



PARIS MASH MEETING

11th edition

**Organized by
Arun Sanyal & Lawrence Serfaty**

**September 11 & 12, 2025
Institut Pasteur, Paris**





PARIS
MASH
MEETING

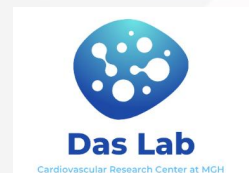
11th edition

September 11 & 12, 2025
Institut Pasteur, Paris



Extracellular Vesicles, miRNAs and inter-organ cross-talk in MASLD

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Massachusetts General Hospital
Harvard Medical School



Presenter Disclosure Information Elements

FINANCIAL DISCLOSURE:

Founder, Equity in LQTT and Switch Therapeutics.

Research Grant: Abbott.

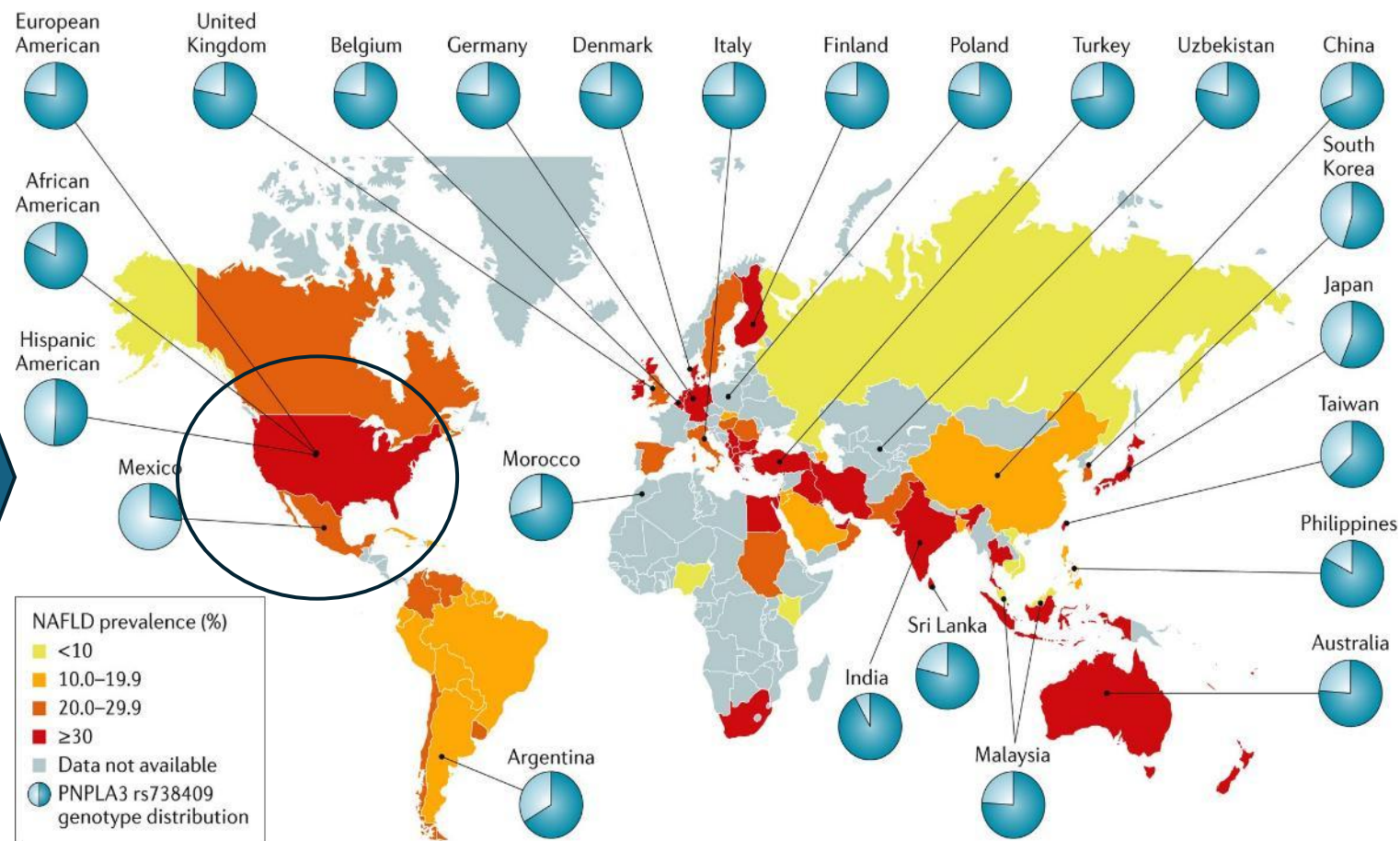
Patents: tDR therapeutics, Tissue-specific EVs

No relevant financial disclosures for the work presented here.

UNLABELED/UNAPPROVED USES DISCLOSURE:

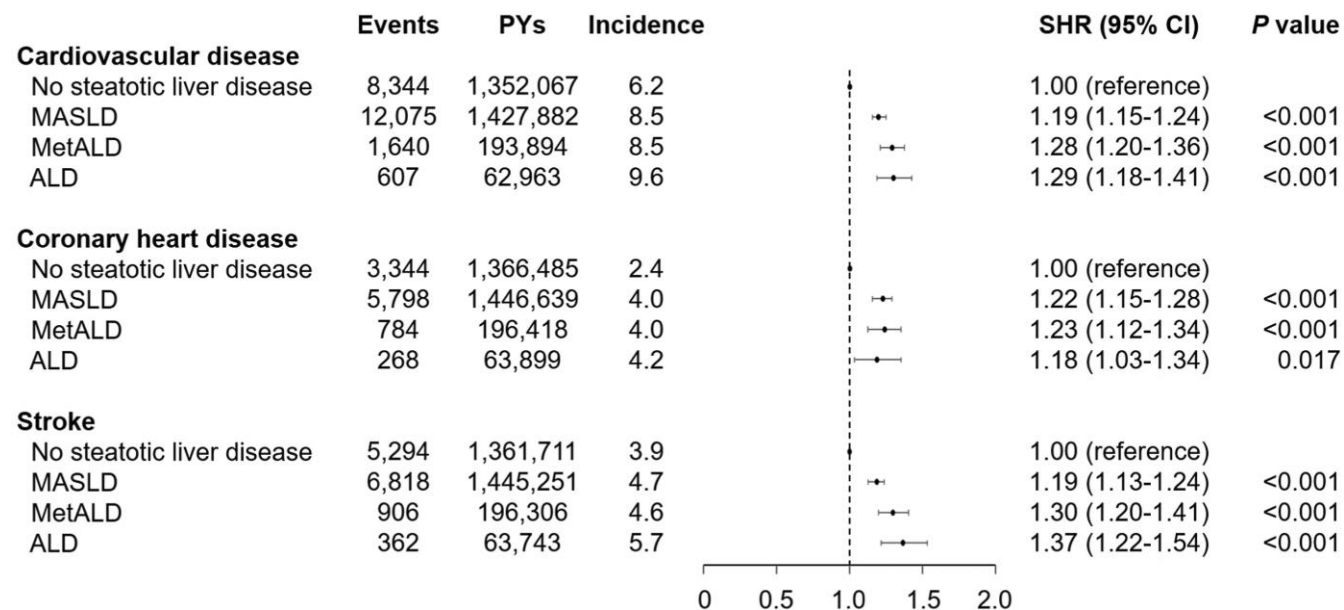
None

Global burden of Metabolic Dysfunction- Associated Steatotic Liver Disease (MASLD)



