

Orally cascade targeting delivery systems alleviate colitis by protecting mitochondria and regulating gut microbiota

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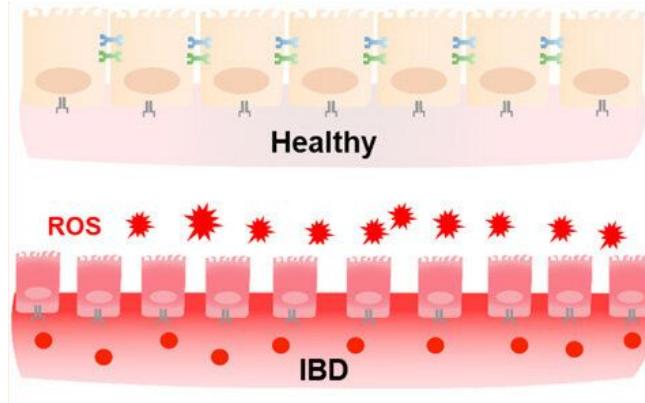


INTEGRATING
Delivery Science
ACROSS DISCIPLINES

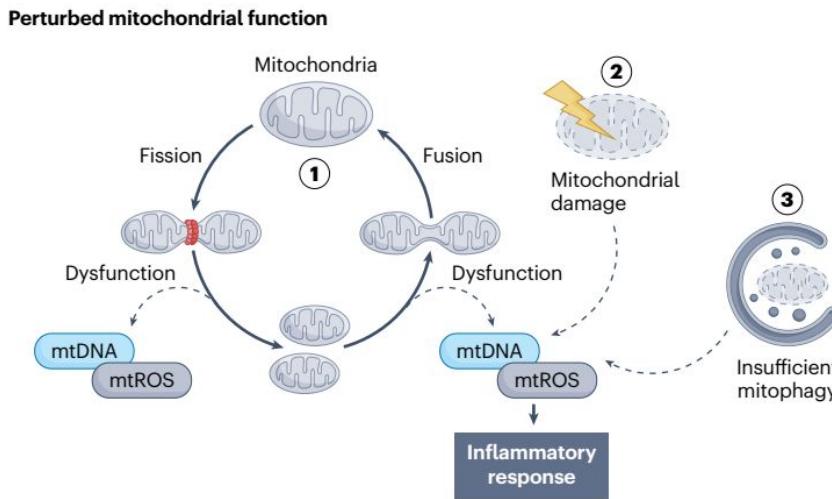


Background

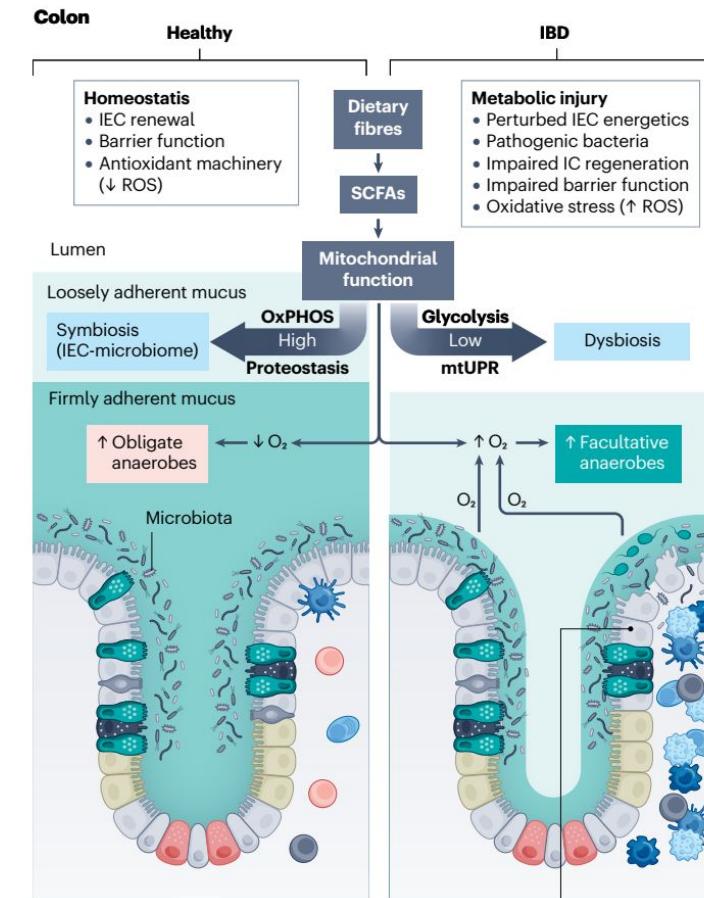
Inflammatory bowel disease (IBD)



