



# *Streptococcus salivarius* mitigates metabolic dysfunction-associated steatotic liver disease by modulating the NLRP3 inflammasome pathway

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## BACKGROUND

Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most prevalent liver diseases worldwide. However, definitive medical treatments have not been established apart from lifestyle modifications. This study aimed to demonstrate the role of gut microbiome in the Western diet-induced MASLD and explore the effects of *Streptococcus salivarius* in the prevention of MASLD by utilizing gut microbiota profiles.

## METHODS

A total of 76 patients' stools (healthy controls [HC, n=19], fatty liver (FL=16), hepatitis (n=24), and cirrhosis (n=17)) were analyzed by 16s rRNA sequencing. For in vivo study, 6 weeks old C57BL/6N mice were fed the Western diet with/without *S. salivarius* for 9 weeks. *S. salivarius* were administered at a concentration of 10<sup>9</sup> CFU/day. We compared liver/body weight ratio (L/B ratio), NAFLD activity score, liver function tests, histopathology, fecal analysis, and markers for inflammation, lipogenesis, and  $\beta$ -oxidation in the liver.

## RESULTS

Figure 1. *S. salivarius* reduces steatosis, ballooning and NAS score in mice liver.

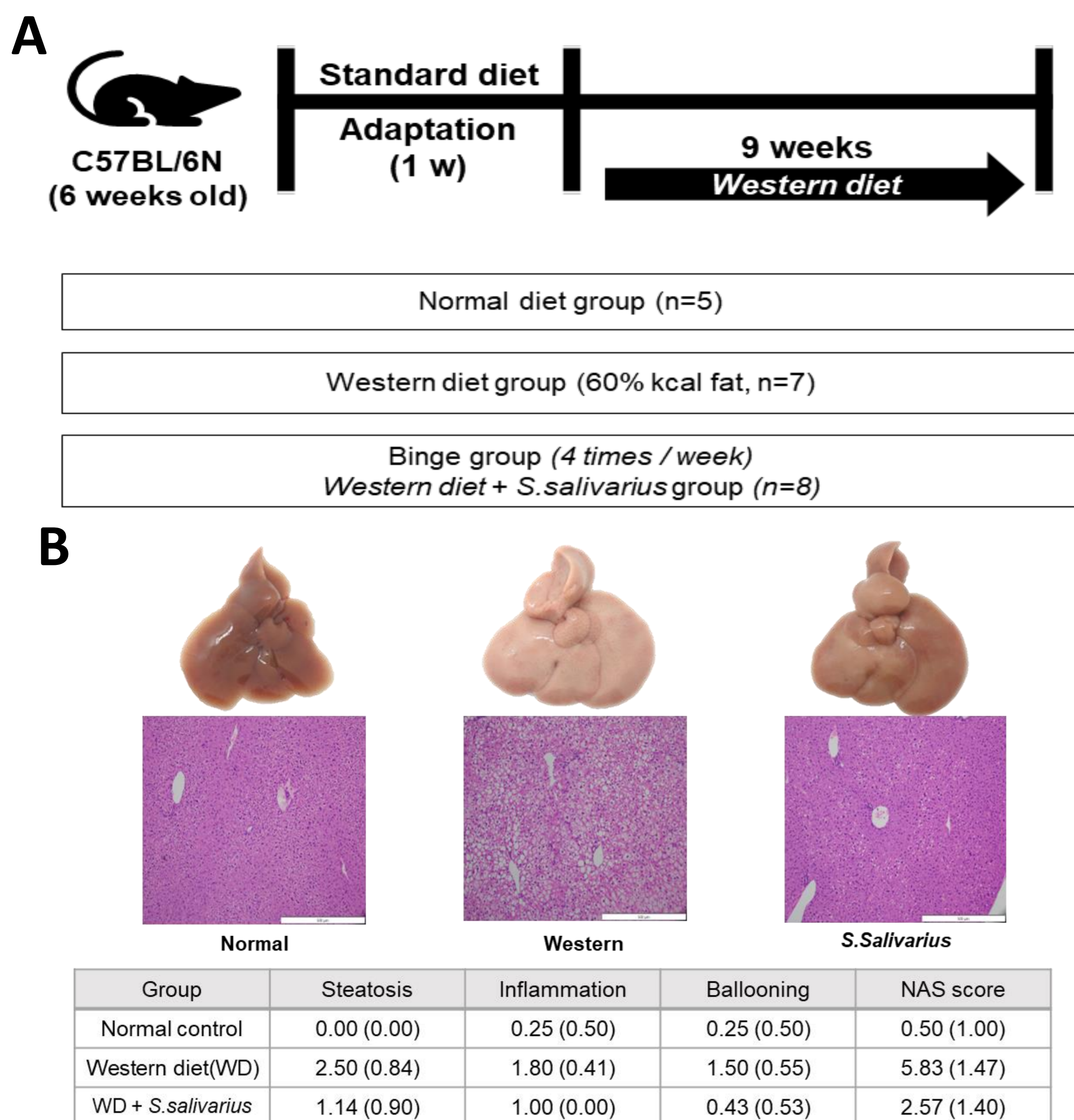
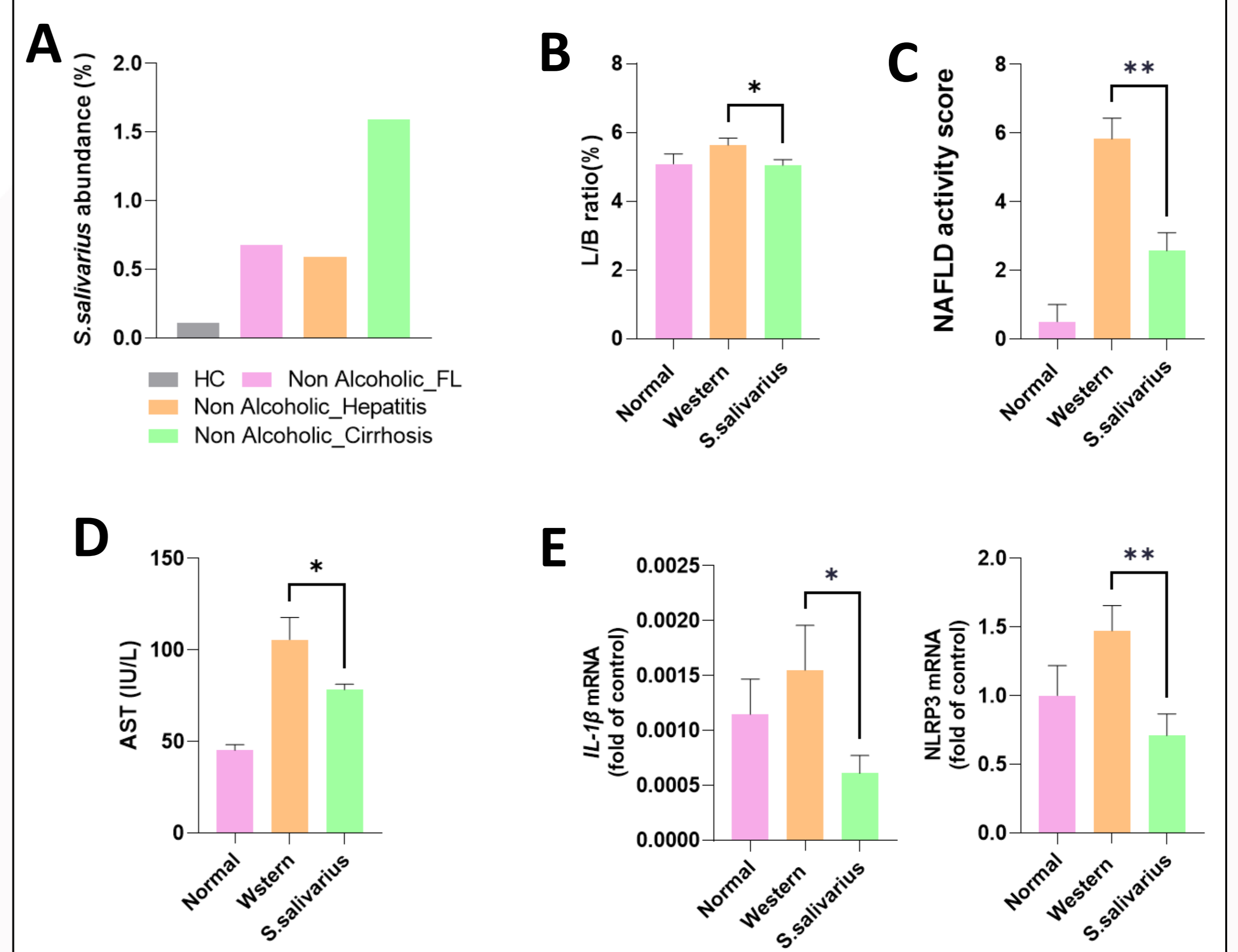
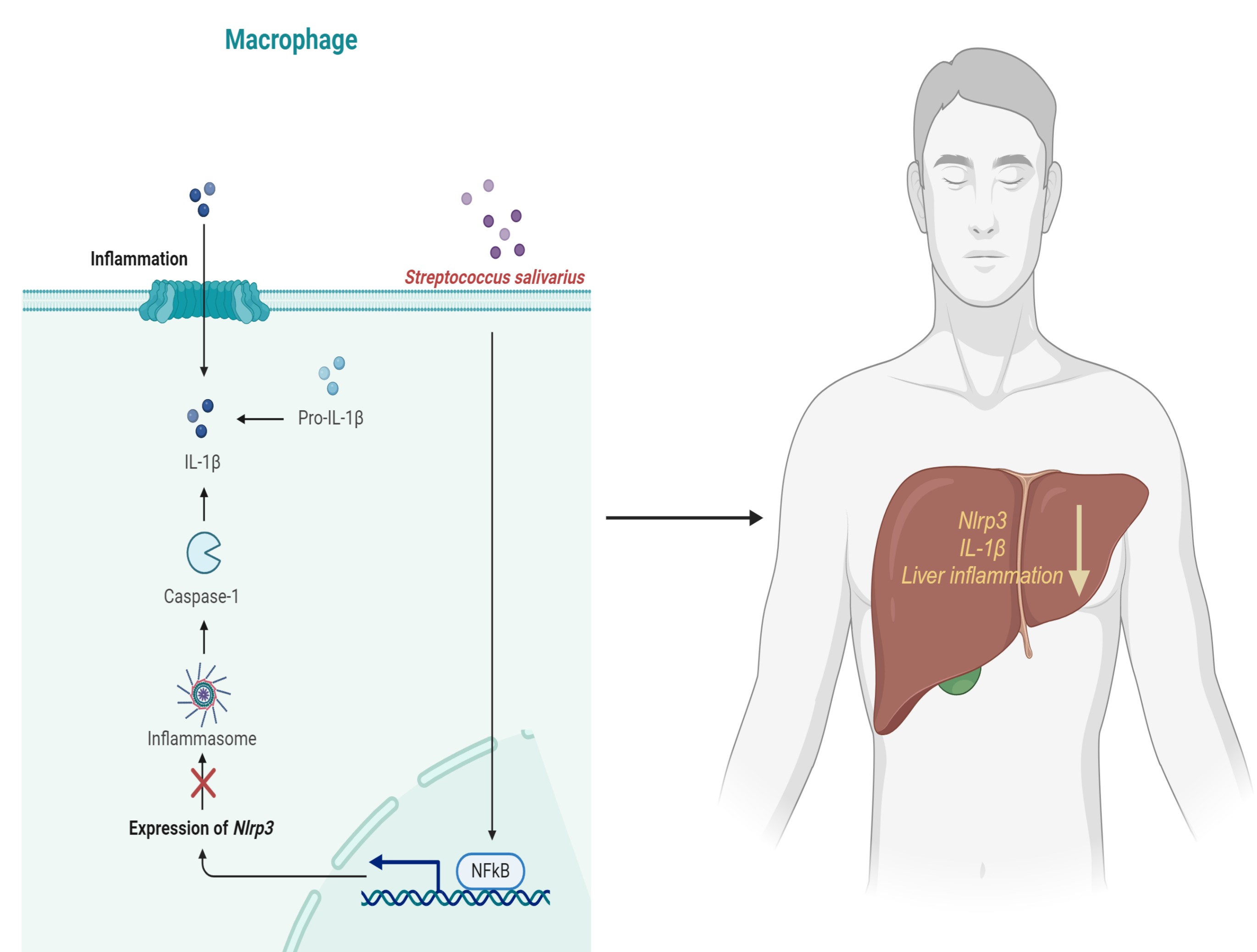