MASLD and the risk of cardiovascular diseases

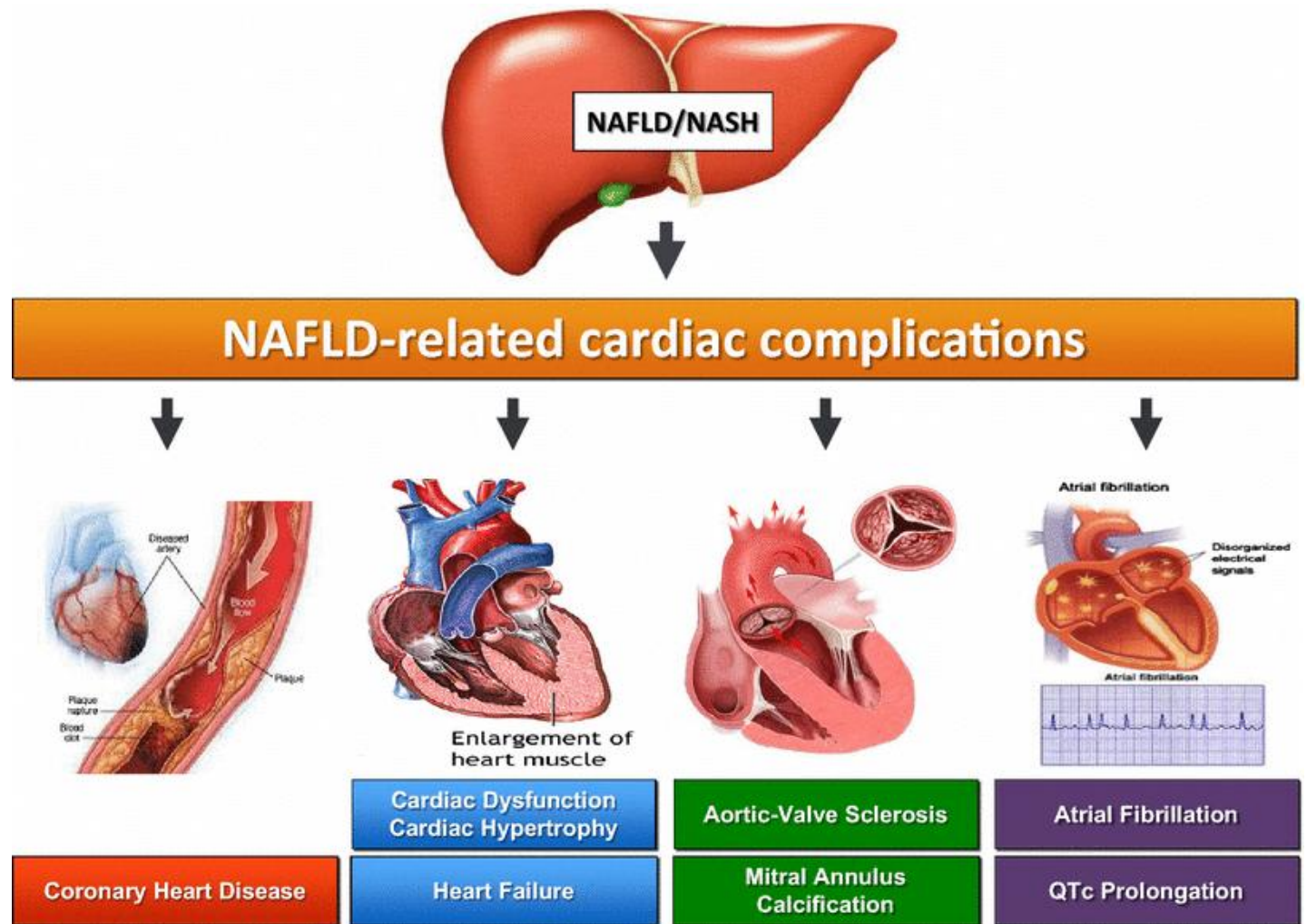
- Epidemiological evidence associating MASLD with increased development of a range of CVD and including association with atherosclerotic CVD events.
- Recent recognition of independent association of MASLD with incident heart failure and MACE (65% increased risk)
- Myocardial metabolic reprogramming and hypertrophy in MASLD.



eClinicalMedicine 2023 65DOI: (10.1016/j.eclinm.2023.102292)

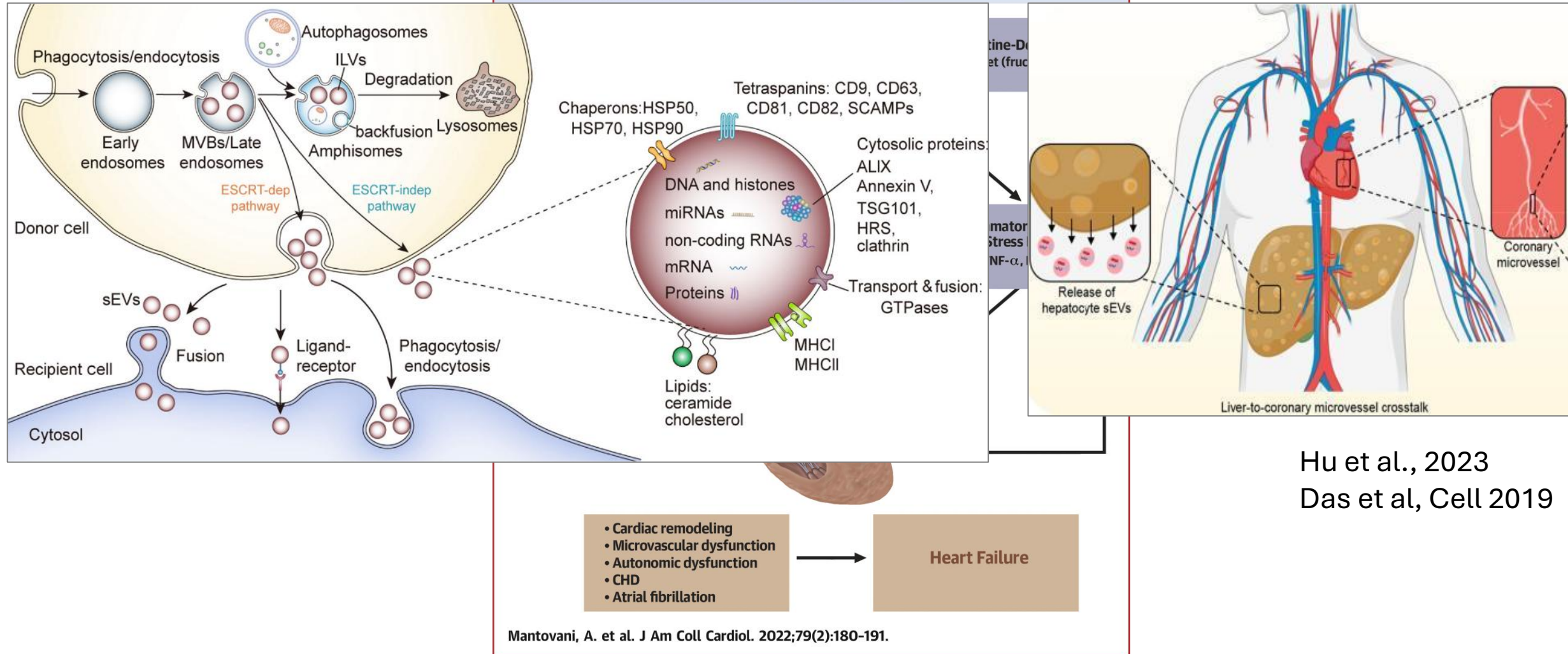
1. Targer et al, J. Hepatology, 2016.
2. Stepanova et al, Clin Gastroenterol Hepatol 2012
3. Wegermann et al, Eur Jnl Heart Failure 2025
4. Sanyal et al, NEJM 2021.
5. Simon et al, Gut 2021.

MASLD and cardiovascular disease



Potential mechanisms for MASLD-associated CVD

CENTRAL ILLUSTRATION: Hepatic and Extrahepatic Factors Affecting Risk of Heart Failure in Nonalcoholic Fatty Liver Disease



Deciphering hepatic-cardiac cross-talk



Do liver EVs transduce the effects of MASLD onto cardiomyocytes?



What phenotypes are elicited in cardiomyocytes by MASLD EVs?



What are the signaling molecules that transduce these effects?



