



# *Akkermansia muciniphila*-derived hypoacylated rough-type lipopolysaccharides alleviate diet-induced obesity via activation of TLR4–IL-23–IL-22 immune axis

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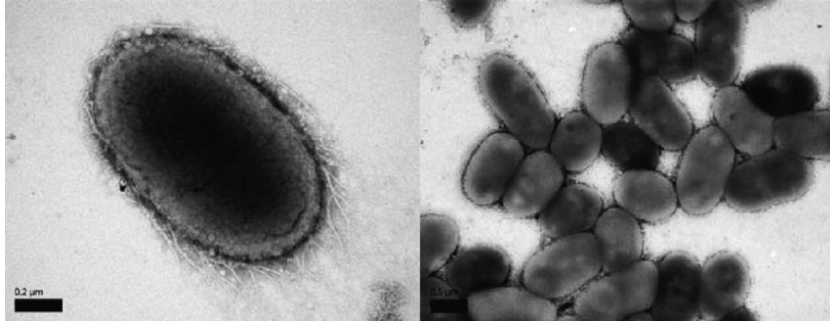
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Li Sun, Yuting Zhang, Wang Dong, Jingzu Sun, Tao Wang, Fei Shao, Huanqin Dai, et al. 2025. *Akkermansia muciniphila*-derived hypoacylated rough-type lipopolysaccharides alleviate diet-induced obesity via activation of TLR4–IL-23–IL-22 immune axis. *iMeta* 4: e70066.

<https://doi.org/10.1002/imt2.70066>

# Background



*Akkermansia muciniphila*



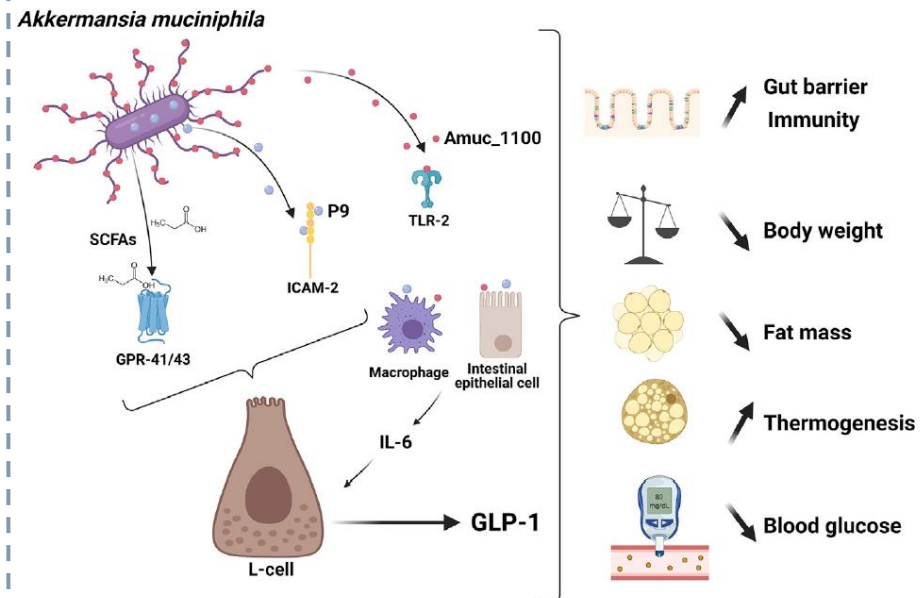
## Efficacy

1. Prevention and treatment of obesity
2. Promote intestinal barrier
3. Manage diabetes
4. Delaying senescence
5. Inhibit inflammation and improve metabolism
6. Prevention of non-alcoholic fatty liver disease

LETTERS  
<https://doi.org/10.1038/s41591-019-0495-2>  
nature  
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## Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study

### *Akkermansia Muciniphila* Protects Against Atherosclerosis by Preventing Metabolic Endotoxemia-Induced Inflammation in *Apoe*<sup>-/-</sup> Mice



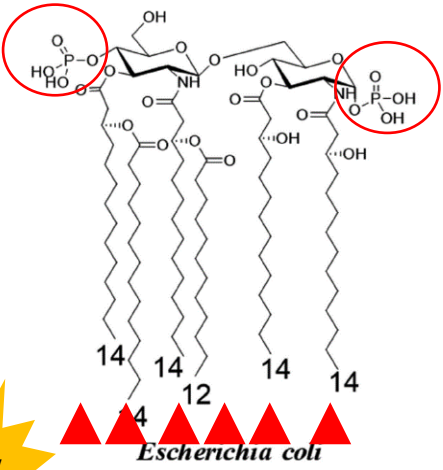
Cell Metab. 2021;33(6):1073-1075.



