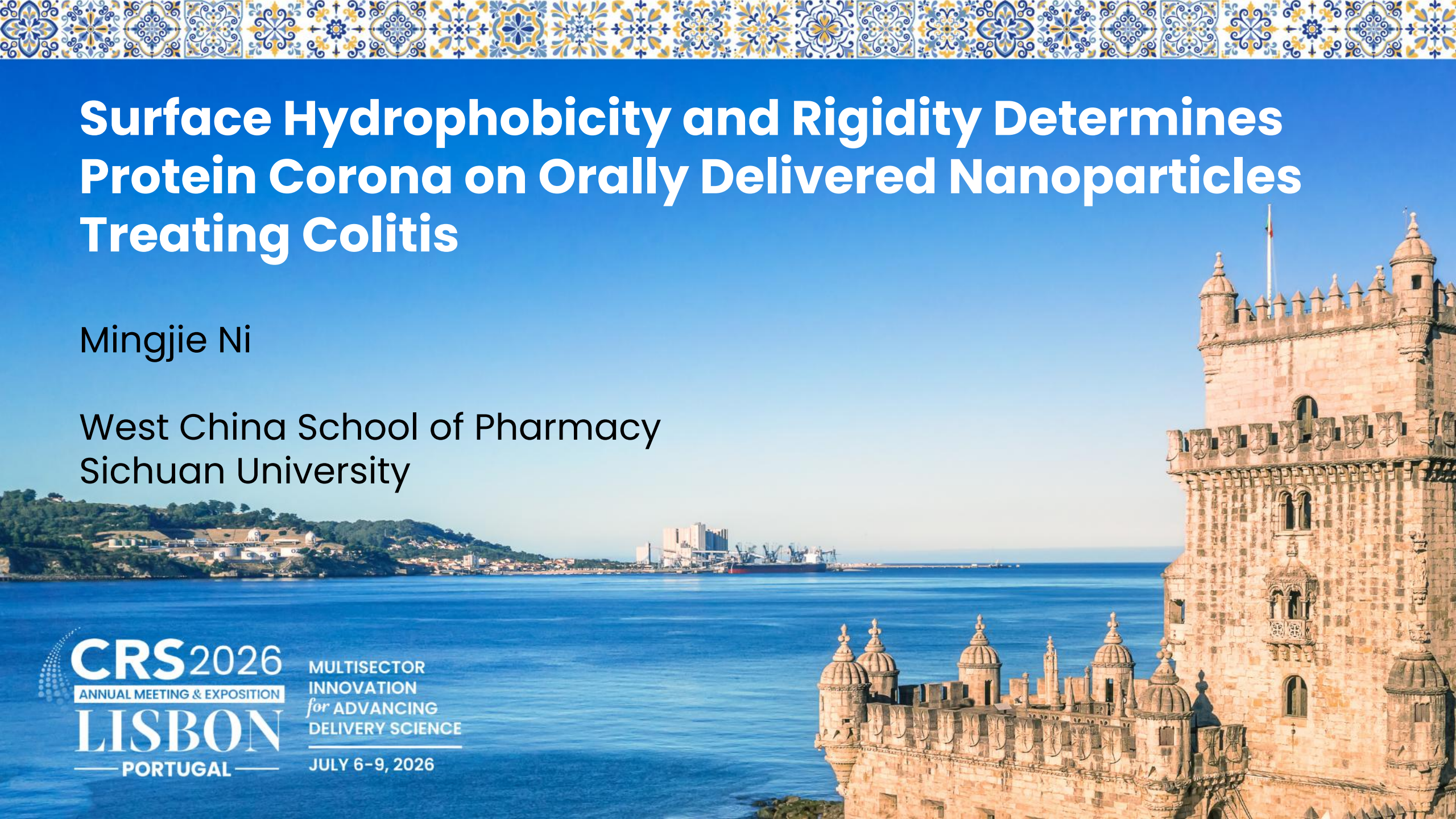




Surface Hydrophobicity and Rigidity Determines Protein Corona on Orally Delivered Nanoparticles Treating Colitis

Mingjie Ni

West China School of Pharmacy
Sichuan University

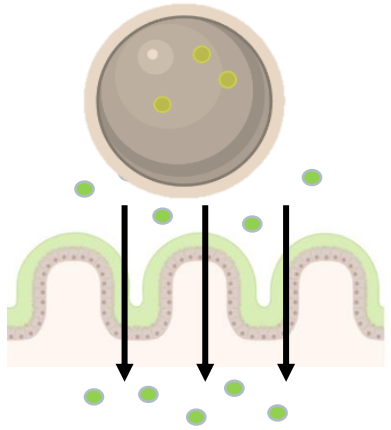


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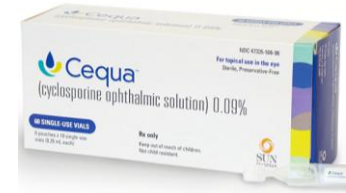
MULTISECTOR
INNOVATION
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DELIVERY SCIENCE

JULY 6-9, 2026

Nanoparticle Delivery Systems: Opportunities and Challenges

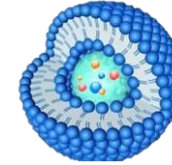


- ✓ Improve drug stability
- ✓ Improve drug dissolution behavior
- ✓ Functional modification to promote uptake



Ophthalmic Cyclosporine
Nanomicellar Solution

Diasome



Oral Liver-Targeted
Insulin Liposomes

× Absorption efficiency
needs improvement



Apical
entry

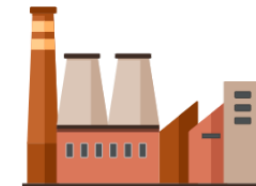


Intracellular
transport



Basolateral
exit

× Complexity of carrier
fabrication



Simple and controllable

Adapting to multiple mucosal barriers

Safe and efficient

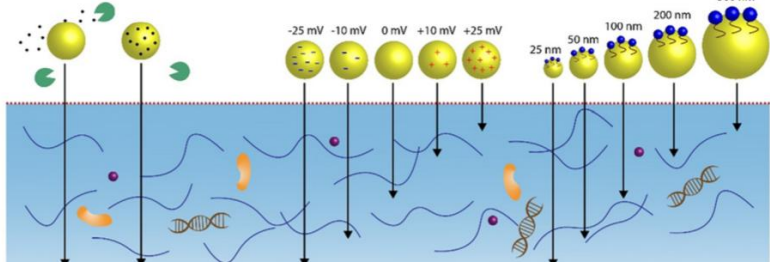
Ref: M. Muttenthaler, P. F. Alewood*, *Nat Rev Drug Discov*, 2021; D. J. Drucker*, *Nat Rev Drug Discov*, 2020

Rational design and optimization of nanocarrier surface properties to improve in vivo delivery efficiency.



Regulation of physicochemical properties

Drug release performance



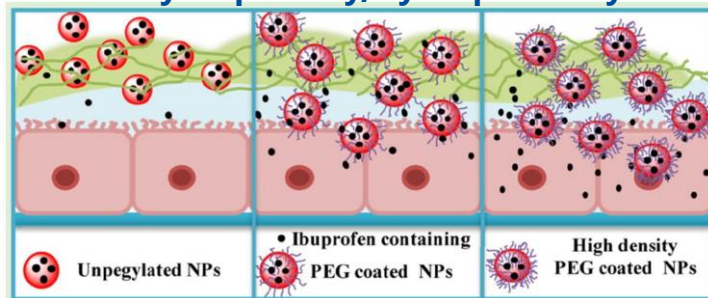
Surface charge

-25 mV -10 mV 0 mV +10 mV +25 mV

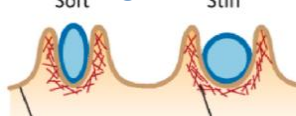
Particle size

25 nm 50 nm 100 nm 200 nm 500 nm

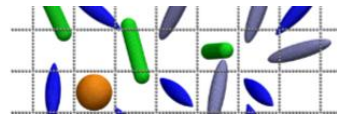
PEG grafting density and surface hydrophilicity/hydrophobicity



