Oral Protein Delivery: Nanoassemblies for Targeted Treatment of Intestinal Diseases

María G. Portela

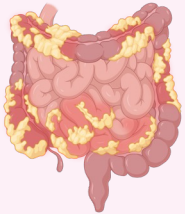
Ana M. López-Estévez, Laura Piñeiro-Alonso, Raquel Castillo-González, Lucía Sancho-Temiño, Noemí Gómez-Lado, María Medel, María J. Vicent, Milagros Castellanos, Pablo Aguiar Fernández, Lola Fernández-Messina, Aránzazu Cruz-Adalia, María José Alonso

CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

INTRODUCTION

INFLAMMATORY BOWEL DISEASE (IBD)



↑ Pro-inflammatory cytokines

TNF-α

INTRODUCTION

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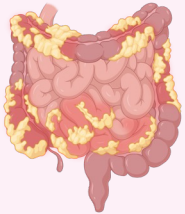
Current therapy:
SC or IV injection of
TNF-α inhibitors



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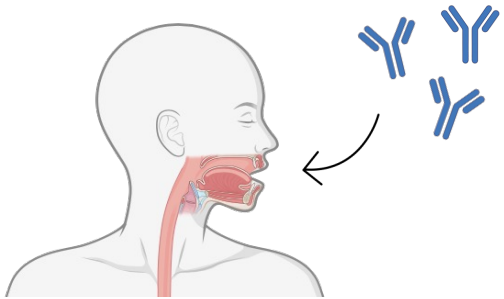
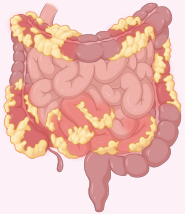


Oral administration



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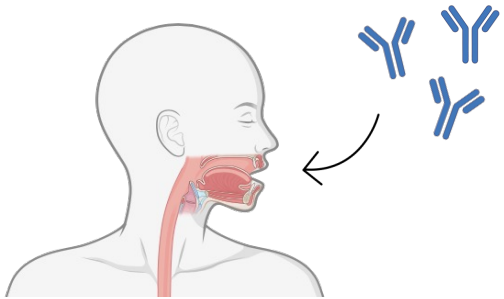

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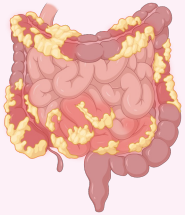
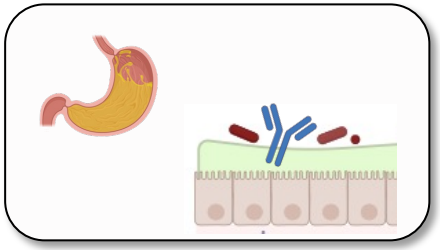


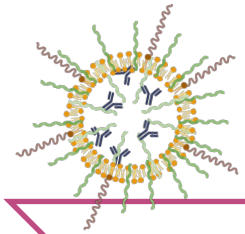
↑ Pro-inflammatory cytokines

TNF-α

CHALLENGES

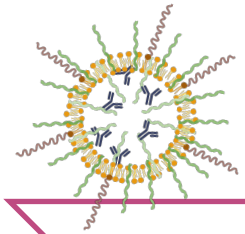


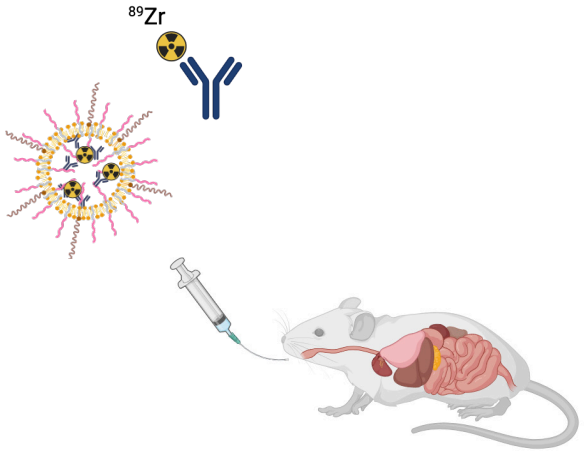
OVERALL AIMS



Design nanosystems for oral delivery of mAb

OVERALL AIMS





Design nanosystems for oral delivery of mAb

Demonstrate that they change the biodistribution profile of the free mAb

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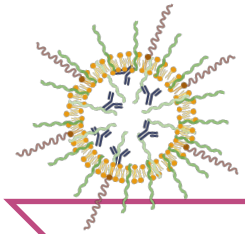
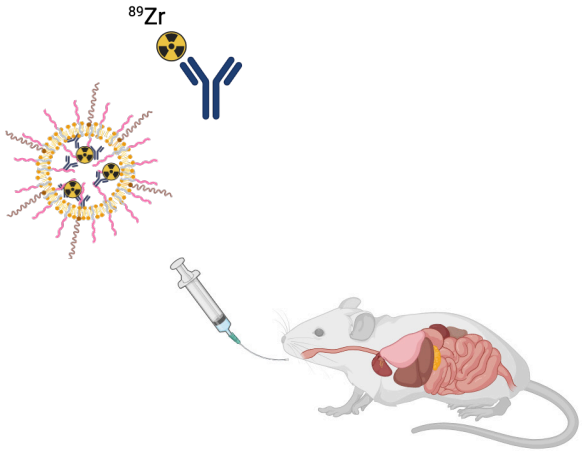
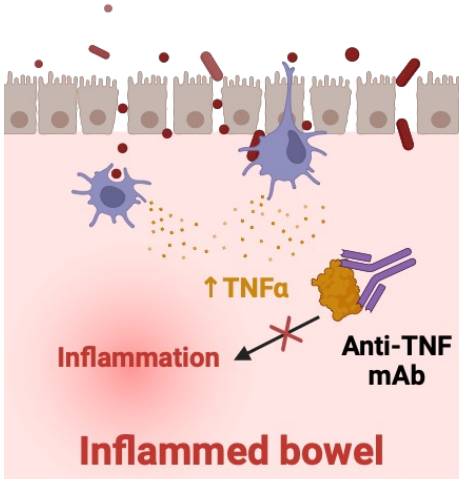