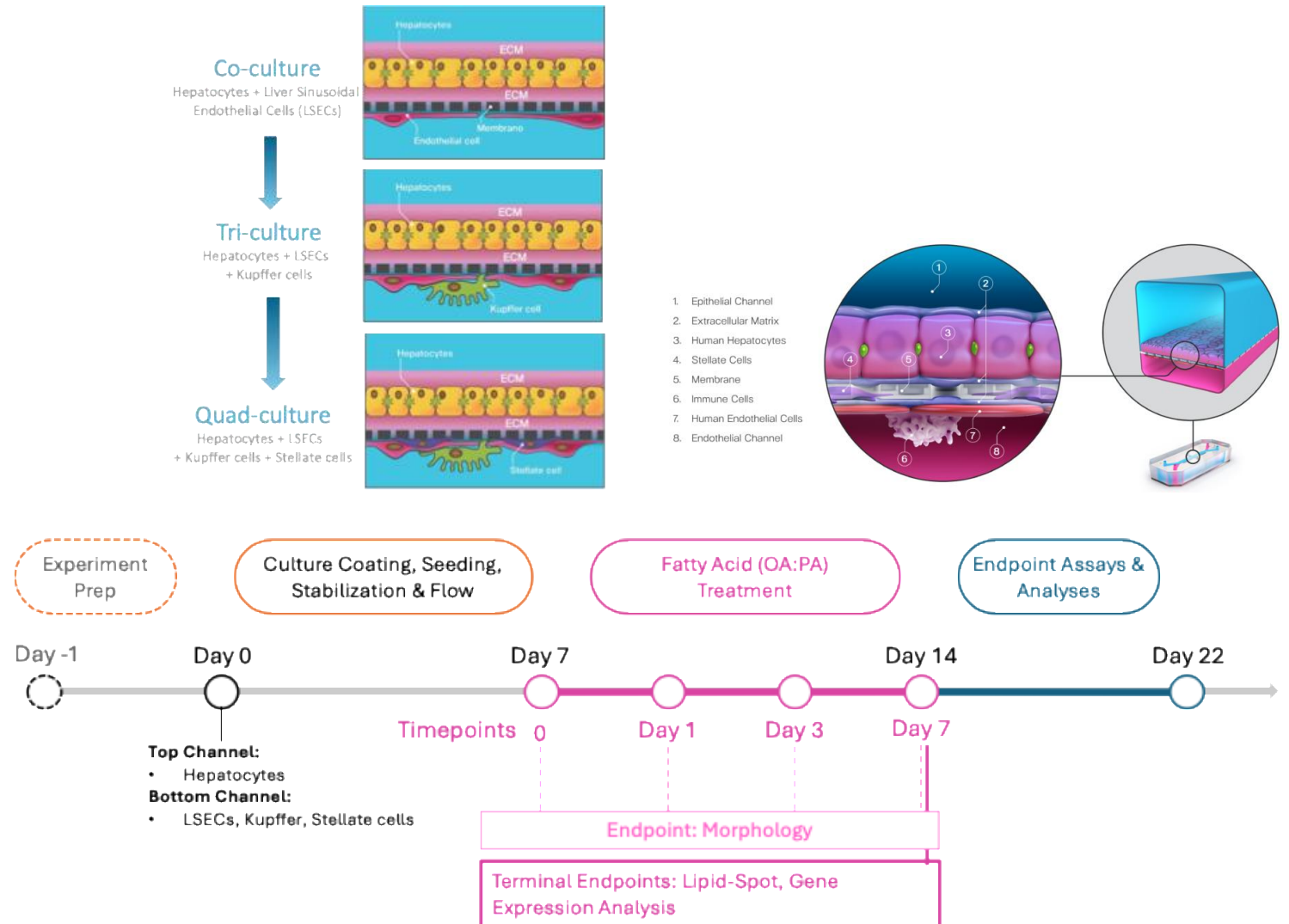
What tools can be used to study these mechanisms?

Human Liver-on-Chip Model (MASLD in a dish)
ExoMap1 mouse model to study EV trafficking.



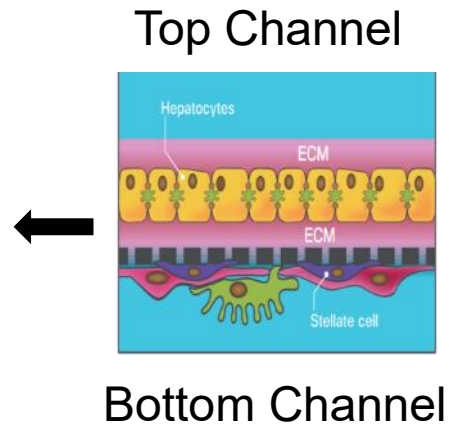
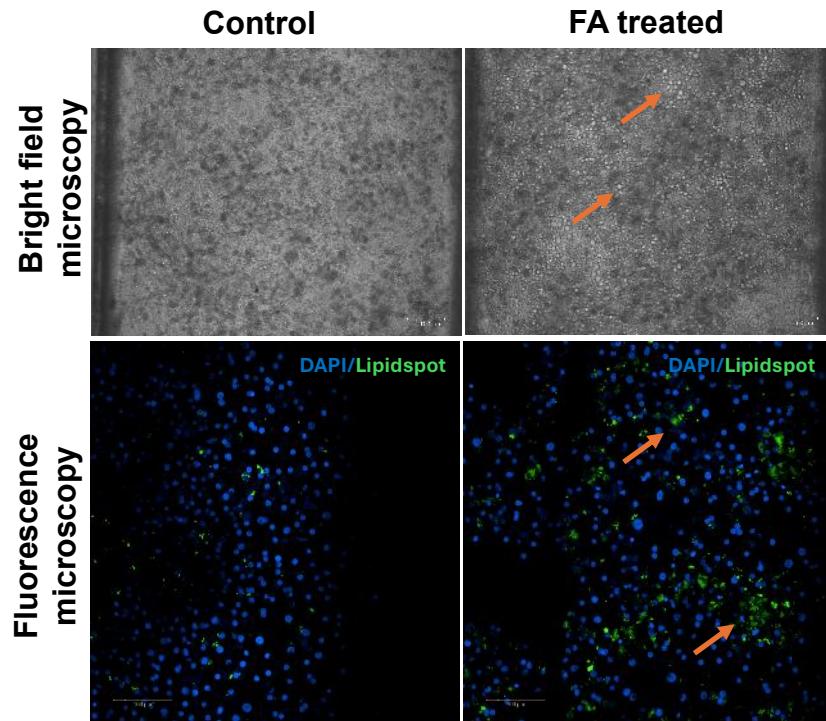
Emeli Chatterjee, PhD
Instructor, MGH/Harvard