mitochondrial dysfunction drives inflammatory responses

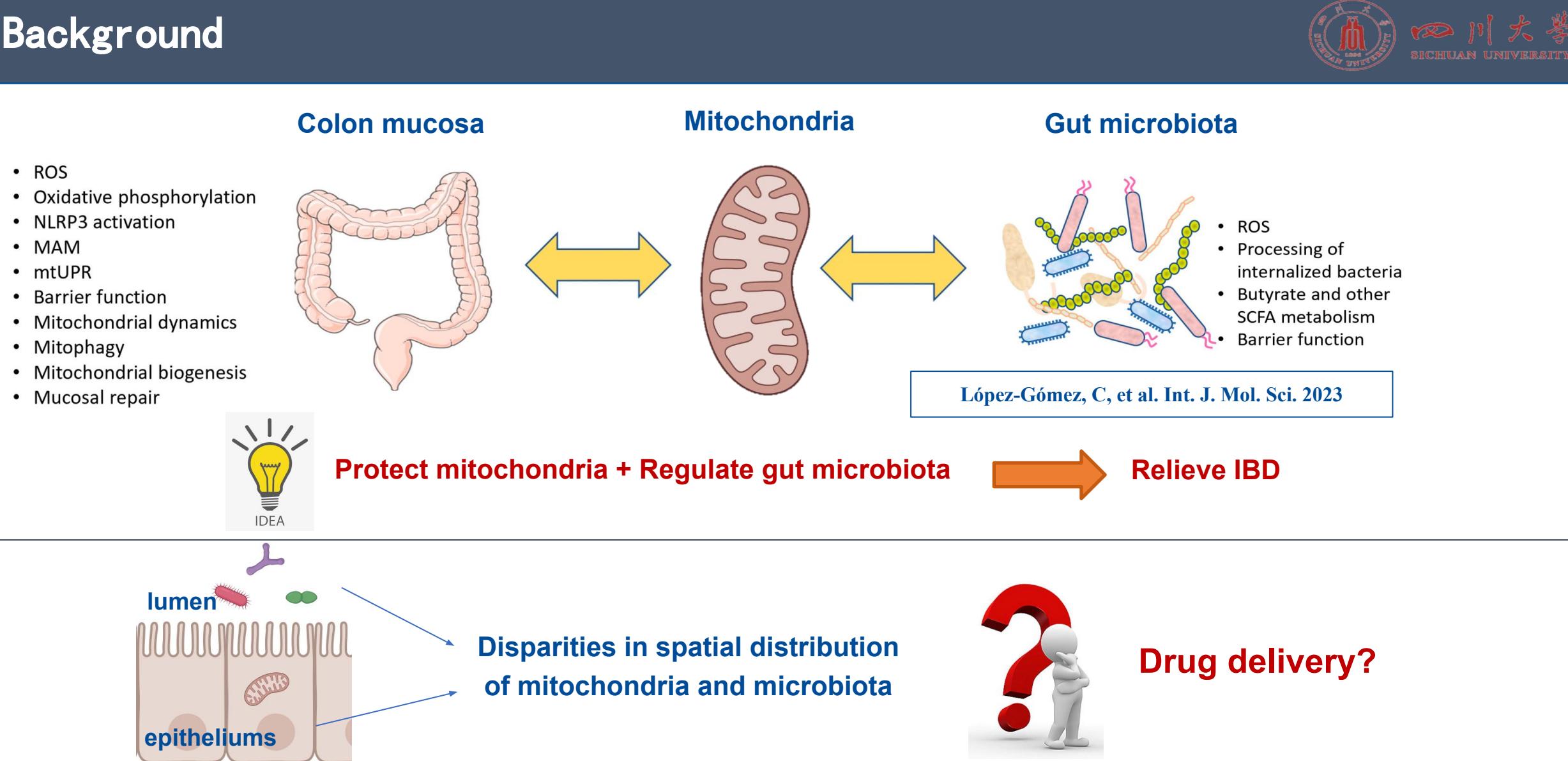


Mitochondrial dysfunction occurs in IBD



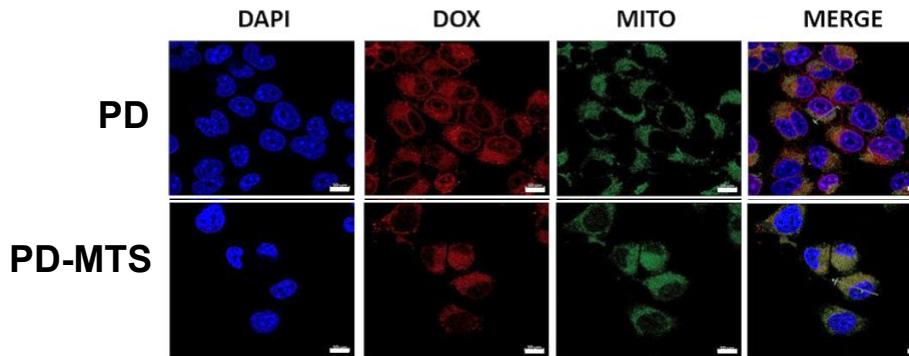
Haque, P.S., Kapur, N., Barrett, T.A. et al. Nat Rev Gastroenterol Hepatol, 2024.

Background



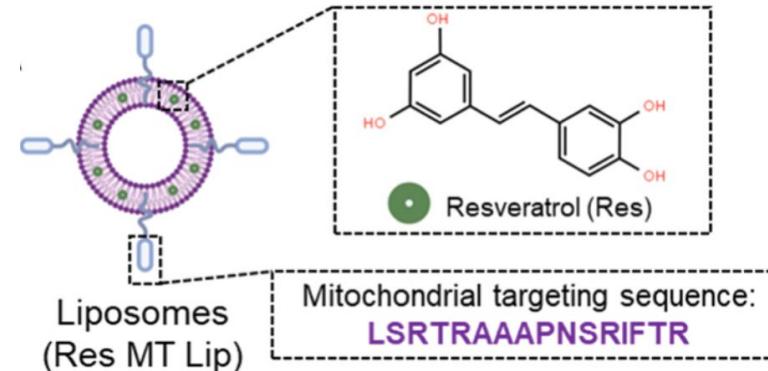
Construction of orally cascade targeting delivery system

Mitochondria-Targeting Sequences (MTS)

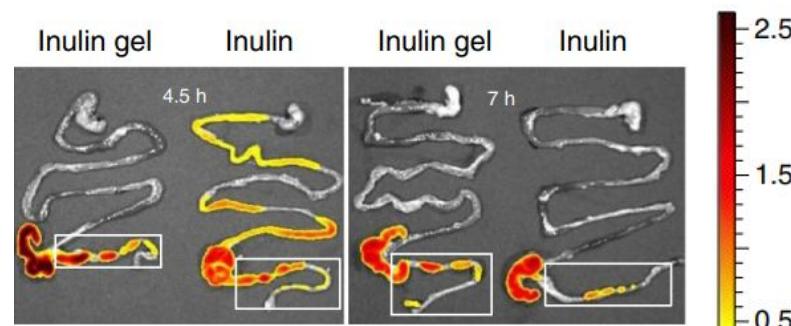


Qiuyi Li, Yuan Huang, et al. *J Control Release.*, 2020.

MTS modified liposomes

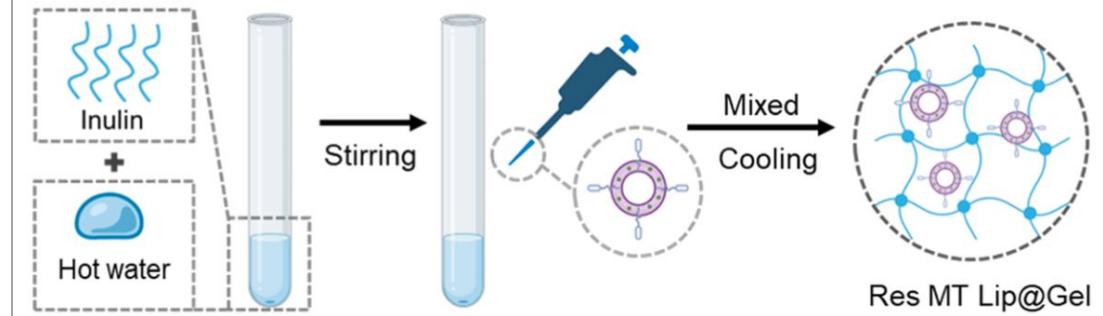


Polysaccharide gel prolongs colonic retention

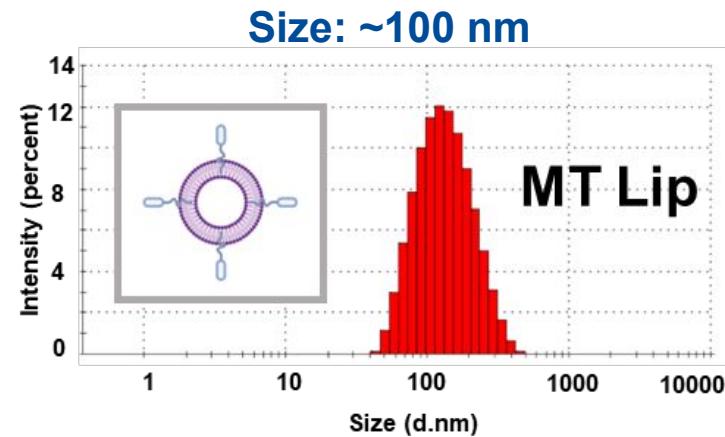


Han, K., Nam, J., Xu, J. et al. *Nat Biomed Eng.*, 2021.

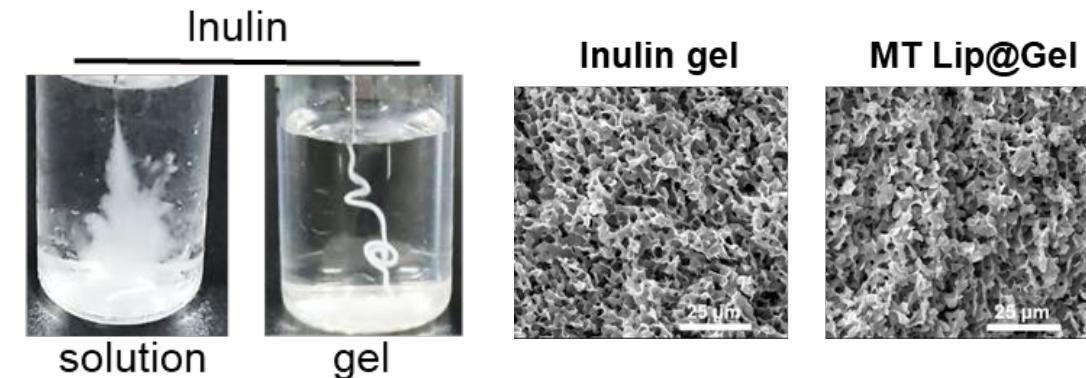
Probiotic inulin gel encapsulated liposomes



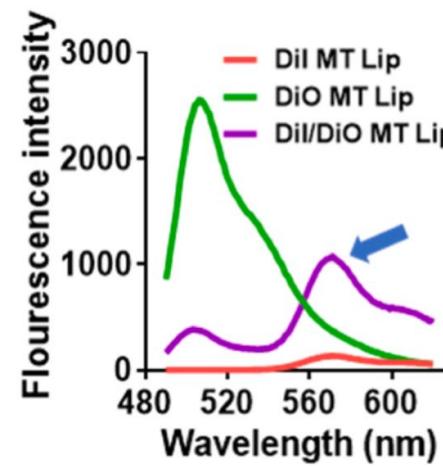
Characterization of orally delivery system