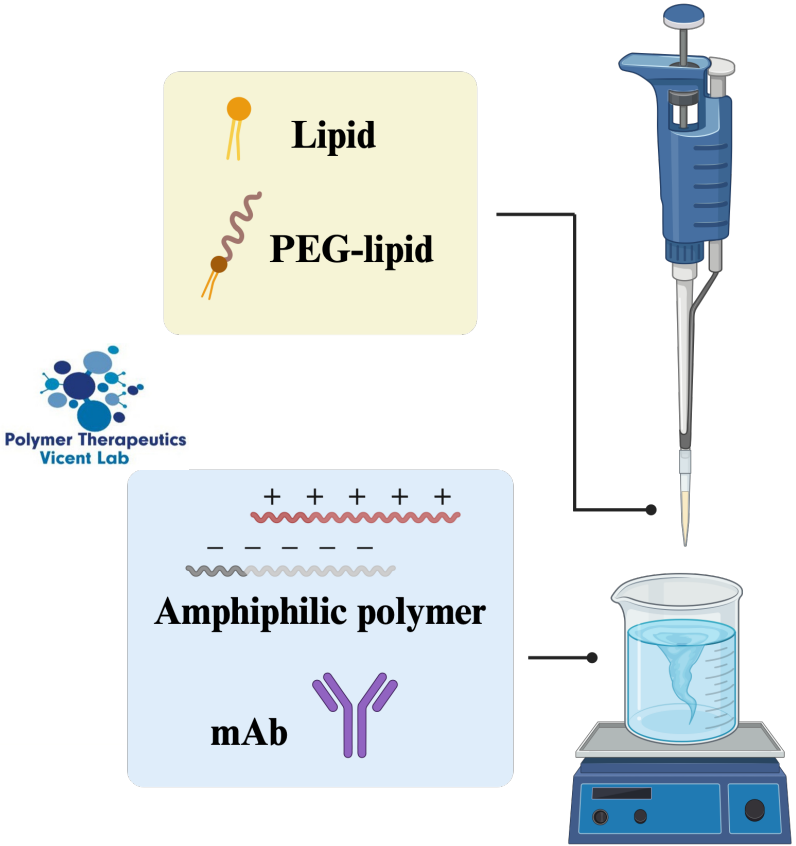


Design nanosystems for oral delivery of mAb

Demonstrate that they change the biodistribution profile of the free mAb

Evaluate their therapeutic efficacy

RATIONAL DESIGN OF NANOSYSTEMS



AM. López-Estévez. *Journal of Controlled Release* (2024); AM. López-Estévez. *Nano Research* (2024); **Under patent application.**

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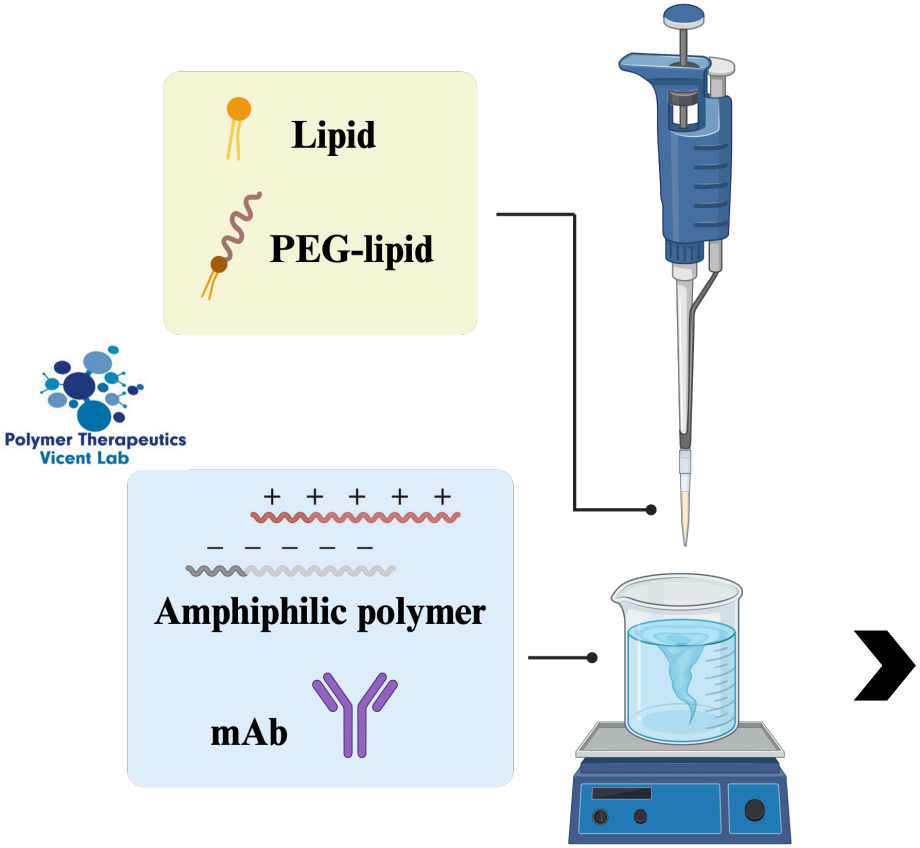
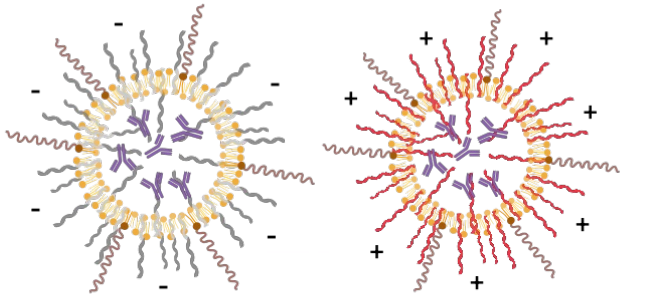


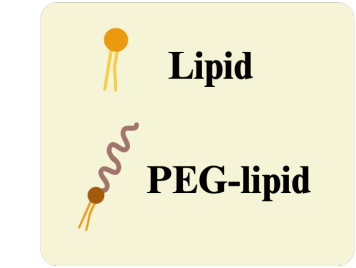


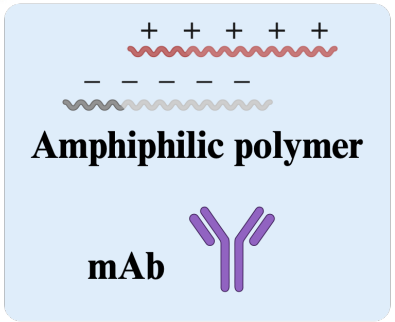
mAb-loaded nanoassemblies (NAs)

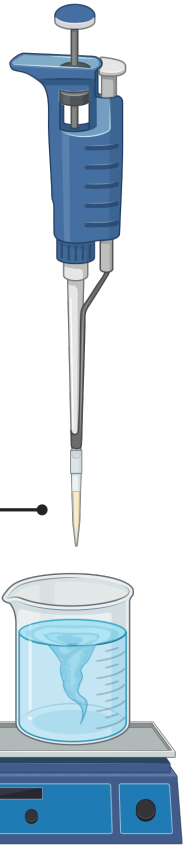
AM. López-Estévez. *Journal of Controlled Release* (2024); AM. López-Estévez. *Nano Research* (2024); **Under patent application.**

RATIONAL DESIGN OF NANOSYSTEMS

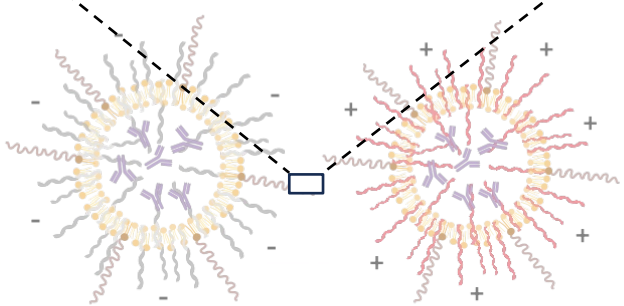
Polymer Therapeutics
Vicent Lab







- Particle size ≤ 100 nm
- PDI < 0.3
- Negative to neutral ζ-potential
- Loading capacity > 10%
- Stable in simulated GI fluids
- Controlled release profile