Rigidity

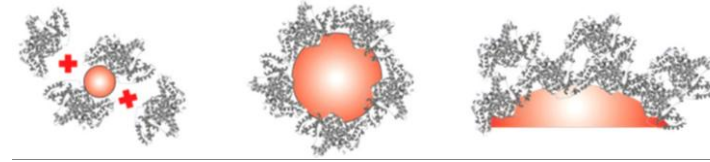


Shape



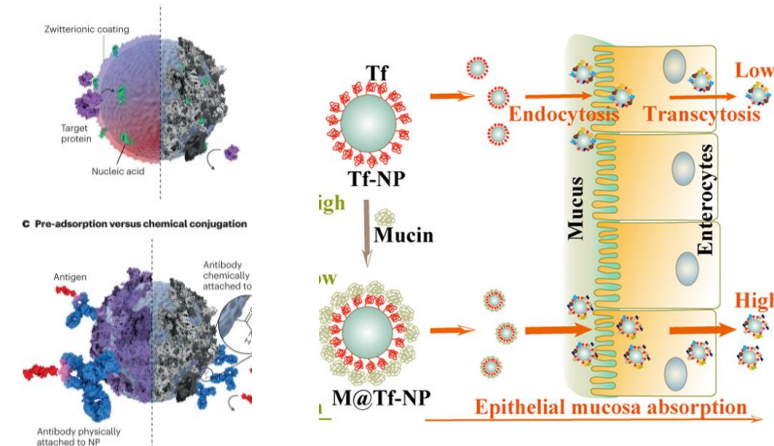
Regulation of biological properties

Protein corona



Reduce blood protein corona to prolong circulation time

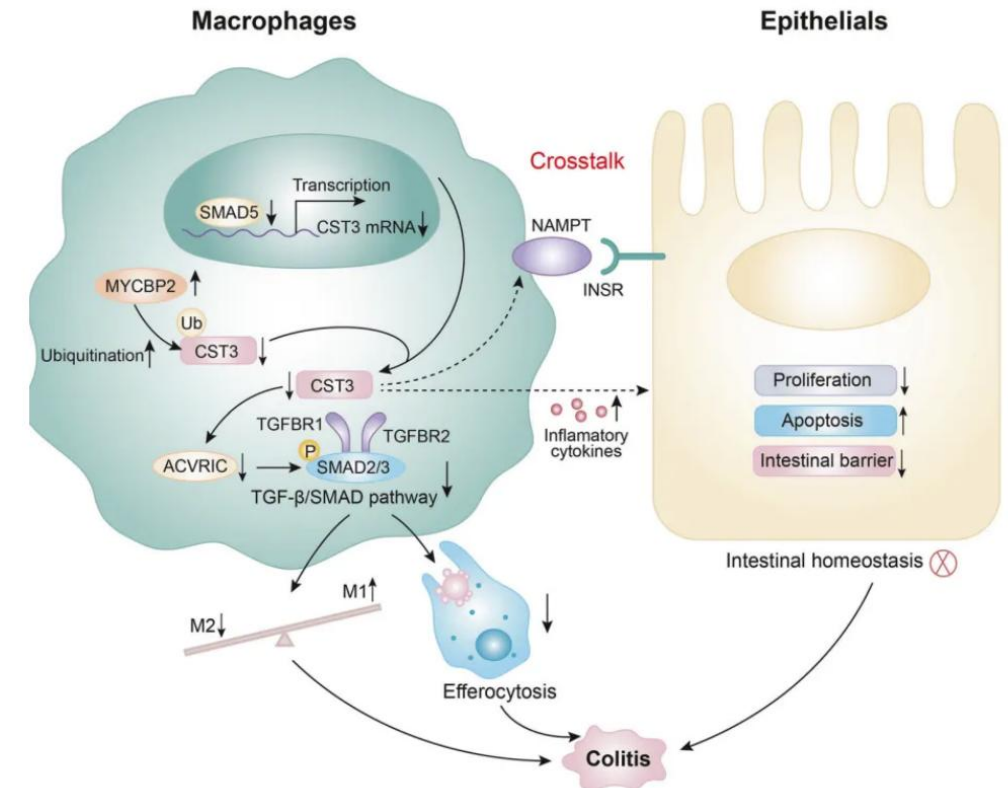
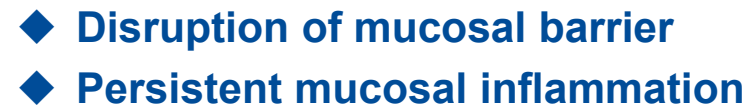
Pre-incubated mucus protein corona to enhance intestinal mucosal absorption



Ref: *Adv. Drug Delivery Rev.*, 2018; *Adv. Drug Delivery Rev.*, 2022; *Nat. Rev. Mater.*, 2023; *ACS Nano*, 2024;

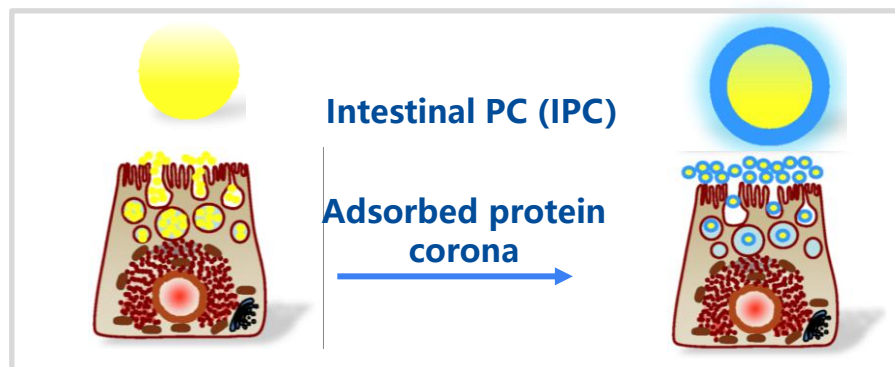
四川大學
SICHUAN UNIVERSITY

Macrophages in IBD

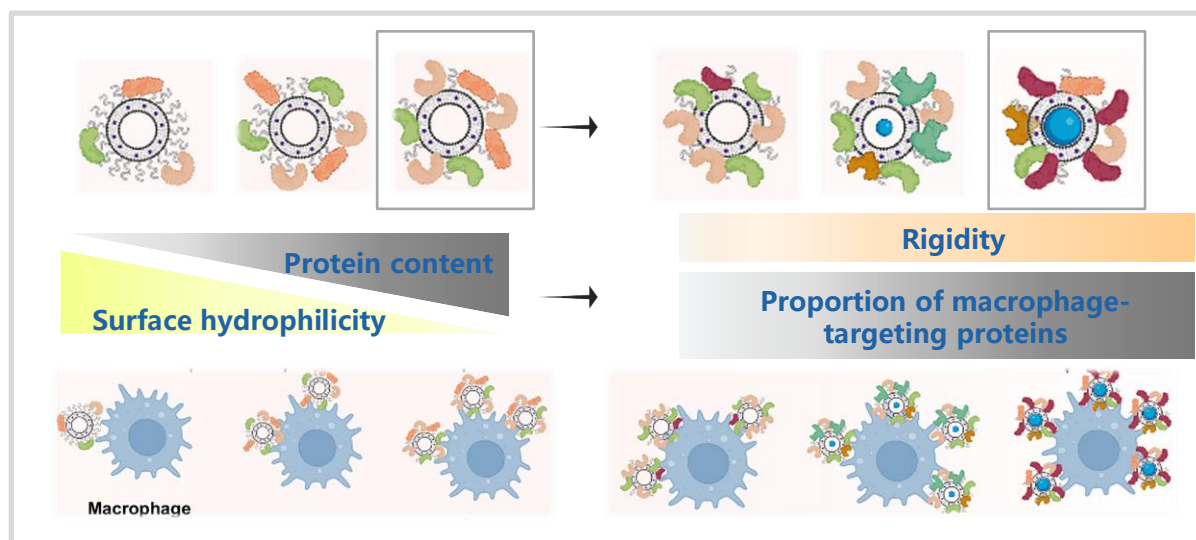
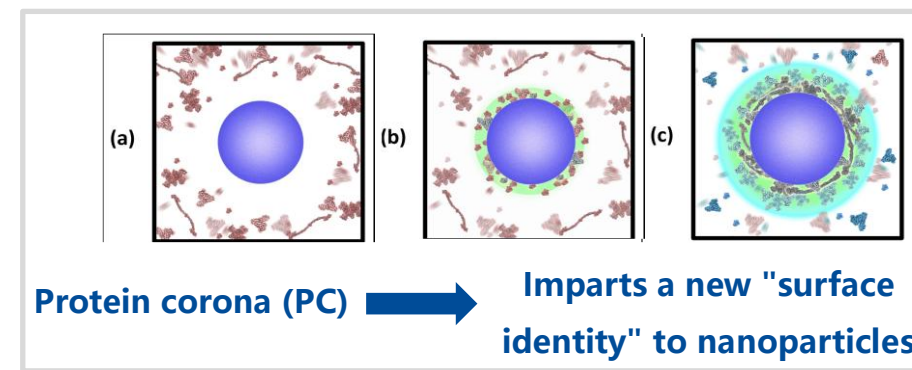


Wang, H., Jiao, C., Xing, H. et al. Cell Death Differ 2026.

