biomarkers to classify disease phenotypes relevant to the onset of diabetic steatosis followed by progression towards liver inflammation.

Methods We compared miR-192-3p level in mice given HFD (high-fat diet), HFFD (high-fat fructose diet), and MCD (methionine-choline deficient diet) diets. Histopathological lesions were analyzed at critical stages to correlate the miRNA expression. In obese individuals diagnosed with DM or not, we examined the miR-192-3p level by droplet digital PCR and characterized serum whole transcriptomes with SEQuoia Complete Stranded RNA Library kits.

Results Along with our reported loss of the overlooked star strand miR-192-3p in db/db mice, we found a high circulating level of miR-192-3p in different diets-induced animals, indicating a heightened inflammatory response in the liver, especially in those given HFFD and MCD diets. Since circulating miR-192-3p surges only in HFFD under an insulin-resistant state but not manifested at all in HFD, its circulating level shall reflect the extent of runaway glycerolipid metabolism. Indeed, we observed a similar expression pattern in serum miR-192-3p for obese individuals (BMI>34), where the miRNA can only be detected in individuals diagnosed with DM. Our transcriptomic analysis identified that PI3K-Akt signaling, FoxO signaling and TGF β signaling pathways were enriched in the hepatocytes with miR-192-3p overexpression. The top differential circulating non-coding transcripts between those individuals with or without diabetes belonged to the ribosomal pathway under the modulating actions of Akt, suggesting the use of these transcripts for a better account of diabetic phenotype.

Conclusions Circulating levels of miR-192-3p and transcripts along its regulated Akt pathway account for visceral obesity and reflect prognostic outcomes to the progression of diabetes. We hereby advocate miR-192-3p as a functional glycerolipid regulator for steatosis in the diabetic liver which offers know-how for better disease staging and treatment regimes.

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SARS-COV-2 PRODUCTIVELY INFECTS HUMAN LIVER AND BILIARY ORGANIDS

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Background SARS-CoV-2 has caused the COVID-19 pandemic, 14-53% with COVID-19 developed hepatic dysfunction. More data is required to ascertain the pattern of liver injury in patients with COVID-19. Here we report the use of human liver and biliary organoids as a tool to investigate the SARS-CoV-2 infection and virus-induced tissue damage ex vivo at the cellular and molecular levels.

Methods Immunofluorescence staining and RT-qPCR was performed to examine the susceptibility and replication of human liver and biliary organoids to SARS-CoV-2. Transmission electron microscopy was performed to investigate the ultrastructure of SARS-CoV-2 infected biliary organoid. The mRNA sequence analysis was performed to determine gene expression changes induced by SARS-CoV-2-infection of biliary organoids.

Results Immunofluorescence staining showed that SARS-CoV-2 spike (S) glycoprotein protein was readily detected in patchy areas of the human liver and biliary organoids, whereas no signal was found in uninfected control. RT-qPCR showed that the SARS-CoV-2 genomic RNAs revealed a dramatic increase of viral load in organoids at 24 h post-infection (MOI=1) and it can remain stable 96 hours in the liver organoids and 48 hours in biliary organoids. Unsupervised transmission electron microscopy (TEM) showed that viral particles occurred in the lumen of the organoid, at the basolateral and apical side of the organoid, even in membrane-bound vesicles. Additionally, RNA-seq revealed early cell response to virus infection, including the well-known upregulation of chemokines and inflammatory cytokines.

Conclusions Therefore, the hepatocytes and bile duct cells have effectively been infected by COVID-19, and human liver and biliary organoids can serve as a pathophysiological model to investigate the underlying mechanism of SARS-CoV-2 infection.

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TYPE 2 RESISTANT STARCH IMPROVES LIVER STEATOSIS INDUCED BY HIGH-FAT DIET RELATING TO GUT MICROBIOTA REGULATION AND CONCENTRATION OF PROPIONIC ACID IN PORTAL VEIN BLOOD IN C57BL/6J MICE

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Background Resistant starch (RS) was approved to regulate glucose and lipid metabolism and gut microbiota in vivo. Our aim was to explore the effect and mechanism of type 2 resistant starch (RS2) on NAFLD mice.

Methods Twenty C57BL/6J male mice were randomly divided into CD group, CD+RS group, HFD group, HFD+RS group (n=5). The NAFLD mouse model was induced by a high-fat diet for 16 weeks. RS2 was supplemented into the diet for 4 weeks subsequently. After treatment, liver steatosis was evaluated by HE staining and NAS score. The serum alanine aminotransferase (ALT), triglyceride (TG), fasting serum glucose (FBG) and insulin resistance index (HOMA-IR) of portal vein blood were detected. The intestinal content of mice was collected for microbiota analysis by 16s amplicon sequencing. The level of short-chain fatty acids (SCFA) in portal vein blood was detected.

Results Compared with HFD group, after RS intervention, the liver steatosis of mice was significantly reduced, and the serum levels of ALT, TG, FBG and HOMA-IR were significantly decreased ($P<0.05$) (IDDF2021-ABS-0207 Figure 1a Type 2 resistant starch improves liver steatosis induced by high-fat diet; Hepatic HE staining of mice) (IDDF2021-ABS-0207 Figure 1b Type 2 resistant starch improves liver steatosis induced by high-fat diet; NAS score of mice (** $P<0.01$)) (IDDF2021-ABS-0207 Figure 1c Type 2 resistant starch improves liver steatosis induced by high-fat diet; Serum levels of ALT in mice (** $P<0.01$) (IDDF2021-ABS-