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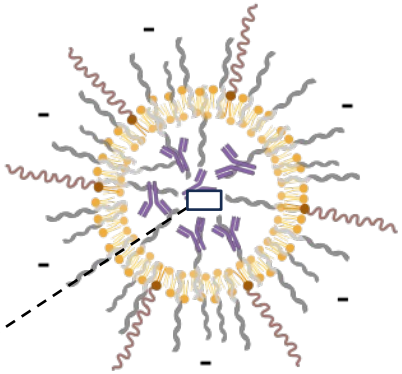
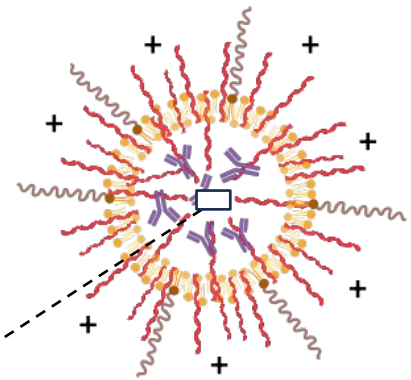
PHYSICOCHEMICAL CHARACTERIZATION

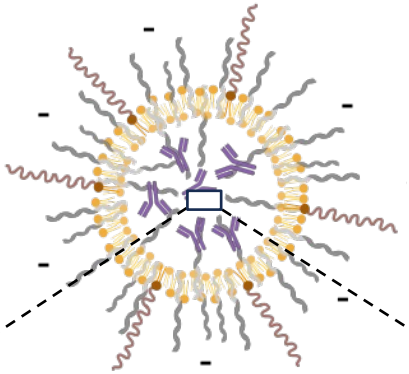


BVZ
Size: 44 ± 4 nm
PDI: 0.24
ζ-potential: -10 ± 2 mV
LC: 20 ± 3%

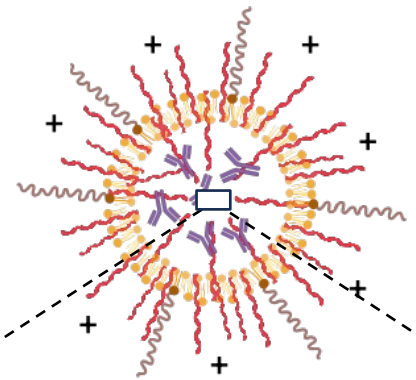


BVZ
Size: 63 ± 5 nm
PDI: 0.17
ζ-potential: +1 ± 2 mV
LC: 16 ± 6%

PHYSICOCHEMICAL CHARACTERIZATION

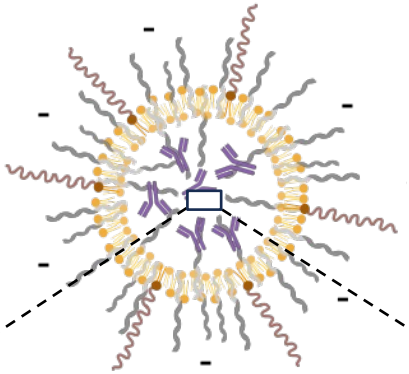


BVZ	antiTNF
Size: 44 ± 4 nm	Size: 53 ± 3 nm
PDI: 0.24	PDI: 0.22
ζ-potential: -10 ± 2 mV	ζ-potential: -8 ± 1 mV
LC: 20 ± 3%	LC: 17 ± 9%



BVZ	antiTNF
Size: 63 ± 5 nm	Size: 65 ± 2 nm
PDI: 0.17	PDI: 0.18
ζ-potential: +1 ± 2 mV	ζ-potential: +2 ± 1 mV
LC: 16 ± 6%	LC: 24 ± 3%

PHYSICOCHEMICAL CHARACTERIZATION



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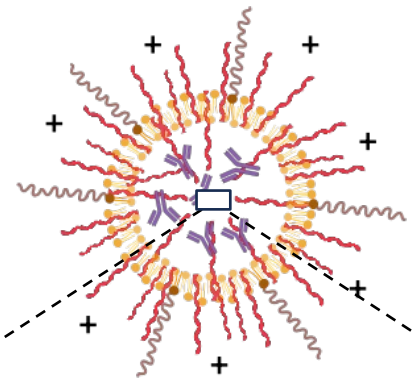

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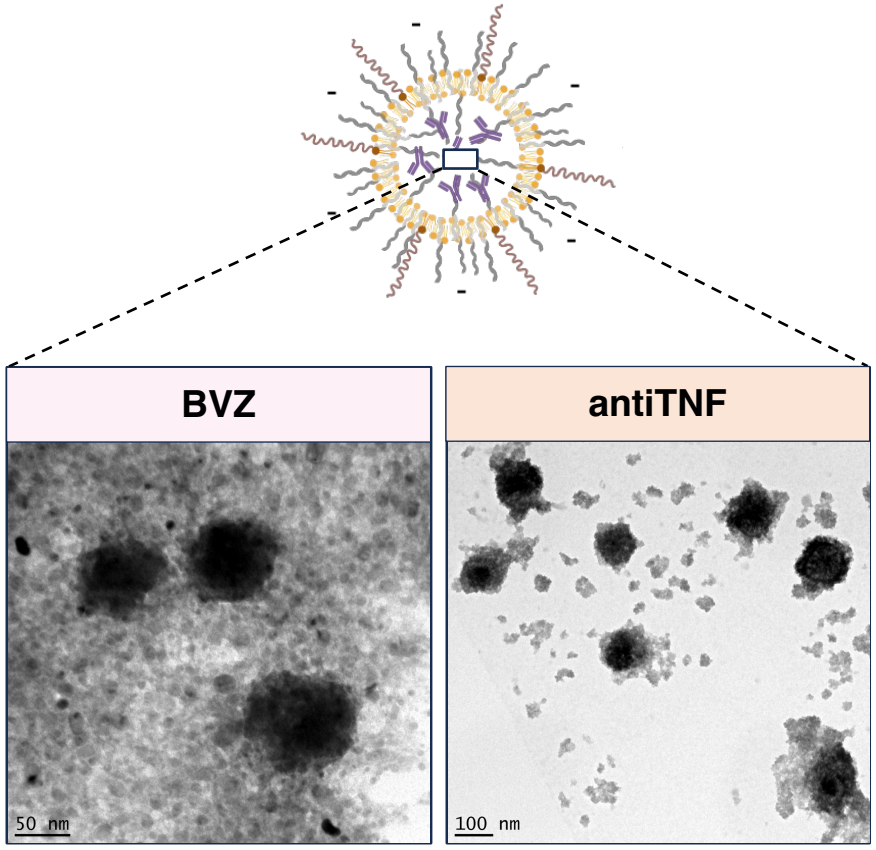
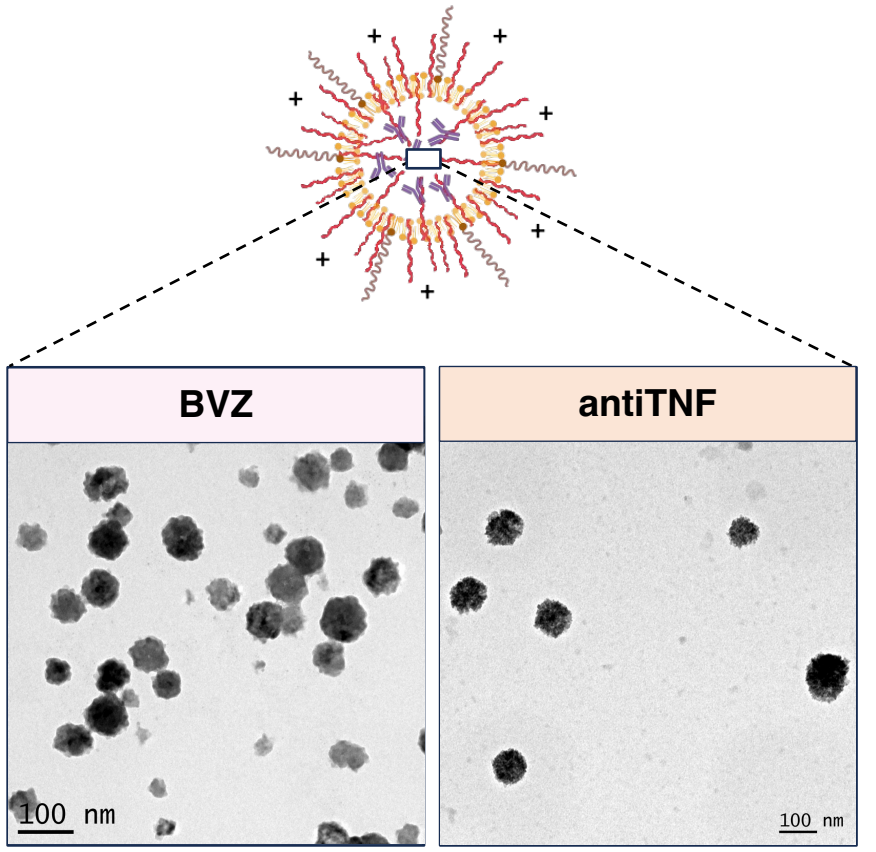
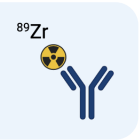
PHYSICOCHEMICAL CHARACTERIZATION