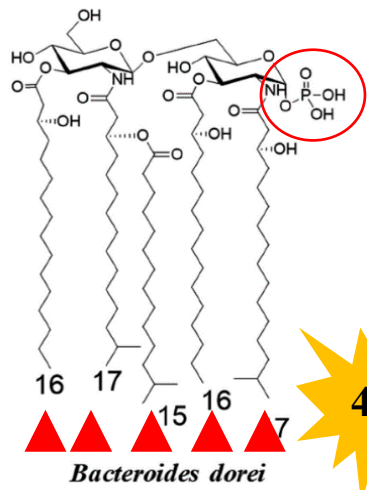
◆ *A. muciniphila* - related products

# Background

2

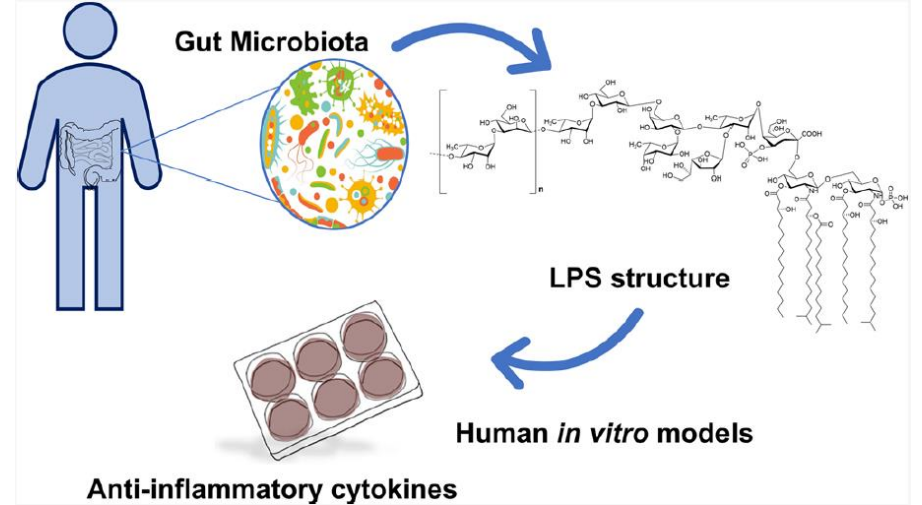
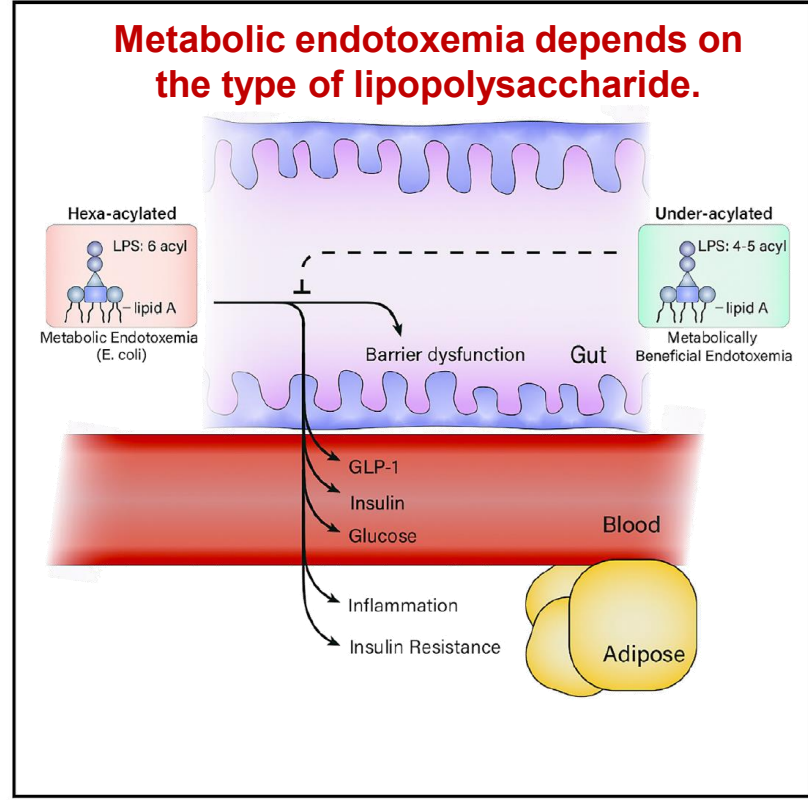


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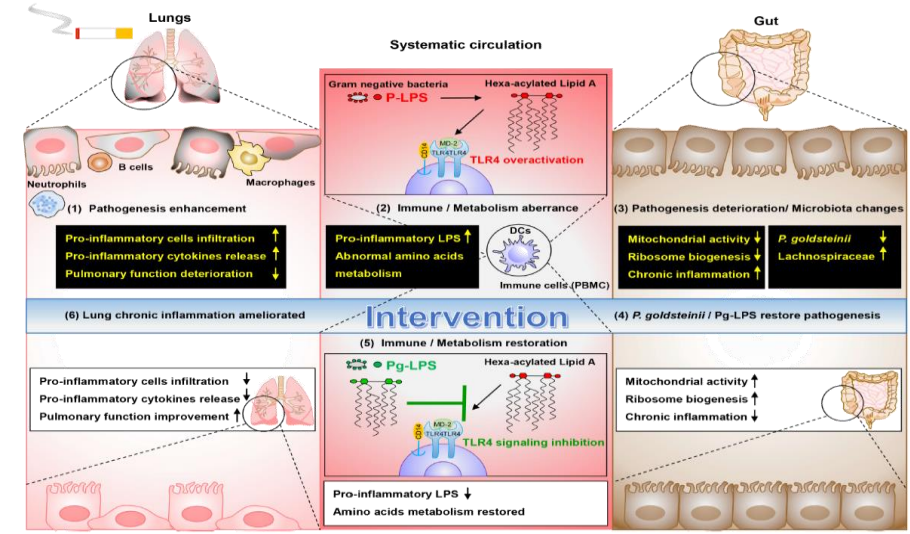


1

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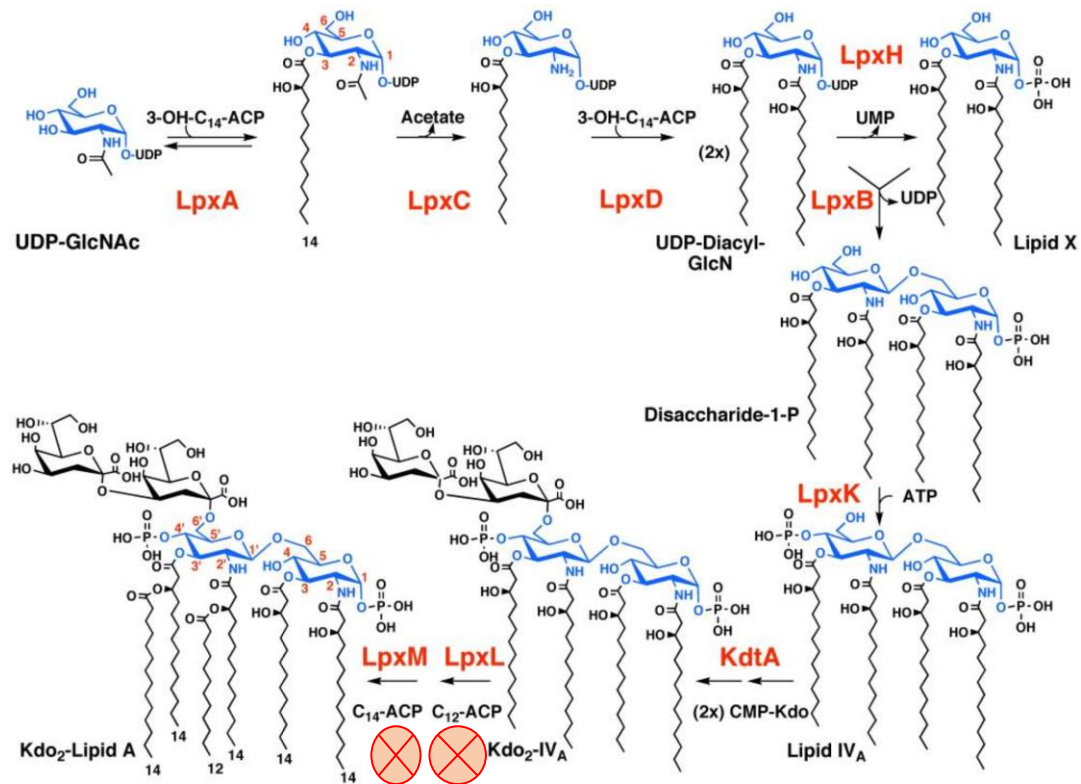
◆ The pentanoylation and monophosphorylation of *Bacteroides vulgaris* LPS exert anti-inflammatory effects through the MD-2/TLR4 signaling pathway.



