



Hypertriglyceridemia-modulated gut microbiota promotes lysophosphatidylcholine generation to aggravate acute pancreatitis in a TLR4-dependent manner

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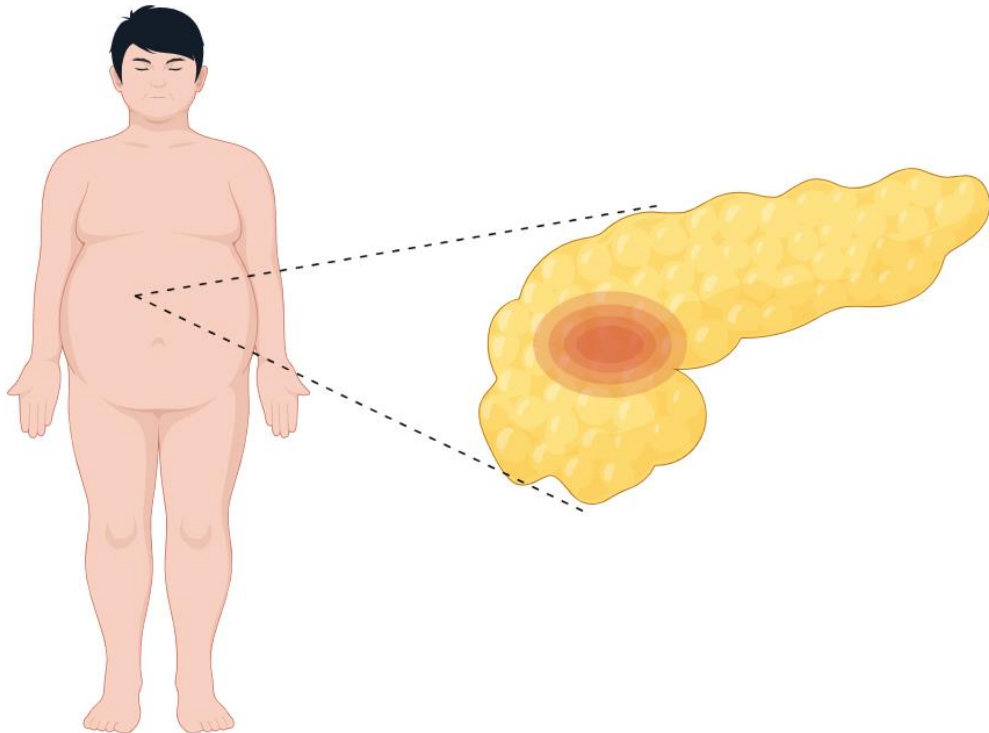


Song, Xiaofan, Lei Qiao, Xina Dou, Jiajing Chang, Xiaonan Zeng, Tianjing Deng, Ge Yang, et al. 2025. Hypertriglyceridemia-Modulated Gut Microbiota Promotes Lysophosphatidylcholine Generation to Aggravate Acute Pancreatitis in a Tlr4-dependent Manner. *iMeta* 4: e70003. <https://doi.org/10.1002/imt2.70003>