TRANSMISSION ELECTRON MICROSCOPY (TEM)



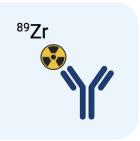


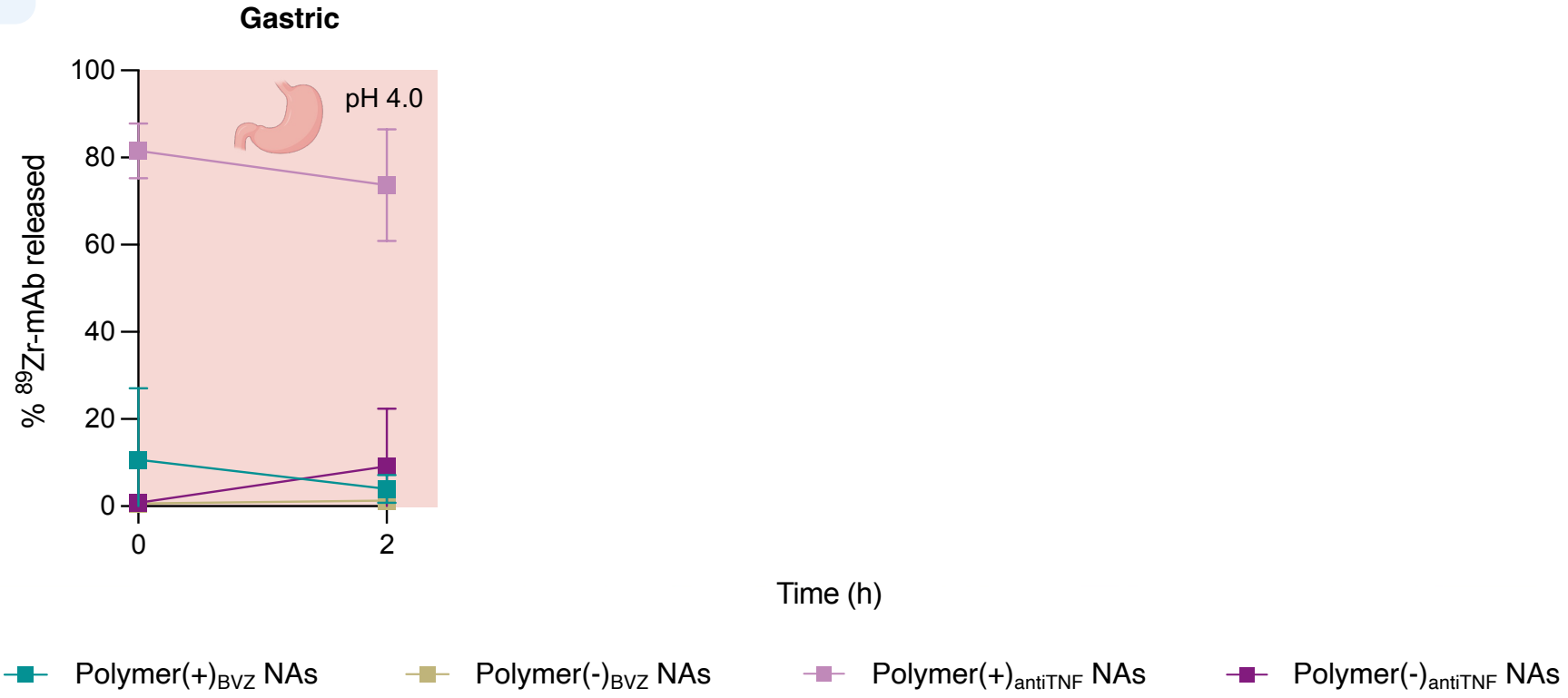
RELEASE



RELEASE

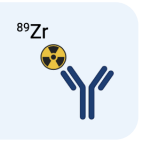
n≥3

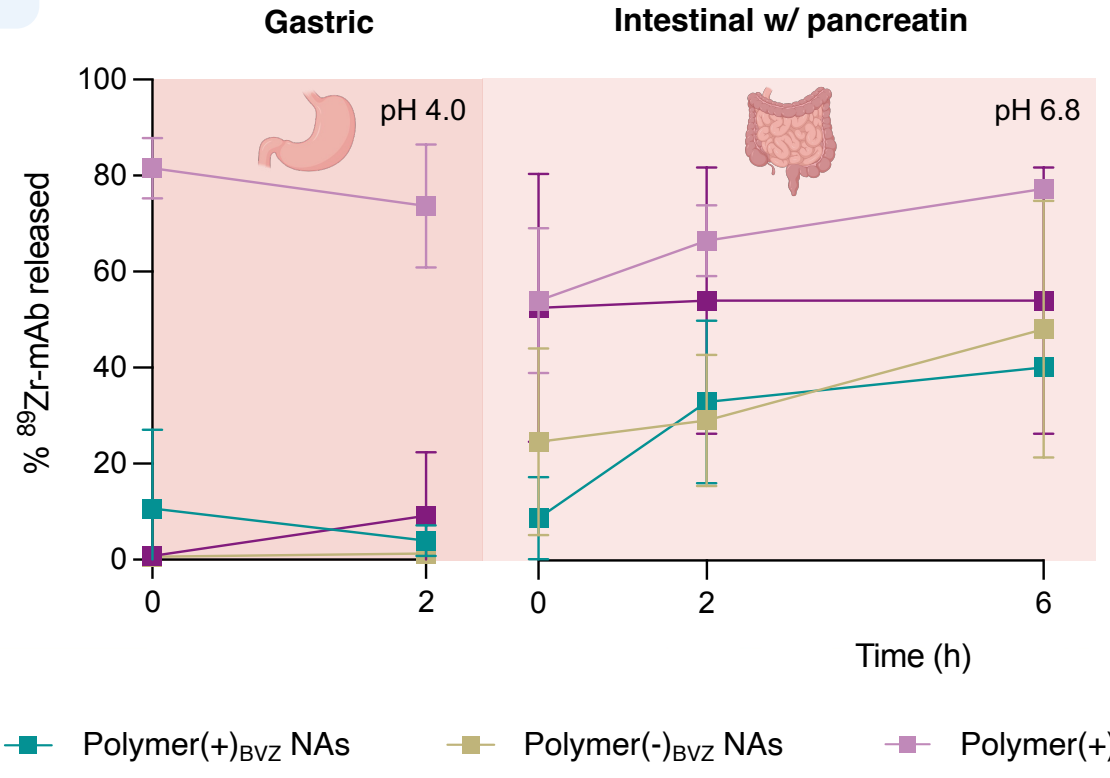

89Zr


Gastric
pH 4.0
100
80
60
40
20
0
% 89Zr-mAb released
0
2
Time (h)
Polymer(+)BVZ NAs
Polymer(-)BVZ NAs
Polymer(+)antiTNF NAs