◆ The pentanoylated lipopolysaccharide of *Bacteroides guttulatus* can improve chronic obstructive pulmonary disease.

# Background

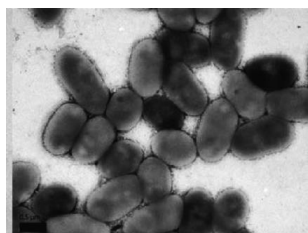
## The biosynthetic pathway of LPS



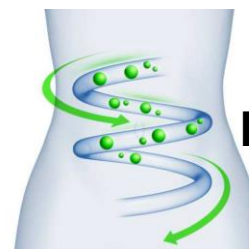
## BLAST

Gene <sup>⊖</sup>	Function <sup>⊖</sup>	<i>E. coli</i> MG1655 <sup>⊖</sup>	<i>A. muciniphila</i> HW07 <sup>⊖</sup>	Identity (%) <sup>⊖</sup>	Query cover (%) <sup>⊖</sup>	E-value <sup>⊖</sup>	<i>A. muciniphila</i> ATCC BAA-835 <sup>⊖</sup>	Identity (%) <sup>⊖</sup>	Query cover (%) <sup>⊖</sup>	E-value <sup>⊖</sup>
<i>lpxA</i> <sup>⊖</sup>	acyl-ACP-UDP-N-acetylglucosamine O-acyltransferase <sup>⊖</sup>	B1XD50 <sup>⊖</sup>	JFJHEM_00188 <sup>⊖</sup>	48.3 <sup>⊖</sup>	87.02 <sup>⊖</sup>	4.5E-74 <sup>⊖</sup>	B2ULY0 <sup>⊖</sup>	48.3 <sup>⊖</sup>	87.02 <sup>⊖</sup>	4.5E-74 <sup>⊖</sup>
<i>lpxB</i> <sup>⊖</sup>	lipid-A-disaccharide synthase <sup>⊖</sup>	B1XD51 <sup>⊖</sup>	JFJHEM_02115 <sup>⊖</sup>	29.7 <sup>⊖</sup>	96.33 <sup>⊖</sup>	3E-48 <sup>⊖</sup>	Q5LH14 <sup>⊖</sup>	29.7 <sup>⊖</sup>	96.33 <sup>⊖</sup>	3E-48 <sup>⊖</sup>
<i>lpxC</i> <sup>⊖</sup>	UDP-3-O-acyl-N-acetylglucosamine deacetylase <sup>⊖</sup>	B1XC73 <sup>⊖</sup>	JFJHEM_01977 <sup>⊖</sup>	38.7 <sup>⊖</sup>	89.83 <sup>⊖</sup>	3.9E+54 <sup>⊖</sup>	B2UNL5 <sup>⊖</sup>	38.7 <sup>⊖</sup>	89.83 <sup>⊖</sup>	3.9E+54 <sup>⊖</sup>
<i>lpxD</i> <sup>⊖</sup>	UDP-3-O-(3-hydroxymyristoyl) glucosamine N-acyltransferase <sup>⊖</sup>	P21645 <sup>⊖</sup>	JFJHEM_00425 <sup>⊖</sup>	33.9 <sup>⊖</sup>	95.01 <sup>⊖</sup>	6.1E-51 <sup>⊖</sup>	B2UND2 <sup>⊖</sup>	33.9 <sup>⊖</sup>	95.01 <sup>⊖</sup>	6.1E-51 <sup>⊖</sup>
<i>lpxF</i> <sup>⊖</sup>	lipid A 4'-phosphatase <sup>⊖</sup>	P10441 <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>
<i>lpxH</i> <sup>⊖</sup>	UDP-2,3-diacylglucosamine diphosphatase <sup>⊖</sup>	P43341 <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>
<i>lpxK</i> <sup>⊖</sup>	tetraacyldisaccharide 4'-kinase <sup>⊖</sup>	B1X855 <sup>⊖</sup>	JFJHEM_00598 <sup>⊖</sup>	30.1 <sup>⊖</sup>	96.64 <sup>⊖</sup>	9.3E-28 <sup>⊖</sup>	B2UPD5 <sup>⊖</sup>	30.1 <sup>⊖</sup>	96.64 <sup>⊖</sup>	9.3E-28 <sup>⊖</sup>
<i>lpxL</i> <sup>⊖</sup>	lauroyl/palmitoleoyl acyltransferase <sup>⊖</sup>	P0ACV0 <sup>⊖</sup>	JFJHEM_01585 <sup>⊖</sup>	23.7 <sup>⊖</sup>	— <sup>⊖</sup>	0.00000012 <sup>⊖</sup>	B2ULH5 <sup>⊖</sup>	23.7 <sup>⊖</sup>	— <sup>⊖</sup>	0.00000012 <sup>⊖</sup>
<i>lpxM</i> <sup>⊖</sup>	Lipid A biosynthesis myristoyltransferase <sup>⊖</sup>	P24205 <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>	— <sup>⊖</sup>
<i>lpxP</i> <sup>⊖</sup>	palmitoleoyl acyltransferase <sup>⊖</sup>	P0ACV2 <sup>⊖</sup>	JFJHEM_01585 <sup>⊖</sup>	21.9 <sup>⊖</sup>	86.93 <sup>⊖</sup>	0.00000012 <sup>⊖</sup>	B2ULH5 <sup>⊖</sup>	21.9 <sup>⊖</sup>	86.93 <sup>⊖</sup>	0.00000012 <sup>⊖</sup>

□ Genome prediction of the genes for the synthesis of secondary fatty acid chains in the lipopolysaccharide biosynthesis pathway of *A.muciniphila*