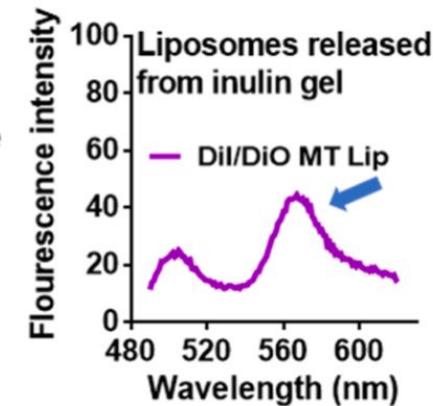
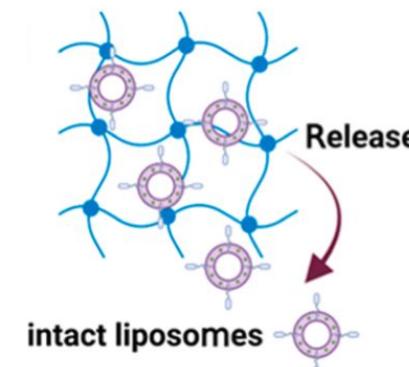
microstructure of inulin gel



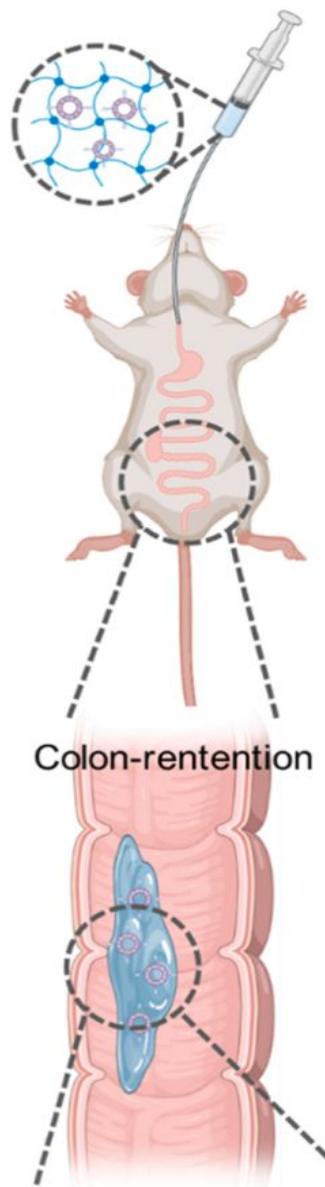
FRET assay for fresh prepared liposomes



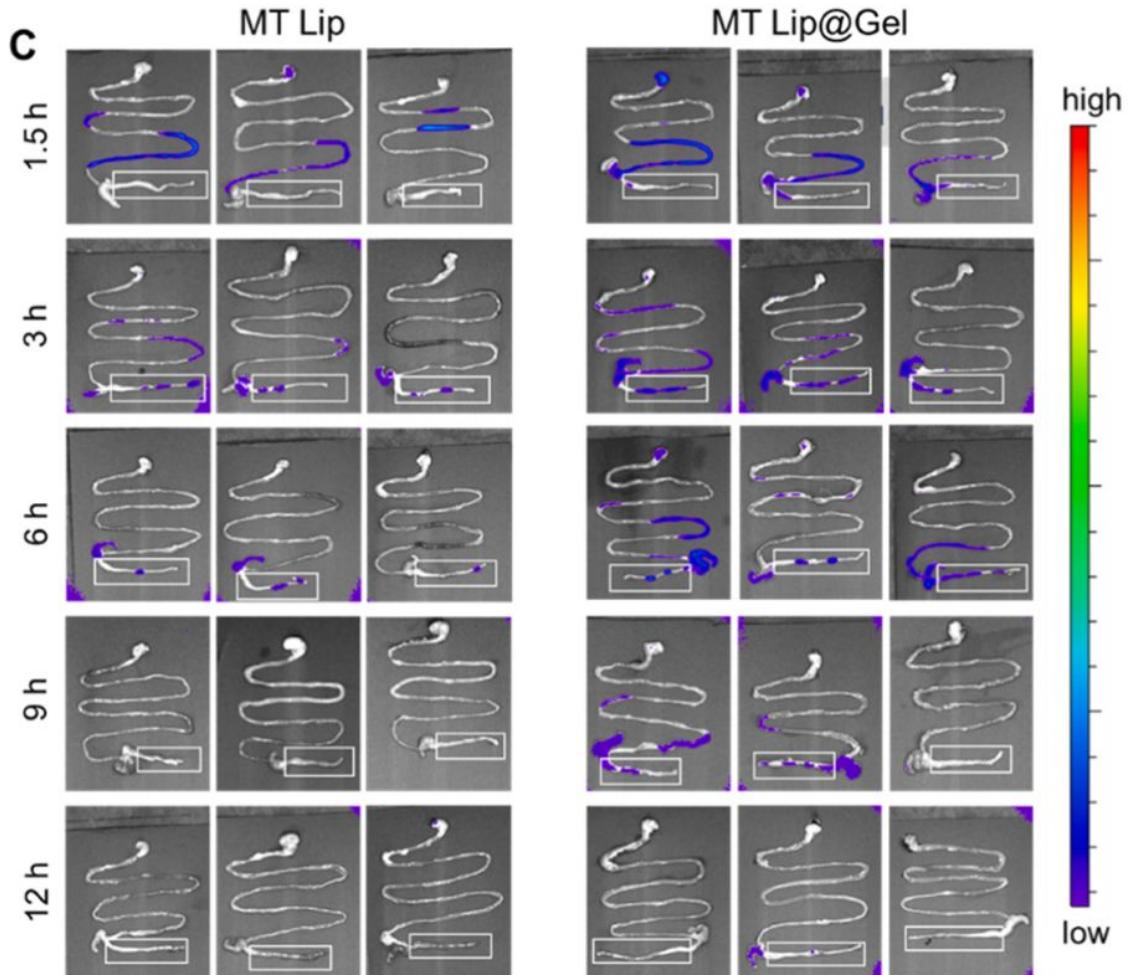
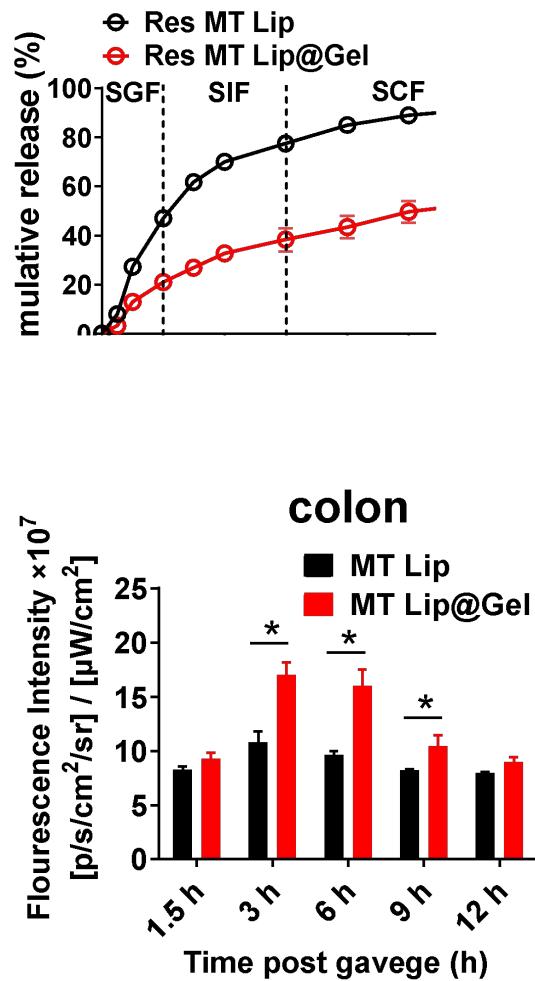
The intact liposomes released from inulin gel