Polymer(-)antiTNF NAs

RELEASE

n≥3





AM. López-Estévez. *ACS Omega* (2025).

RELEASE

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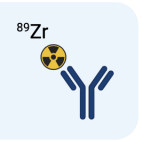

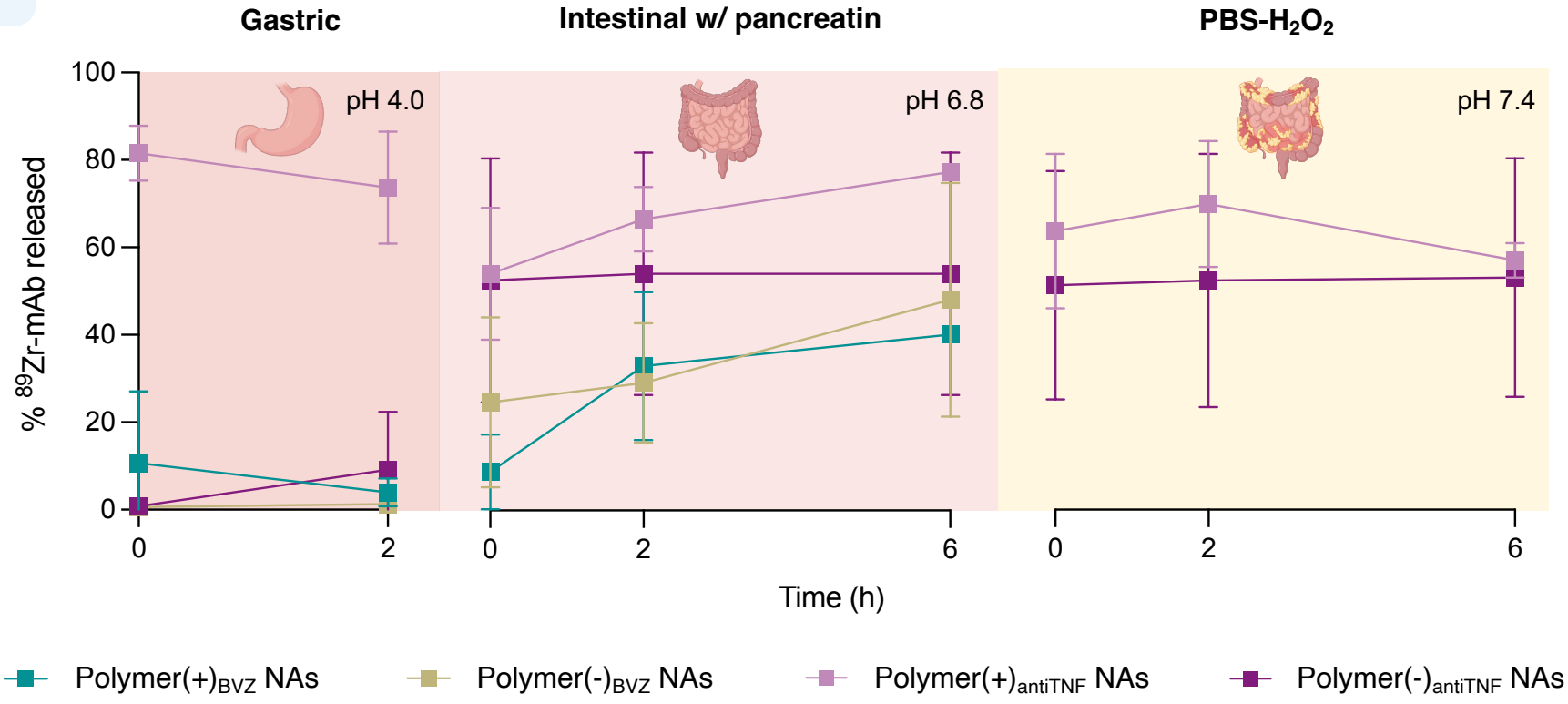

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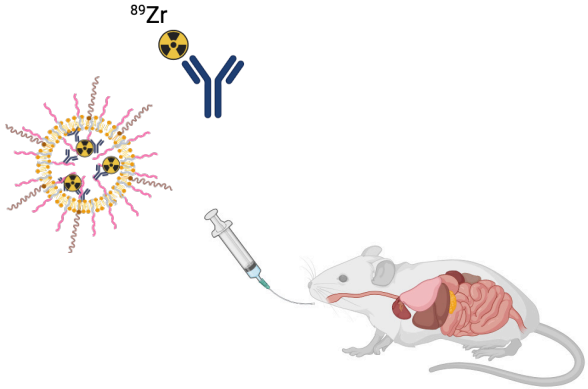
IN VIVO. BIODISTRIBUTION