Introduction

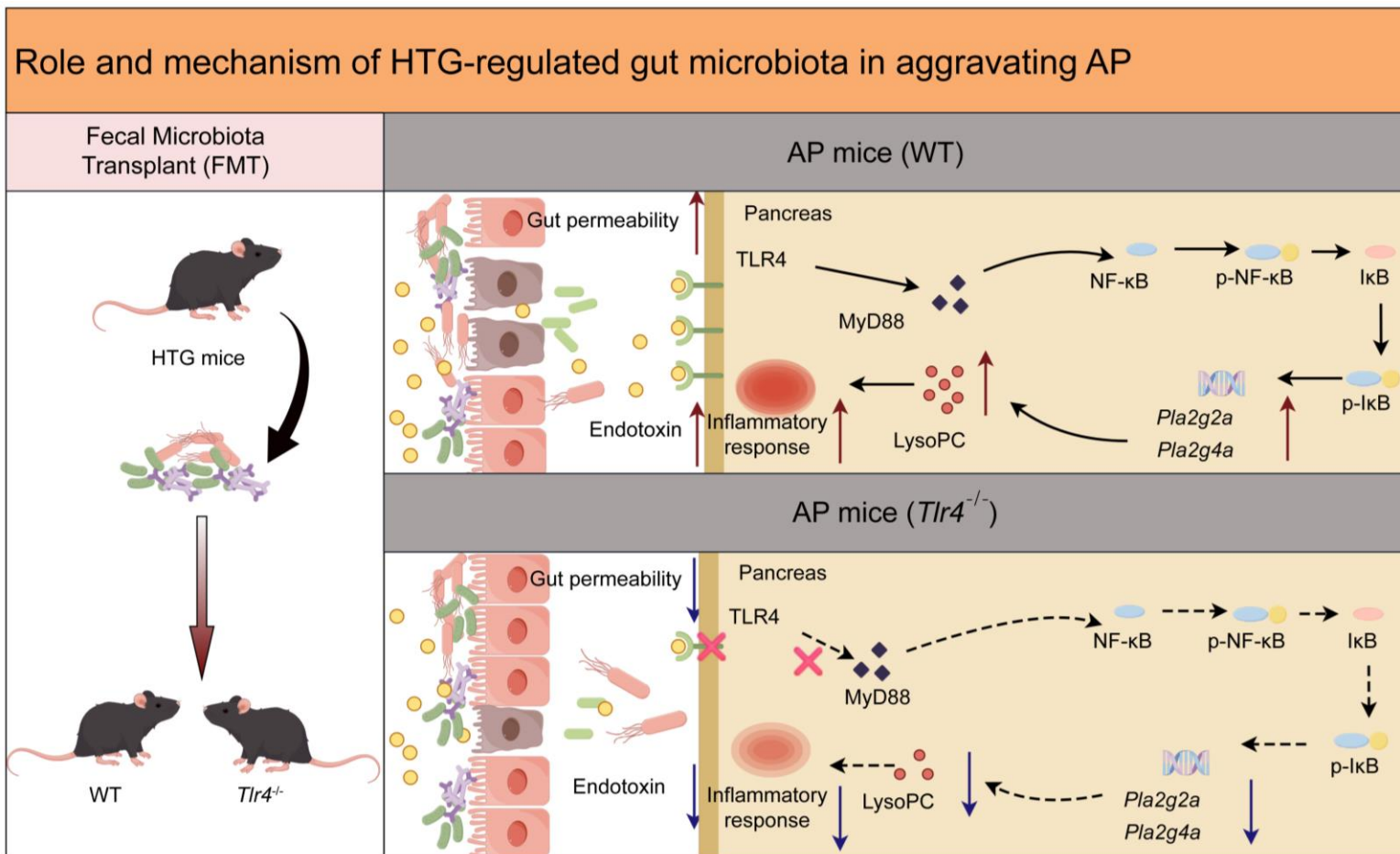
Hypertriglyceridemic acute pancreatitis



- ❑ Acute pancreatitis (AP) is mainly caused by the abnormal activation of pancreatic enzymes secreted by the pancreas, leading to the autodigestion of pancreatic tissue.
- ❑ With the rapid development of the social economy, people's lifestyles have changed, and hypertriglyceridemia (HTG) has become the third leading cause of AP.
- ❑ Patients with HTG - AP are more prone to developing severe conditions, more likely to experience persistent multiple organ failure (lasting > 48 hours), and have a higher mortality rate (36% - 50%).
- ❑ This study aims to start from the gut microbiota and explore the role and mechanism of the interaction between the gut microbiota and the host in the process of HTG exacerbating AP.



Highlights



- ❑ In HTG mice, changes in the composition and function of the gut microbiota lead to a significant increase in endotoxin levels.
- ❑ HTG can further exacerbate the impairment of intestinal barrier function in AP mice, thereby increasing the risk of intestinal bacterial translocation.
- ❑ The gut microbiota regulated by HTG promotes the production of LysoPC in a TLR4 - dependent manner, thus exacerbating AP.