Figure 2. *S. salivarius* improves liver function and develops a community of gut microbiota by suppressing IL-1 $\beta$  and NLRP3.



## CONCLUSION

In the human stool microbiota analysis, the species level of *S. salivarius* increased in cirrhosis group. In the animal study, Western diet group showed elevation in the proportion of Proteobacteria and Firmicutes and reduction in Bacteroidetes. *S. salivarius* groups revealed significant improvement in liver enzymes (AST 78.3 $\pm$ 8.6, P=0.03), L/B ratio (5.0 $\pm$ 0.5, P=0.03) and improved NAS (2.6 $\pm$ 1.4, P<0.01) compared with the untreated group (AST 105.7 $\pm$ 32.1; L/B ratio 5.6 $\pm$ 0.5; NAS 5.8 $\pm$ 1.5). Moreover, *S. salivarius* supplementation downregulated the expression of inflammation biomarkers (IL-1 $\beta$ , P=0.05; Nlrp3, P<0.01). *S. salivarius* supplementation ameliorates MASLD progression, and dysbiosis through the modulation of gut microbiota resulting in improving hepatic inflammation.



Our study highlighted the association between gut microbiota and MASLD through the gut-liver axis. We confirmed the potential of *S. salivarius* on the prevention of MASLD progression and the detailed mechanisms for the novel therapy.