Human Liver-on-Chip Model to study MASLD

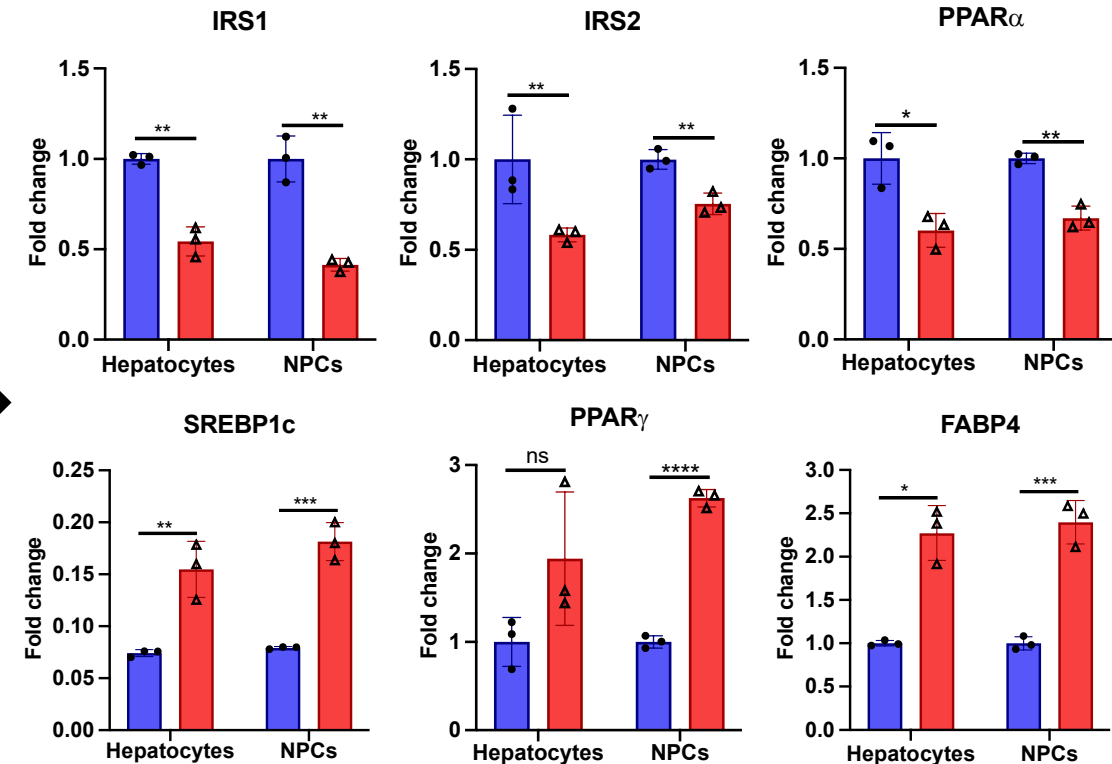


LOC-MASLD phenocopies human MASLD phenotypes

Increased lipid droplet accumulation



Gene expression analysis for MASLD on LOC model

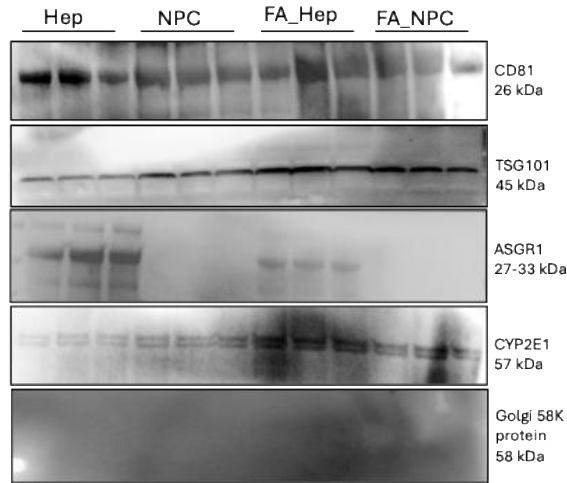


Control LOC
FA treated LOC

MASLD-induced changes in hepatocyte EVs

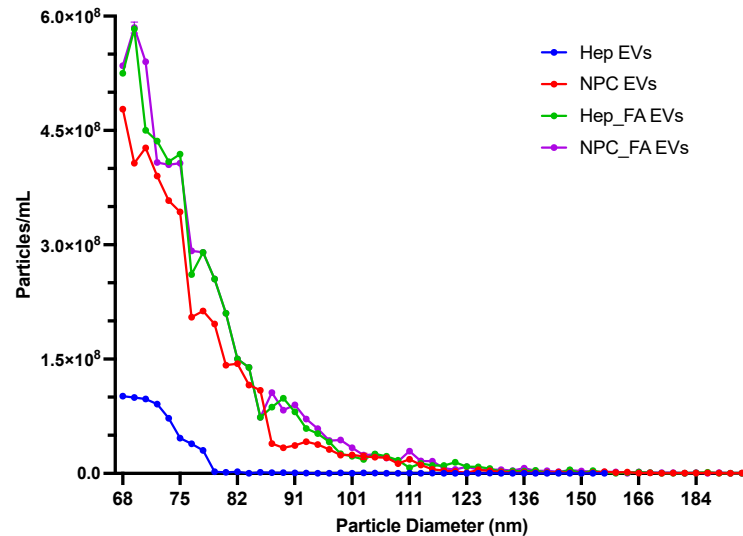
A.

Immunoblotting



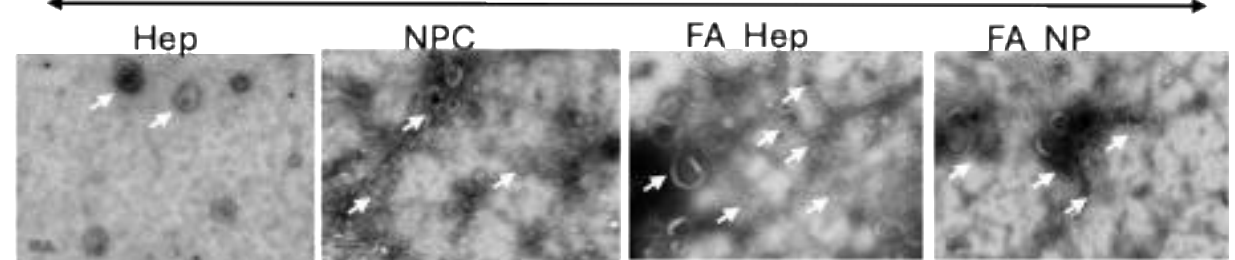
Microfluidic RPS

B.



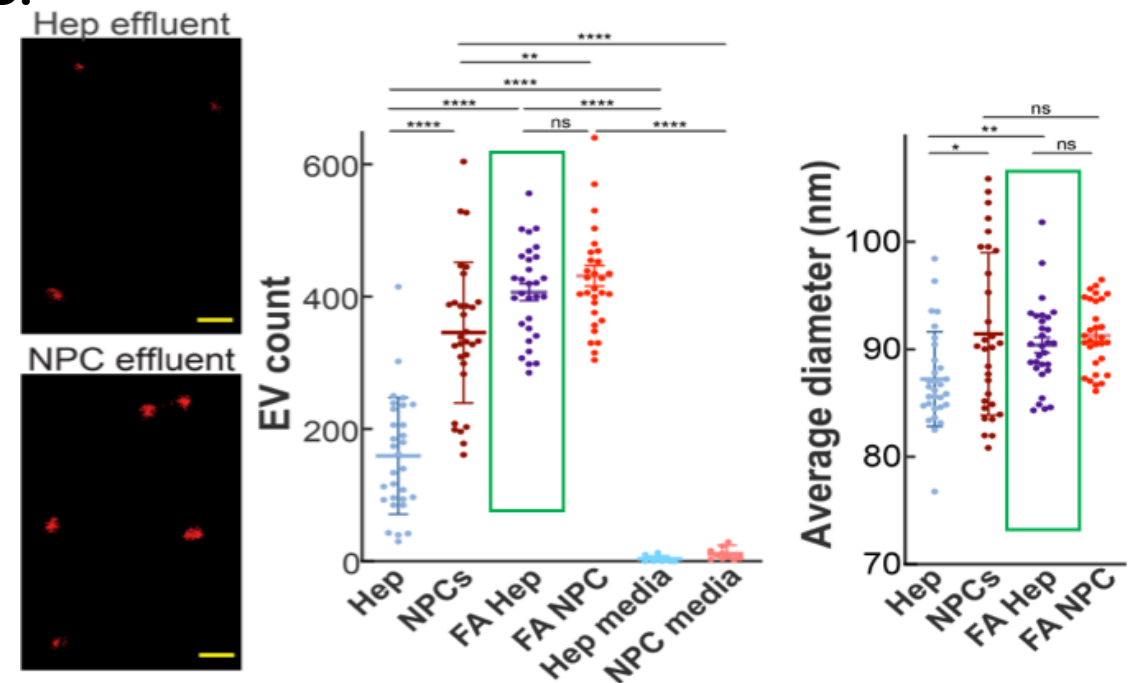
C.

TEM of LOC effluent derived EVs



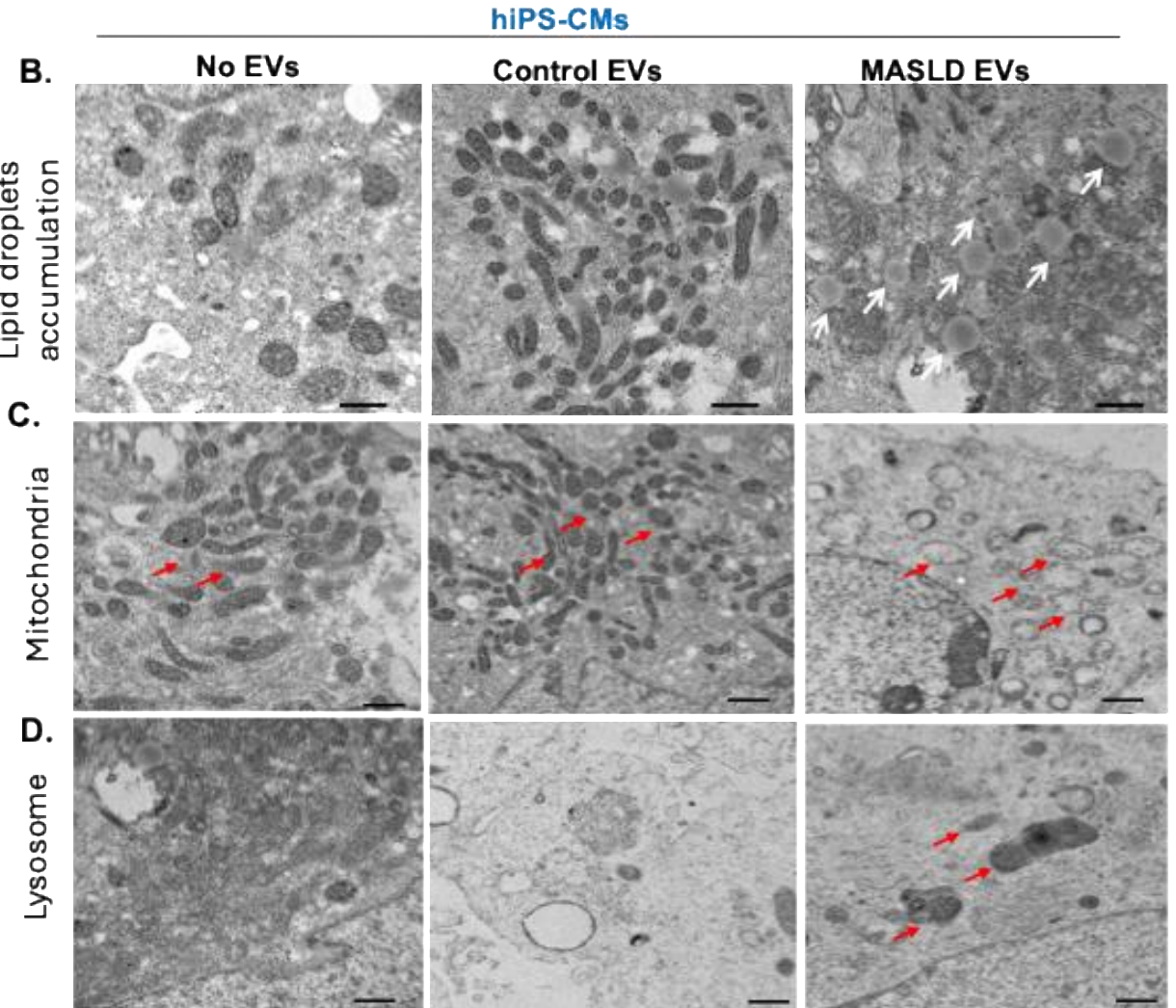
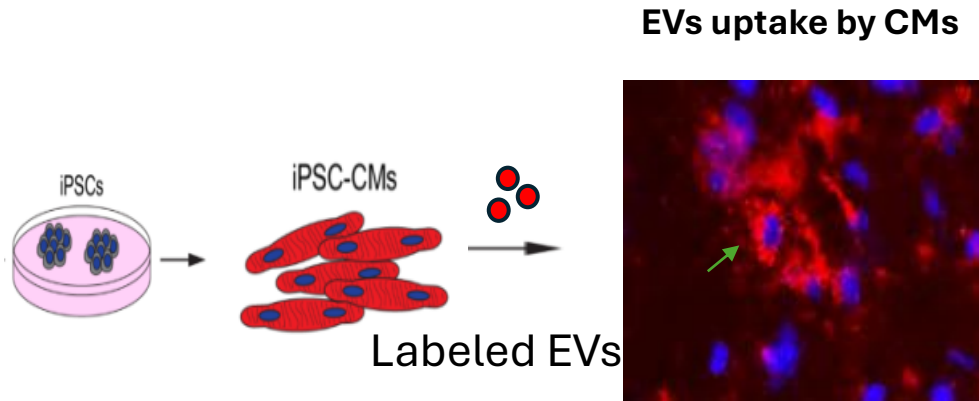
D.

