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齐齐哈尔市肿瘤医院
Qiqihar Cancer Hospital

吸烟与非酒精性脂肪肝

中心实验室
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Gut bacteria alleviate smoking-related NASH by degrading gut nicotine

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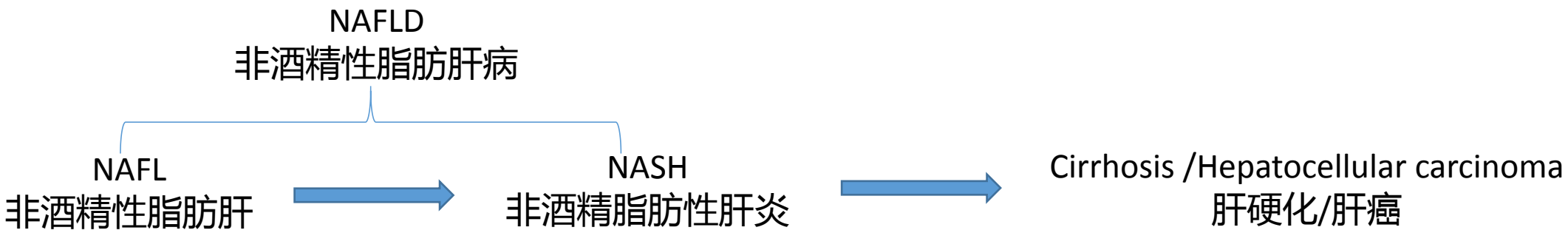
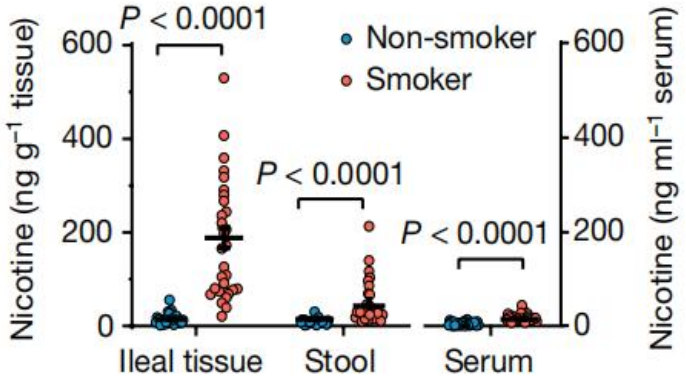
2022年10月19日，北京大学基础医学院姜长涛团队联合美国国立卫生研究院的Frank J. Gonzalez发表



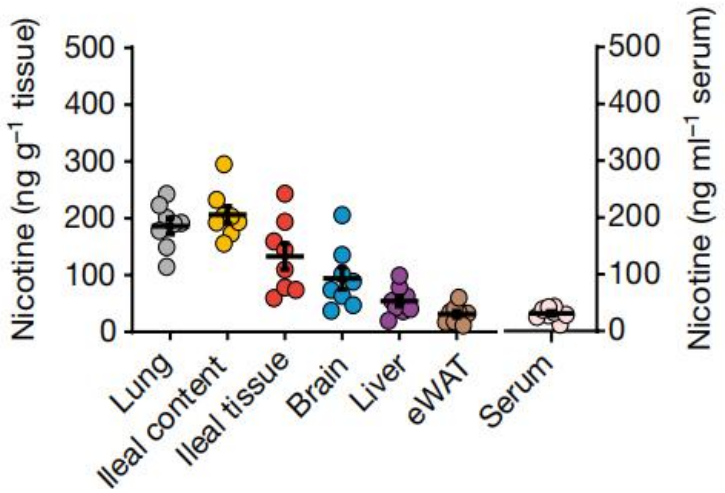
1.Gut bacteria degrade ileal nicotine

(1) To confirm whether nicotine accumulates in the intestine during tobacco smoking.

a 30 non-smokers and 30 smokers

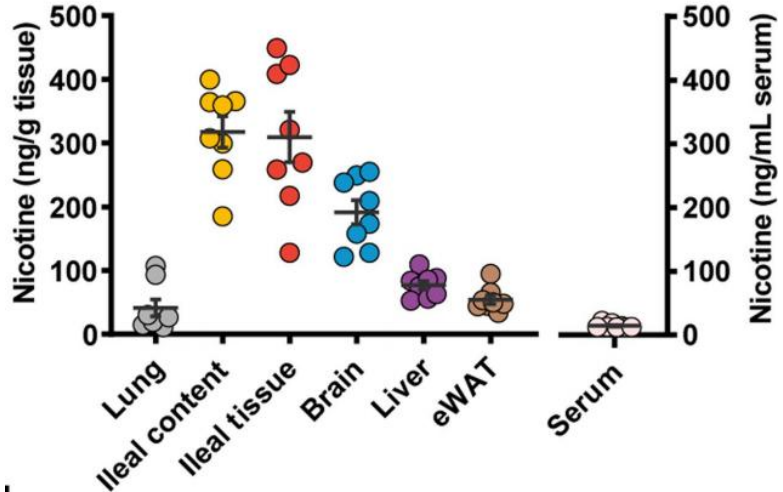


b smoke exposure SPF mice (C57BL/6J)

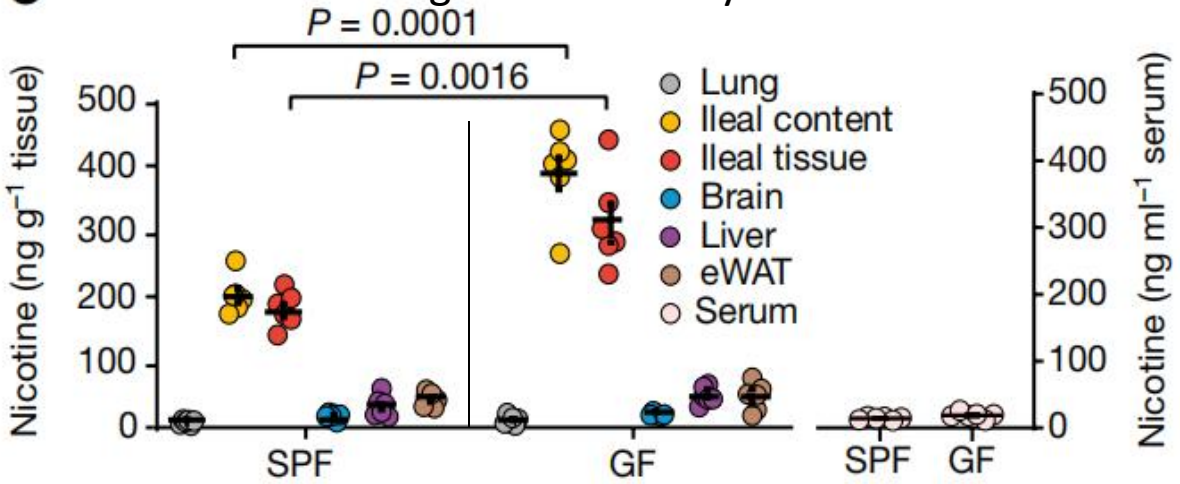


These results indicate that nicotine levels during smoking accumulate in the intestine to a relatively large degree, which may be of pathophysiological significance.