Results

◆ HTG Can Exacerbate Pancreatic Injury and Inflammatory Responses in AP Mice

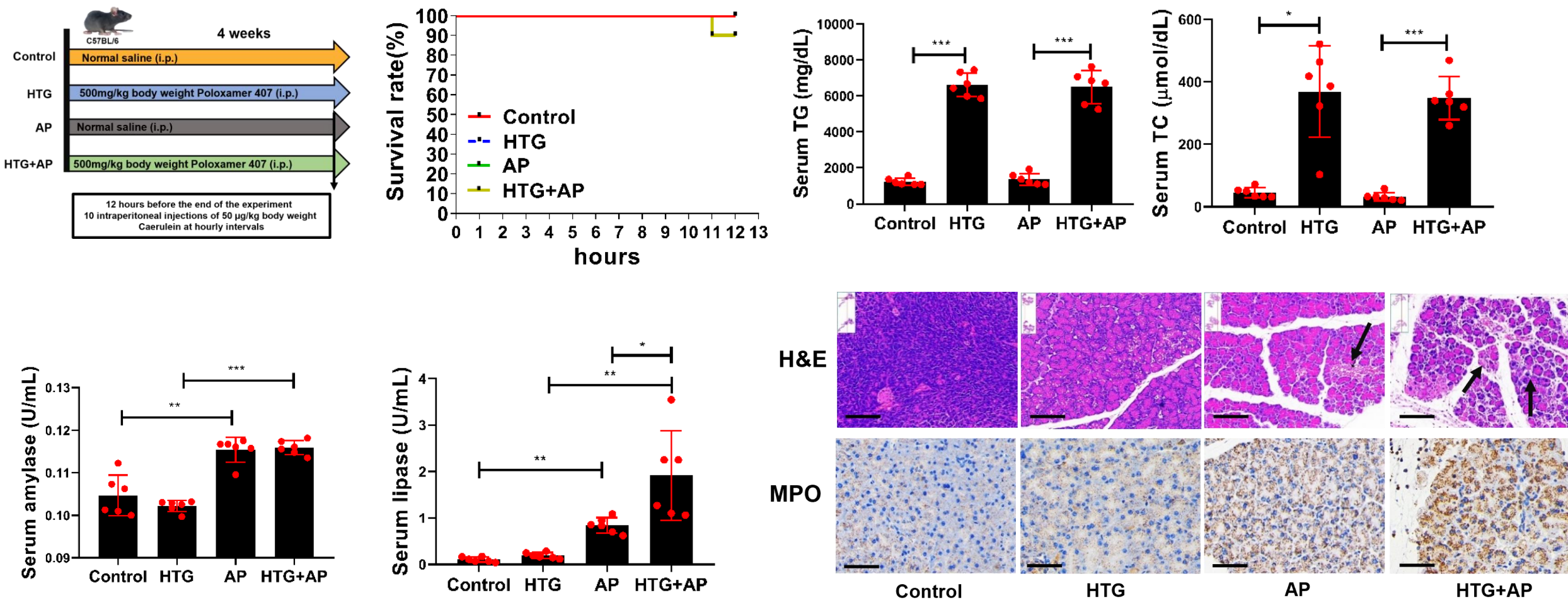


Figure 1. HTG can exacerbate pancreatic injury and inflammatory responses in AP mice



Results

◆ HTG Can Lead to Disorders in the Composition and Function of the Gut Microbiota in Mice