Orally cascade targeting: colon-cell-mitochondria

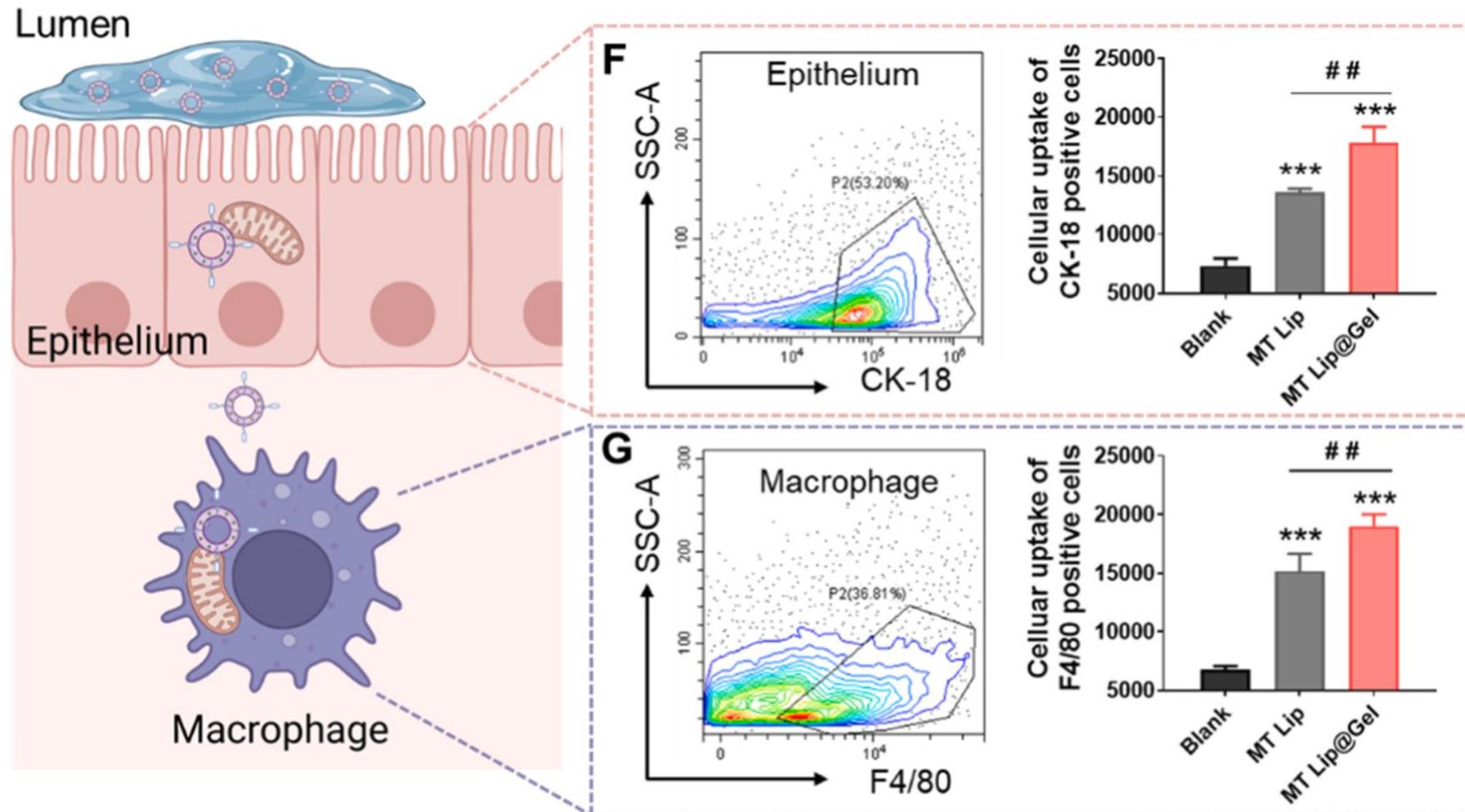


Inulin gel decrease drug leakage in stomach and small intestine



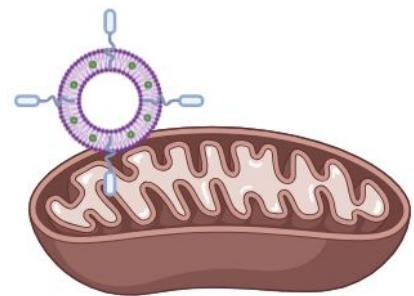
Inulin gel prolongs colonic retention

Orally cascade targeting: colon- cell -mitochondria

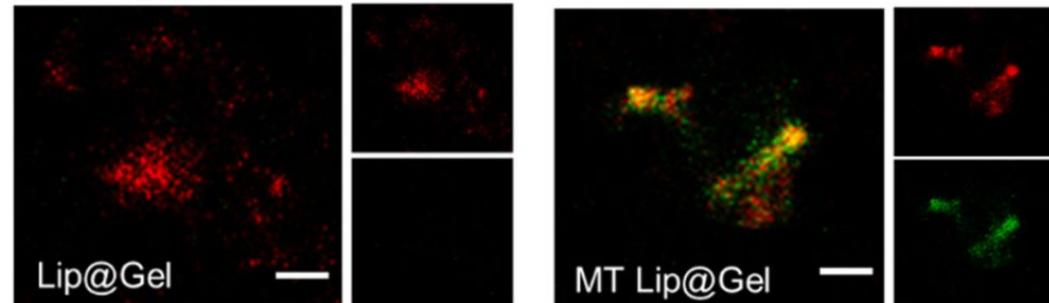


- liposomes were delivered to colonic macrophages and epitheliums
- increasing colonic retention via inulin gel could enhance the cellular uptake

Orally cascade targeting: colon-cell- mitochondria

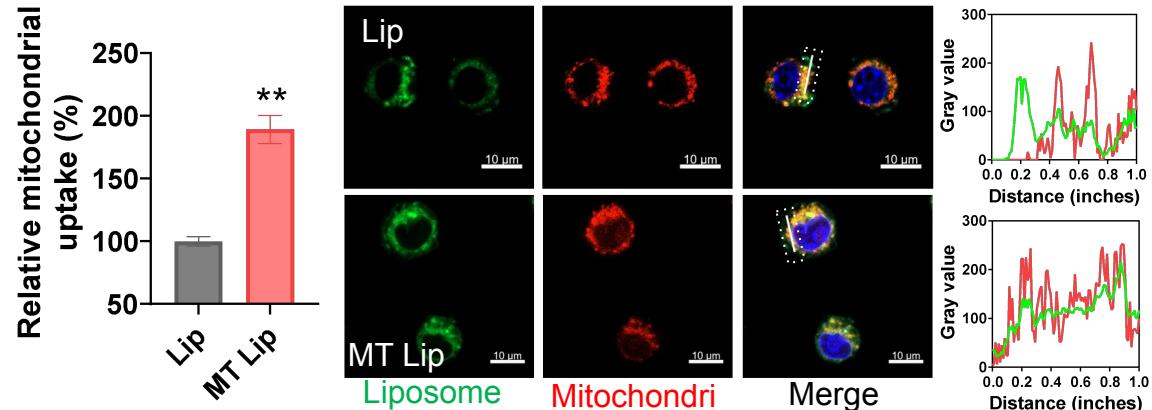


Red: Mitochondria isolated from colon tissue
Green: Preparations



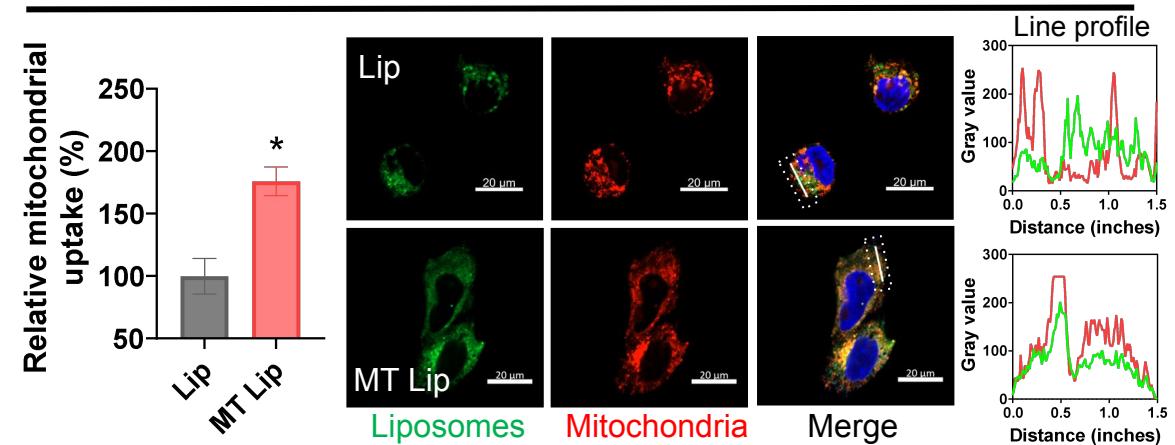
Liposomes accumulated in colonic mitochondria