Single EV Analysis

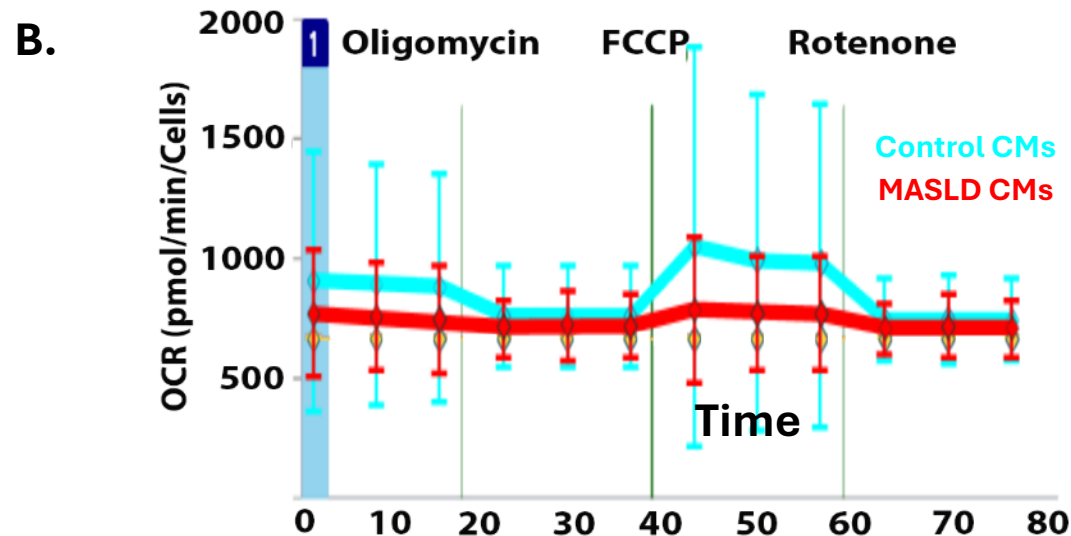
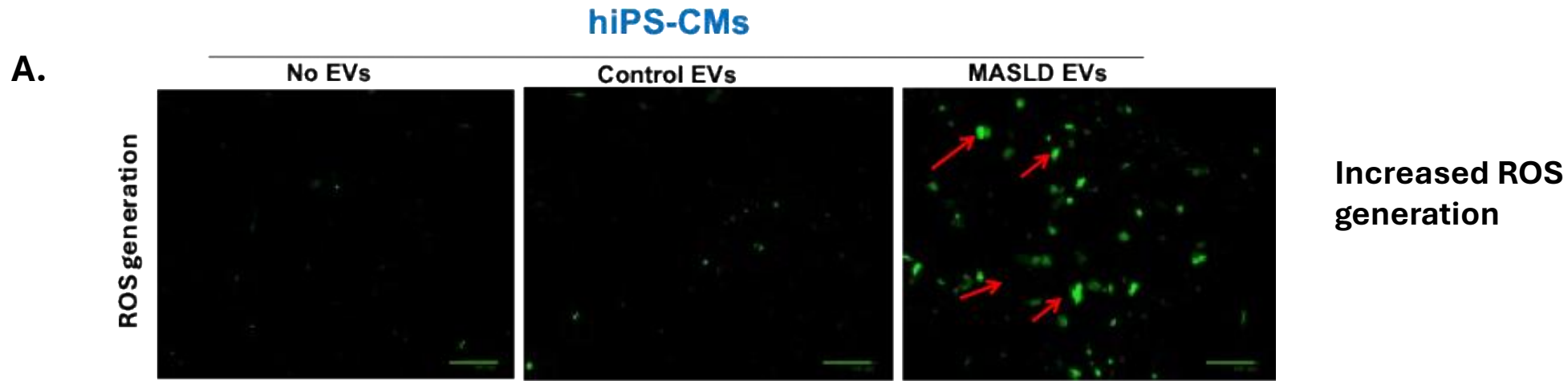


MASLD EVs are taken up by CMs and cause profound structural changes in mitochondria

A.



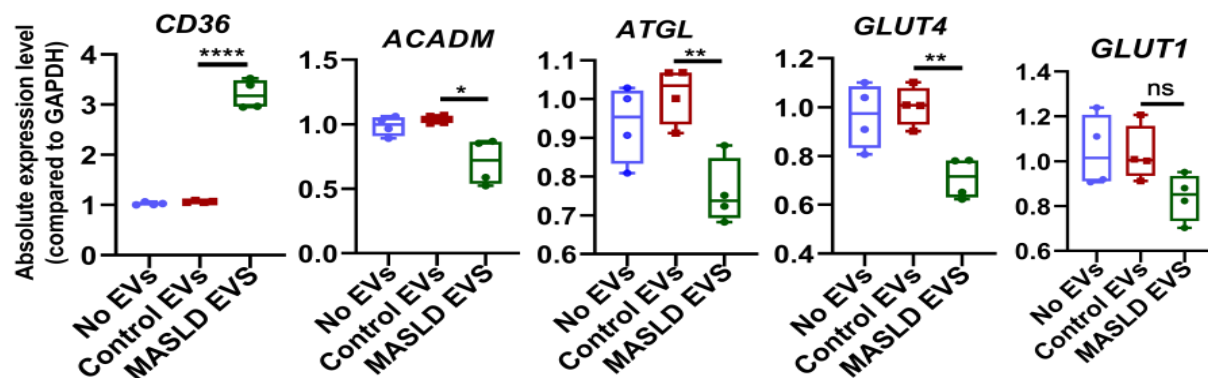
Increased ROS and mitochondrial respiratory depression in MASLD-EV exposed CMs



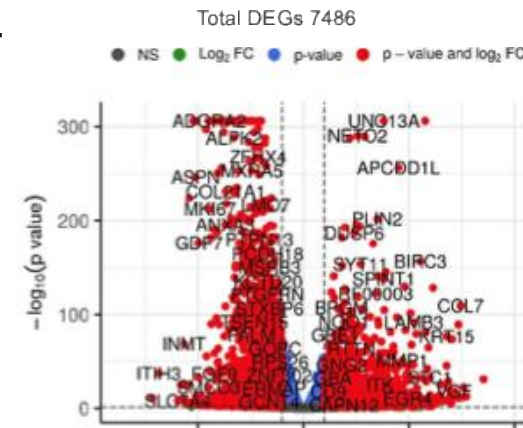
- Impaired Glycolysis
- Blunted maximal respiratory capacity
- Unchanged non-mitochondrial oxygen consumption

Transcriptional remodeling in MASLD-EV exposed cardiomyocytes

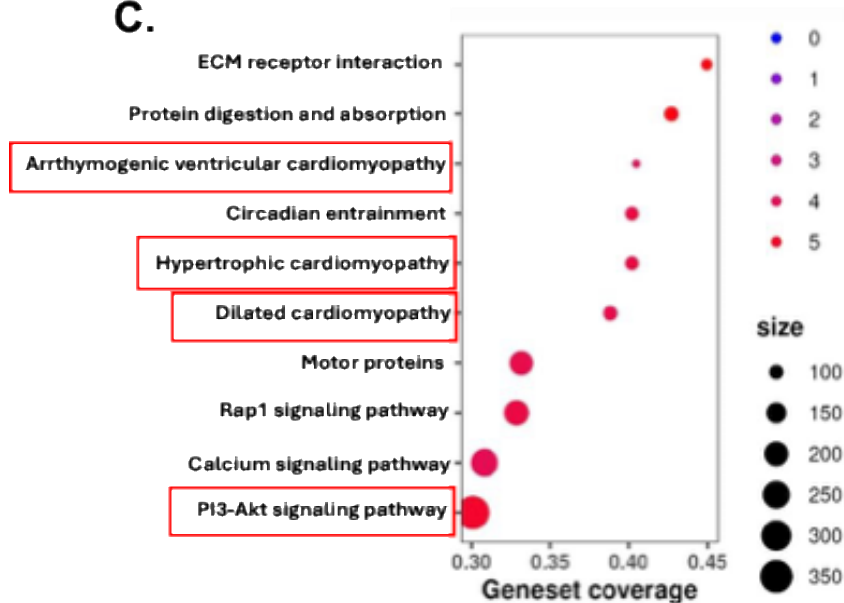
A



B.