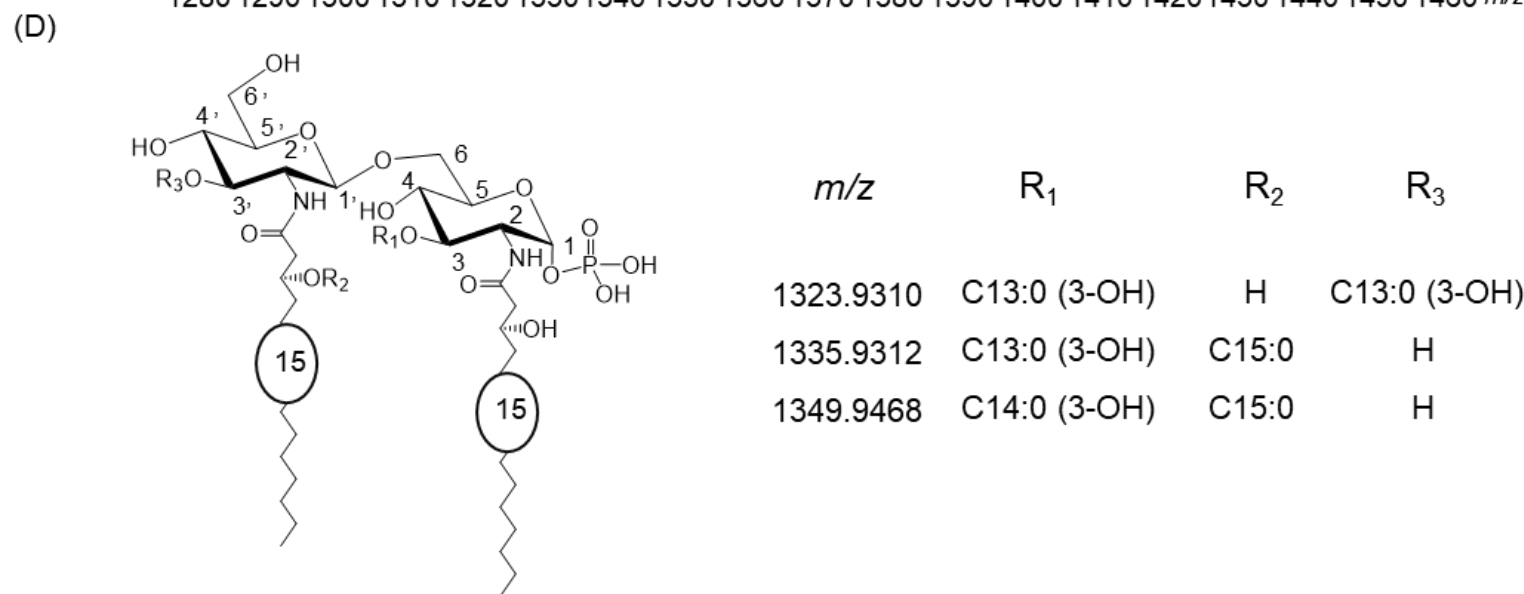
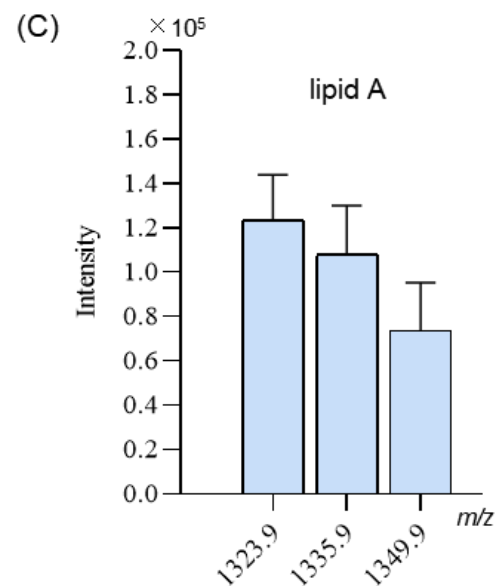
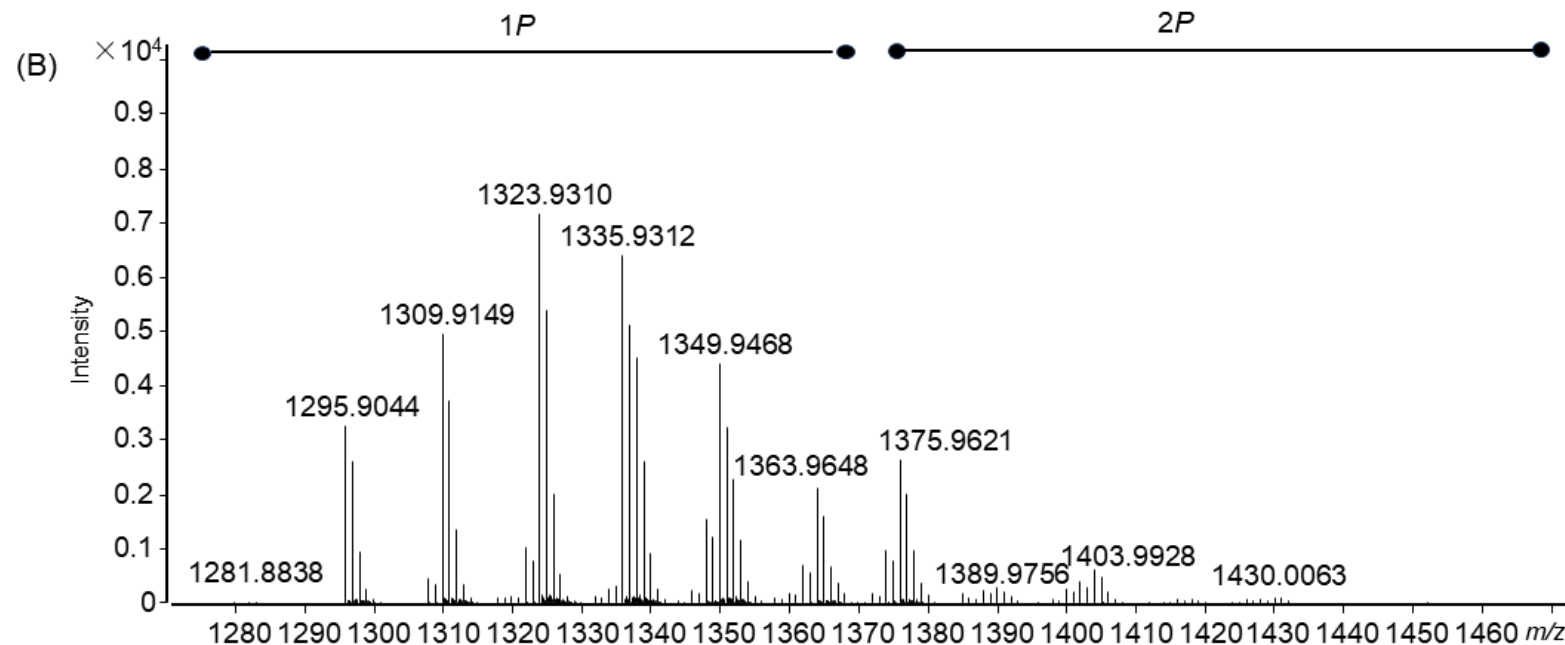
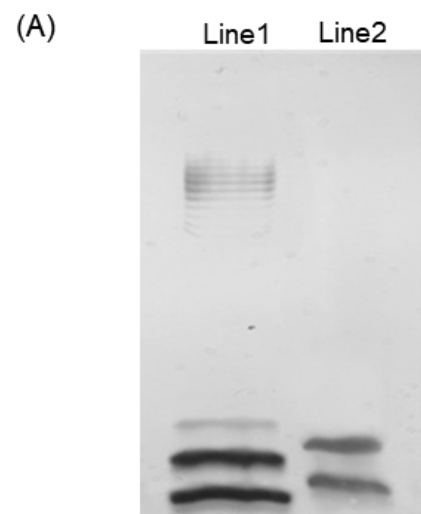
→ *A.muciniphila* LPS → ?