INMUNO-PET IMAGING



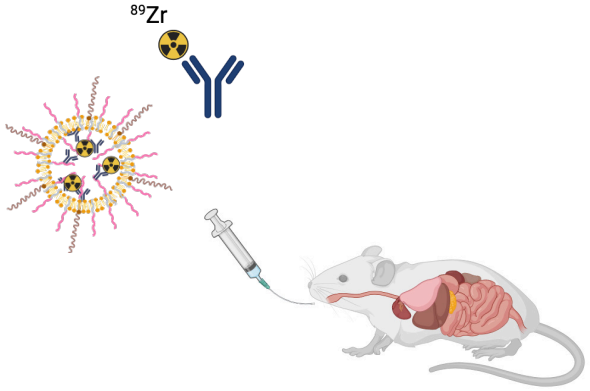
Oral administration

Healthy rats

IN VIVO. BIODISTRIBUTION

INMUNO-PET IMAGING

n≥2



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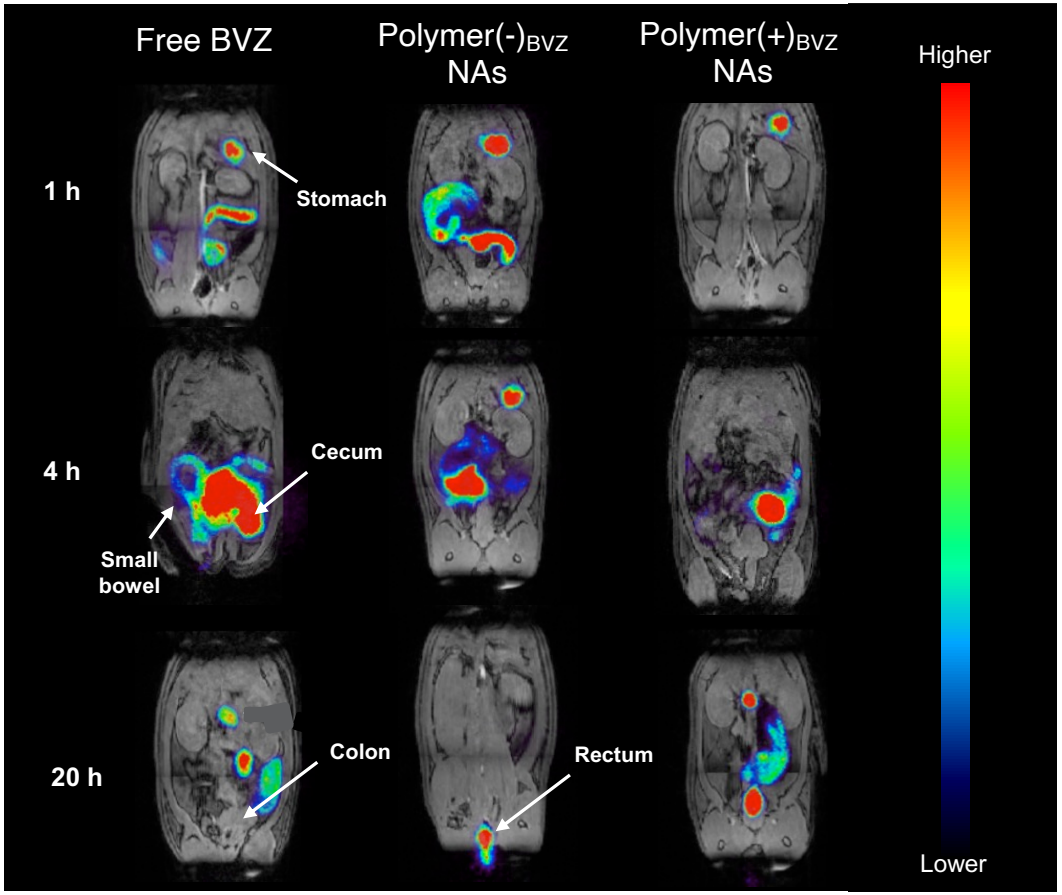
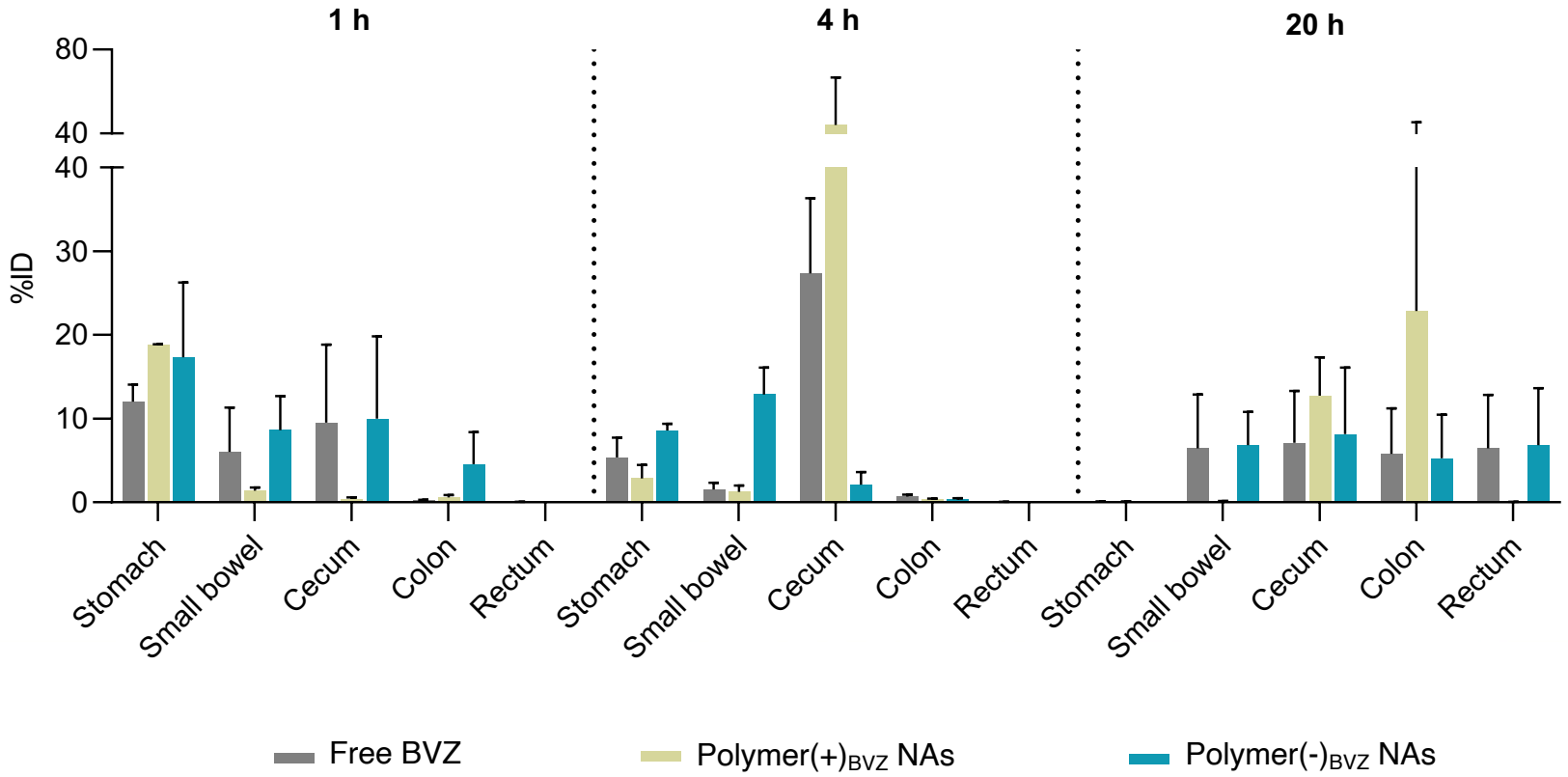