Modulation of disease-specific IPC on nanoparticle surfaces



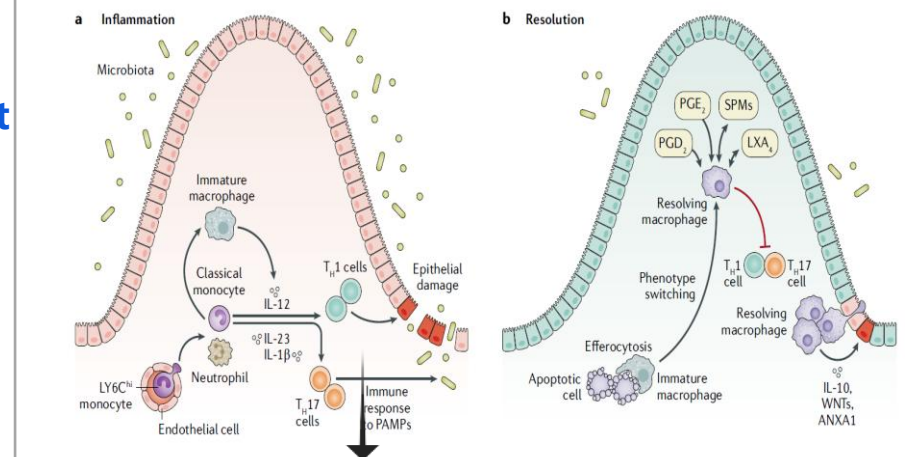
Alters **surface properties** of nanoparticles to influence protein corona formation



Regulation of nanocarrier physicochemical properties

Oral treatment of colitis

Local delivery (colonic macrophages): Colitis-IPC

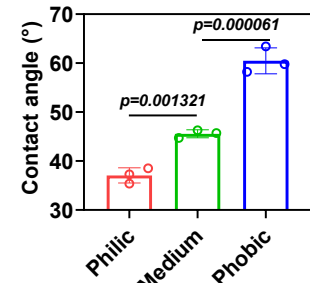
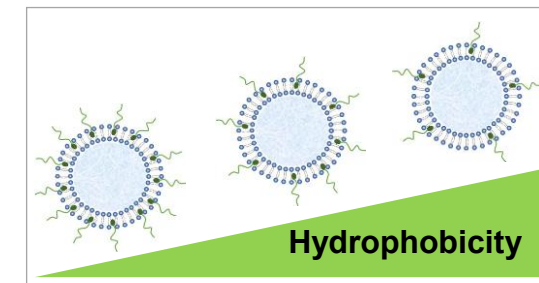
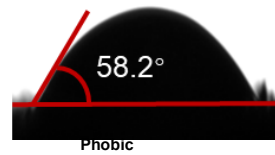
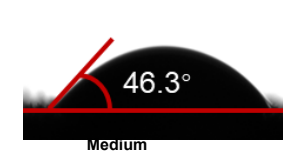
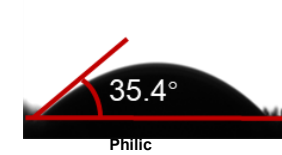
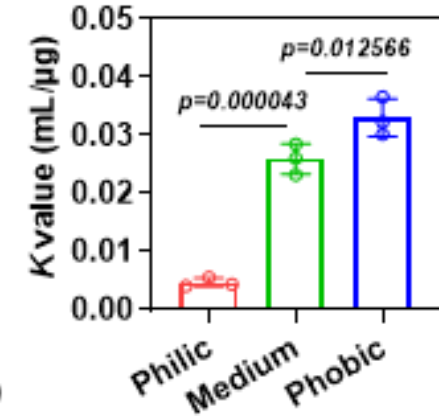
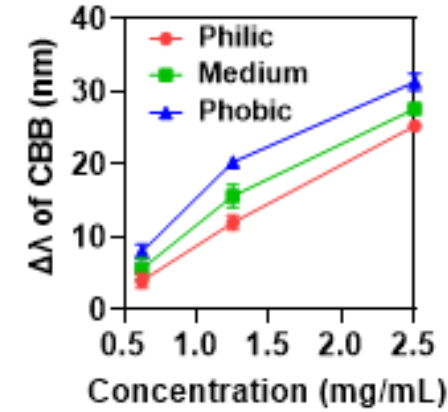
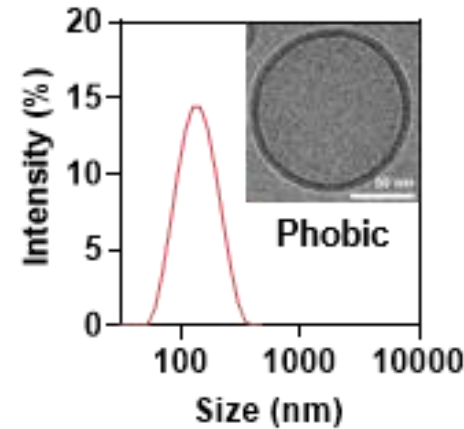
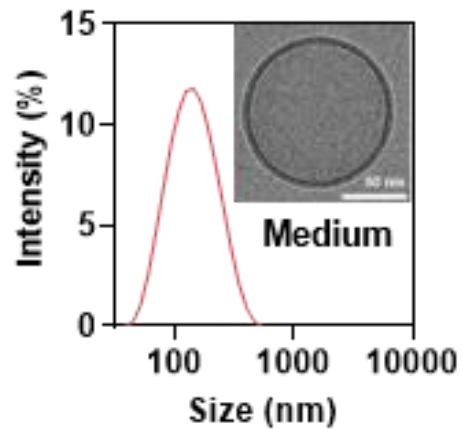
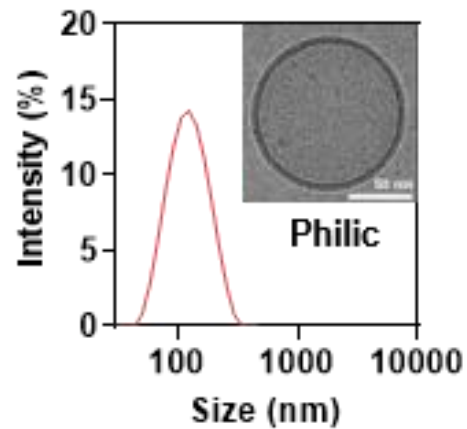
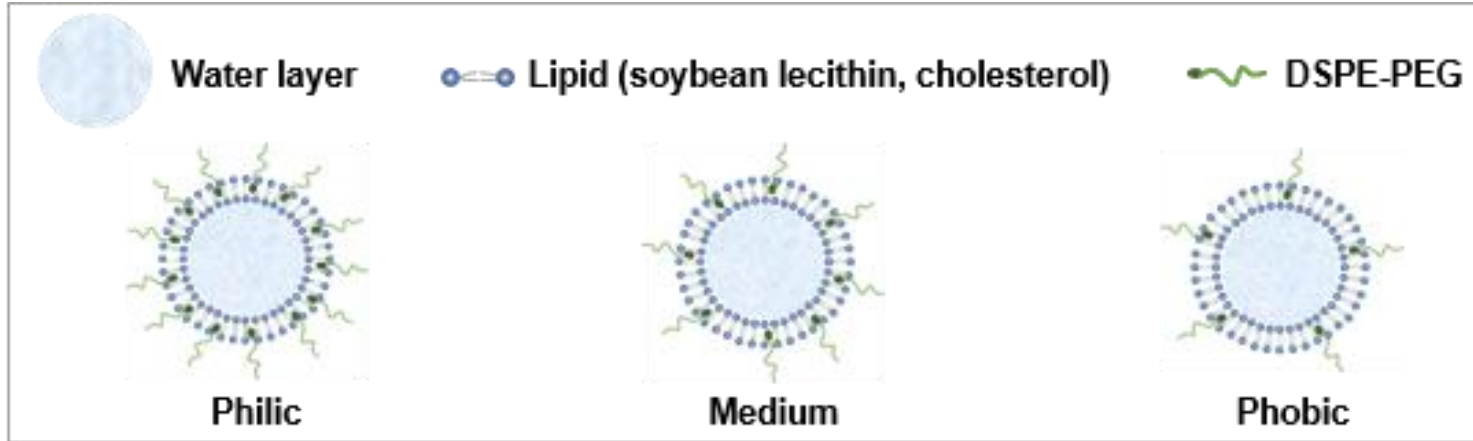


Customize a specific IPC for colitis treatment ?

Ref: *Nat. Rev. Drug Discovery*, 2020 ; *ACS Appl. Mater. Interfaces*, 2020; *Nat. Rev. Gastroenterol. Hepatol.*, 2019; *Inflammatory bowel diseases*, 2018 ; *Curr. Opin. Colloid Interface Sci.*, 2019 ; *Biomacromolecules*, 2019.



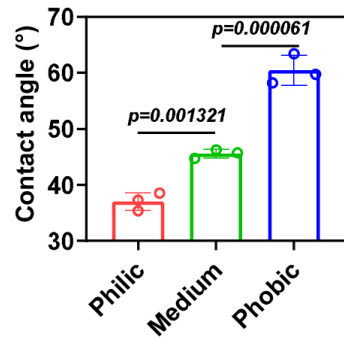
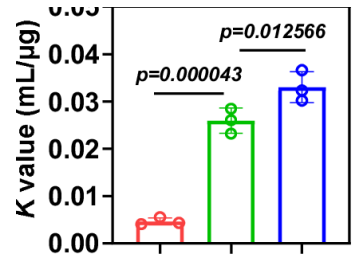
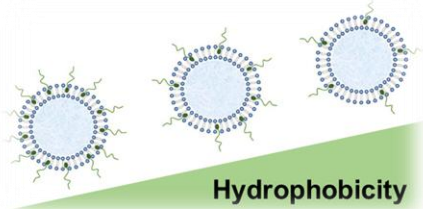
Preparation and characterization of liposomes with different surface hydrophilicity/hydrophobicity