Improve metabolism



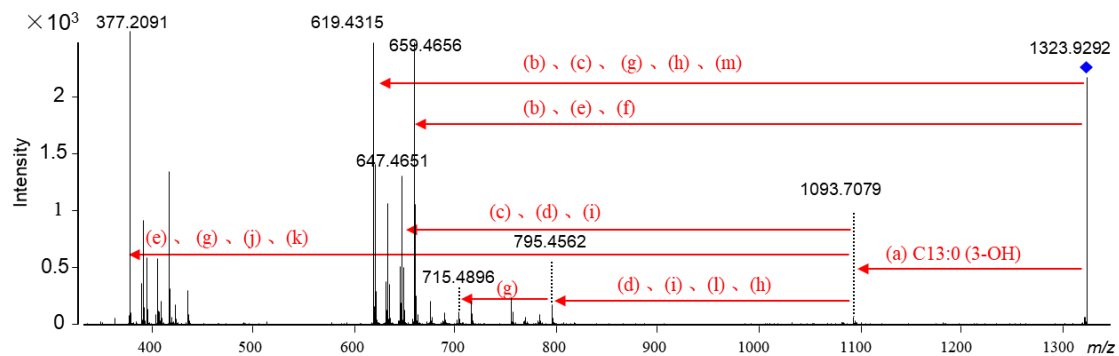
# The silver-stained SDS-PAGE and the representative chemical structure of lipid A