S.C.injection mouse model

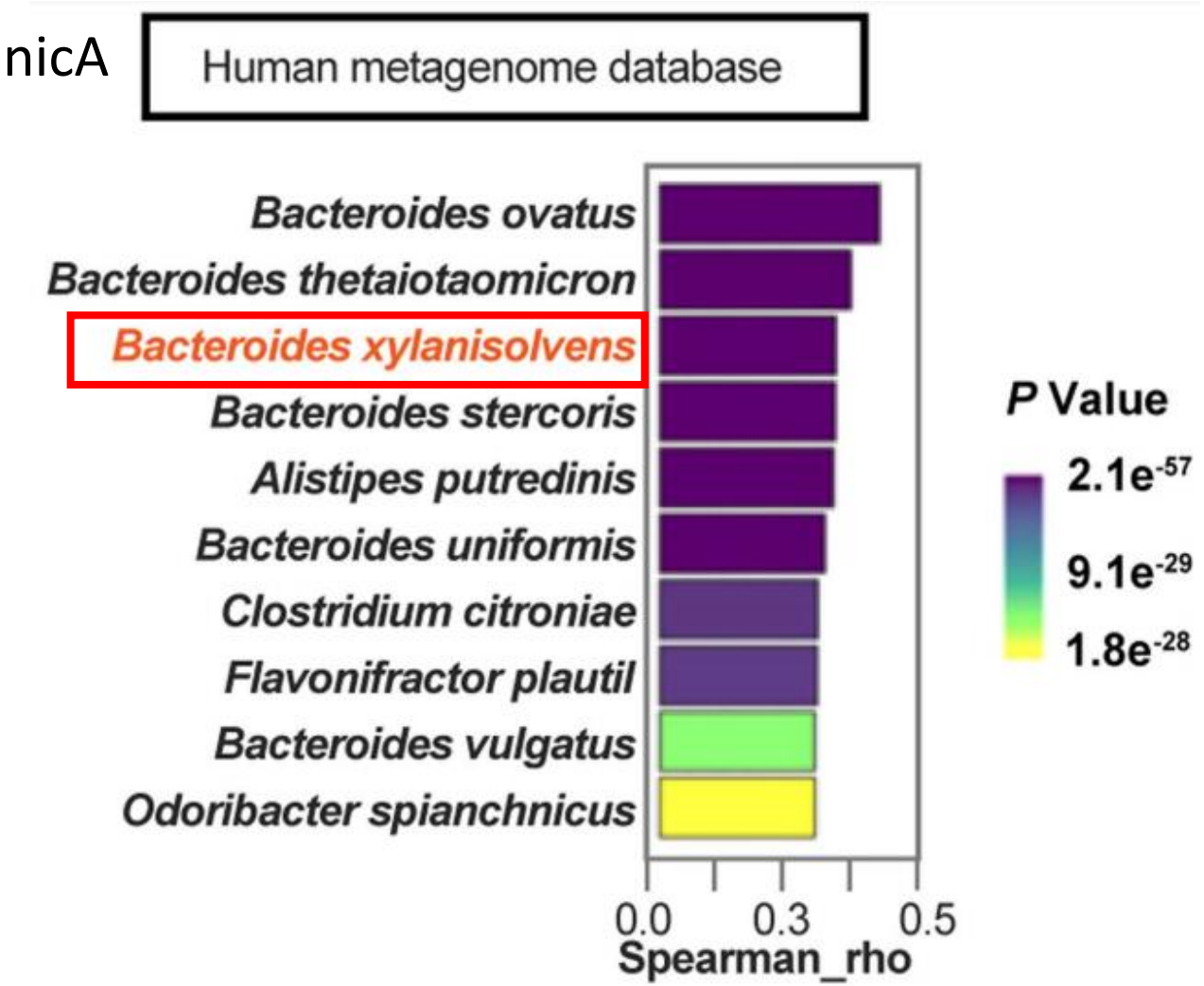


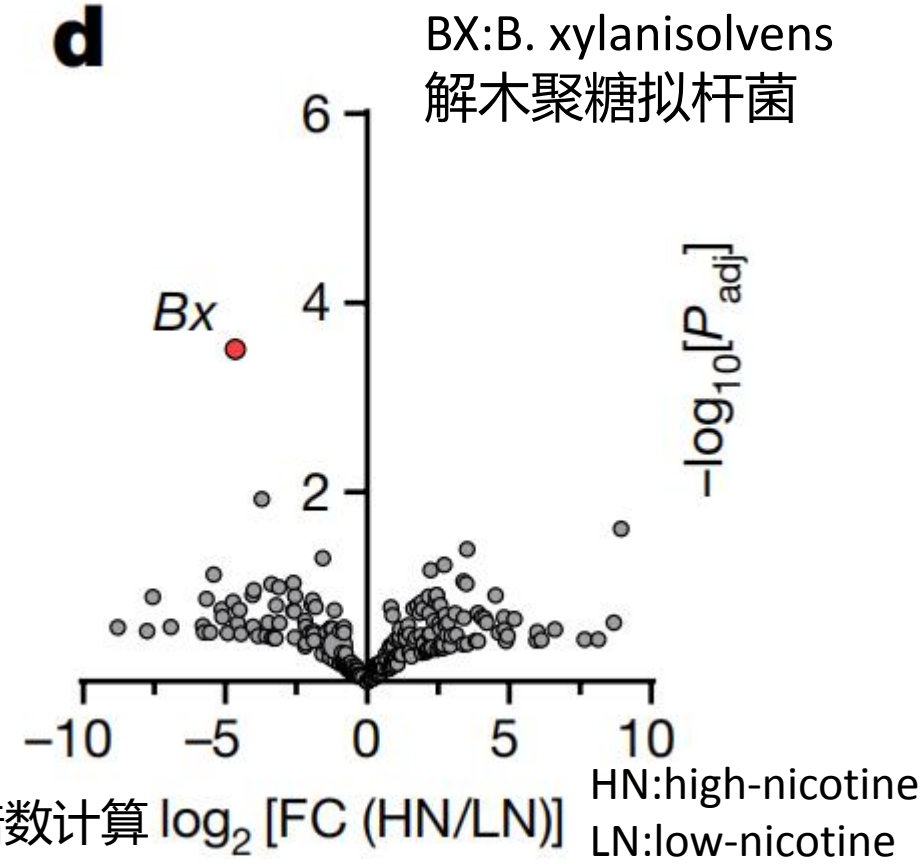
c nicotine drinking water delivery model