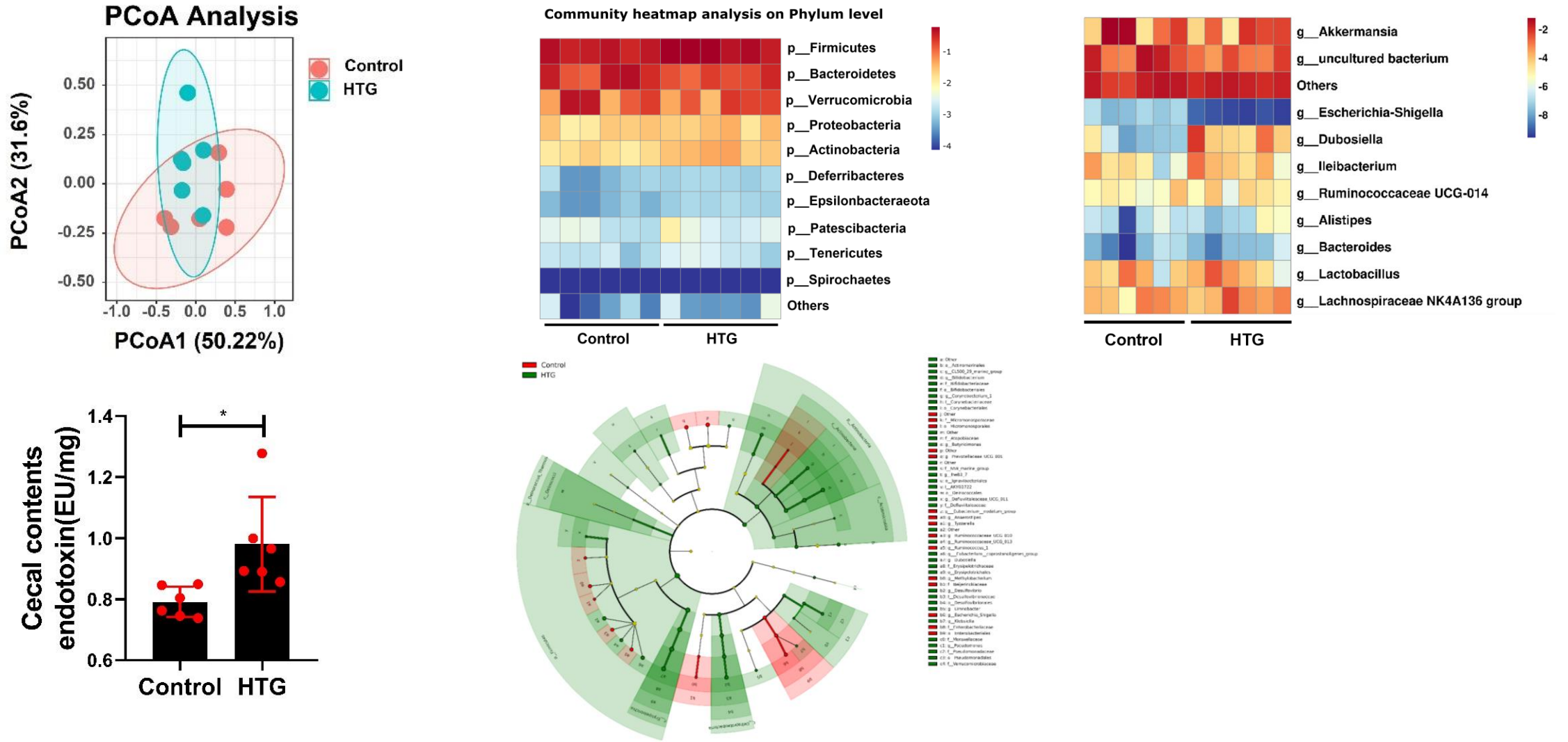


Figure 2. HTG can cause disorders in the composition and function of the gut microbiota in mice

Results

◆ The Involvement of Gut Microbiota in the Process of HTG Aggravating AP

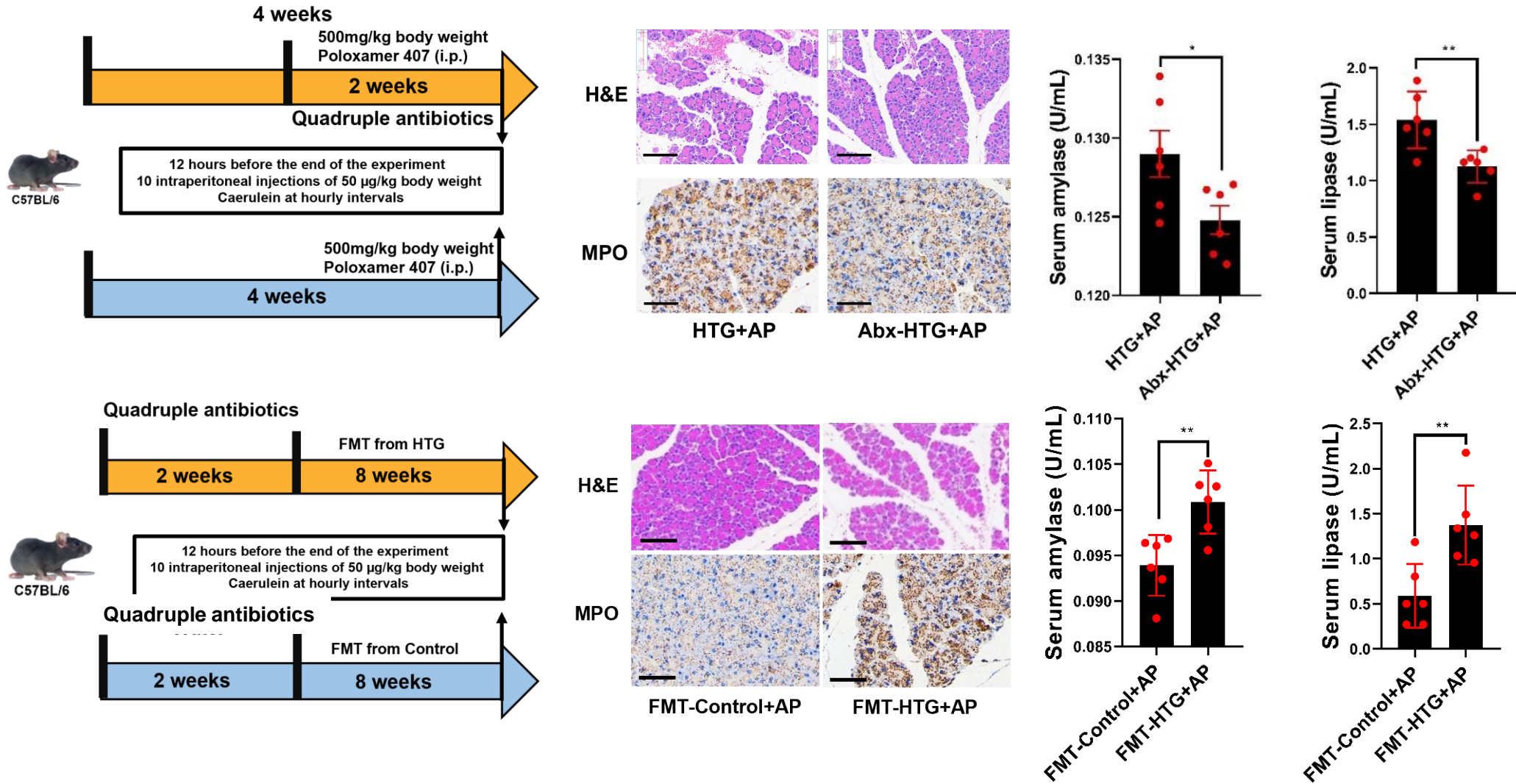


Figure 3. The Involvement of Gut Microbiota in the Process of HTG Aggravating AP



Results

◆ The Gut Microbiota Regulated by HTG: Promoting Glycerophospholipid Metabolism and Lysophosphatidylcholine Production