RAW264.7



Liposomes targeted to mitochondria in macrophages

Caco-2

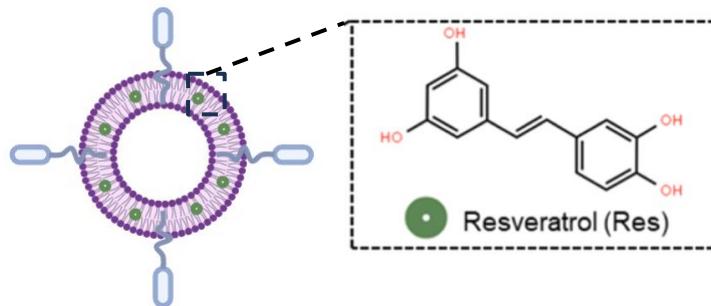


Liposomes targeted to mitochondria in epithelium

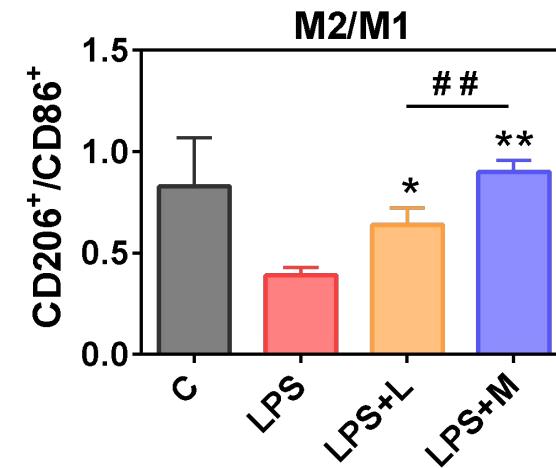
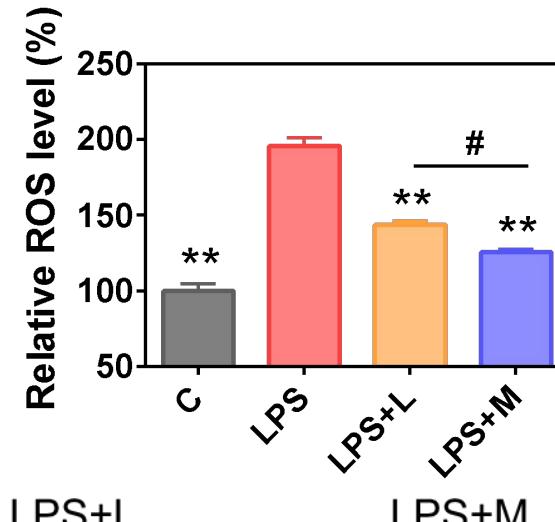
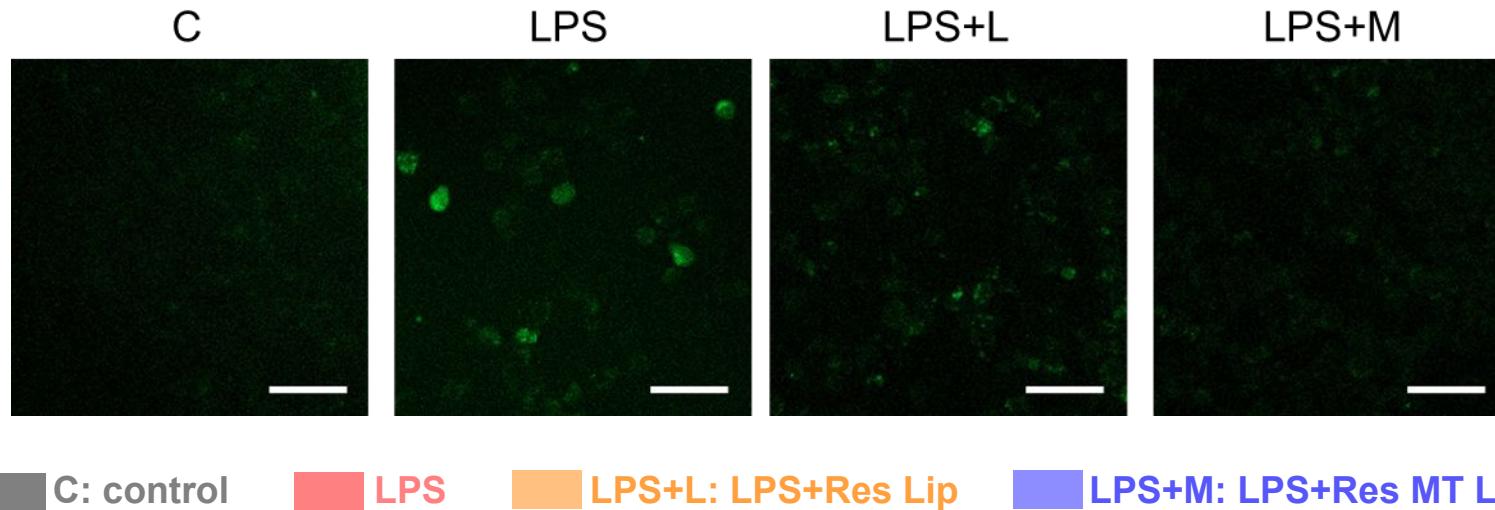
Res MT Lip facilitated ROS-scavenging in macrophages



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Resveratrol loaded mitochondrial targeting liposomes (Res MT Lip)