Suggest that endogenous gut bacteria contribute to nicotine degradation

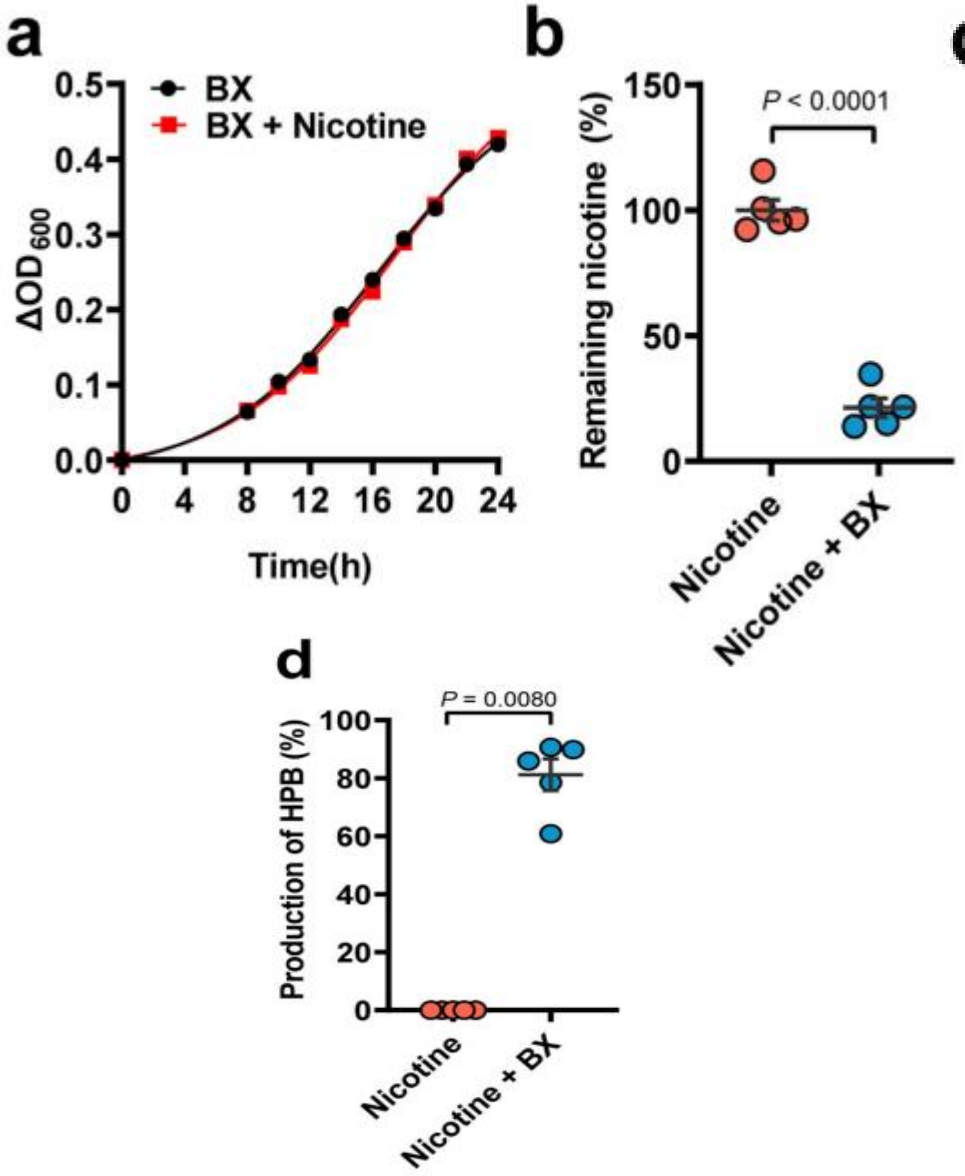
（2）To identify the specific endogenous nicotine-degrading gut microbiota in humans.

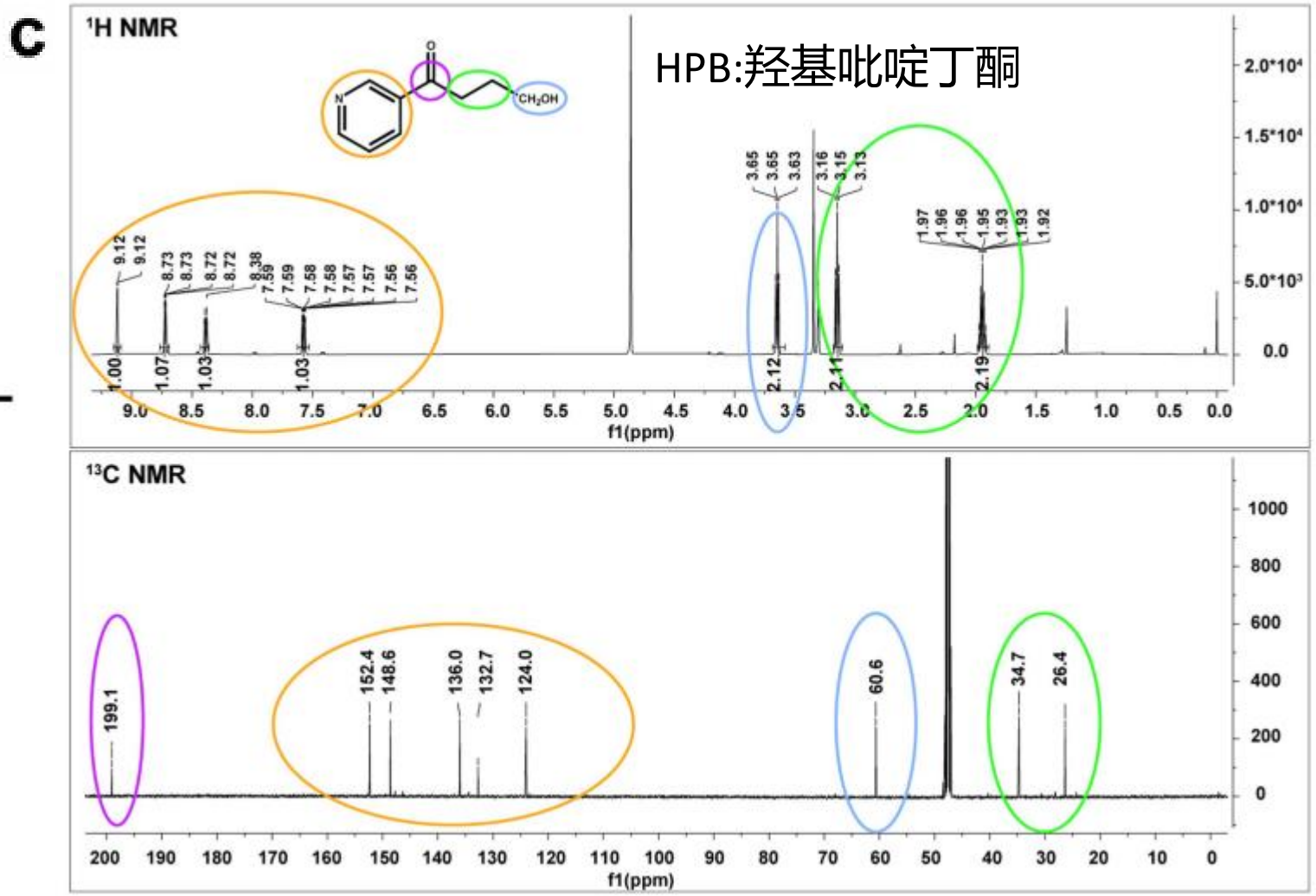




Stool samples from 30 smokers were analysed using a metagenomics study to identify the most correlative species with reduced ileal nicotine concentrations.

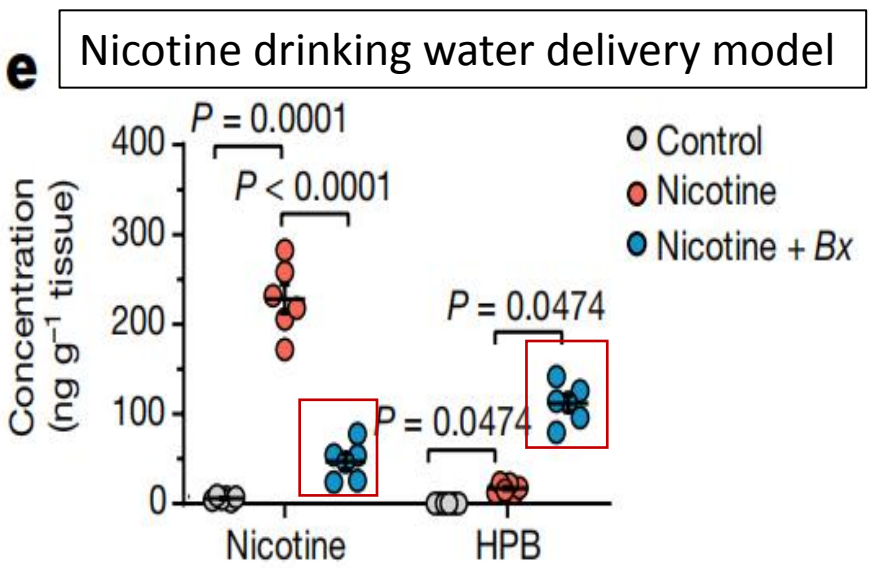
（3）To examine the degraded metabolites of nicotine in B. xylanisolvens.