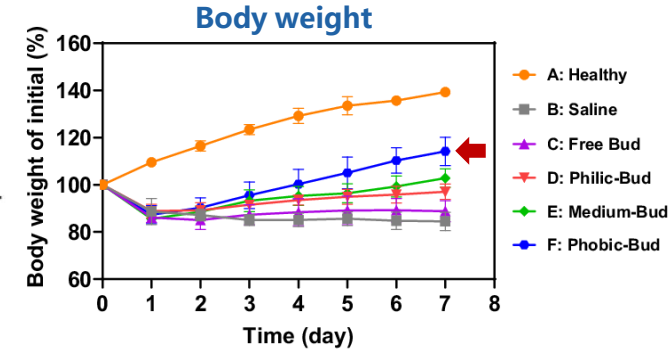
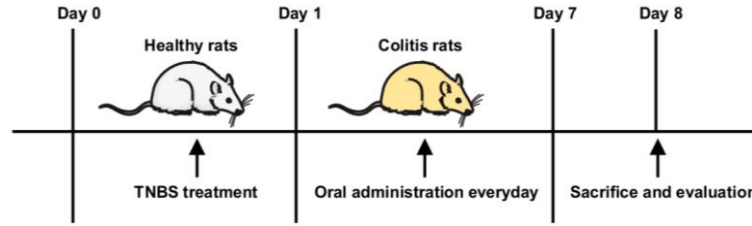
Reducing surface hydrophilicity improves the therapeutic effect of drug-loaded nanoparticles in colitis



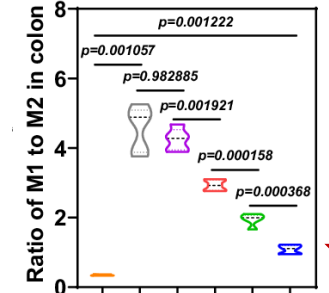
Hydrophilicity modulation



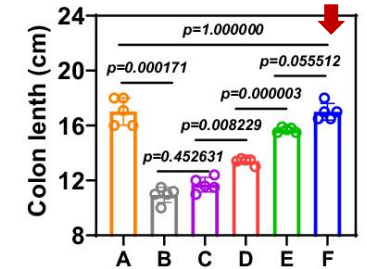
Treatment of acute colitis



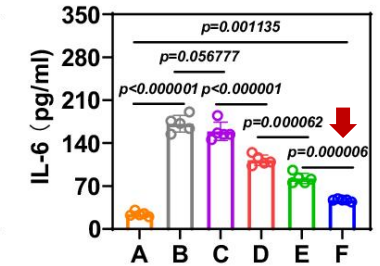
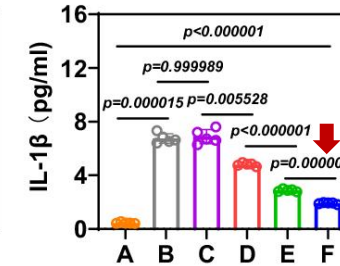
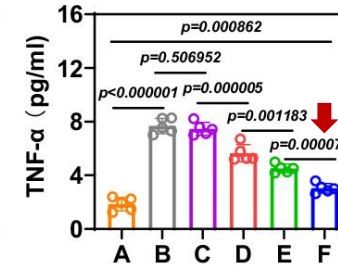
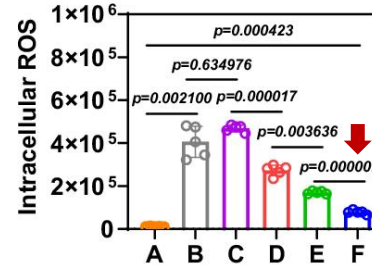
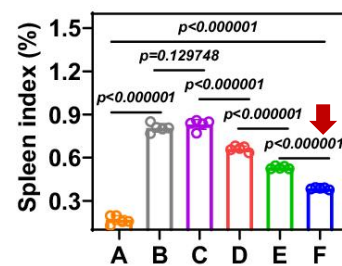
Macrophage polarization level



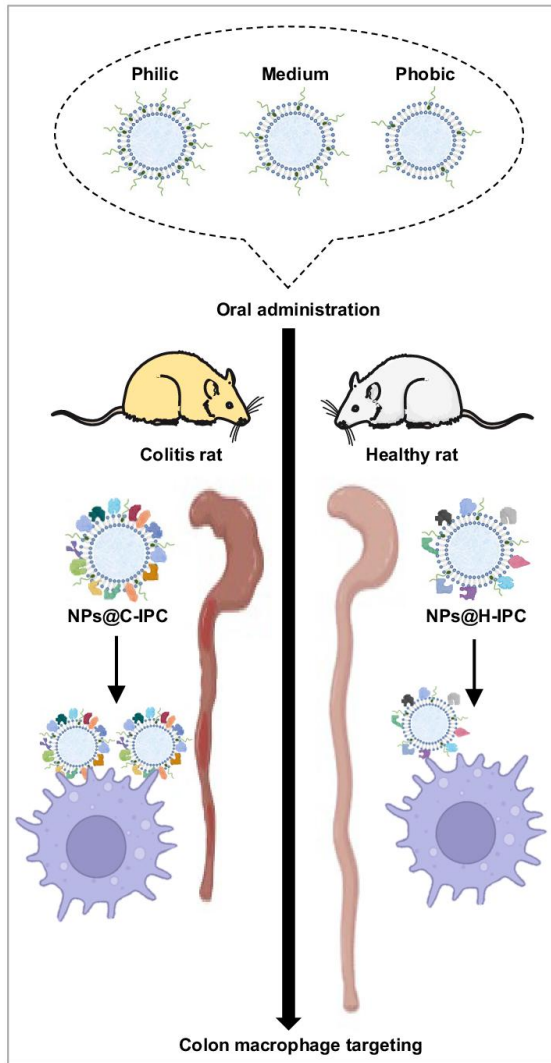
Colon length



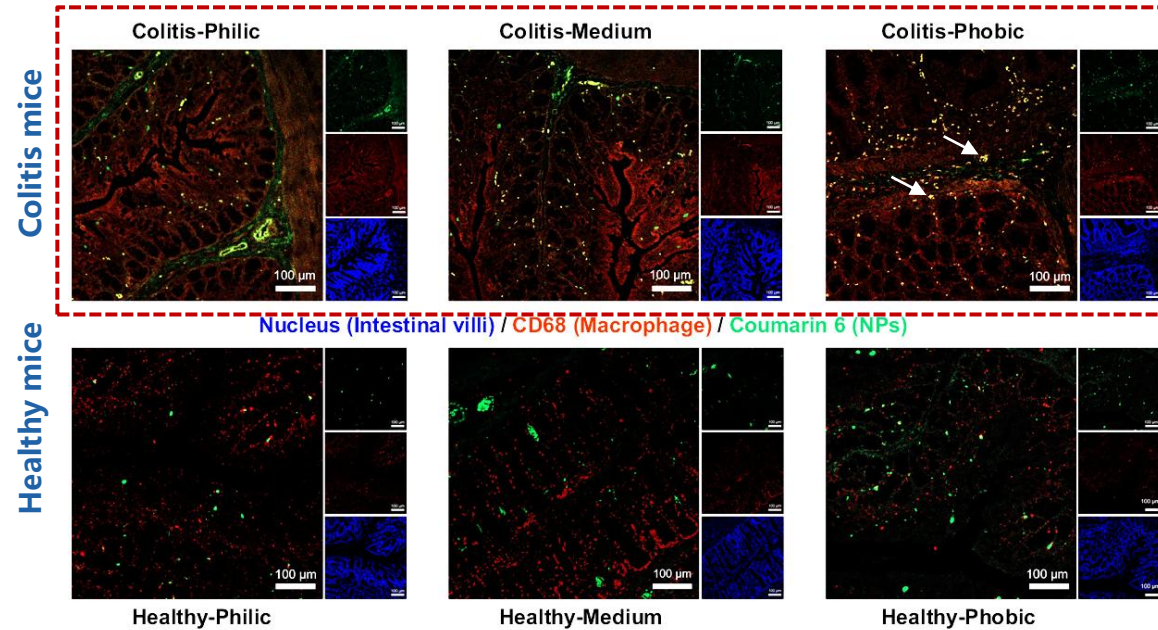
Inflammatory cytokine levels



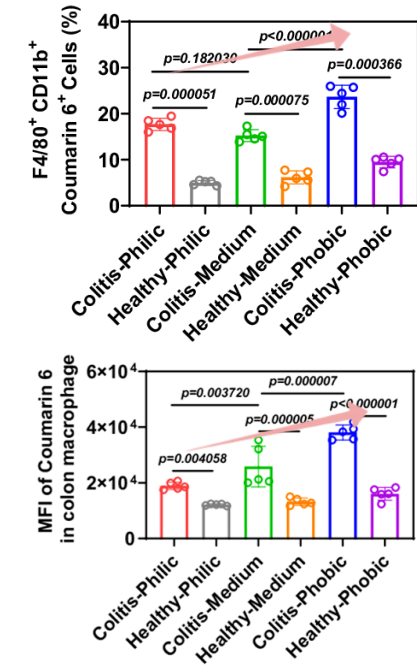
Low-hydrophilicity nanoparticles specifically target colonic macrophages in colitis mice



Colocalization of orally administered nanoparticles with different hydrophilicity and colonic macrophages