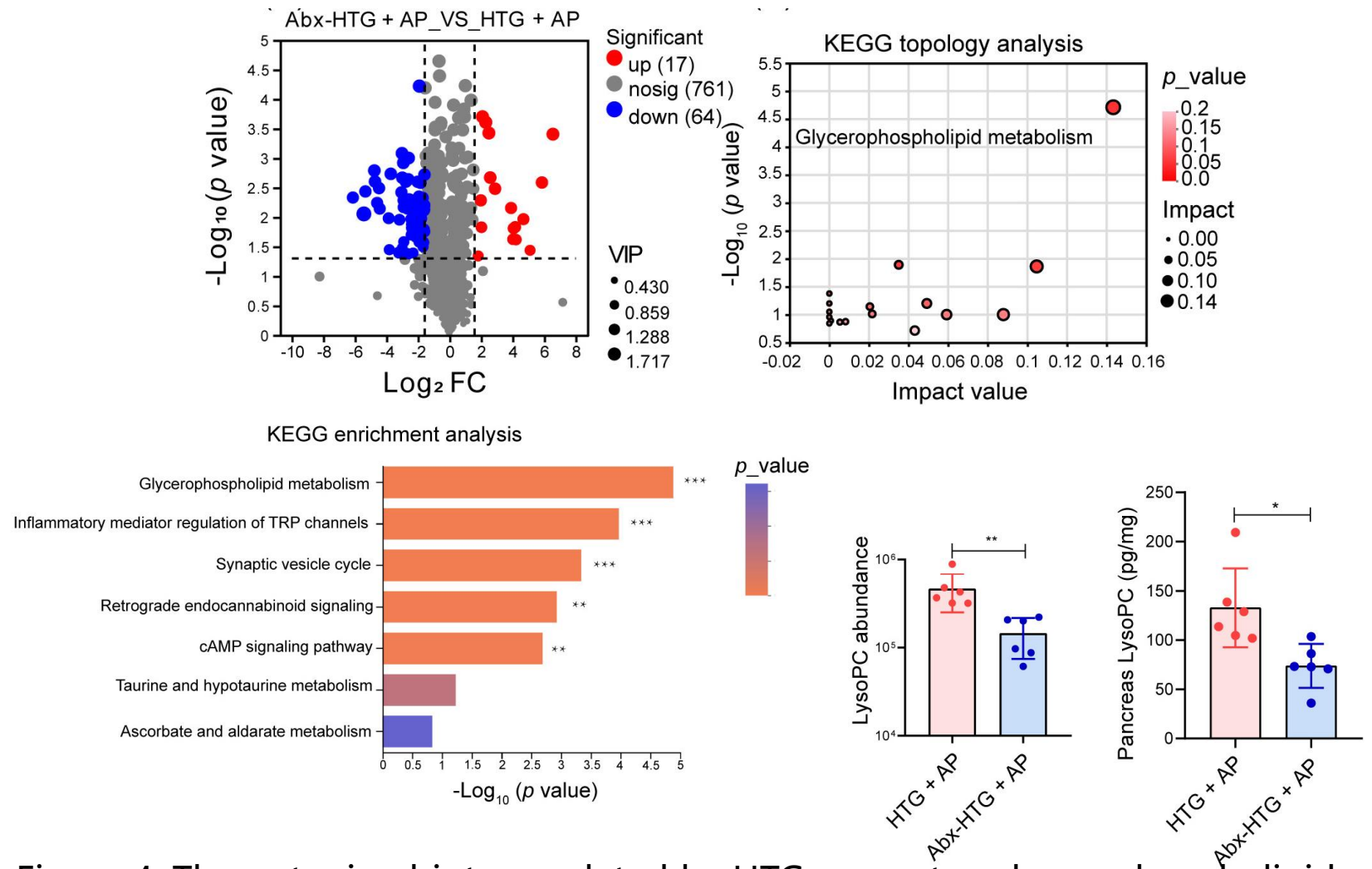


Figure 4. The gut microbiota regulated by HTG promotes glycerophospholipid metabolism and lysophosphatidylcholine production