C.

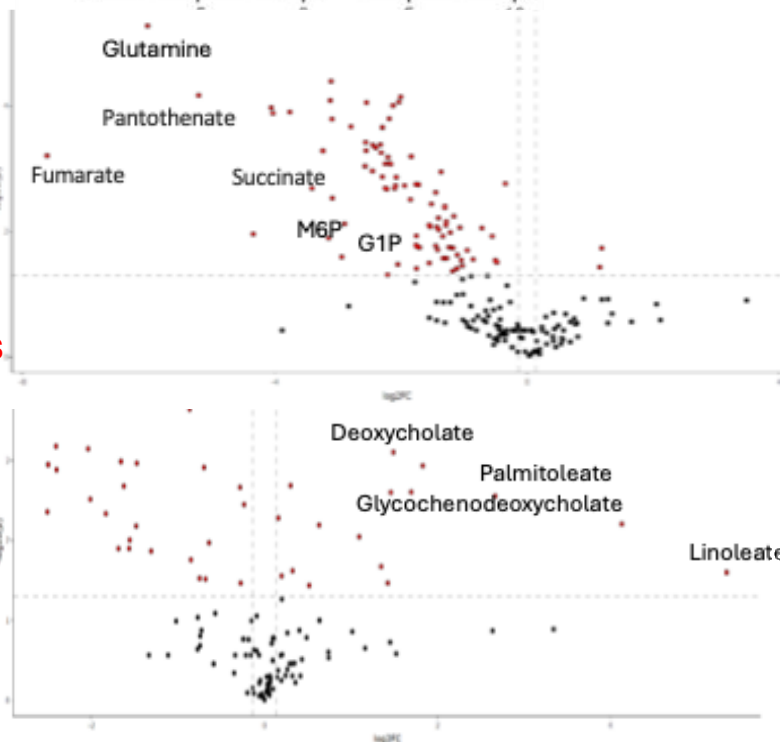


iPSC-CMs

Dysregulated FAO/Glycolysis

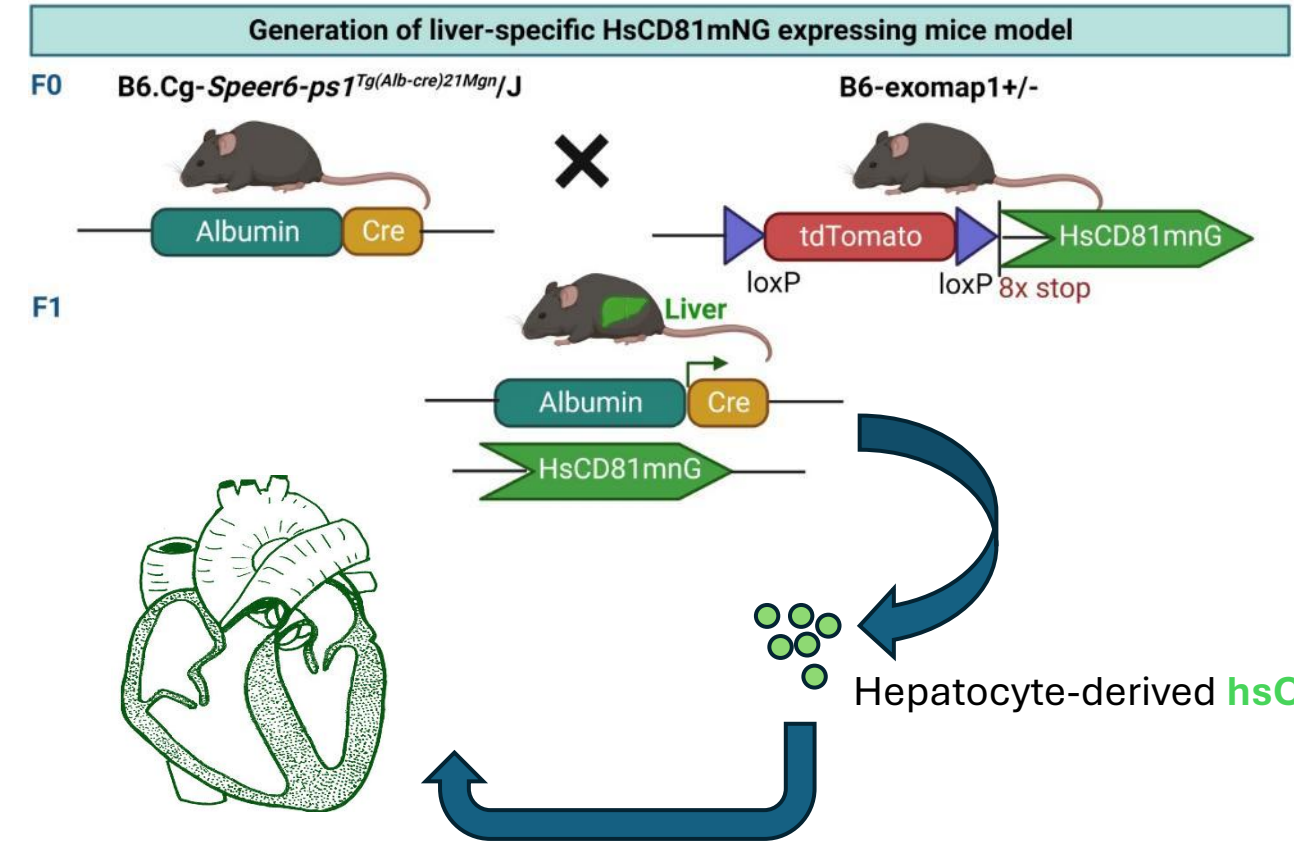
iPSC-CM Media

D

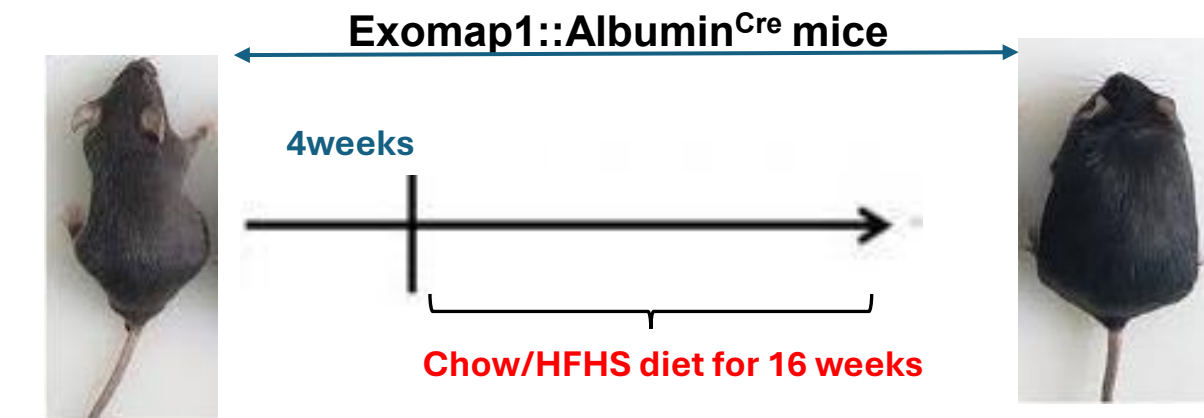


A transgenic mouse model to study EV-mediated interorgan cross-talk

A.



