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Summary

IMPAIRMENT OF REGENERATIVE AND METABOLIC PATHWAYS IN DUODENAL ORGANOIDS FROM PATIENTS WITH MASLD-CIRRHOSIS

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Duodenal organoids from patients with MASLD-cirrhosis demonstrate profound energetic, mitochondrial, and antioxidant impairments compared to non-fibrotic MASLD.

KEY POINTS

- Organoids from MASLD-cirrhosis patients showed approximately 600 dysregulated transcripts involving stem cell regeneration, pluripotency, mitochondrial metabolism, and hypoxia pathways.
- Energetic status was impaired in both differentiated and undifferentiated cirrhotic organoids, with lower triphosphate sum, ATP/ADP ratio, and NAD+/NADH ratio indicating declined phosphorylating capacity and mitochondrial derangement.
- Cirrhotic organoids exhibited reduced levels of glutathione, NADPH, and UDP-glucuronic acid, reflecting impaired antioxidant defense and xenobiotic response.
- The study characterizes intestinal epithelial dysfunction in MASLD-cirrhosis as a cluster of regenerative and metabolic disturbances, providing an in vitro organoid model for gut-liver axis research.

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