Results

◆ TLR4 Mediates LysoPC Production in Mouse Primary Pancreatic Acinar Cells

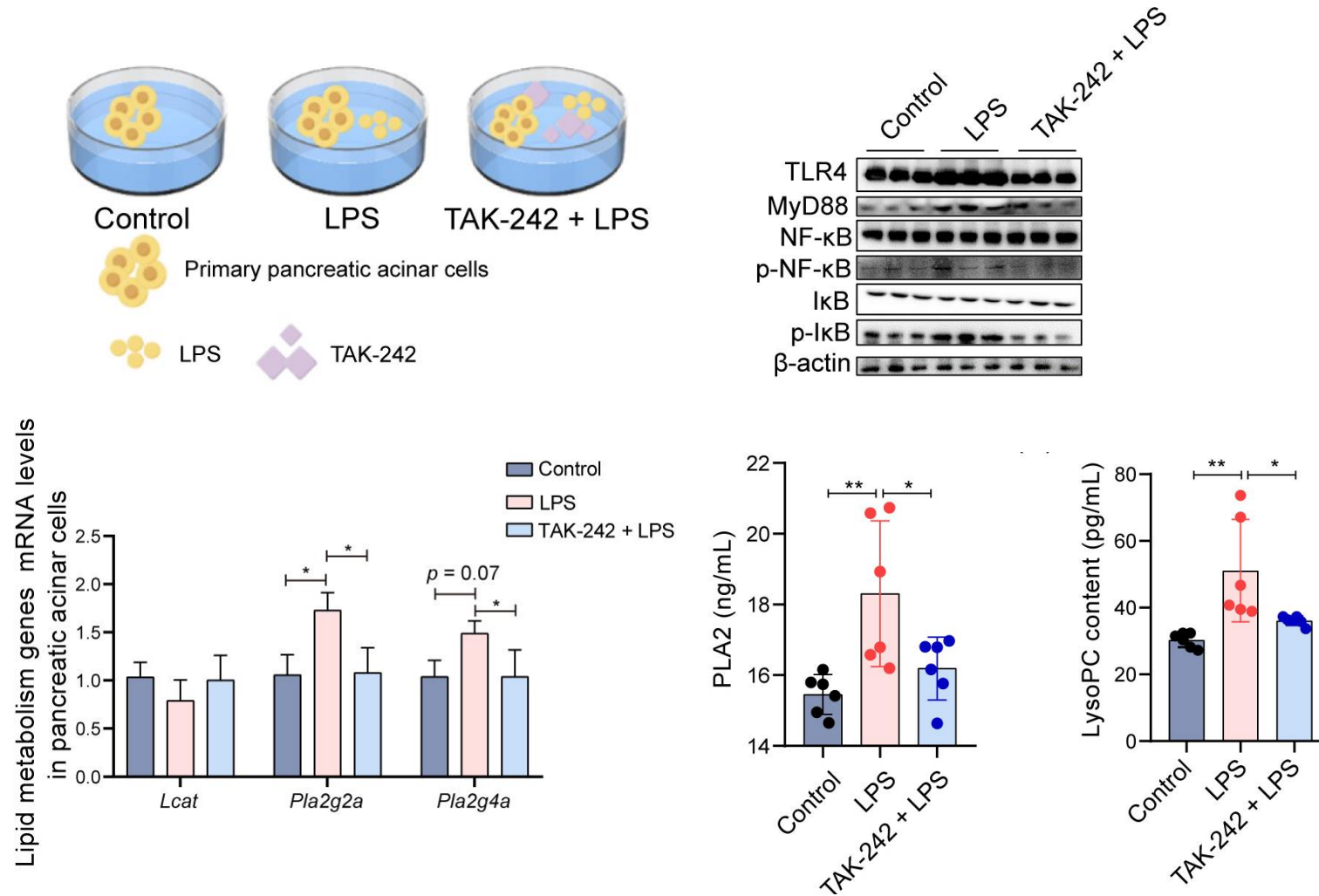


Figure 5. TLR4 Mediates LysoPC Production in Mouse Primary Pancreatic Acinar Cells

Results

◆ HTG - regulated Gut Microbiota Promotes LysoPC Production in a TLR4 - dependent Manner

