique subsets



Immunophenotyping model

CD3+	CD66b-	CD66b-	CD66b-	CD3-	CD3-	CD14-	HLADR-	CD66b d+	CD3-	CD14-	CD3-	CD3-	CD3-
CD66b-	CD3+	CD3+	CD3+	CD14-	CD19-	CD3-	CD66b-	CD16+	CD19-	CD3-	CD19-	CD19-	CD14-
CD19-	CD8-	CD8 d	CD4-	CD56-	CD56-	CD123-	CD123 d+	HLADR-	CD66b-	CD19-	CD14-	CD14-	CD16 d-
CD8+	CD4+	CD4-	CD14-	CD16 d-	CD66b-	CD66b-	CD38 d+	HLADR-	CD56-	HLADR-	CD20-	CD20-	CD66b-
CD4-	CD14-	CD14-	CD161 d+	CD19+	HLADR d+	CD45RA+	CD294+	HLADR-	CD294+	CD66b-	HLADR d+	CD20-	CD20-
CD14-	TCRgd-	TCRgd+	TCRgd-	CD20+	CD11c+	CD56 d+	CD123+	CD123-	CD66b d+	HLADR d+	CD11c+	CD19 d+	CD19 d+
CD161-	CD11c-		CD28+	HLADR d+				CD45-			CD11c-	CD123-	CD56-
TCRgd-			CD15-								CD123+	CD16 d-	CD38++
CD123-			CD161++										CD38 d+
CD11c-													HLADR++
													CD294-

T CD8 stages 1

CCR7+	CCR7 d-	CCR7-
CD27+	CD27 d+	CD27-
Naive & central memory	Effector memory	Terminal effector

T CD8 stages 2

CD45RA+	CD45RA-
Naive	Central memory

T CD4 stages

CCR7+	CCR7+	CCR7-	CCR7-
CD27+	CD27+	CD27+	CD27-
CD45RA+	CD45RA-	CD45RA-	CD45RA-
Naive	Central memory	Effector memory	Terminal memory

T CD4 subsets

CXCR3+	CXCR3-	CXCR3-	CD25+
CCR6-	CCR6-	CCR6+	CD127-
CCR4-	CCR4+	CCR4+	CCR4+
CXCR5-	CXCR5-	CXCR5-	HLADR-
Th1	Th2	Th17	Treg

B cell stages

CD27-	CD27+
Naive	Memory

Monocyte stages

CD14+	CD14 d-	CD14-
CD38+	CD38 d-	CD38-
Classical	Transitional	Non-classical

NK stages

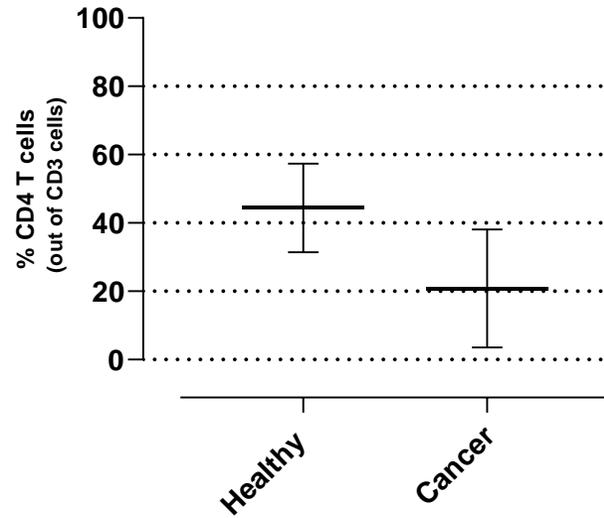
CD57-	CD57+
Early	Late

- + Select brightest peak in expression profile
- ++ Select brightest peak in expression profile
- Select dimmest peak in expression profile
- d+ Select positive plus dim peaks in expression profile
- d- Select negative plus dim peaks in expression profile
- ↑ ↓ Expression profiles used in immunophenotyping model (Up/down arrows denote step up/down in intensity)
- Cell Immune cell type identified by immunophenotyping model
- Cell Immune cell type identified by staging
- Cell Immune cell type identified by TriCOM analysis tool

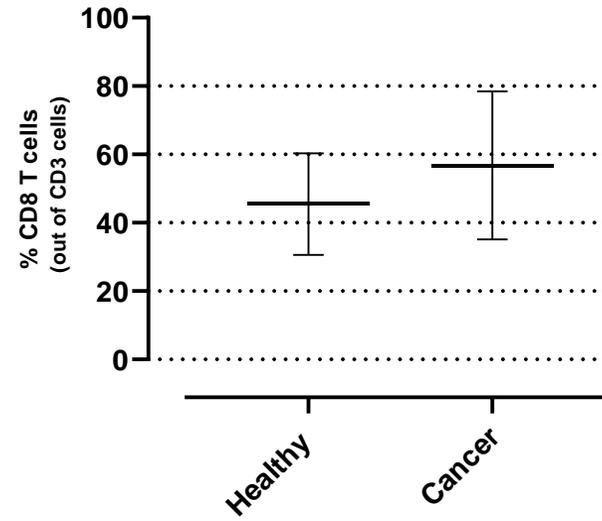
- Parameter used in clean up model
- Model tool: Staging
- Model tool: Fit used to identify Stage