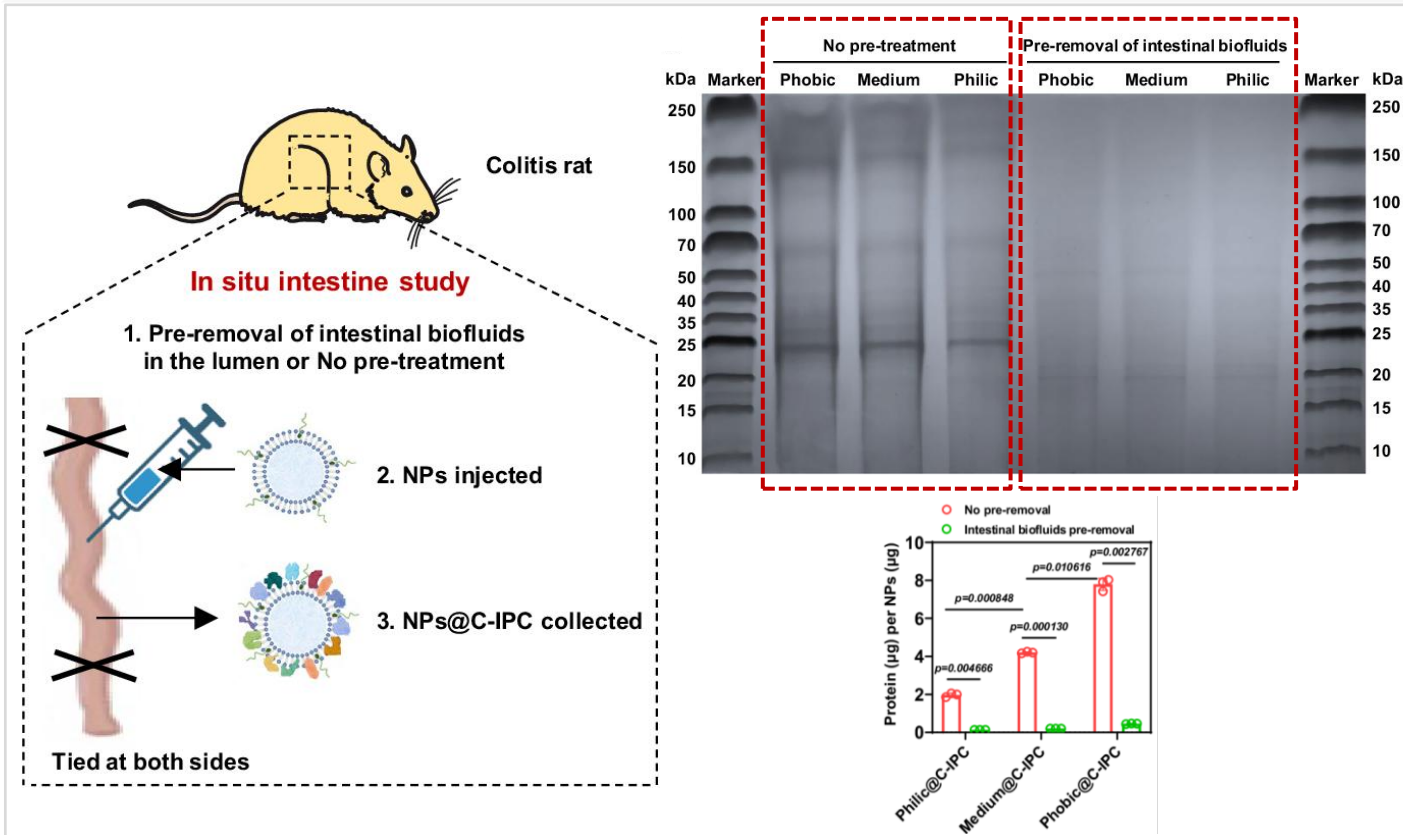
Uptake by macrophages in colitis mice



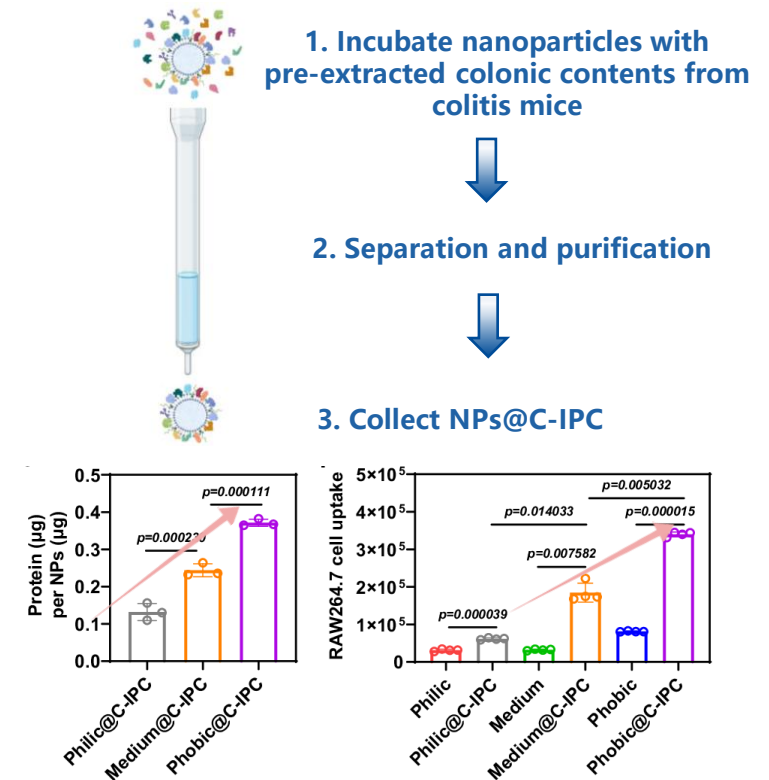
- ◆ Compared with healthy group, oral nanoparticles show stronger colocalization with macrophages in colitis mice
- ◆ As hydrophilicity decreases, the uptake of oral nanoparticles by macrophages in colitis mice is also enhanced

Surface hydrophilicity affects the protein content of colitis-specific IPC on orally delivered nanoparticles

Composition and content determination of IPC formed in vivo



Content determination and macrophage uptake of IPC formed in vitro

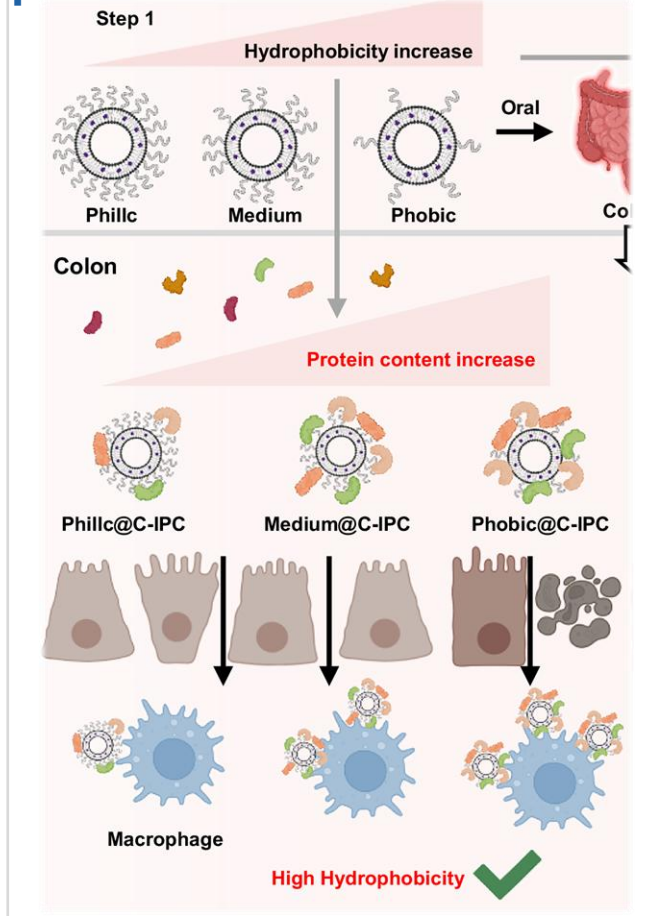


◆ IPC content increased with decreasing hydrophilicity, and macrophage uptake was significantly enhanced

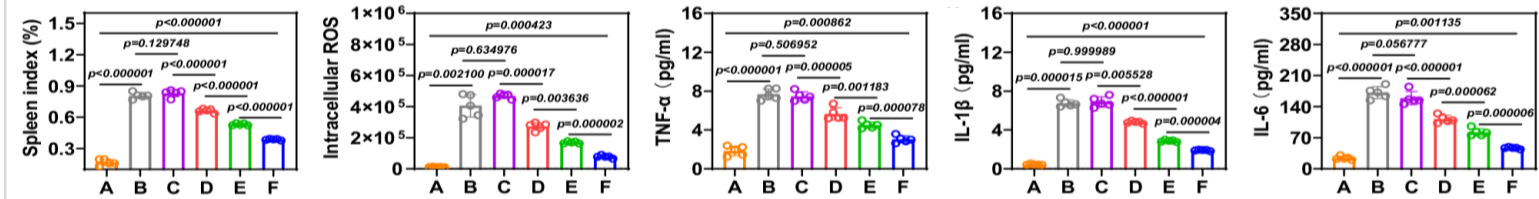
Does rigidity modulation affect the protein types of colitis-specific IPC on oral nanoparticles?