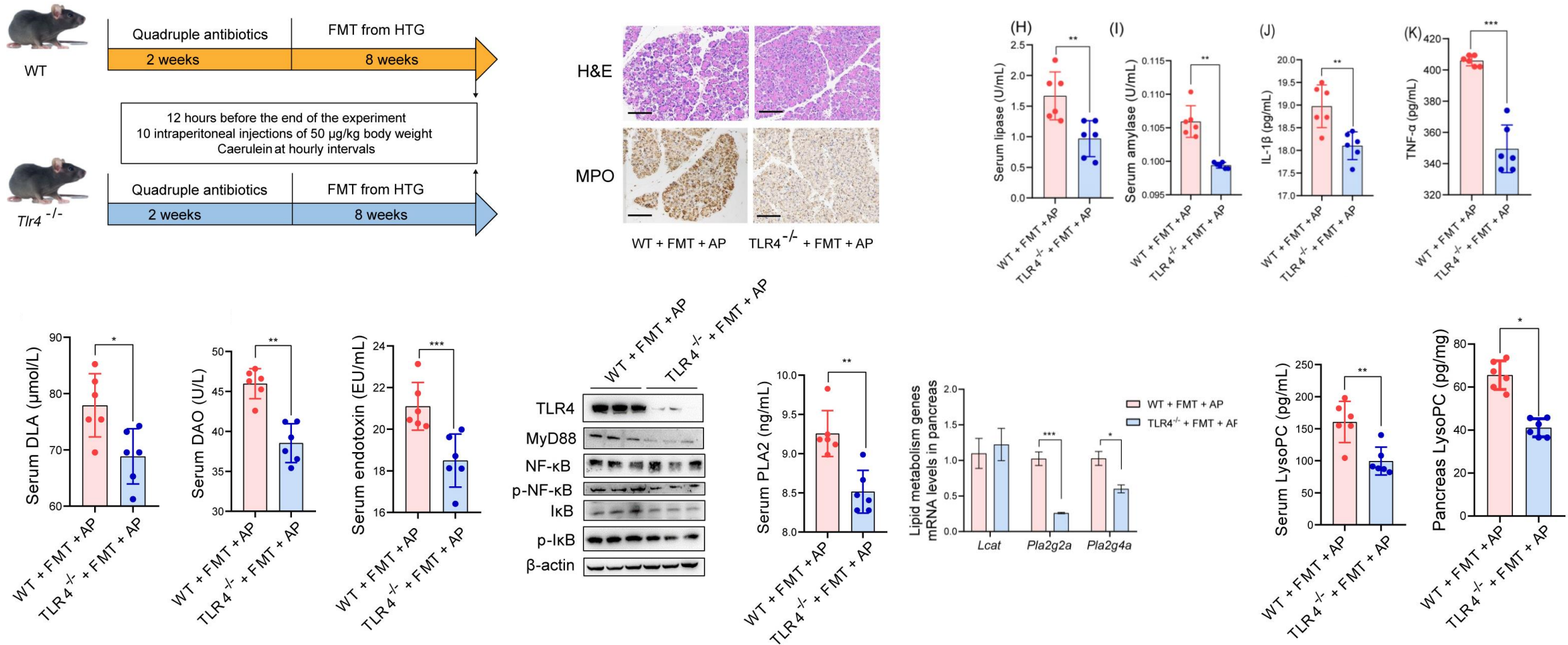


Figure 6. The gut microbiota regulated by HTG promotes the production of LysoPC in a TLR4 - dependent manner