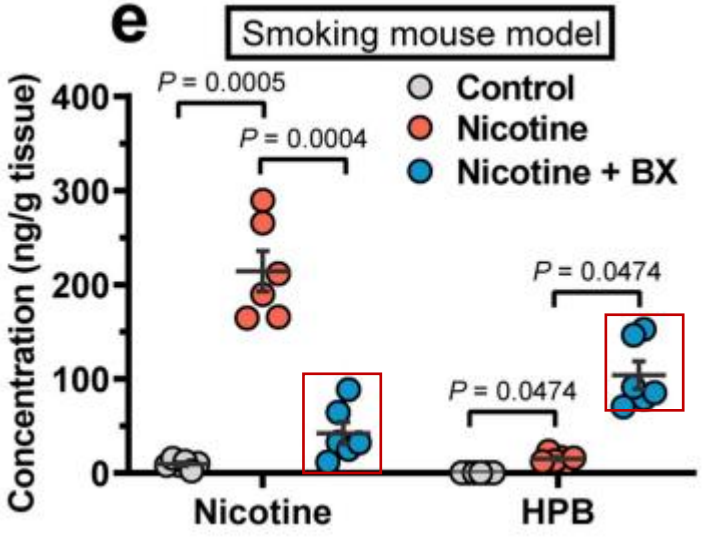


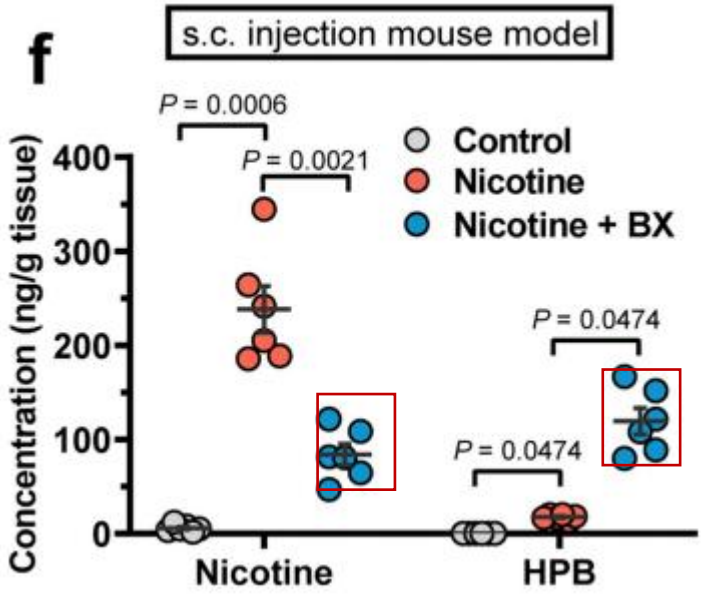


液相二级质谱（三重四级杆LC-MS/MS）对尼古丁代谢物进行分析，用氢谱和碳谱进行了表征

（4）To verify the nicotine-degrading properties of B. xylanisolvens in vivo.