IN VIVO. BIODISTRIBUTION

INMUNO-PET IMAGING

n≥2

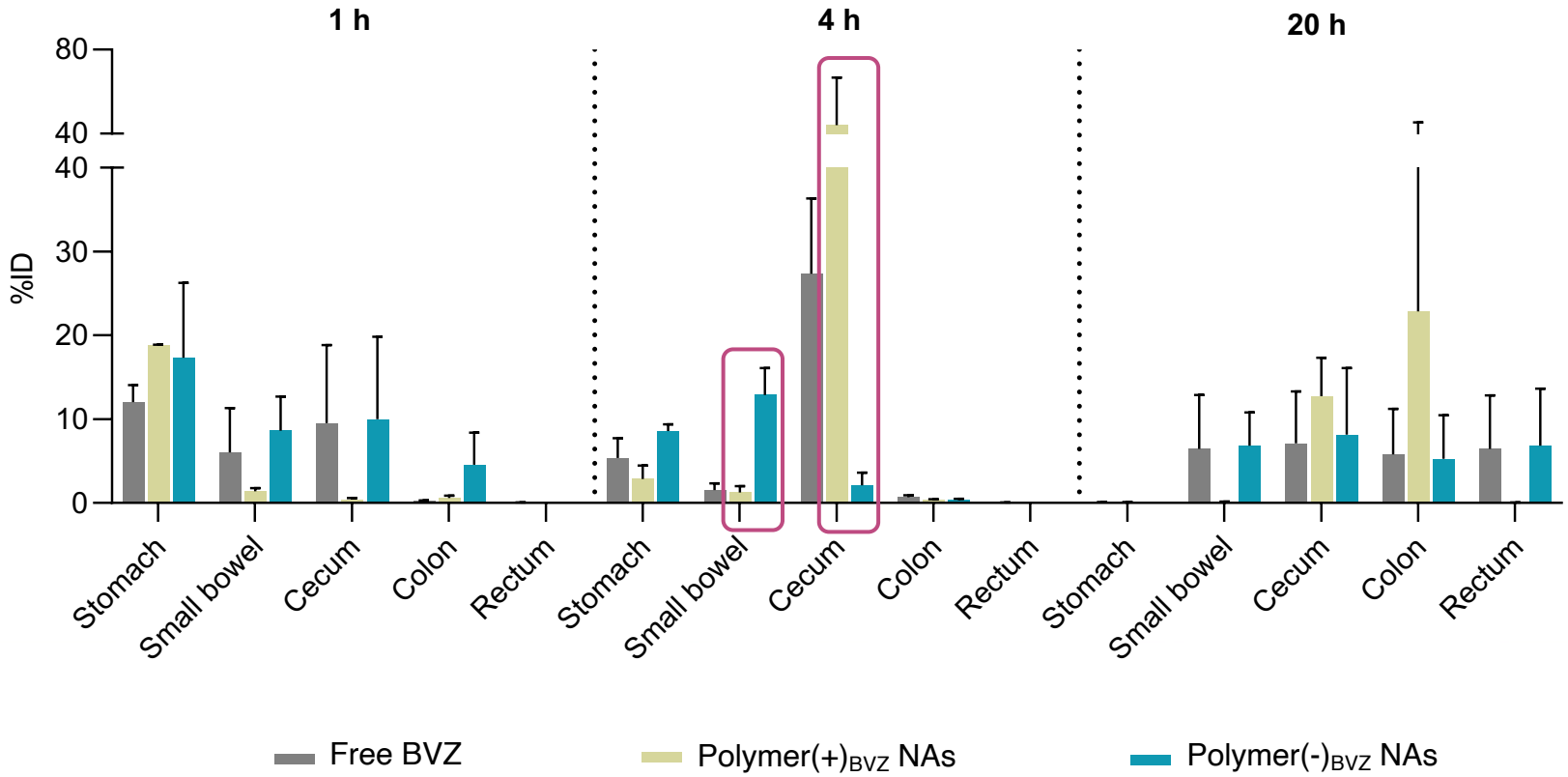


Injected dose (ID)