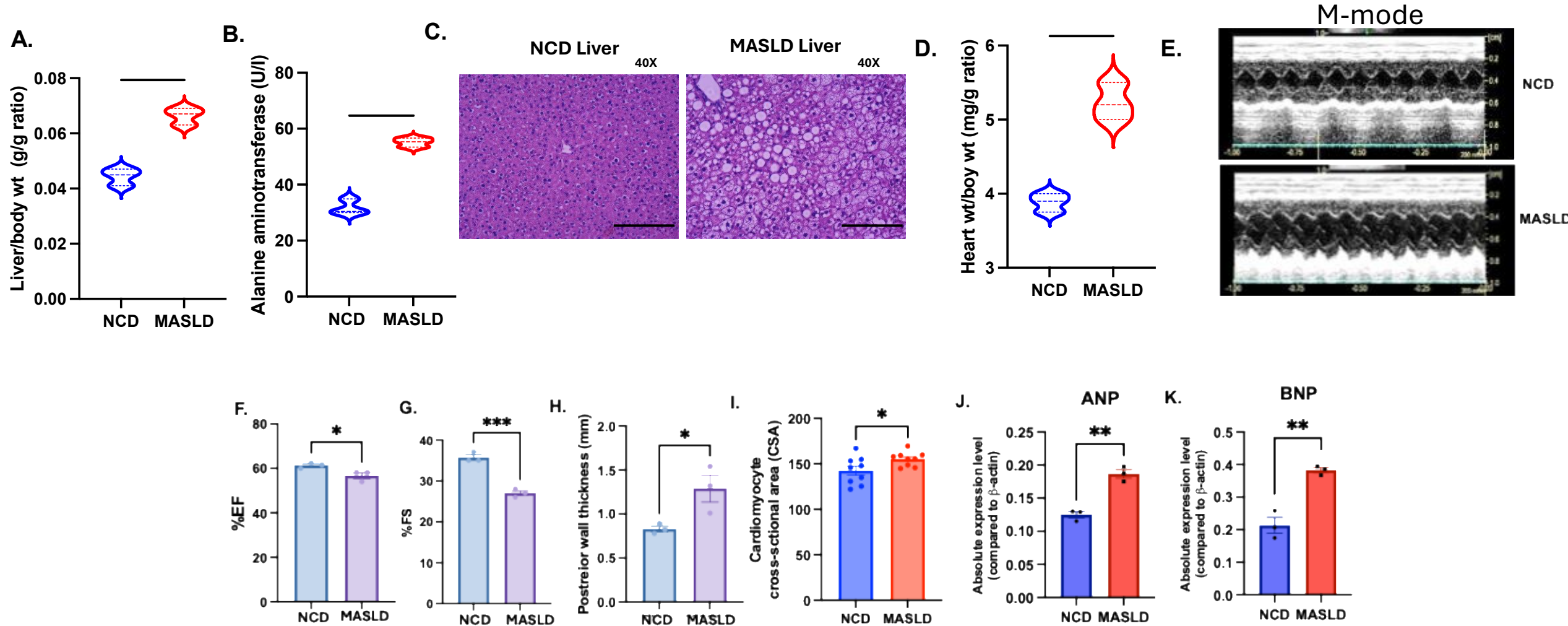
B.



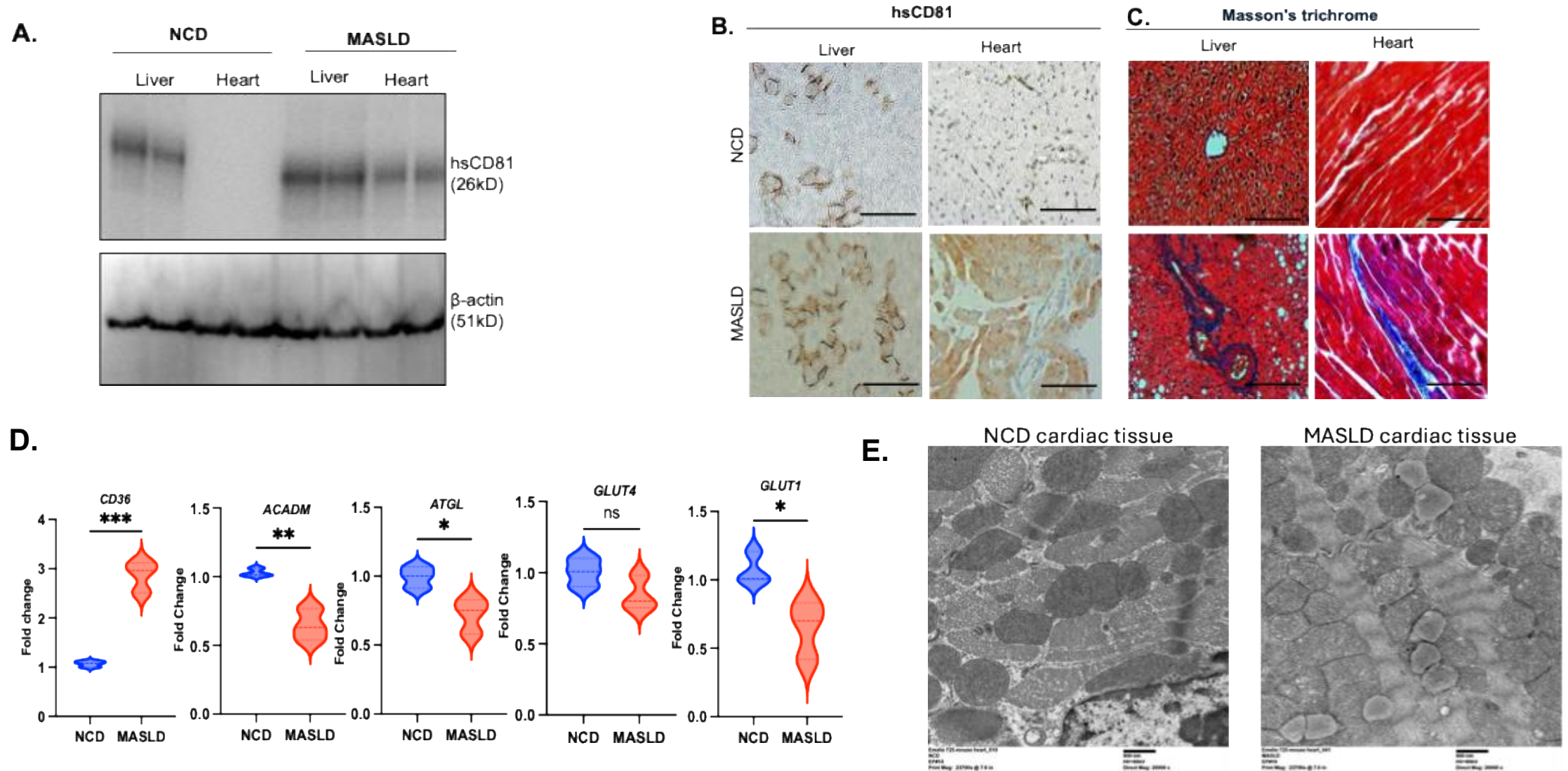
Transfer of hepatocyte EVs containing hsCD81/mNeon and functional Cre marks recipient heart cells

(Fordjour, F.K., Abuelreich, S., Hong, X., Chatterjee, E., et al. 2023)

HFHS Mouse Model develops MASLD features and cardiac hypertrophy with cardiac dysfunction

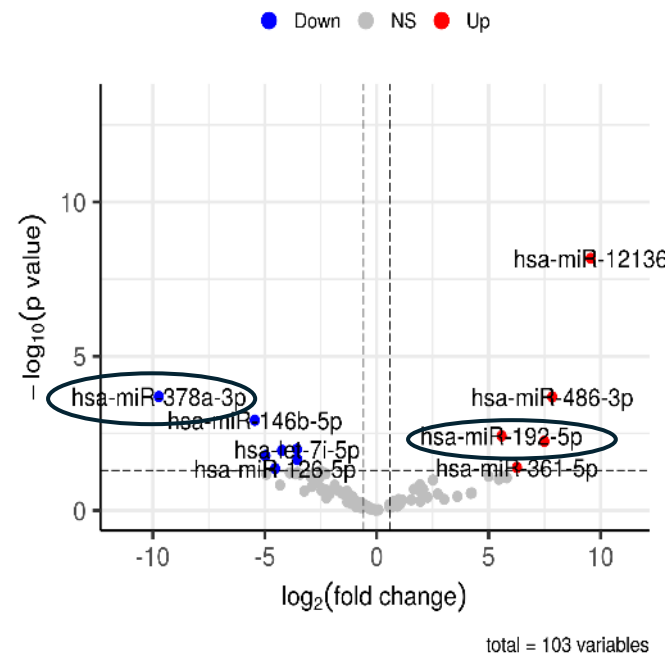


Liver EVs traffic to the heart in MASLD and phenocopy transcriptional changes seen in human CMs