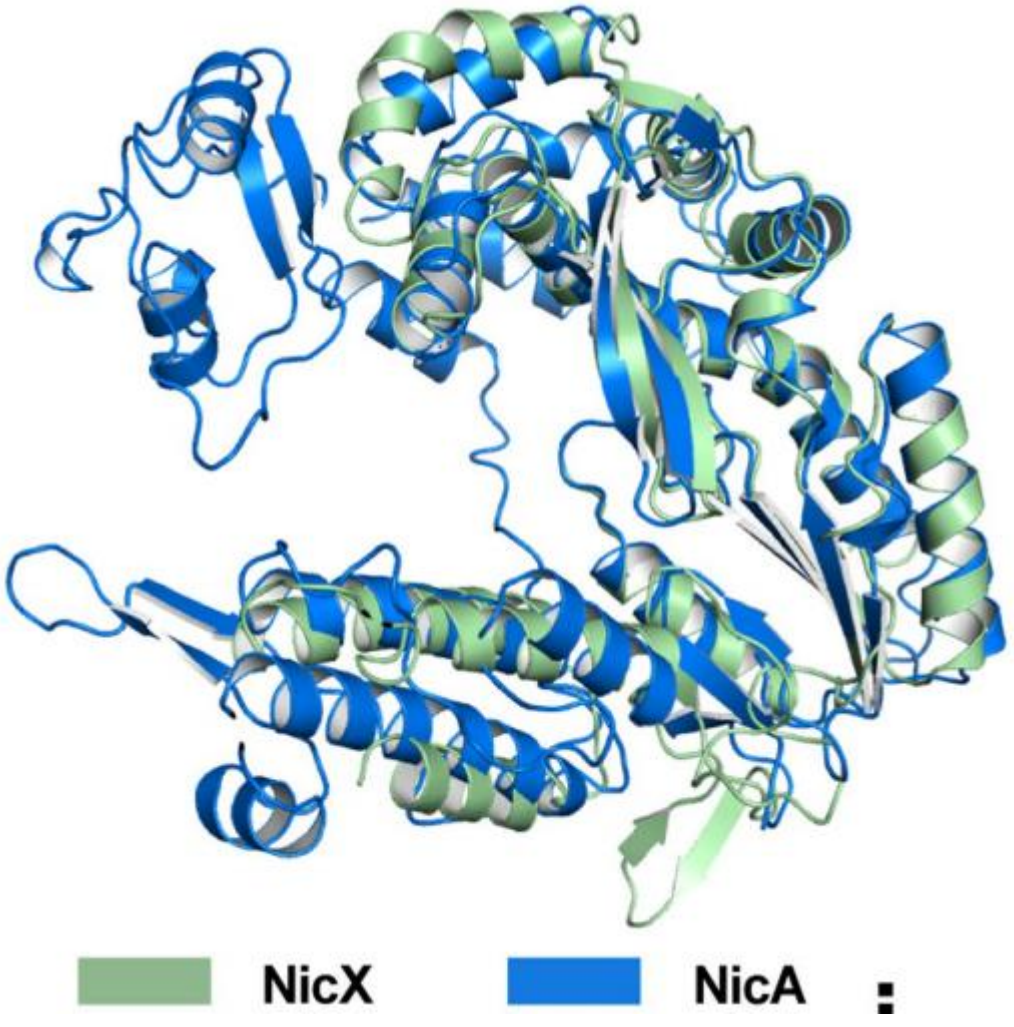


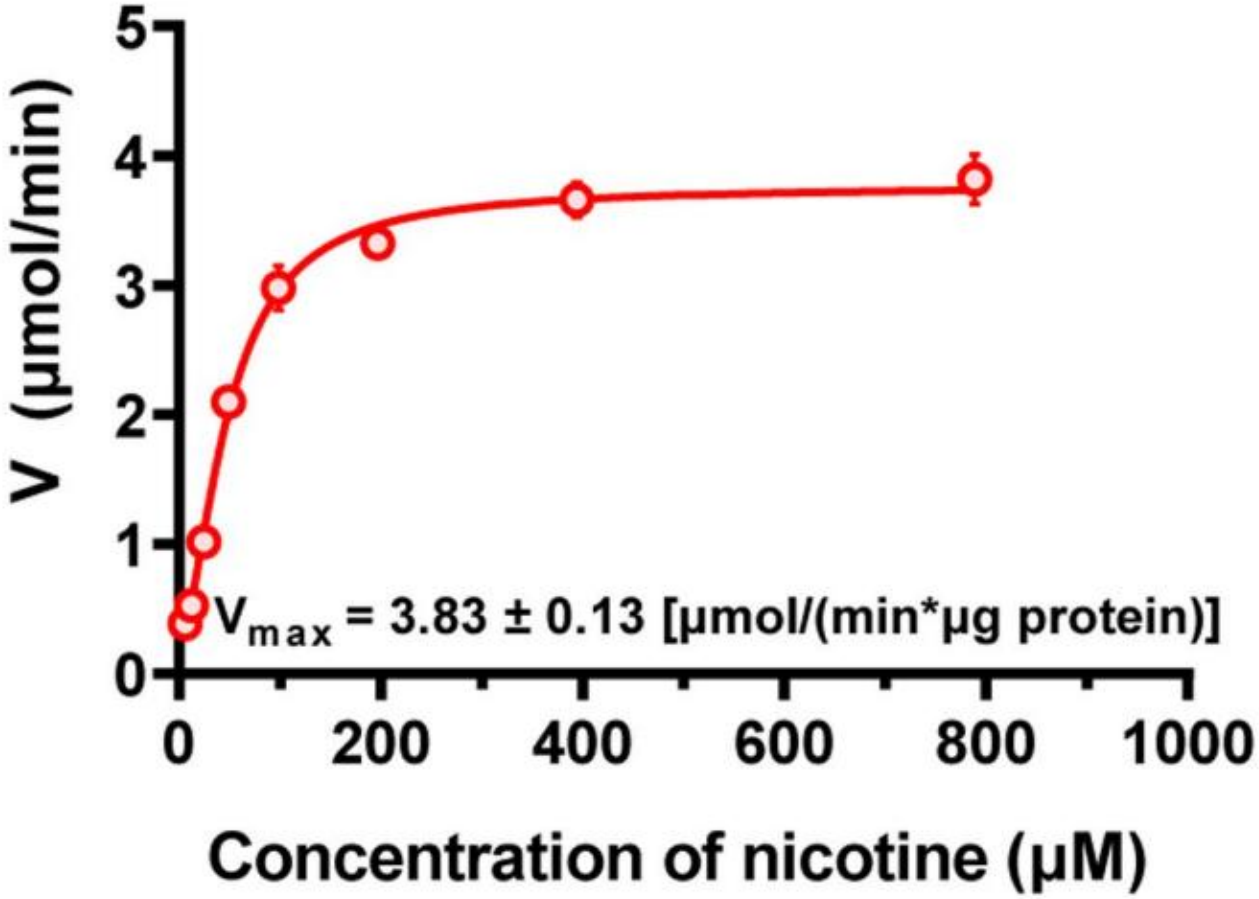




colonized B. xylanisolvens into SPF mice

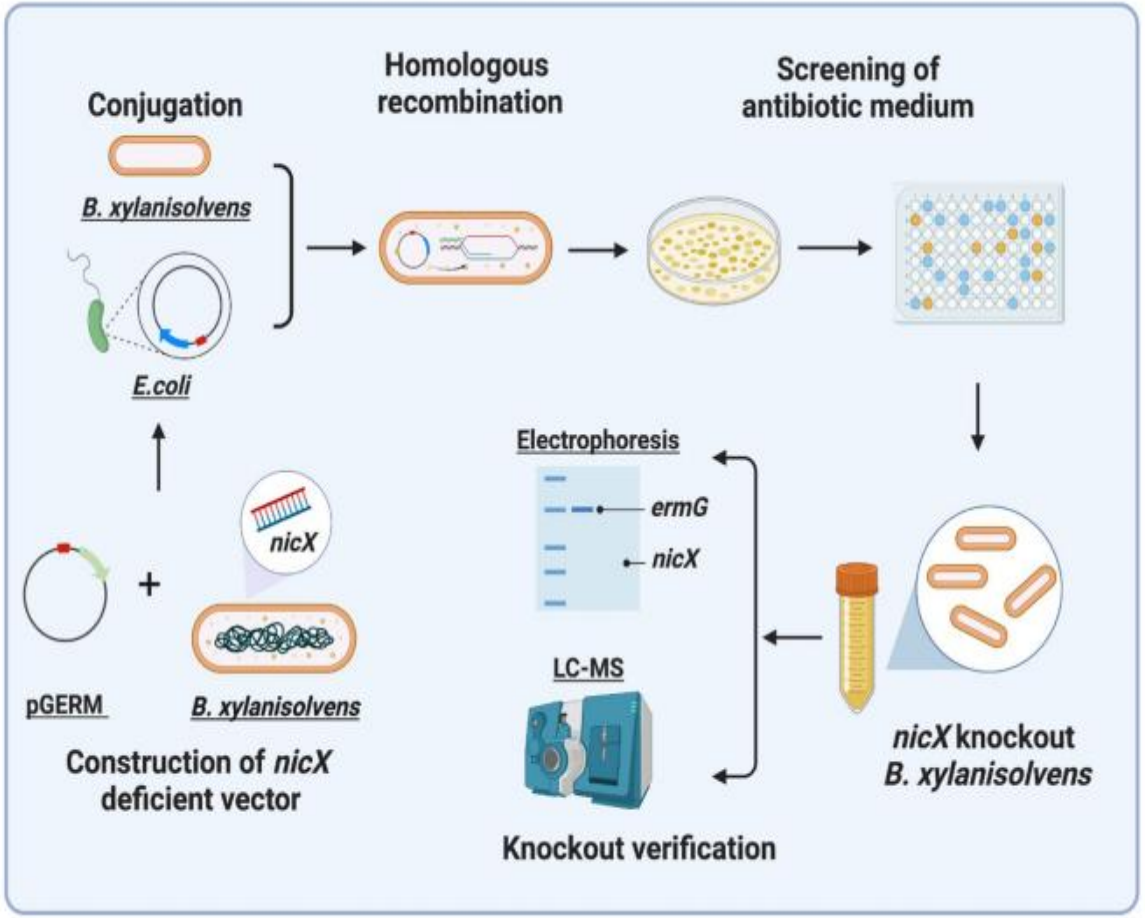
（5）whole-genome sequencing of B. xylanisolvensand performed to examine the biosynthetic gene responsible for the catabolism of nicotine in B. xylanisolvens.

