Cyy-287, a novel pyrimidine-2,4-diamine derivative, efficiently mitigates inflammatory responses, fibrosis and lipid synthesis in obesity-induced cardiac and hepatic dysfunction (#91103)

Authors clearly explained NF-kB and AMPK signaling pathways and derived hypothesis based on their previous research. Their novel compound, Cyy-287, has a great potential for impeding obesity-induced deterioration of cardiac and hepatic functions. They demonstrated well signaling axes related to HFD induced inflammation with supporting data. Also, this compound is worthy to look into further for other disease such as type 2 diabetes.

Minor revision

1. At line 124,
    a. the sum of fat, protein, and carbohydrate is 50%. What is the rest of 50% for the standard control diet?
    b. Please briefly describe 'adaptive feeding' strategy
2. In their previous study (doi: 10.3724/abbs.2022139), authors administrated 15mg/kg of cyy-287 via i.p. and showed about less than 5% of the compound was found in the liver. In this study, the compound was administrated by gavage and the max dose is 20mg/kg. Given the previous study that shows low affinity for liver, why did author choose the administration method? Did author measured cyy-287 distribution in other organ? How did they come up with the max dose?
3. Please fix the typo. 'Cyy-287 mitigates hepatic fat accumulation and damage through p38 MAPK/NF- kB dowregulation and activating AMPK in HFD mice