Revealing the immune microenvironment of NASH-associated HCC

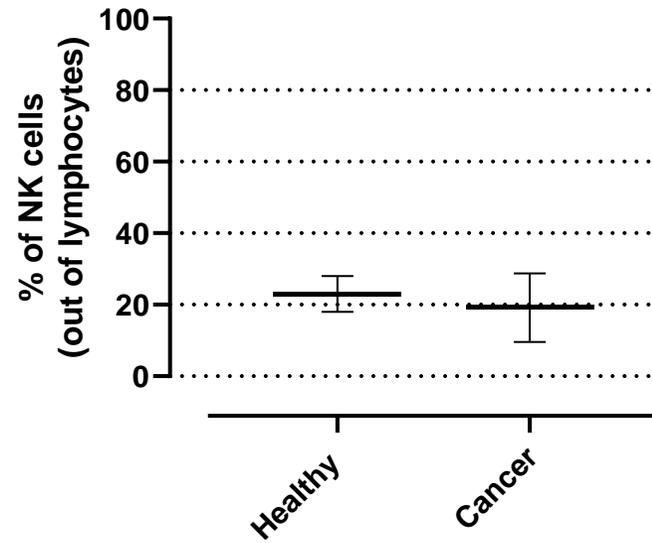
CD4 T cells



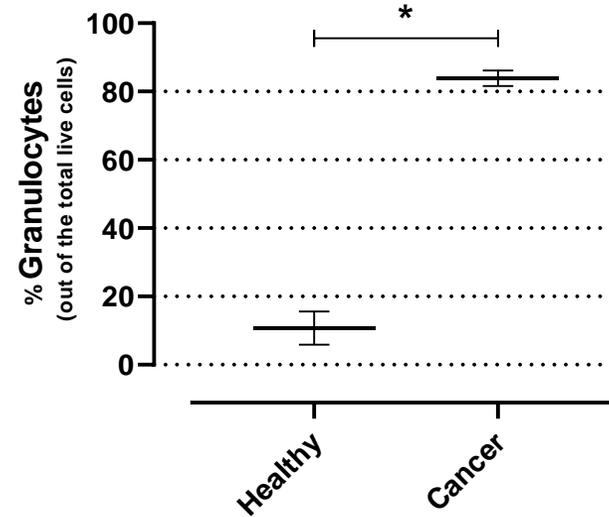
CD8 T cells



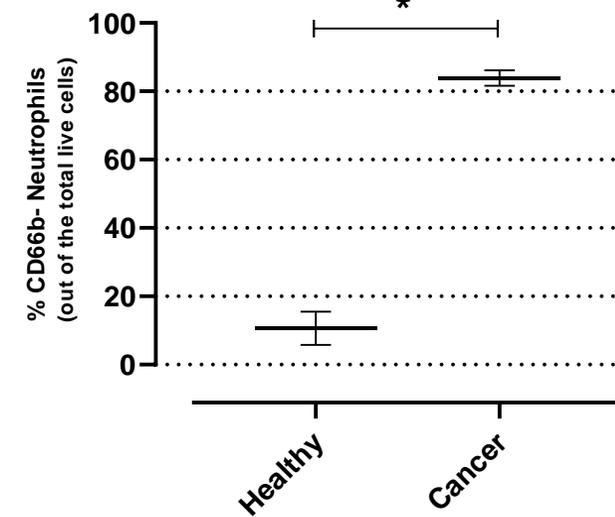
NK cells



Granulocytes

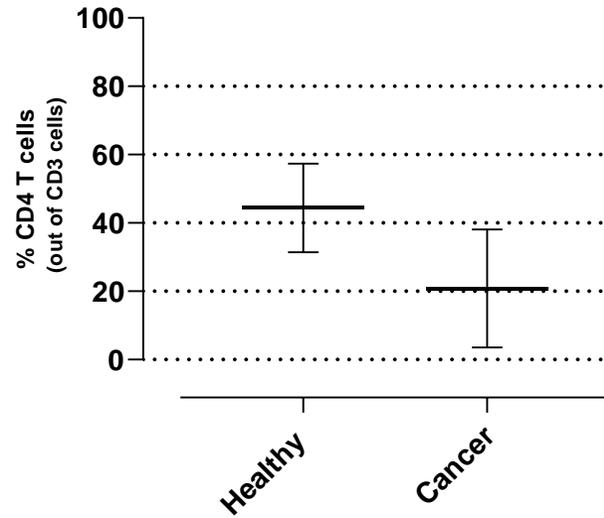


CD66b- Neutrophils

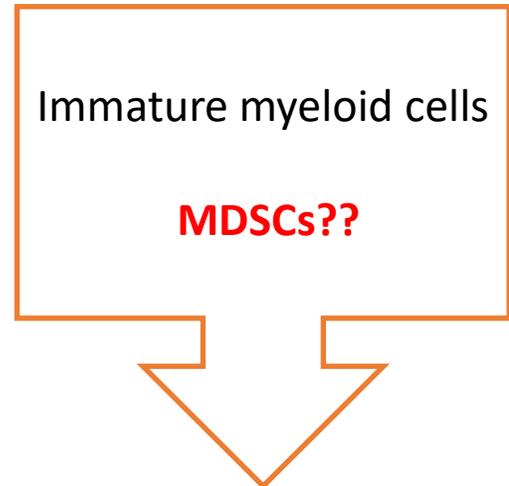