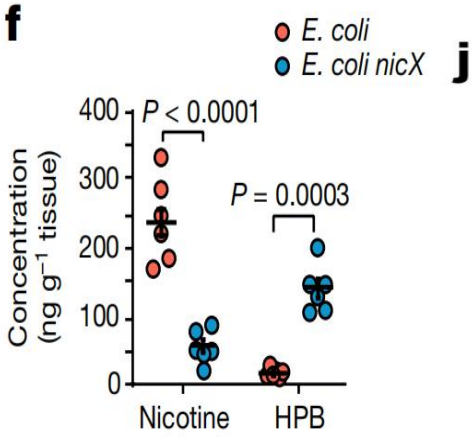


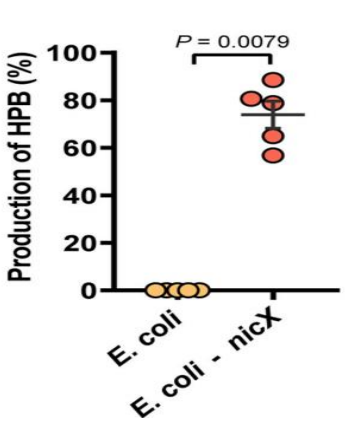


NicX degraded nicotine with a Vmax of 3.83 ± 0.13 μmol min−1 per μg protein in vitro

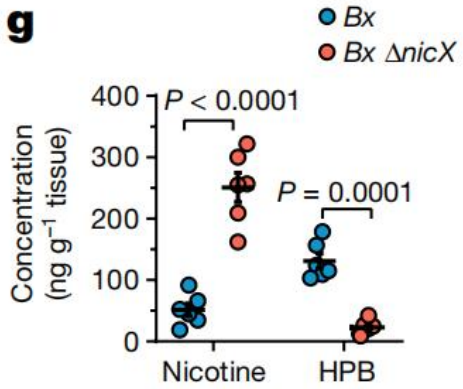
(6)To further verify the nicotine-degrading ability of NicX

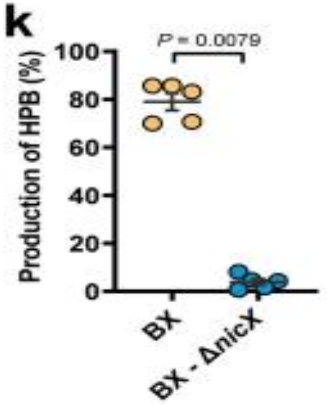






Compared with wild-type (WT) E. coli, nicX-knockin E. coli gained the ability to degrade nicotine and produce HPB in vitro and in vivo



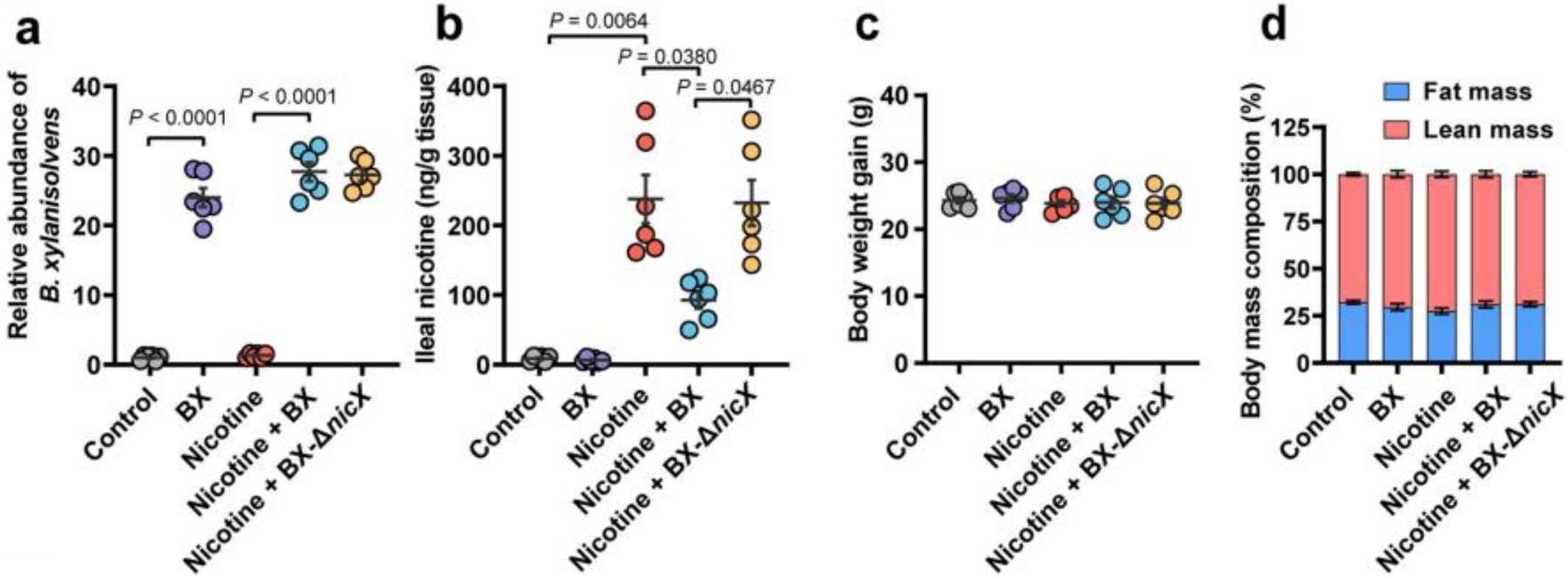


NicX deficiency in B. xylanisolvens resulted in the loss of its nicotine-degradation ability

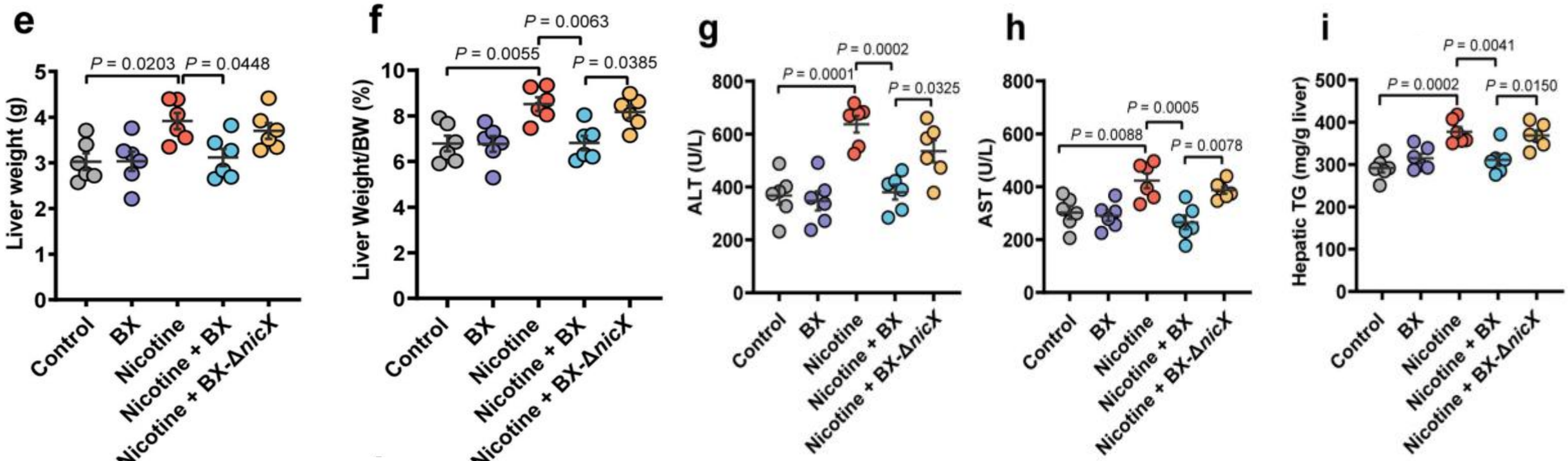
In summary, the results show that nicotine accumulates in the intestine during various routes of nicotine administration, and B. xylanisolvens has the ability to degrade nicotine in the presence of NicX.

