

Drug screening and efficacy tests in 3D human liver MASH spheroids

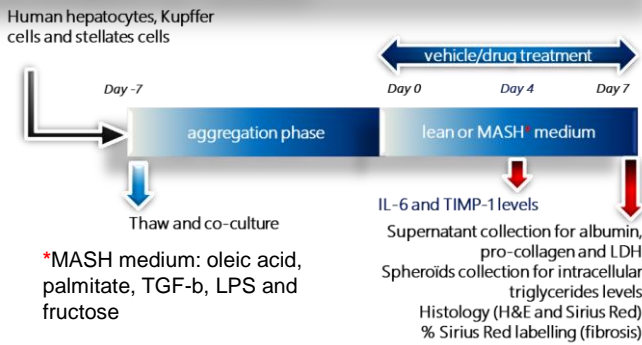
✓ A 3D human liver spheroids system with MASH to quickly confirm the efficacy of our drugs targeting steatosis, inflammation and fibrosis.

Key benefits

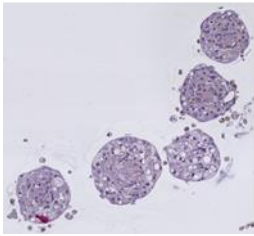
A co-culture system of human hepatocytes, human Kupffer cells and human stellate cells in lean and MASH conditions for rapidly testing your compounds targeting hepatic steatosis, inflammation and fibrosis.

→ Get your study report ~1 month after the experimental phase

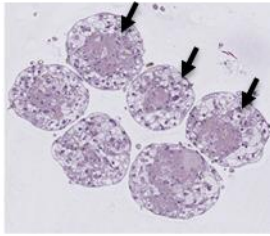
EXPERIMENTAL DESIGN



Lean spheroids

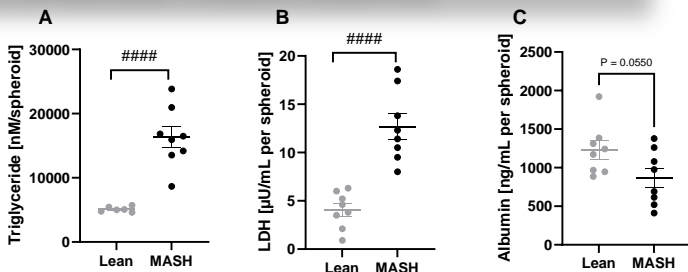


MASH spheroids

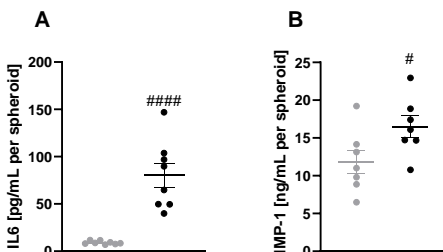


Hematoxylin and Eosin staining confirms MASH phenotype by showing hepatocyte ballooning with displaced nuclei (black arrows)

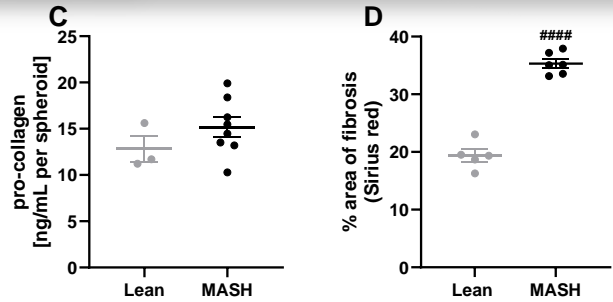
3D SPHEROIDS CHARACTERISTICS



Compared to lean control, MASH spheroids show hepatic steatosis with greater triglycerides content (panel A), leading to lipotoxicity and cell damage as shown by the higher LDH levels (panel B), and dysfunctional hepatocytes with lower albumin secretion (panel C). #### p < 0.001 vs. lean.

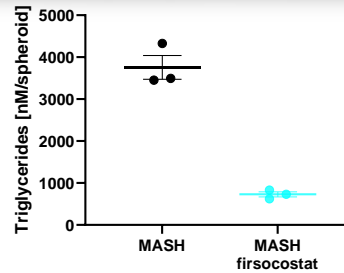


MASH spheroids shows strong increase in pro-inflammatory cytokine IL-6 secretion (panel A) and significantly higher levels of the pro-fibrotic marker (B) TIMP-1 on day 4 of MASH culture. #p < 0.05 and ####p < 0.0001 vs. lean.

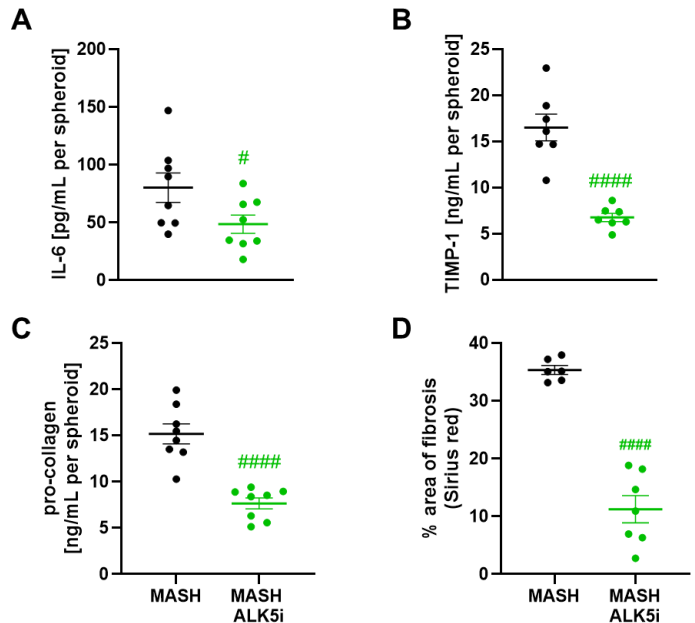


A trend towards higher pro-collagen levels (panel C) and a strongly increased % area of fibrosis as measured by Sirius Red staining (panel D) confirm the evident fibrotic phenotype of MASH human spheroids. #### p < 0.0001 versus lean.

MASH SPHEROIDS PHARMACOLOGICAL VALIDATION



Left panel: Firsocostat, an acetyl-coenzyme A carboxylase (ACC) inhibitor reduces intracellular triglycerides levels in MASH spheroids.



Reduction of inflammation and fibrosis in MASH human spheroids under anti-fibrotic treatment with an ALK5 inhibitor (ALK5i). Compared to MASH, ALK5i significantly reduced secretion of pro-inflammatory cytokine IL-6 (panel A) and pro-fibrotic marker TIMP-1 (panel B) on day 4, pro-collagen levels (panel C) and % area of fibrosis as measured by Sirius Red staining (panel D). #p < 0.05 and ####p < 0.0001 vs. MASH.