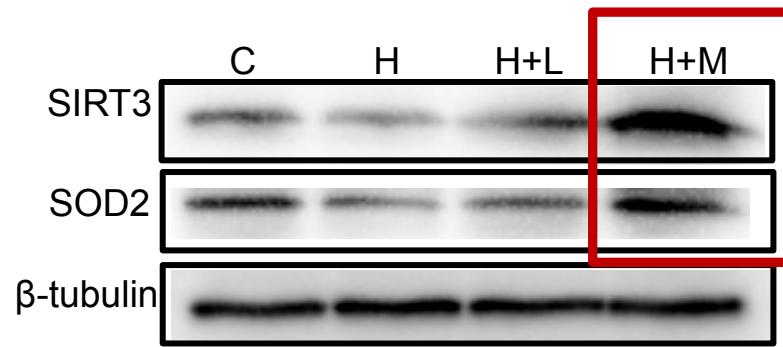


□ Mitochondrial-targeted Res MT Lip facilitated ROS-scavenging

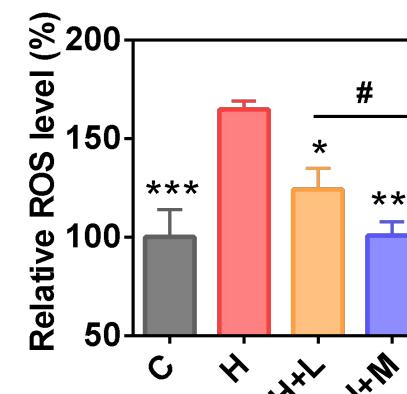


Res MT Lip facilitated wound healing in epitheliums

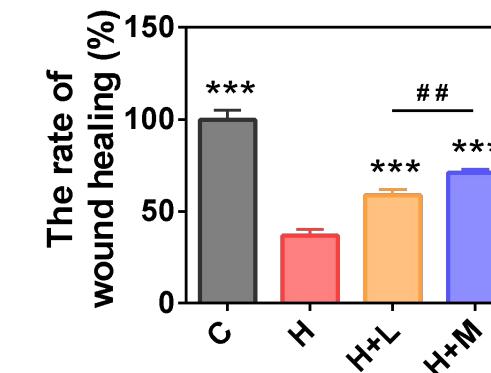
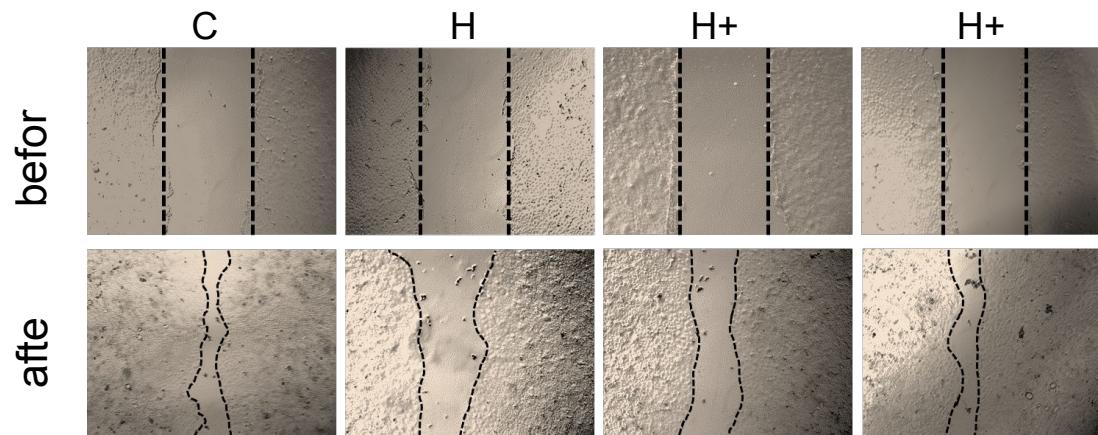
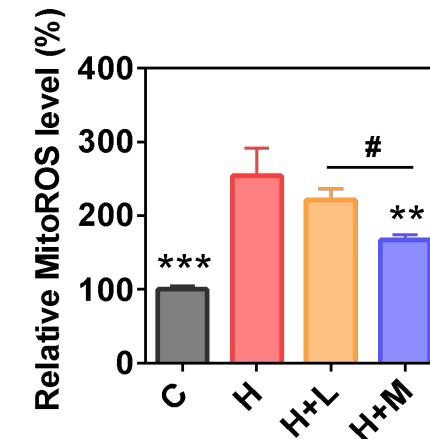
Activate SIRT3 for mitochondrial protection