Results

◆ LysoPC Can Exacerbate Pancreatic Injury and Inflammatory Response in AP Mice

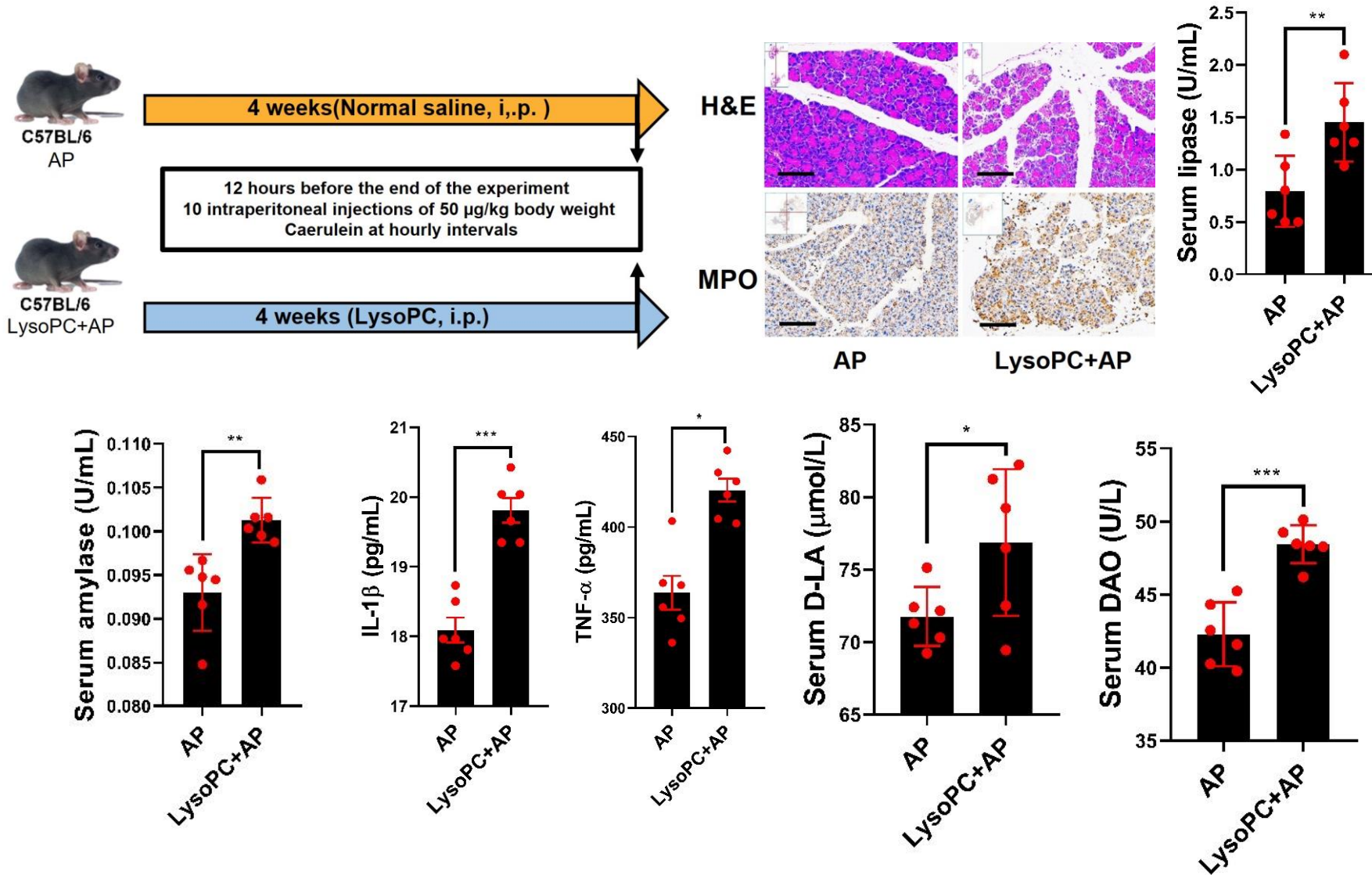


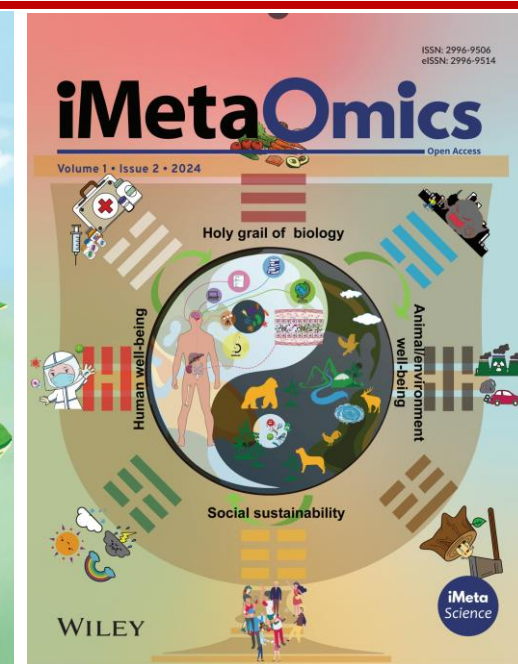
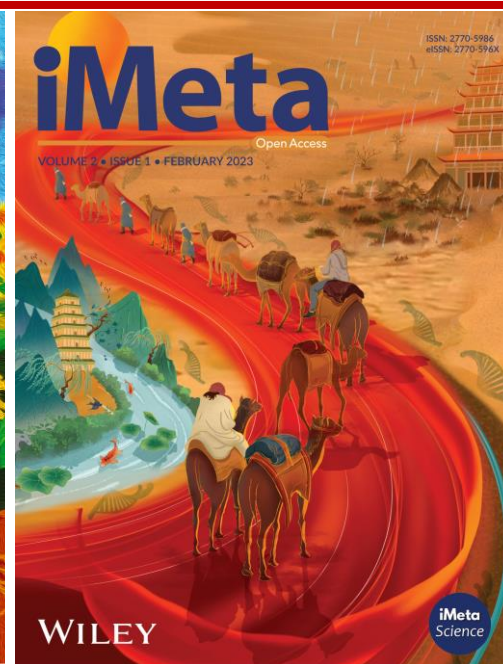
Figure 7. LysoPC can exacerbate the degree of pancreatic injury and inflammatory response in AP mice



Summary



- ❑ In this study, we found that HTG exacerbates pancreatic injury and inflammatory responses in AP mice in a gut microbiota - dependent manner.
- ❑ HTG can cause disorders in the composition and function of the gut microbiota in mice, leading to an increase in endotoxin content.
- ❑ The gut microbiota regulated by HTG promotes glycerophospholipid metabolism and LysoPC production in a TLR4 - dependent manner, thus exacerbating the severity of AP.

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