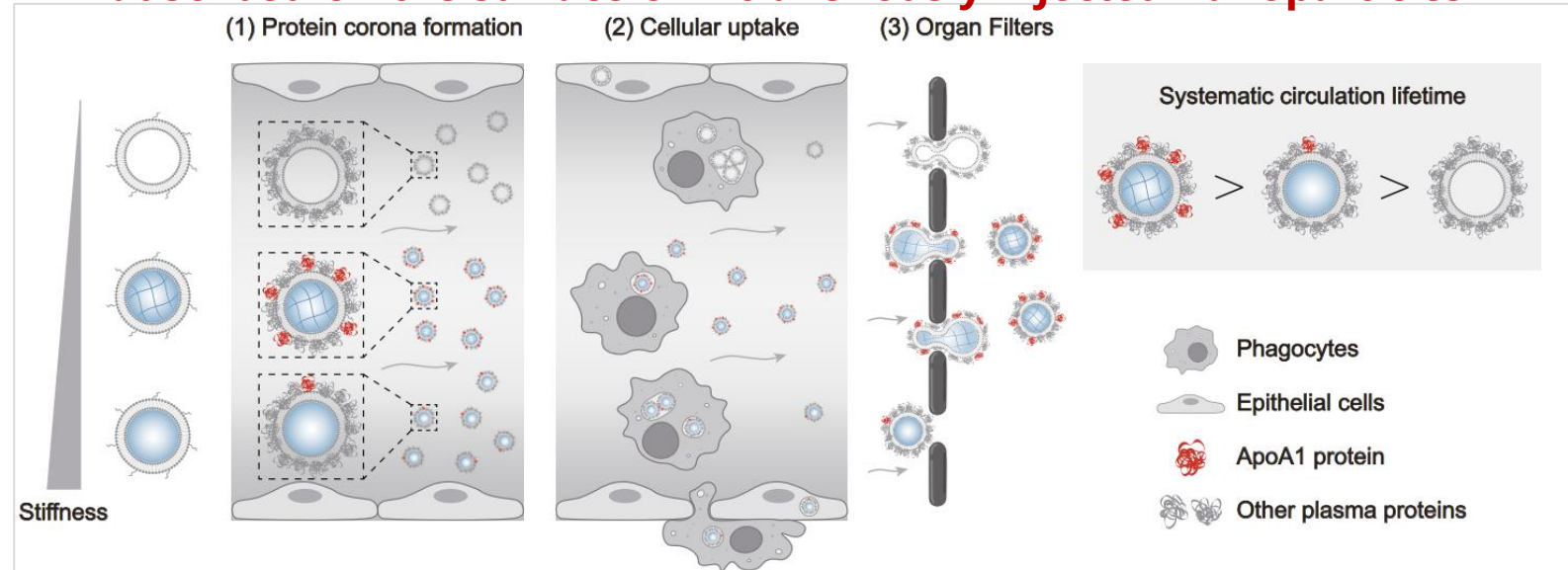
① Only changes the IPC protein content on the surface



② Therapeutic efficacy needs further improvement



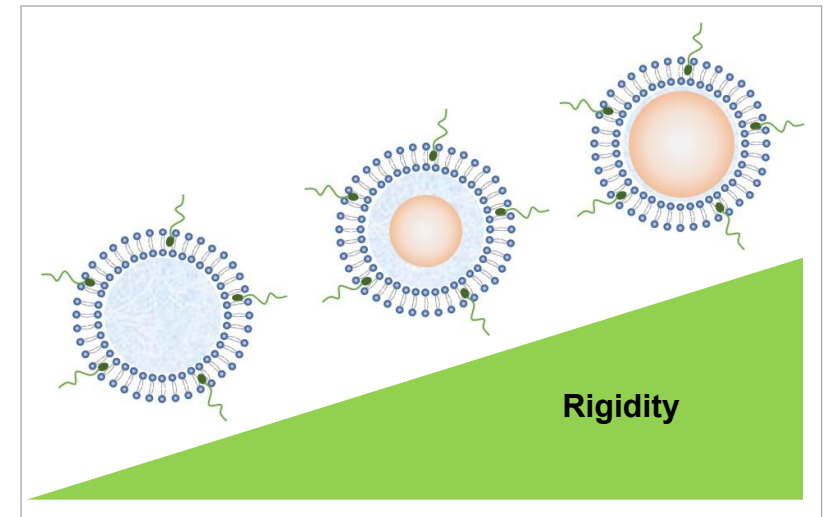
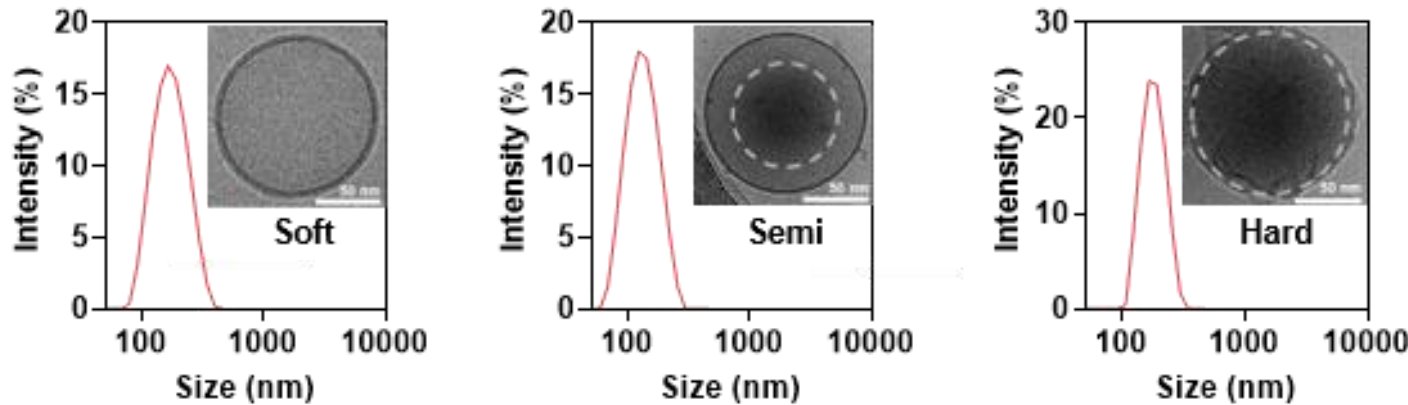
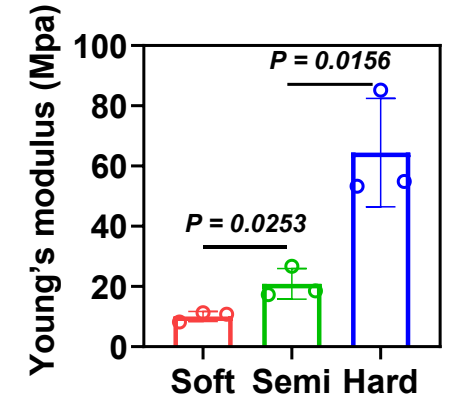
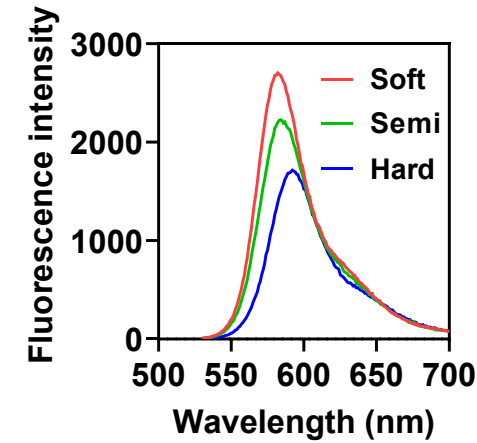
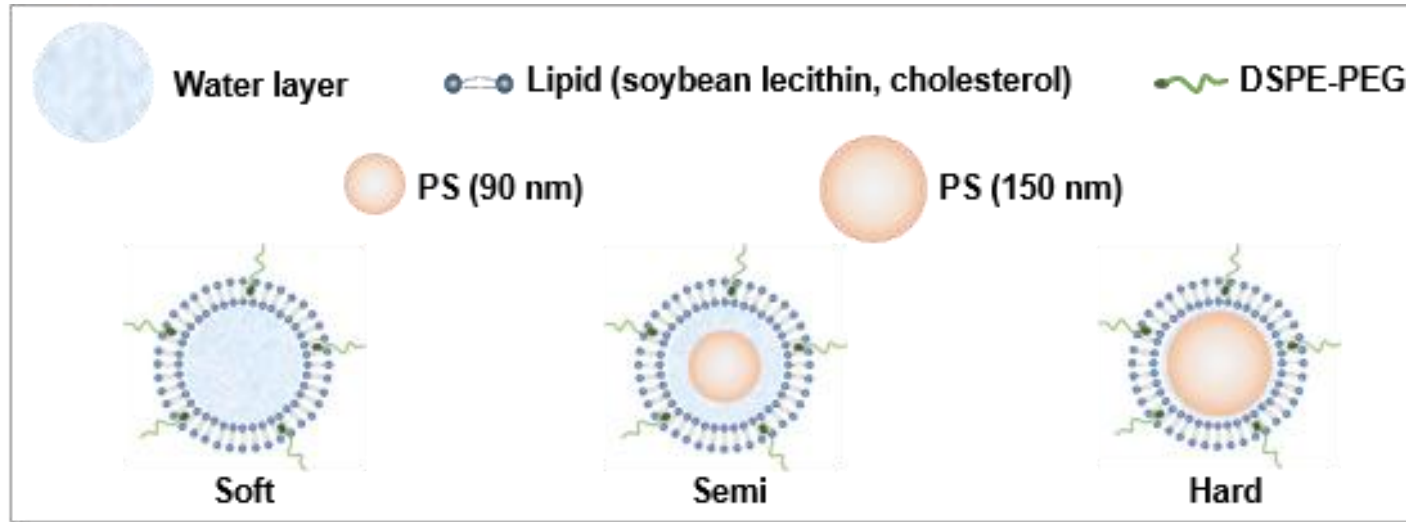
Increased rigidity can affect the protein types of the protein corona adsorbed on the surface of intravenously injected nanoparticles



Ref: C. X. Zhao*, *Nat. Commun.* 2022.