IN VIVO. BIODISTRIBUTION

INMUNO-PET IMAGING

n≥2

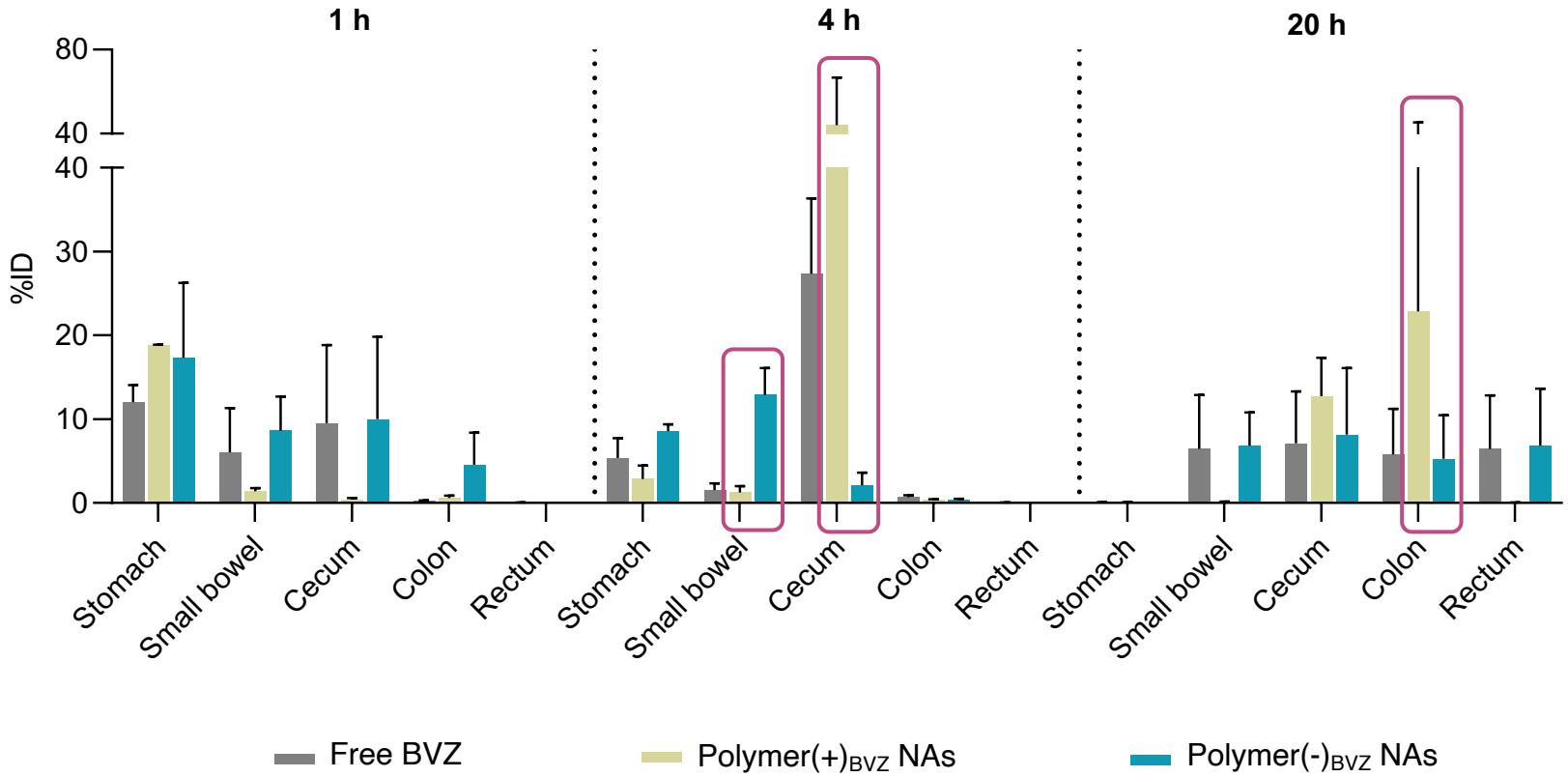


Injected dose (ID)

IN VIVO. BIODISTRIBUTION

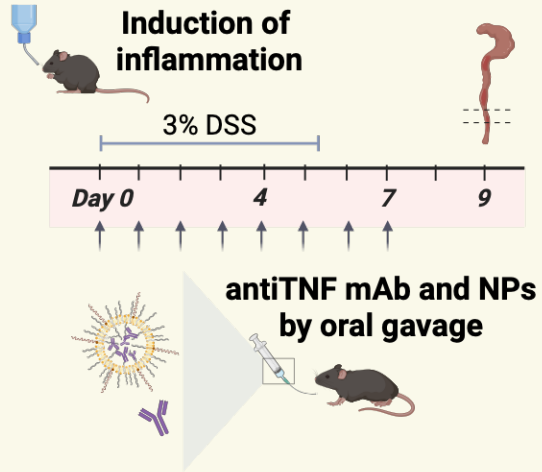
INMUNO-PET IMAGING

n≥2



Injected dose (ID)

IN VIVO. EFFICACY

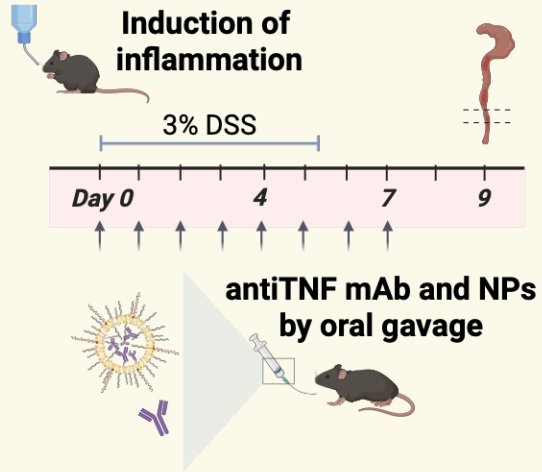


Oral administration

DSS-induced colitis mice

IN VIVO. EFFICACY

n≥3



Oral administration

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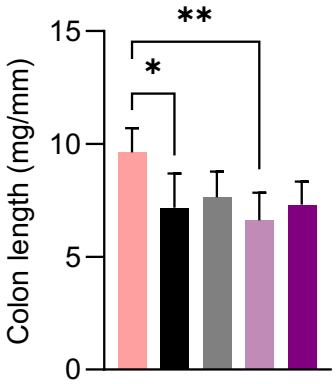
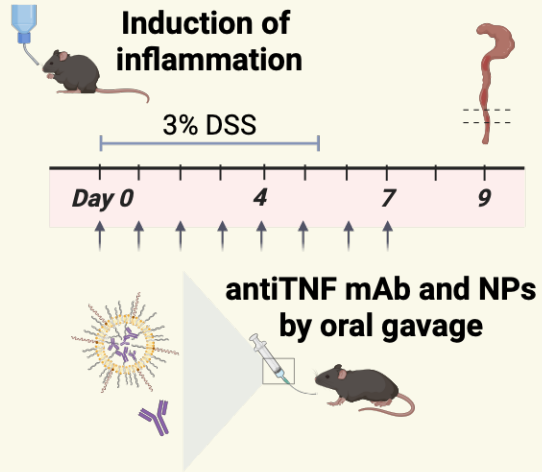


Healthy control | DSS control | Free antiTNF mAb | Polymer(+)$_{antiTNF}$ NAs | Polymer(-)$_{antiTNF}$ NAs

IN VIVO. EFFICACY

n≥3



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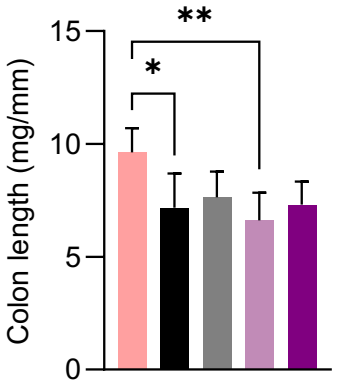

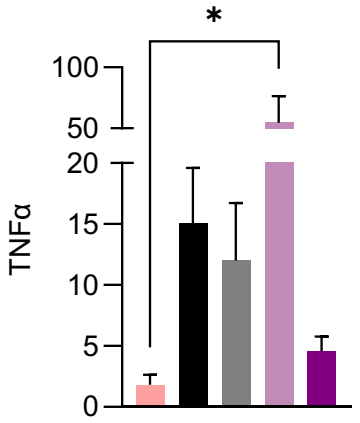

CYTOKINE ANALYSIS

Healthy control | DSS control | Free antiTNF mAb | Polymer(+)$_{antiTNF}$ NAs | Polymer(-)$_{antiTNF}$ NAs

OVERALL CONCLUSIONS

- **mAb-loaded NAs exhibited desirable features for overcoming oral biological barriers.**
- **The NAs change the biodistribution profile of the free mAb in a healthy murine model.**
- **In an acute colitis mice model, the Polymer(-)$_{antiTNF}$ NAs reduce the production of pro-inflammatory cytokines and may provide superior protection against inflammation.**

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Further studies are underway to fully elucidate their mechanism of action and translational potential.

ACKNOLEDGMENTS

Inés Rubio
Cris Iglesias
Elisa Battistini
Julia Baena
Jorge Ruz
Paloma Rial
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Belén Cuesta
Puri Domínguez
Lucía Sanjurjo
Elena Ibeas
Natalia Carballo
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