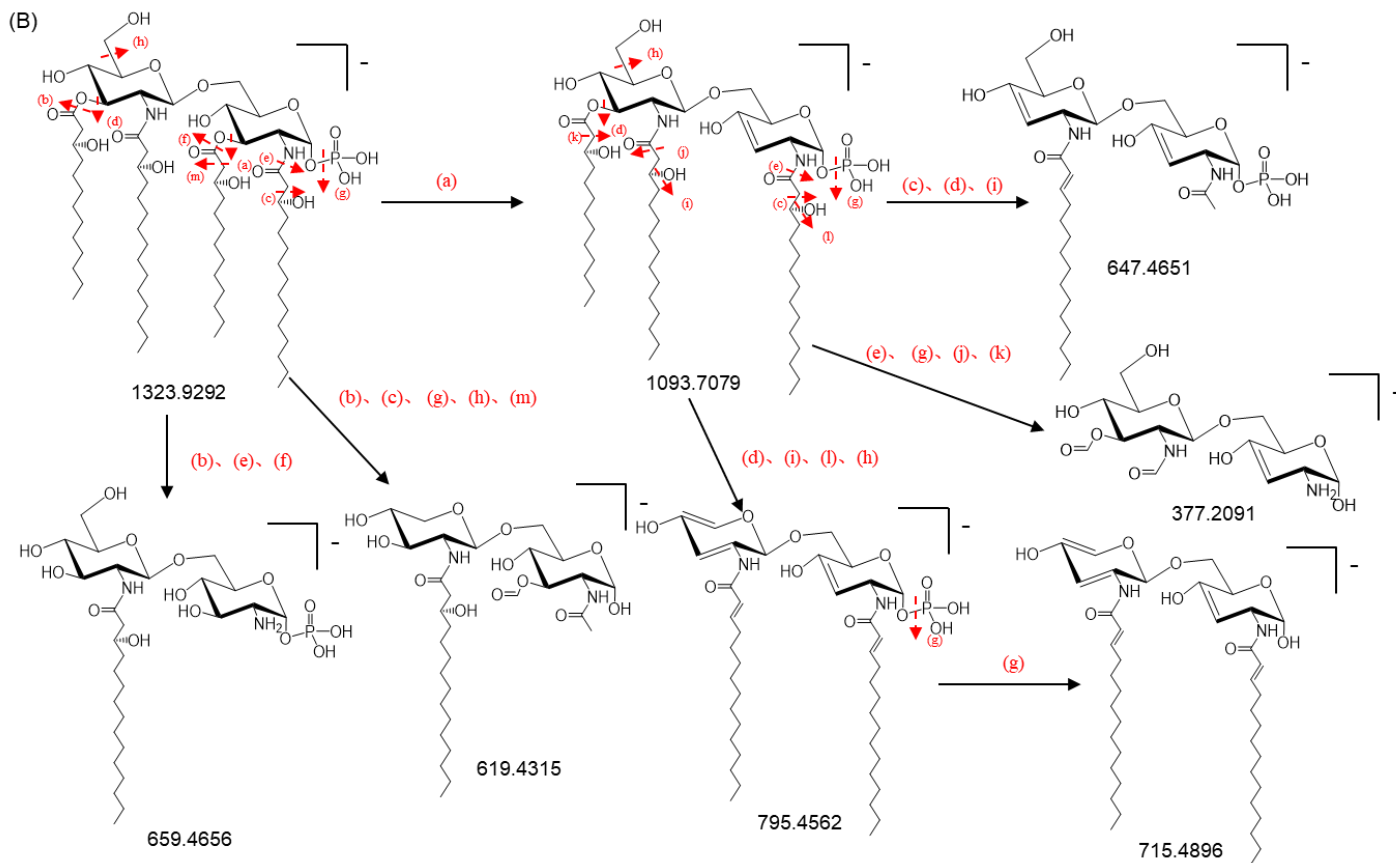


# HPLC-ESI-MS2 spectroscopic analysis of the lipid A in *A. muciniphila* LPS (ALPS)

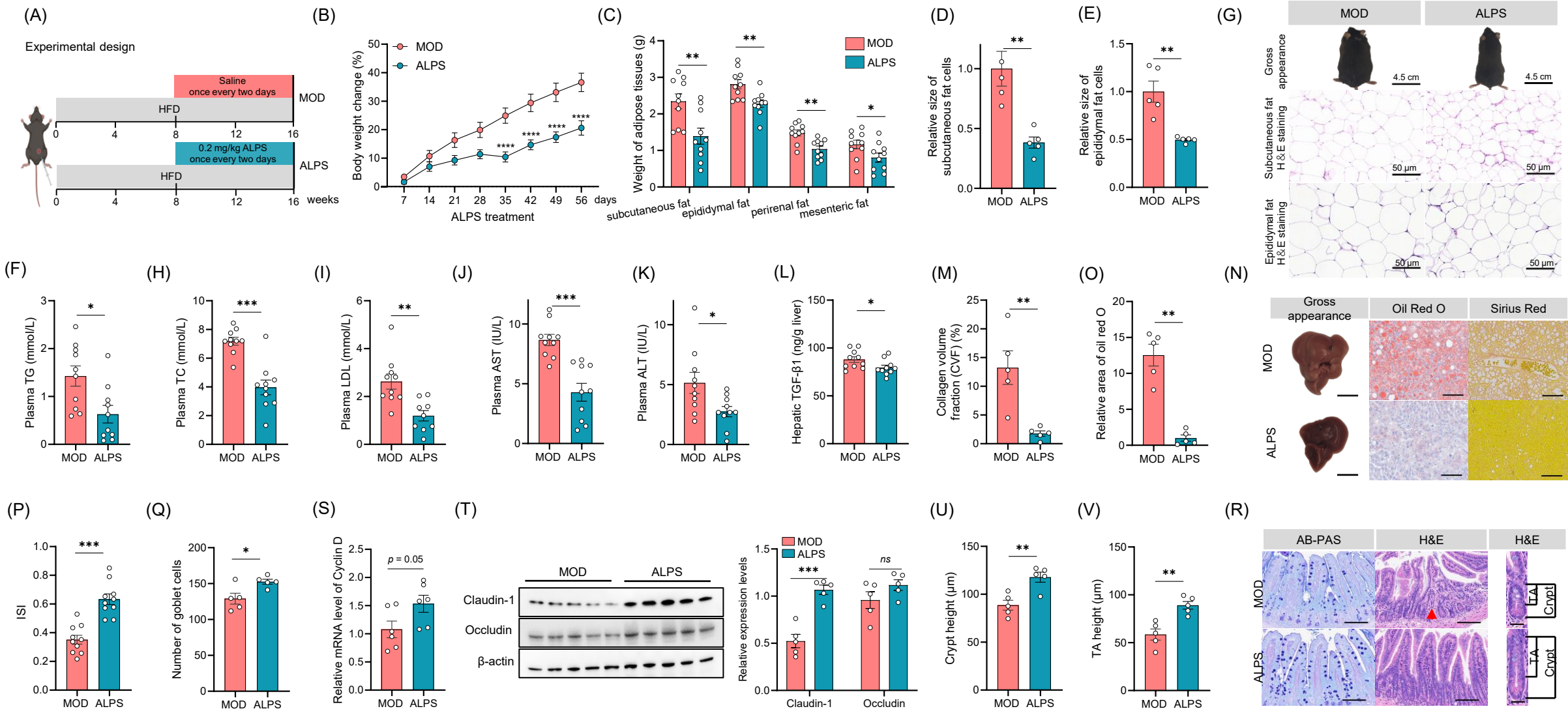
(A)



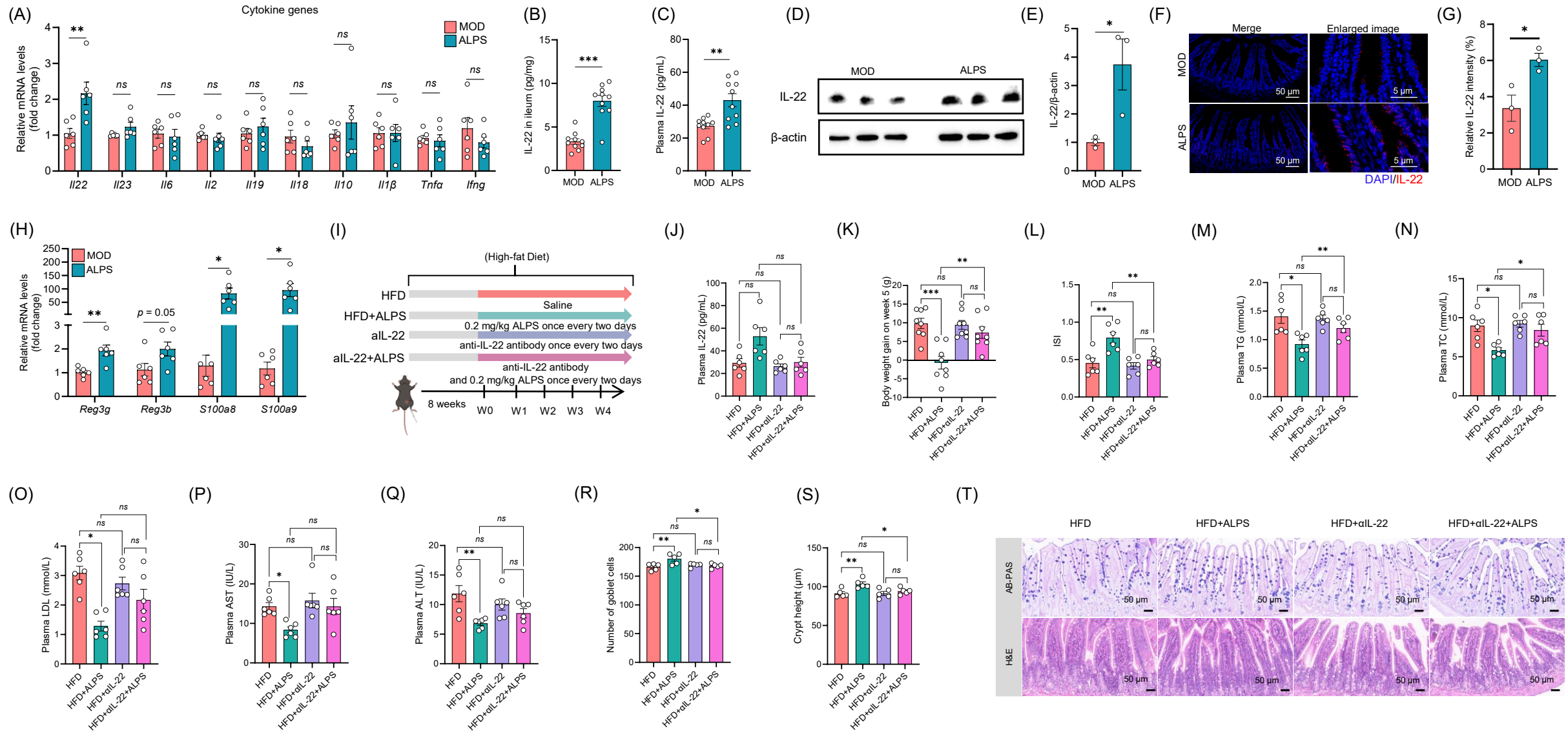
(B)