2.Nicotine degradation delays NAFLD progression

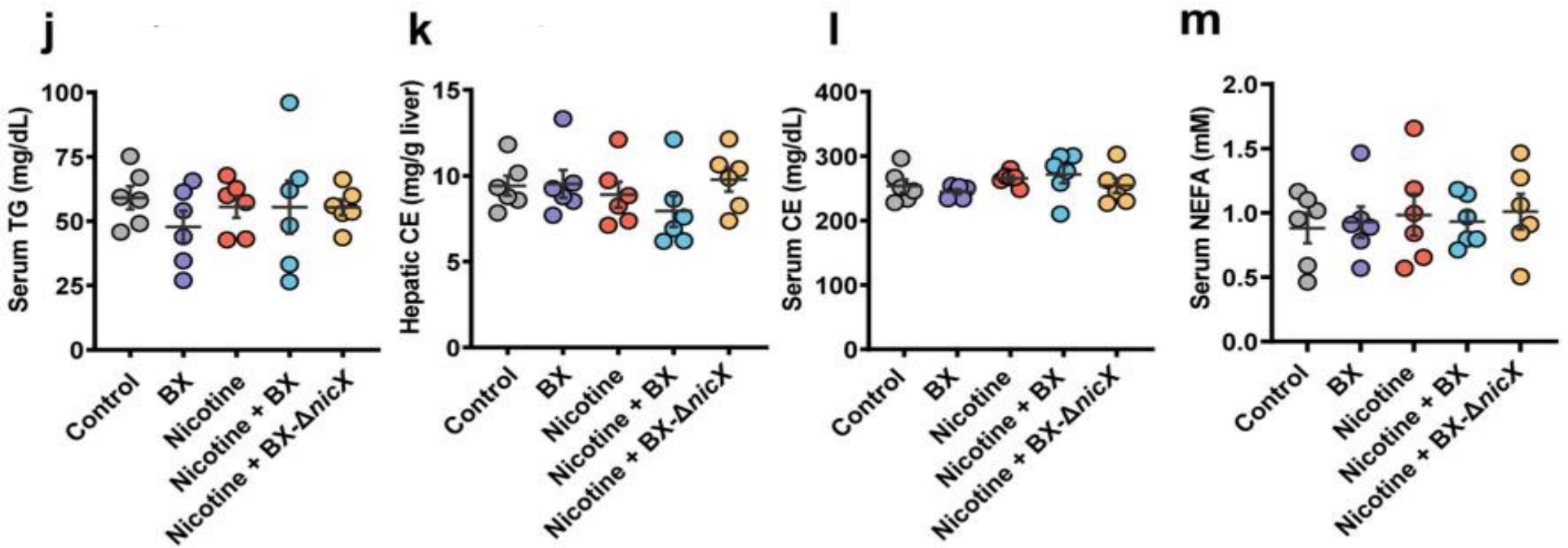
(1)To determine the role of intestinal nicotine accumulation and the effect of its degradation by B. xylanisolvens in NAFLD progression



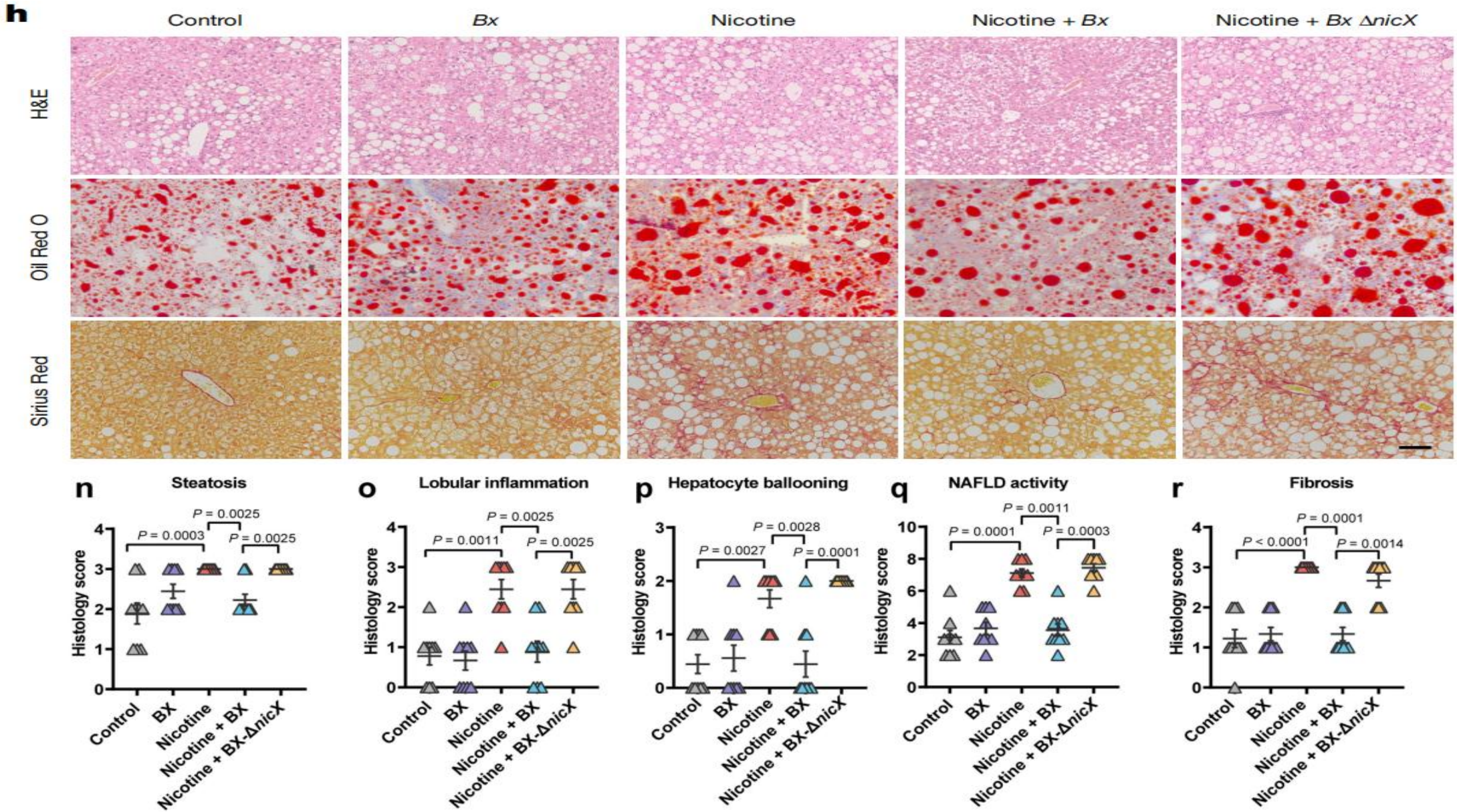
SPF mice treated with PBS (control), B. xylanisolvens, nicotine water, B. xylanisolvens plus nicotine water or nicX-knockout B. xylanisolvens plus nicotine water were administered a high-fructose and high-cholesterol diet (HFHCD) for 20 weeks.


e
Liver weight (g)
P = 0.0203
P = 0.0448
f
Liver Weight/BW (%)
P = 0.0063
P = 0.0055
P = 0.0385
g
ALT (U/L)
P = 0.0002
P = 0.0001
P = 0.0325
h
AST (U/L)
P = 0.0005
P = 0.0088
P = 0.0078
i
Hepatic TG (mg/g liver)
P = 0.0041
P = 0.0002
P = 0.0150
Control
BX
Nicotine
Nicotine + BX
Nicotine + BX-ΔnicX