ROS scavenging



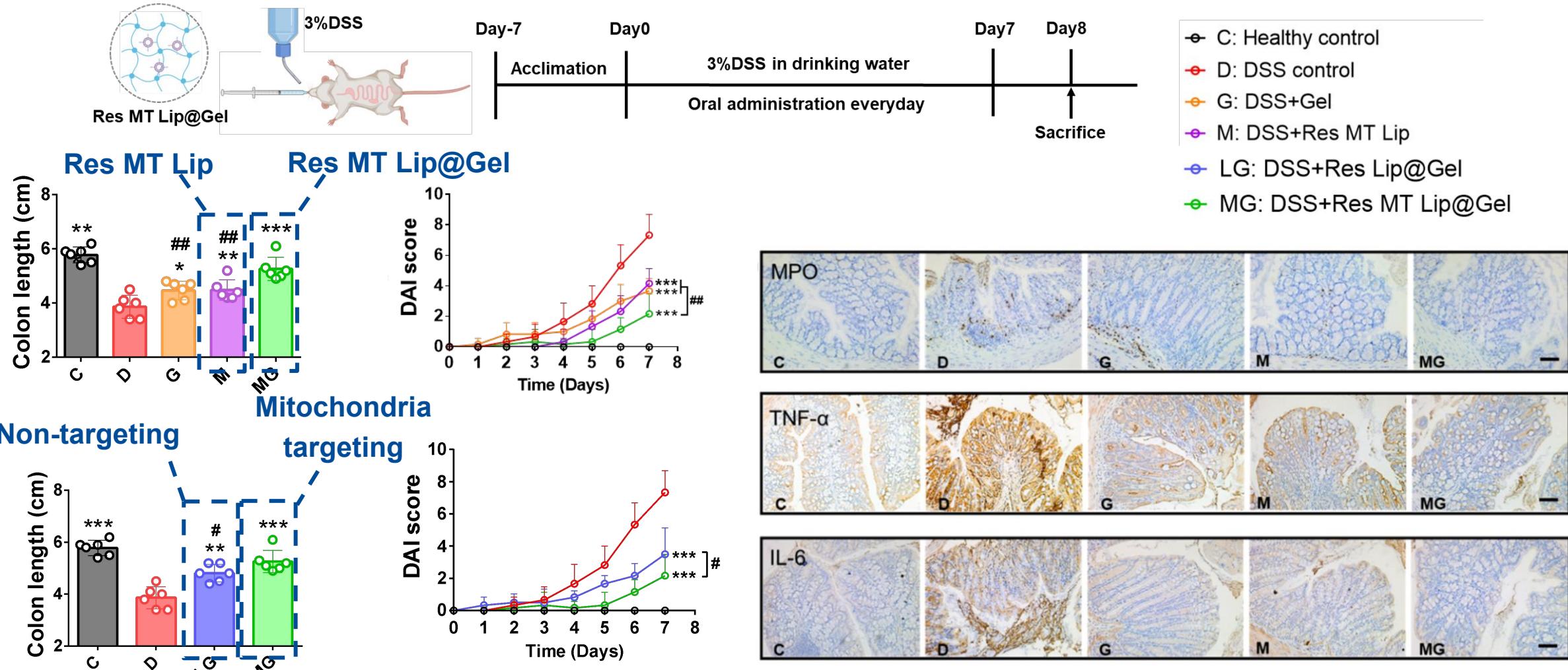
Decrease mitochondrial ROS



Protect epitheliums under oxidative damage

C: control H: H₂O₂ H+L: H₂O₂+Res Lip H+M: H₂O₂+Res MT Lip

Res MT Lip@Gel relieved DSS-induced acute colitis



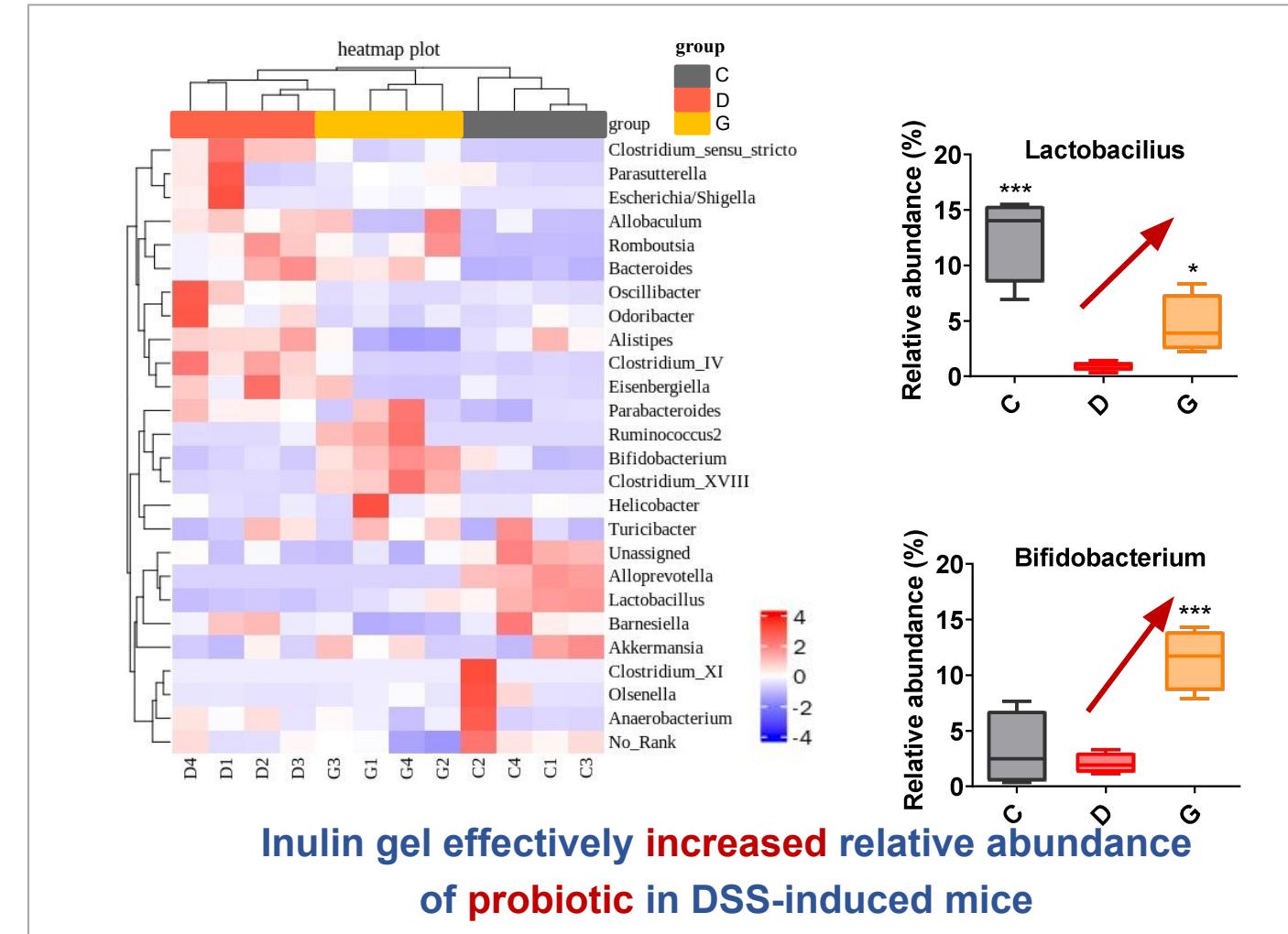
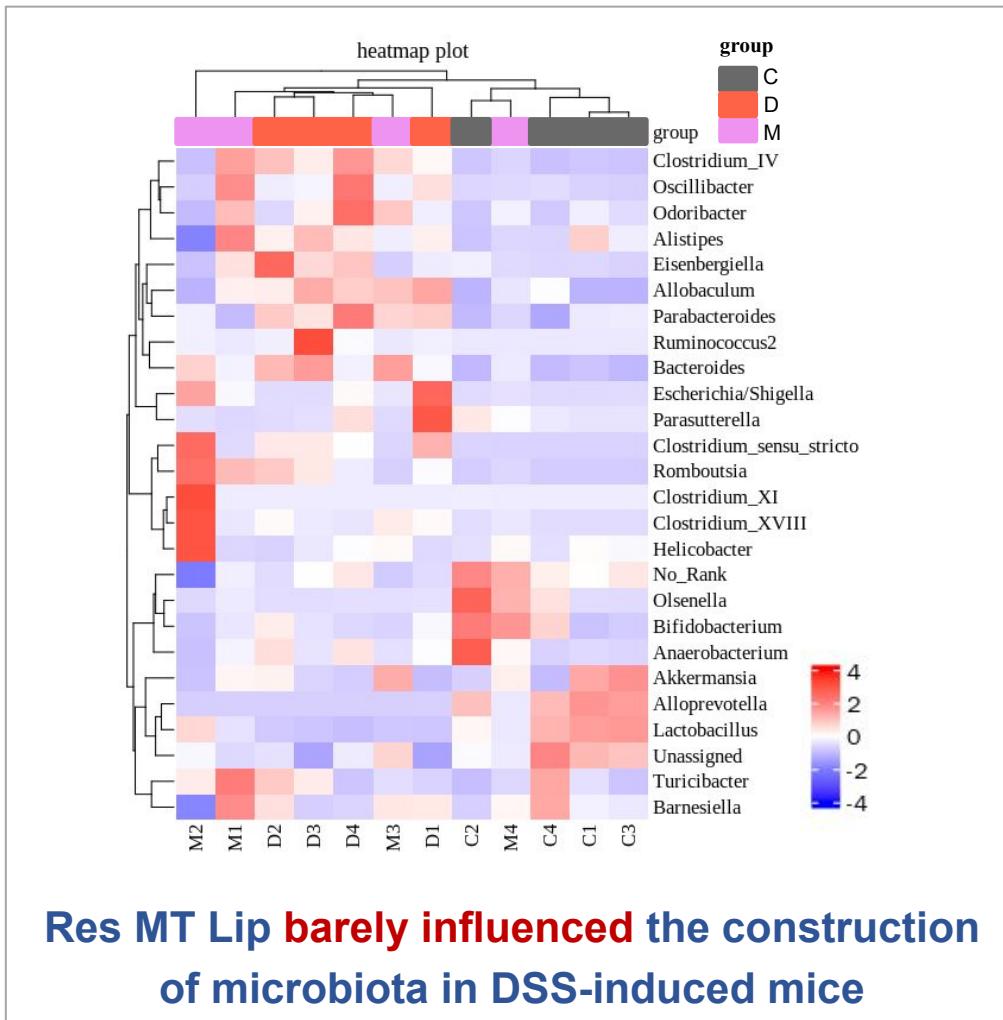
Inulin gel modulated gut microbiota