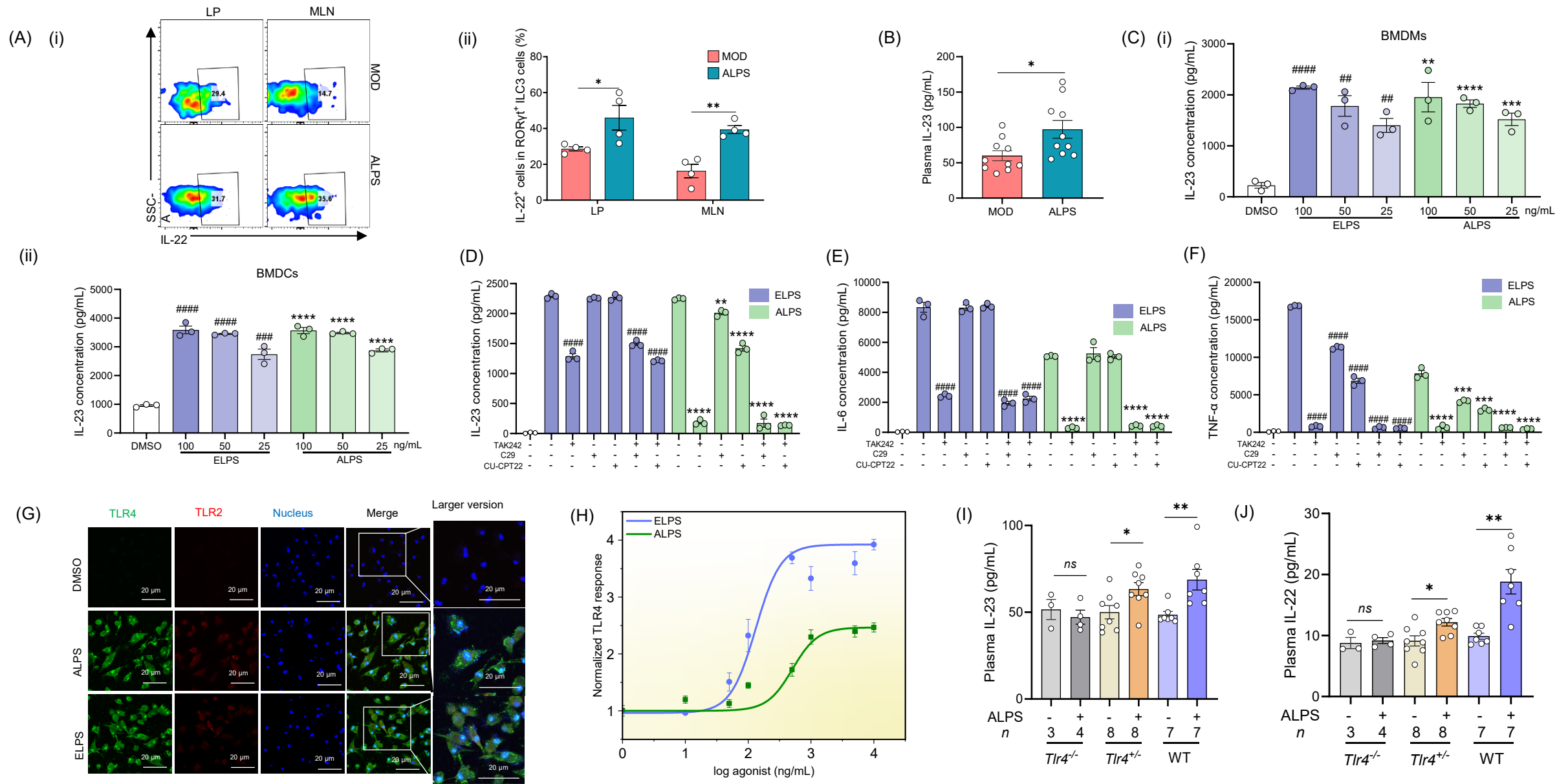
# ALPS protects against metabolic disorders in diet-induced obese (DIO) mice



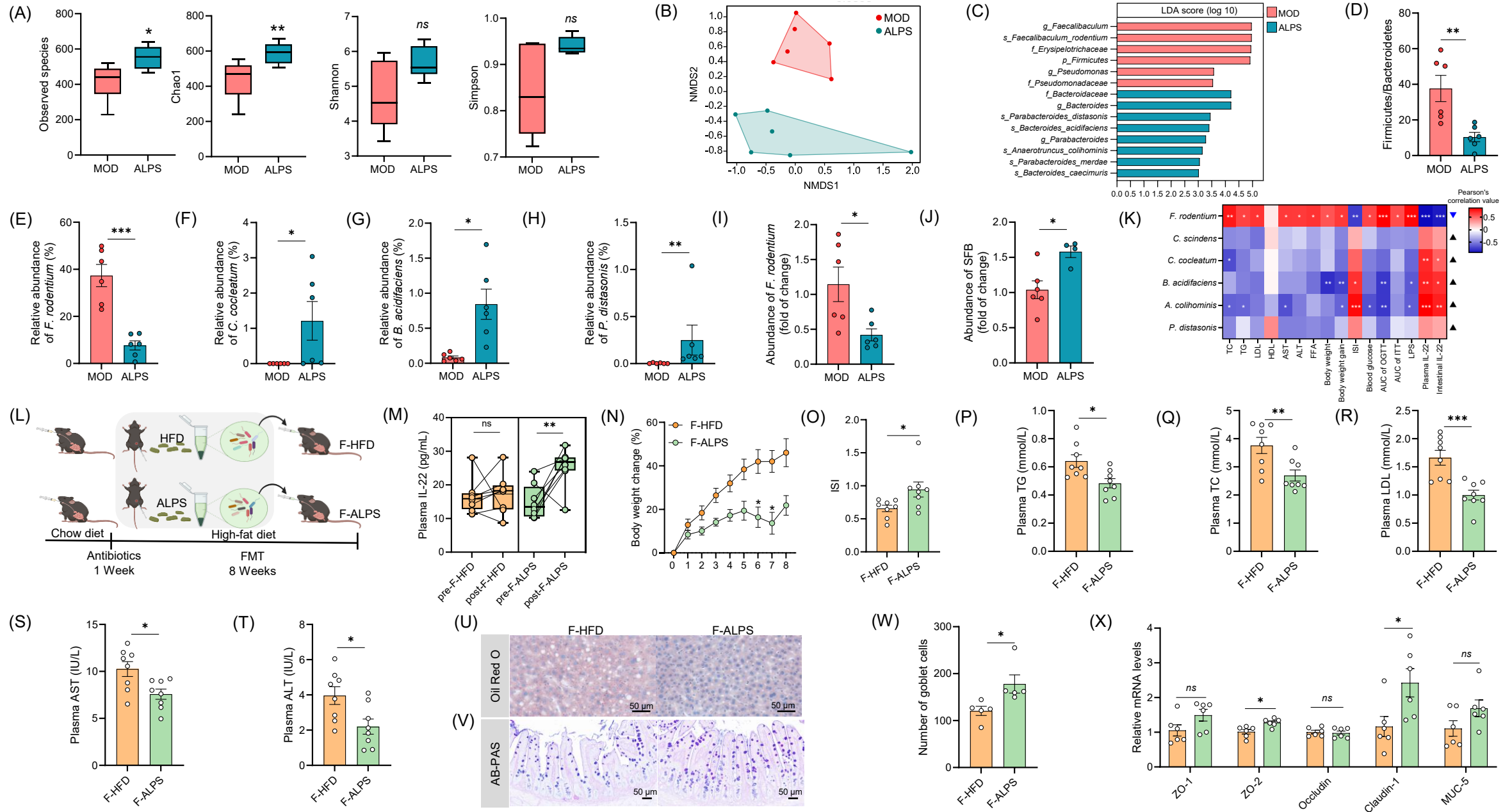
# A. muciniphila LPS (ALPS) promotes IL-22 production in DIO mice