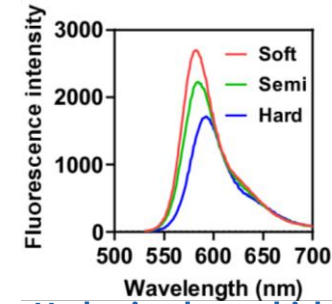
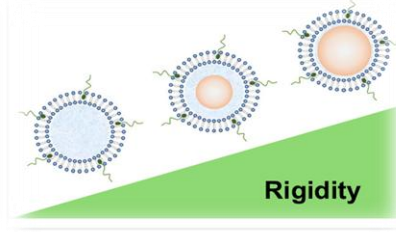
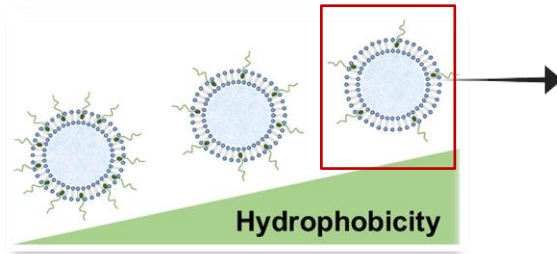
Preparation and characterization of liposomes with different rigidity



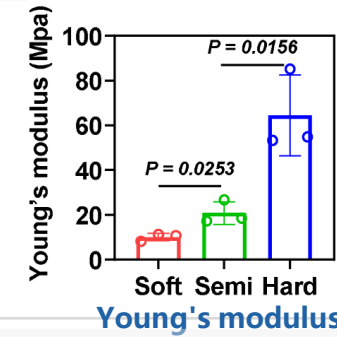
Combined regulation of surface hydrophilicity and rigidity further enhances the therapeutic effect in colitis



Hydrophilicity-rigidity modulation

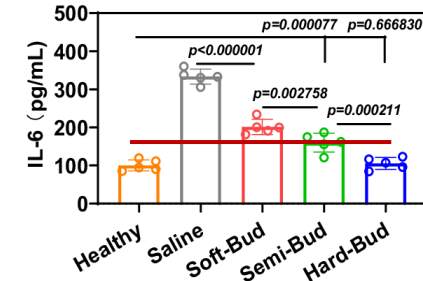
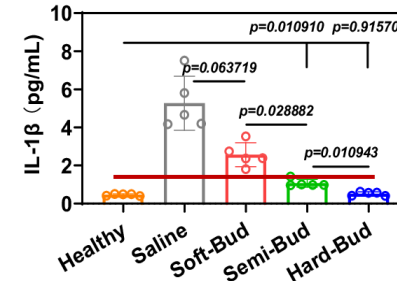
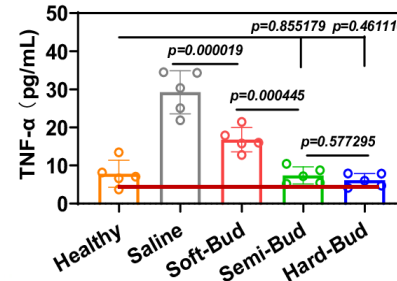
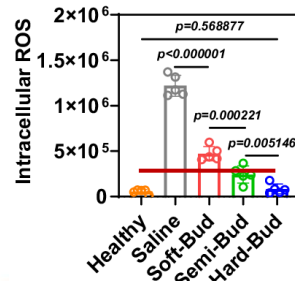
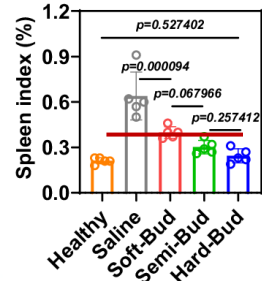
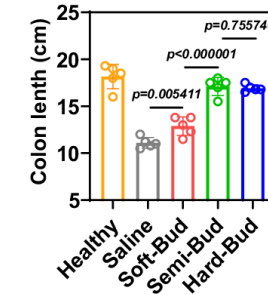
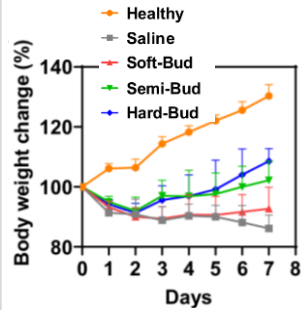


Hydration layer thickness



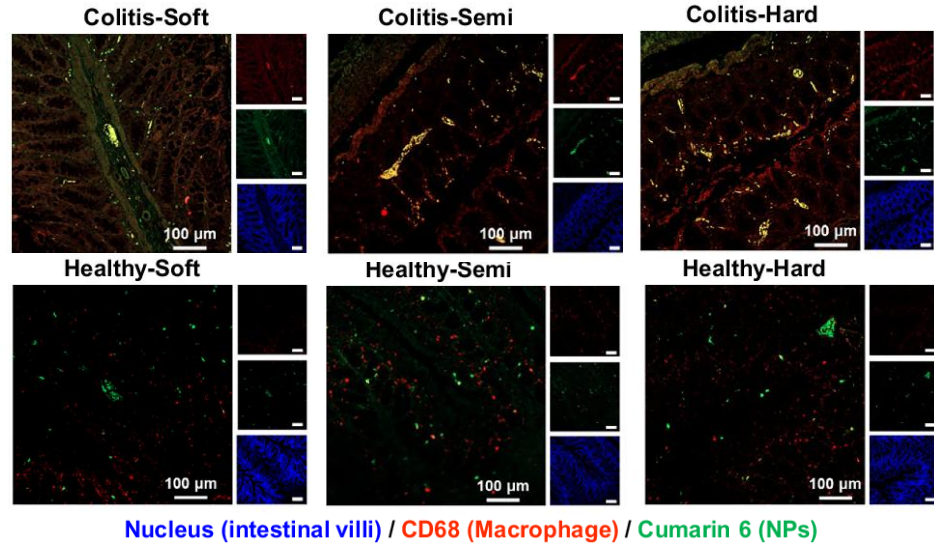
Young's modulus

Treatment of acute colitis

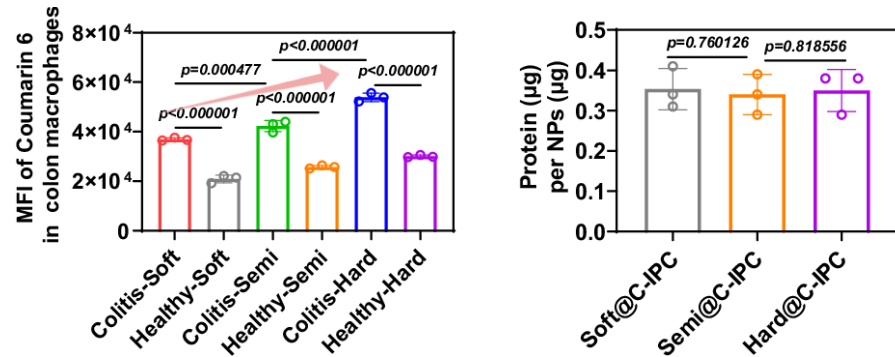


Increasing rigidity enhances the proportion of macrophage-targeting proteins in C-IPC

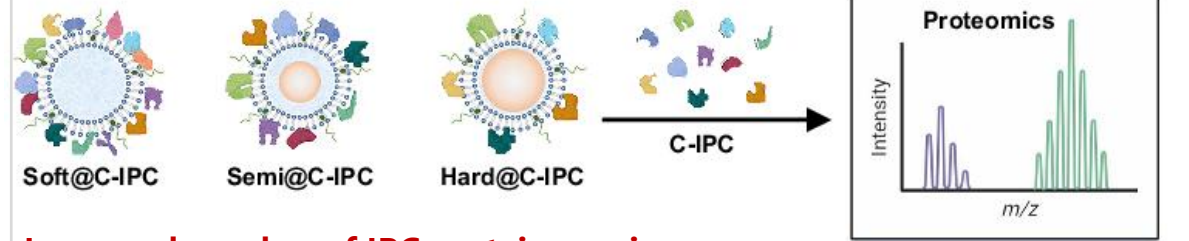
Colocalization and uptake by colonic macrophages