C: Healthy control

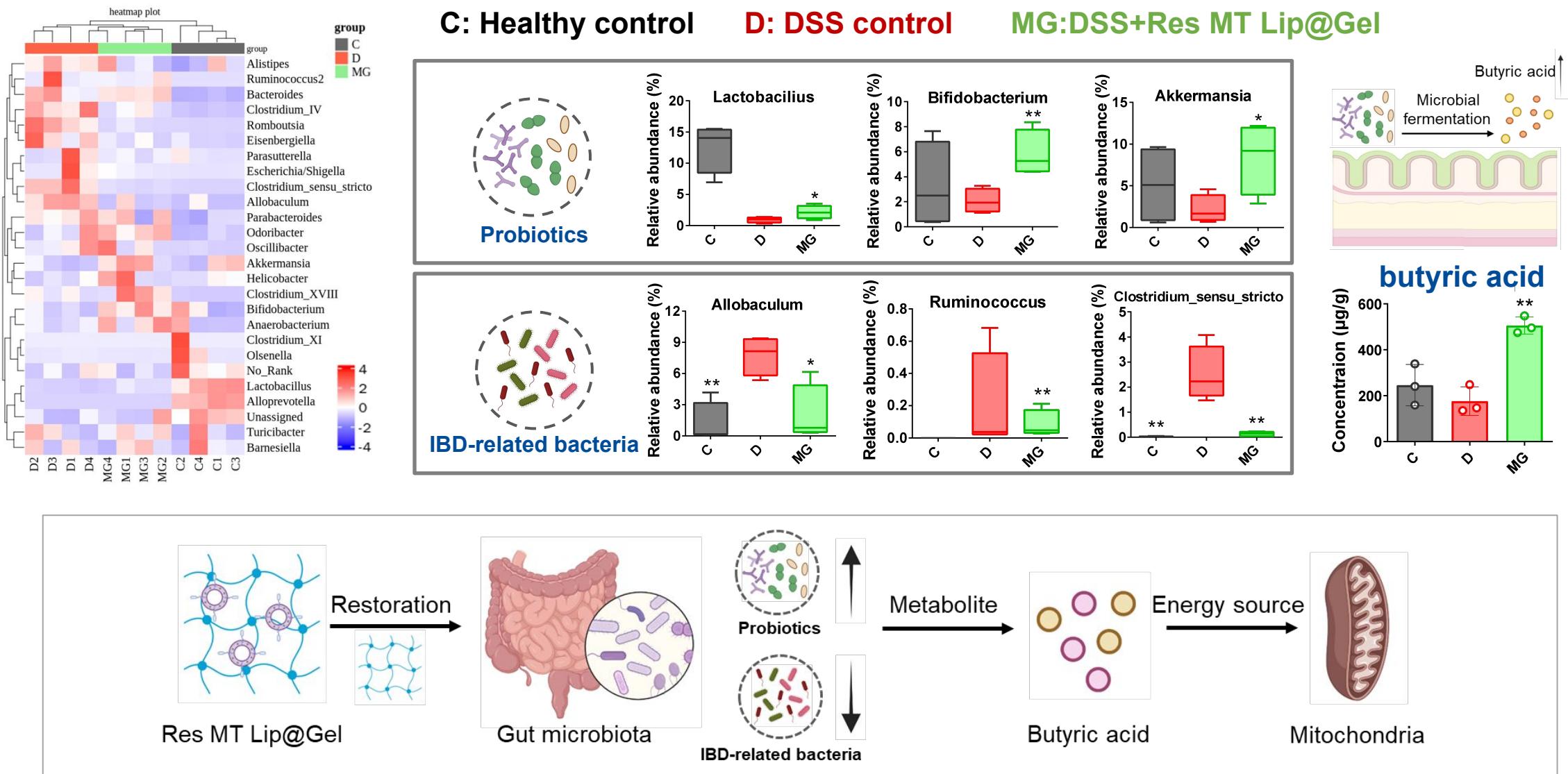
D: DSS control

M:DSS+Res MT Lip

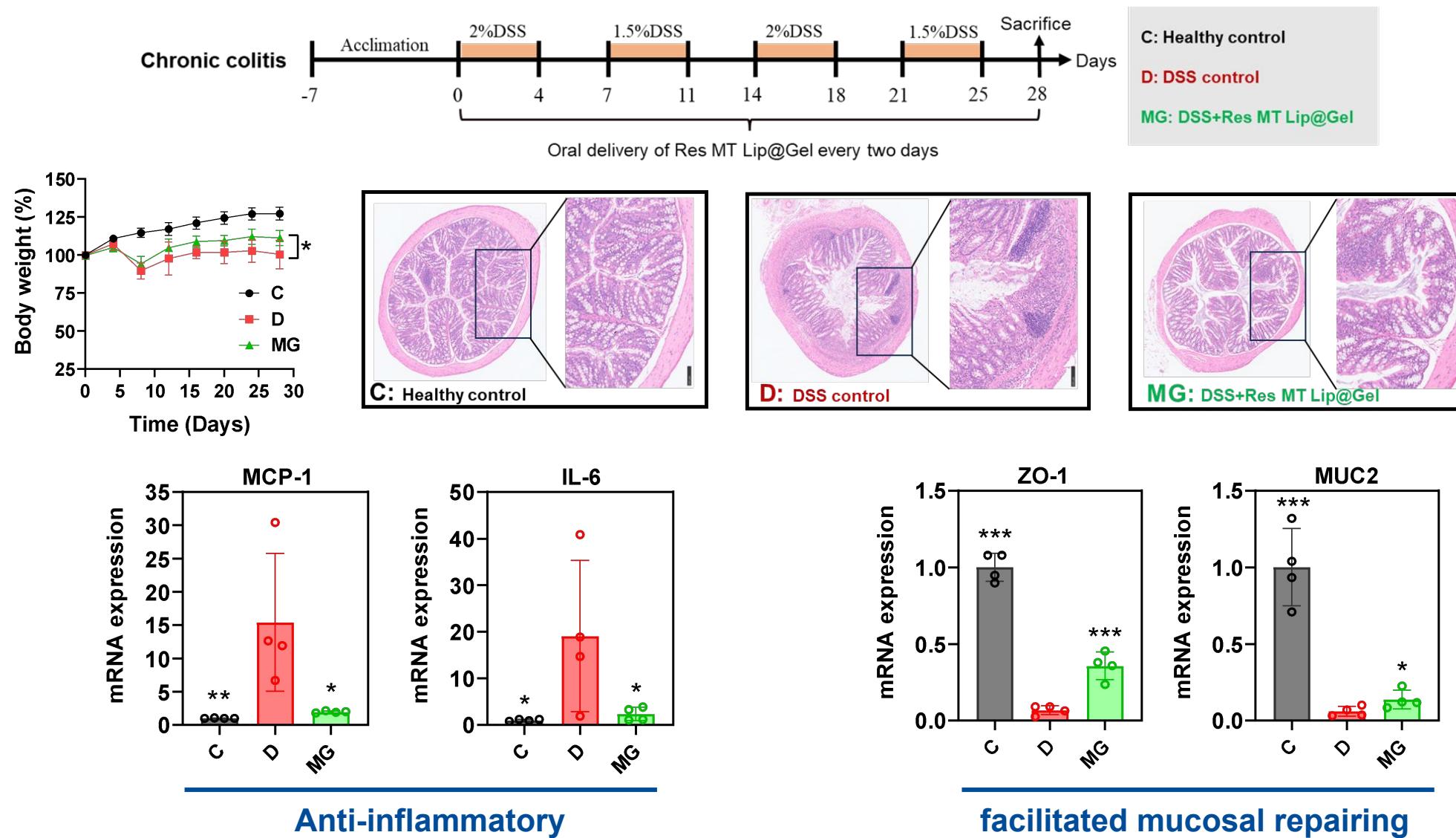
G:DSS+Gel



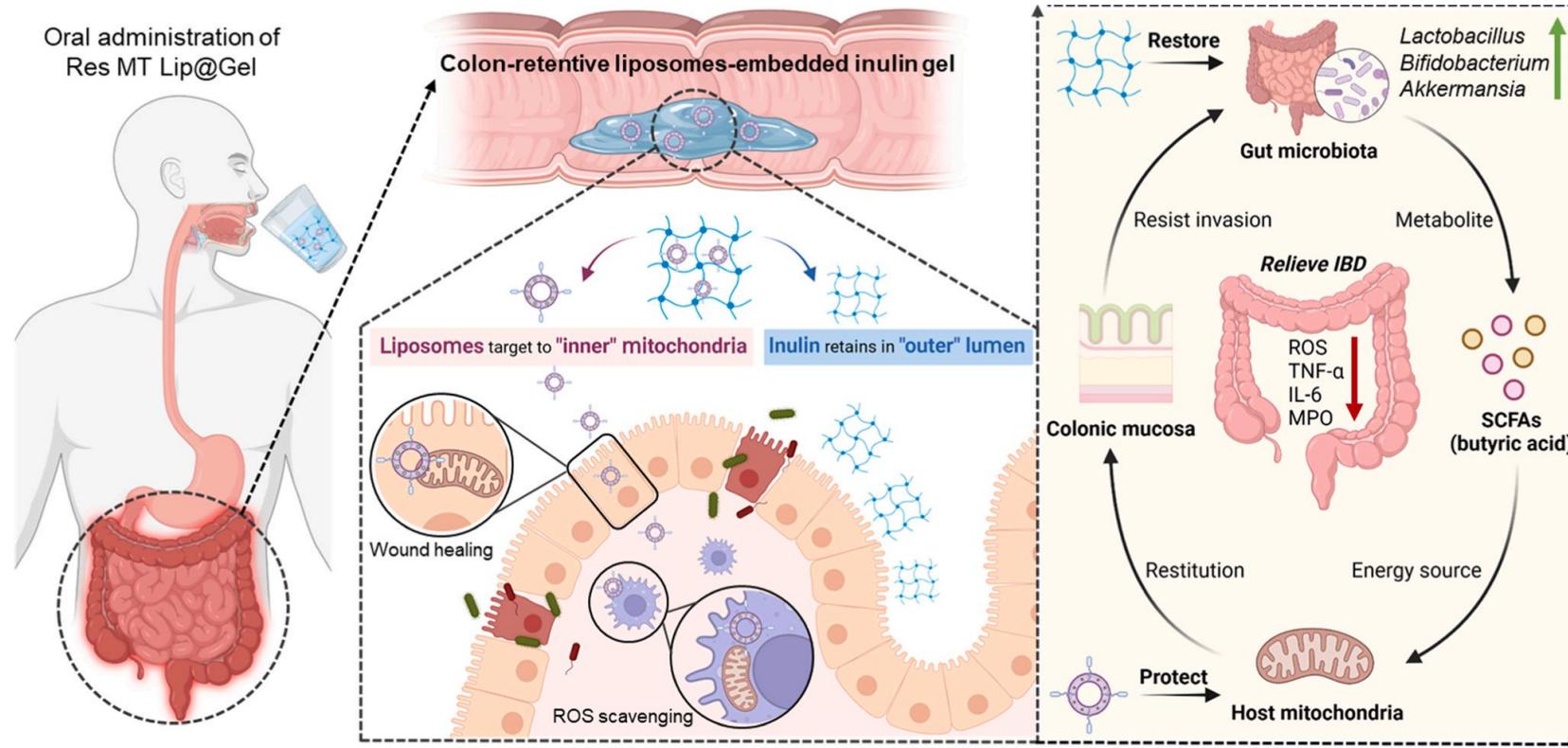
Res MT Lip@Gel inherited the microbiota-regulation of



Res MT Lip@Gel relieved DSS-induced chronic colitis



Orally cascade targeting delivery system



- ◆ Targeted delivery to colonic mitochondria
- ◆ Protect mitochondria and regulate gut microbiota
- ◆ Alleviating acute and chronic colitis

Acknowledgement 613 Huang's Lab



Prof. Yuan Huang



A.P. Zhou Zhou



A.P. Lian Li



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Mucosal delivery systems

- Oral drug delivery
- Inhaled drug delivery
- Mucosal delivery of protein and peptide drugs

Subcellular-targeted delivery systems

- Mitochondrial targeted delivery
- Endoplasmic reticulum targeted delivery
- Nuclear targeted delivery



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Thanks for listening



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