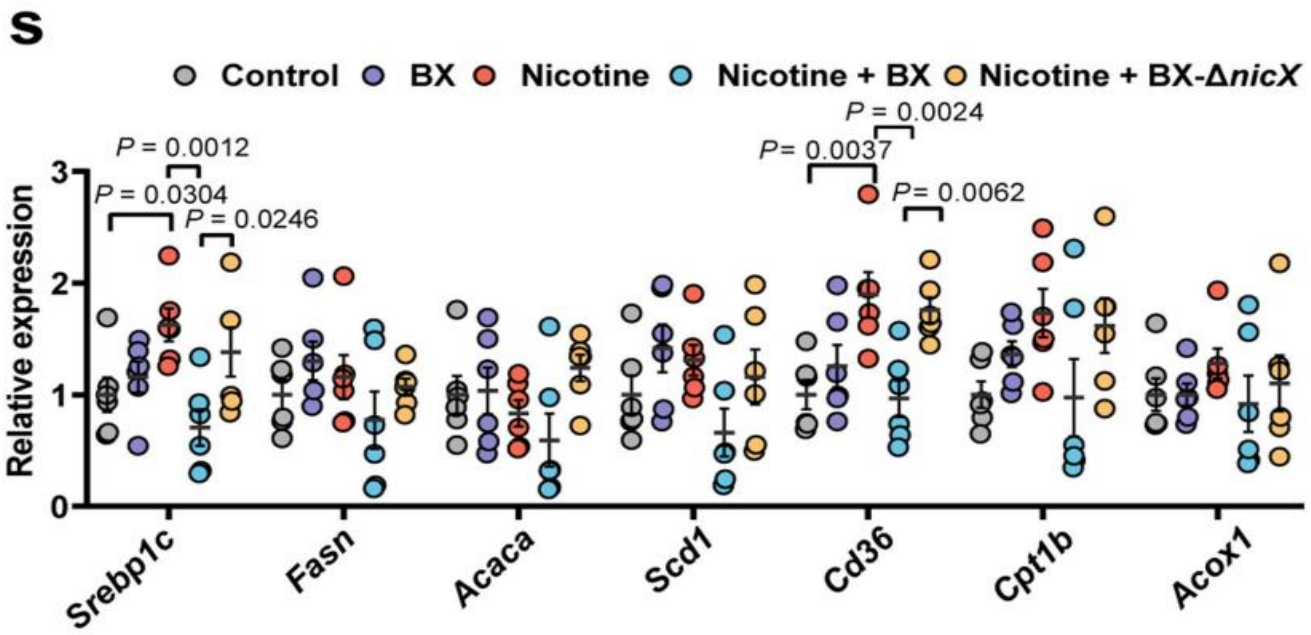
No significant differences in the serum triglyceride, the hepatic and serum cholesterol ester and serum non-esterified fatty acid levels were found between the two groups

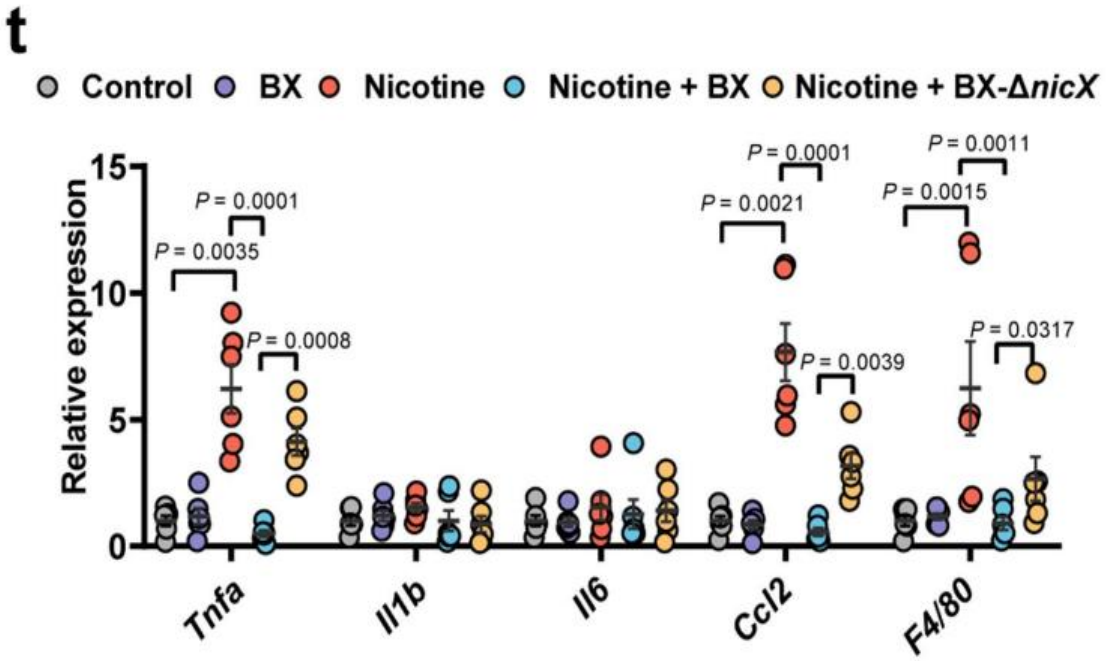


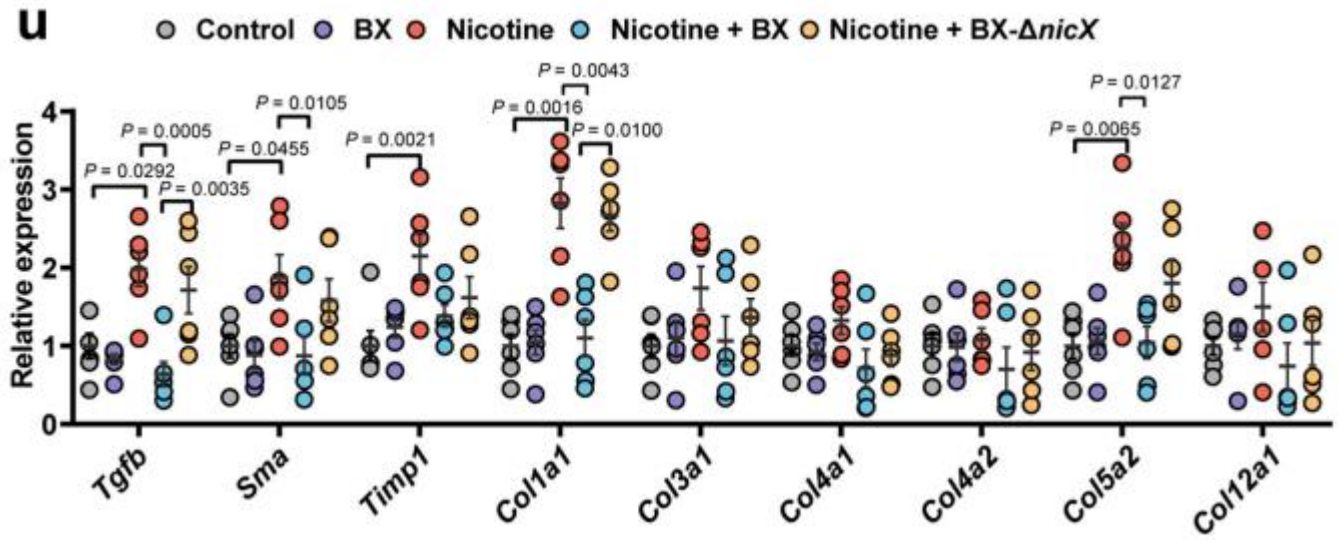
nicotine supplementation in the water accelerated NAFLD progression , and this acceleration was accompanied by more severe hepatic steatosis, inflammation and fibrosis



Furthermore, increases in the relative expression of mRNAs involved in hepatic lipid metabolism, proinflammatory cytokine production and collagen synthesis were induced by nicotine-supplemented water treatment







Together, these data suggest that the colonization of nicotine-degrading bacteria could reduce nicotine-induced NASH, and this effect is dependent on the expression of NicX

谢 谢 ！