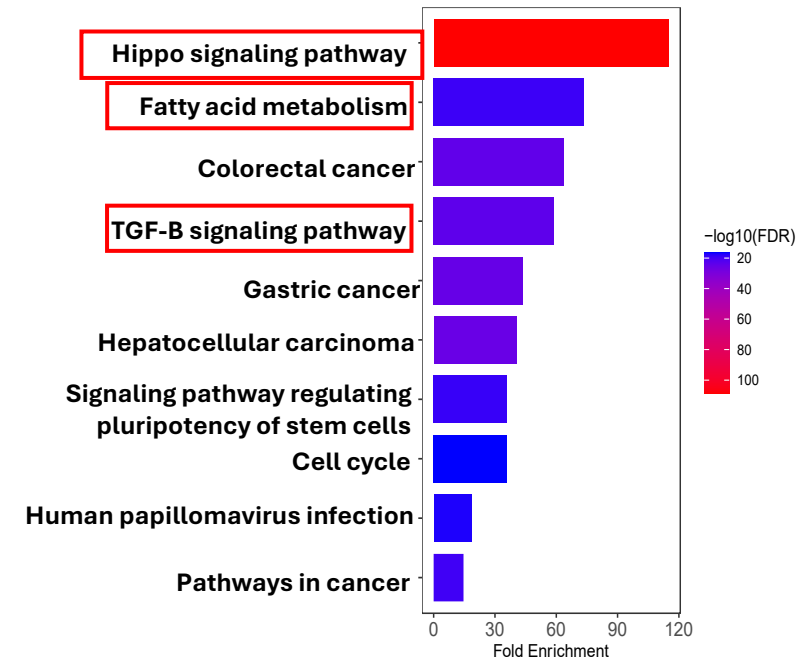
Differentially expressed miRNAs in MASLD EVs regulate transcriptional networks dysregulated in MASLD-HF

A. Small RNA content in Control vs MASLD EVs

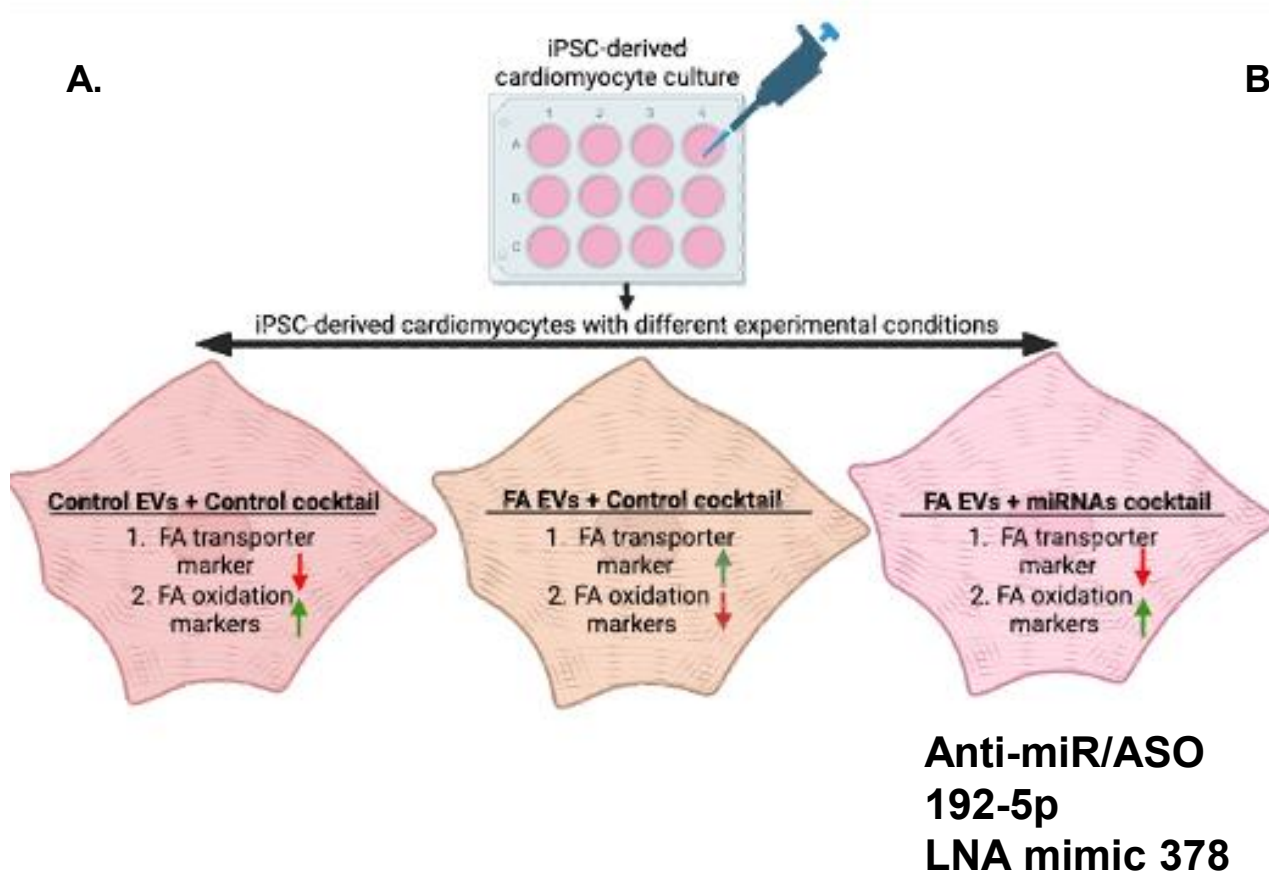


B.

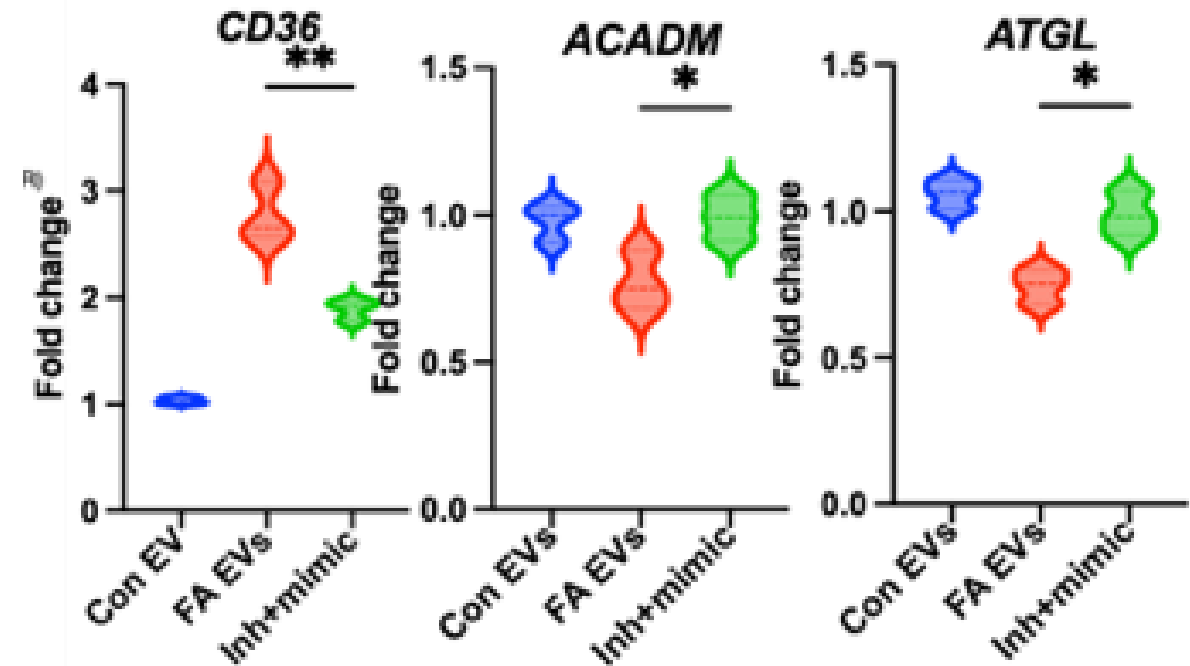
Top 10 genesets



Targeting MASLD-EV miRNAs in CMs reverses transcriptional dysregulation



B.



Summary: the MASLD- cardiac connection



MASLD is associated with higher risk of incident HF and other CVD conditions.



Hepatocyte-derived EVs in a MASLD model are increased and have distinct biophysical and cargo miRNAs.



MASLD liver EVs induce profound metabolic dysregulation, mitochondrial dysregulation and cardiac hypertrophy in cardiomyocytes.



Liver EVs target the heart in MASLD but not at baseline.



MiRNAs in MASLD-liver EVs may be key mediators of pathogenesis.

Contributors and Collaborators

- **Das Lab**

- **Emeli Chatterjee**
- **Priyanka Gokulnath**
- **Michail Spanos**
- **Lingfei Sun**
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- **Wora Limipitikul**
- **Nedyalka Valkov**
- **Rodos Rodosthenous**
- **Francois Cherbonneau**

- **Vanderbilt**

- **Ravi Shah**
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- **Michael Betti**
- **Quanhu Sheng**

- **NYU**

- **Mike Pacold**

- **ERCC**

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- **Tijana Talisman (COH)**
- **Elizabeth Hutchins**
- **Bessie Meechovet**
- **Louise Laurent (UCSD)**

**Funding: NIH Common Fund
(UH3 TR002878), U01
HL126497, AHA SFRN for DM,
NHLBI R35 150807, RO1 150401
NIDDK R01DK133847**