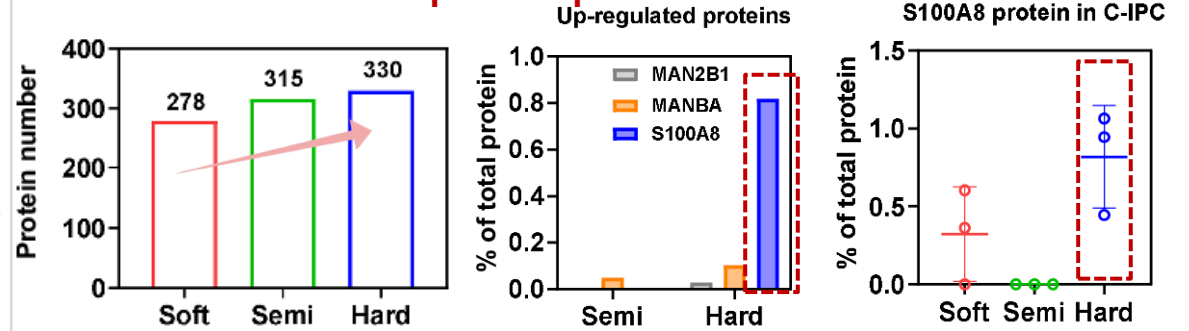
Unchanged IPC protein content



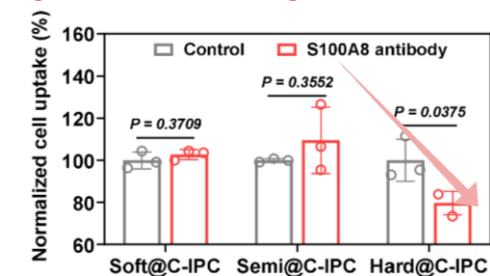
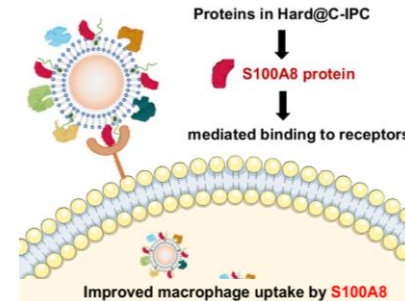
Proteomic analysis of IPC on nanoparticles with combined hydrophilicity-rigidity modulation



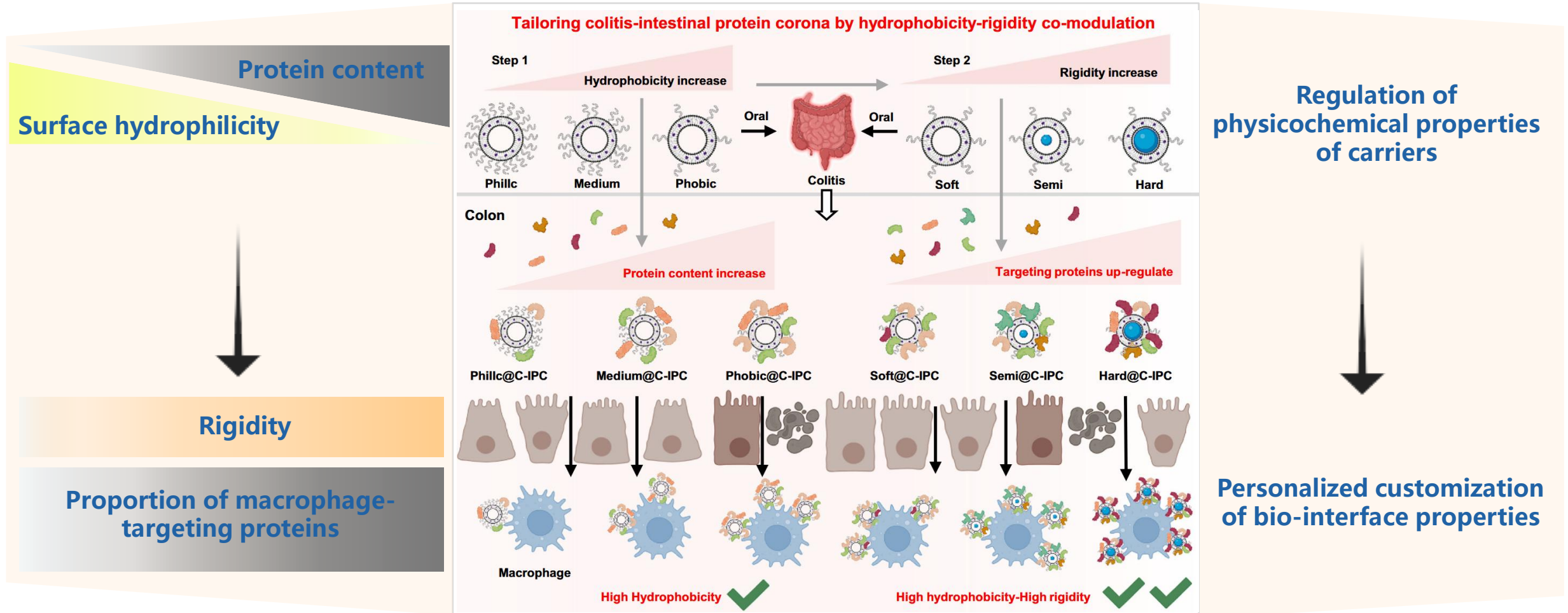
Increased number of IPC protein species



Macrophage-targeting proteins in C-IPC are significantly upregulated



Personalized regulation of nano-bio interface properties based on delivery goals



Jiawei Wu⁺, Mingjie Ni⁺, Yuan Huang* et al. *Nat. Commun.*, 2026



Prof. Yuan Huang

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



A.P. Zhou Zhou



A.P. Lian Li



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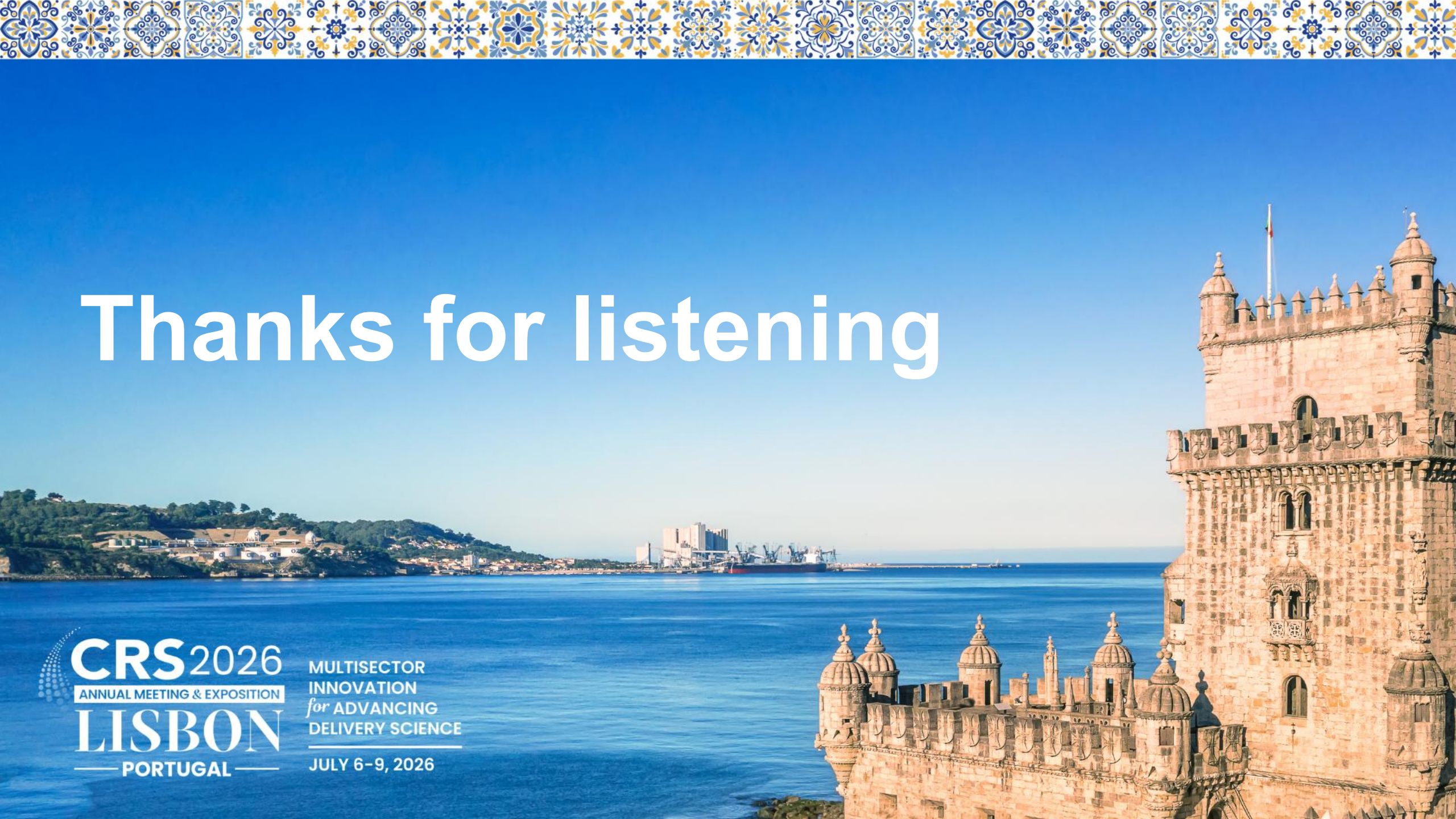


the Regional Innovation and Development Joint Fund of National Natural Science Foundation of China (U22A20356)
West China School of Pharmacy & CREDIT Pharmaceutical Graduate Conference Exchange Fund





Thanks for listening



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