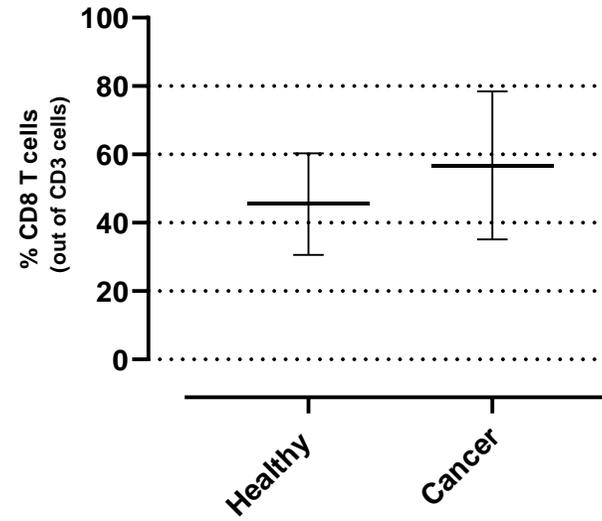


Revealing the immune microenvironment of NASH-associated HCC

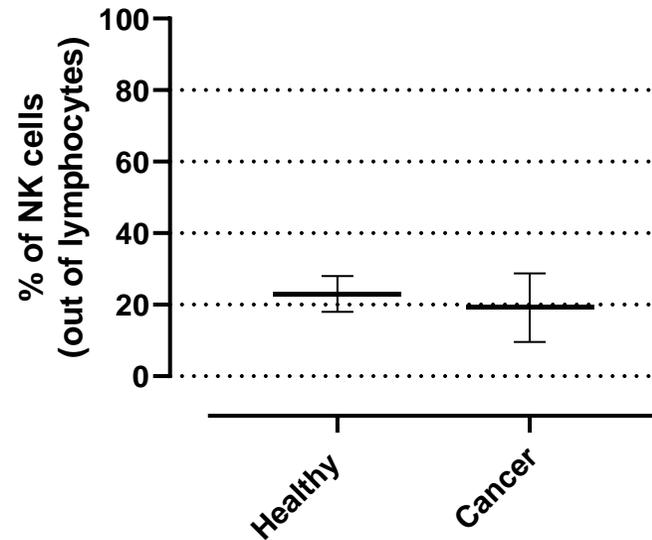
CD4 T cells



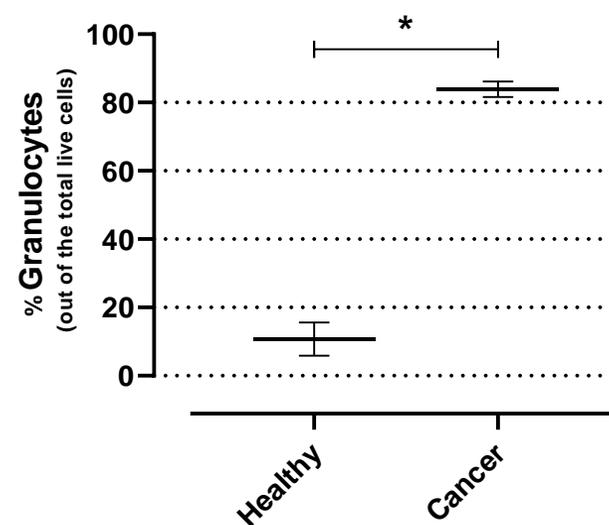
CD8 T cells



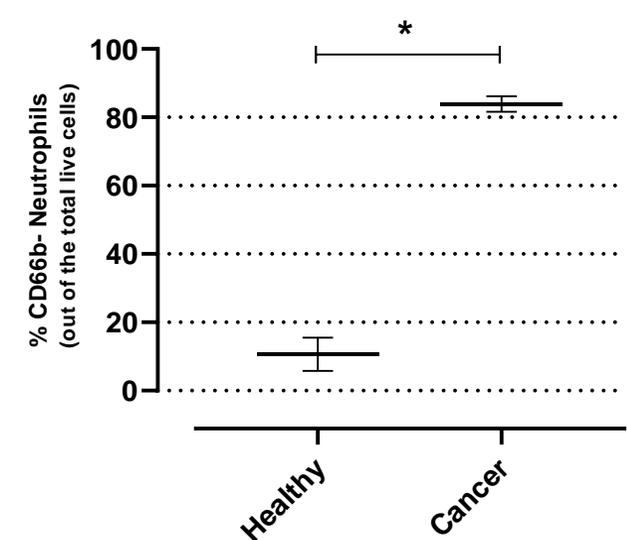
NK cells



Granulocytes



CD66b- Neutrophils



Acknowledgments

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