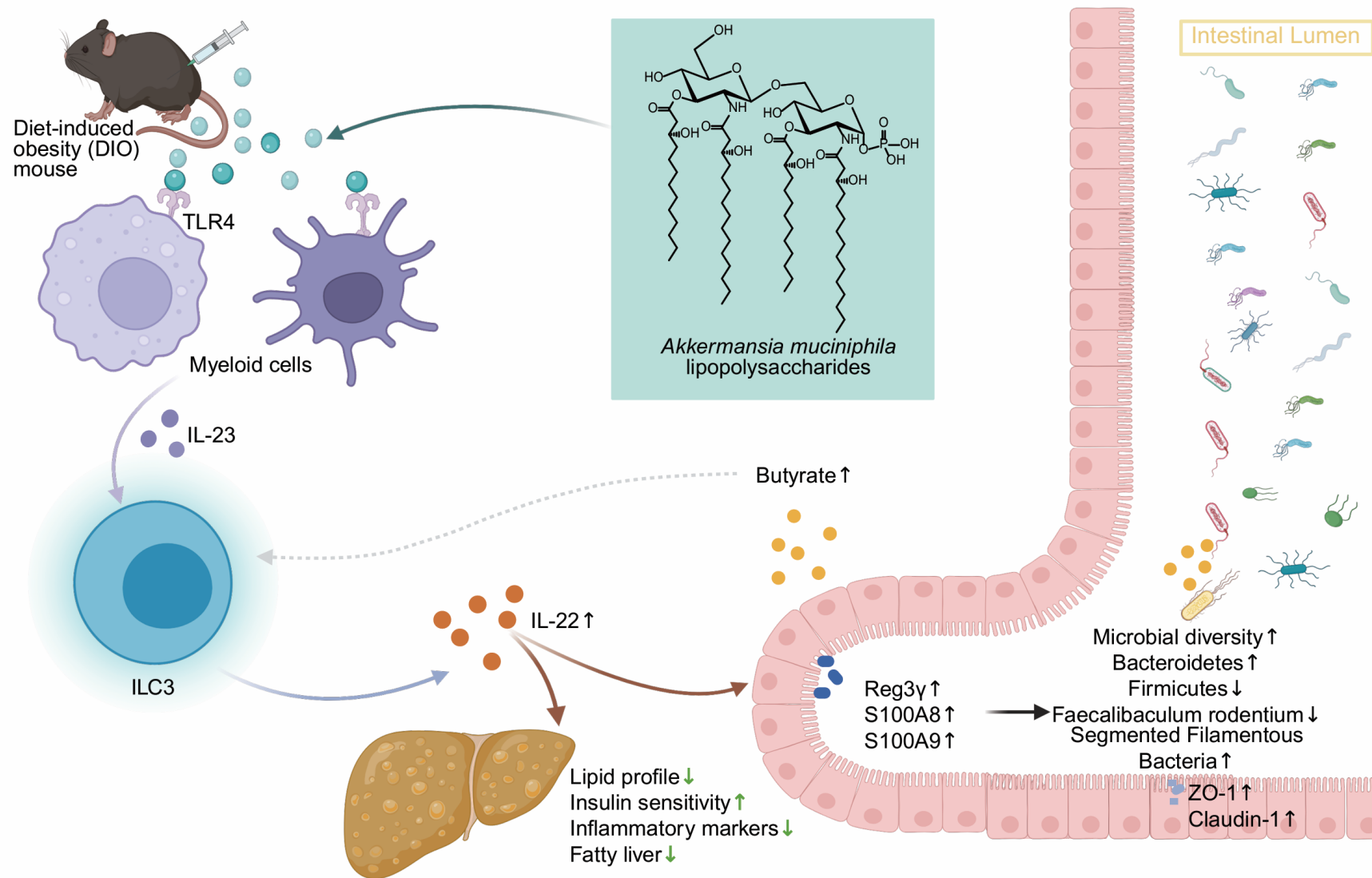
# *A. muciniphila* LPS (ALPS) activates the TLR4-IL-23-IL-22 signaling pathway



# Alteration of gut microbiota by *A. muciniphila* LPS (ALPS) and the protective effect of ALPS-induced gut microbiota in DIO mice



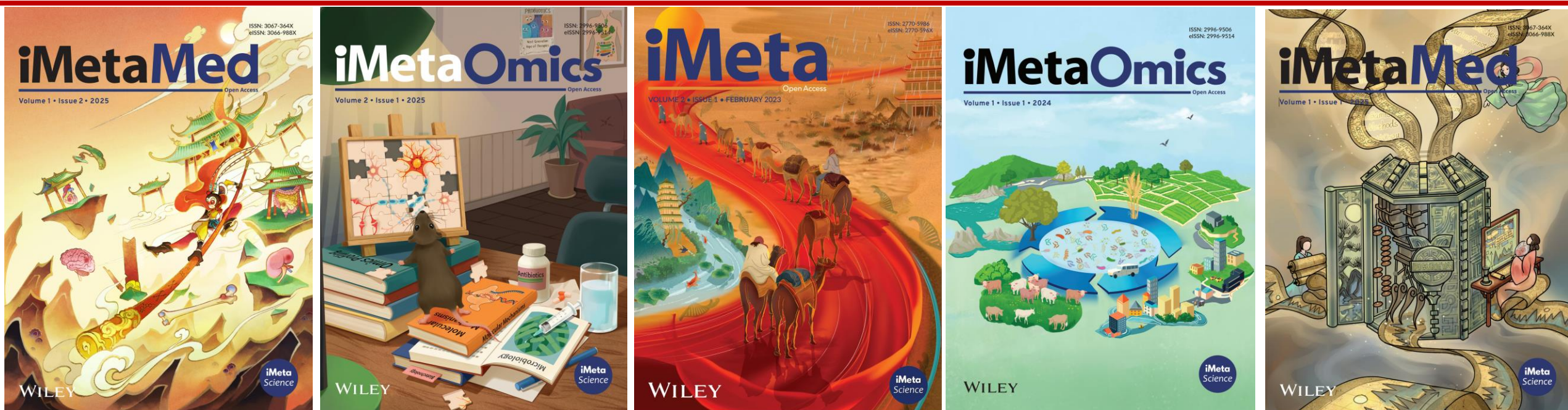
# Summary



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