

Bioengineered Bacteria Delivery System Enhances Tumor Pyroptosis Through Preventing ESCRT-Dependent Cell Membrane Repair

Zhaoting Li (Ph.D.)

University of Wisconsin-Madison

CONTROLLED RELEASE SOCIETY

CRS 2023 ANNUAL MEETING & EXPOSITION

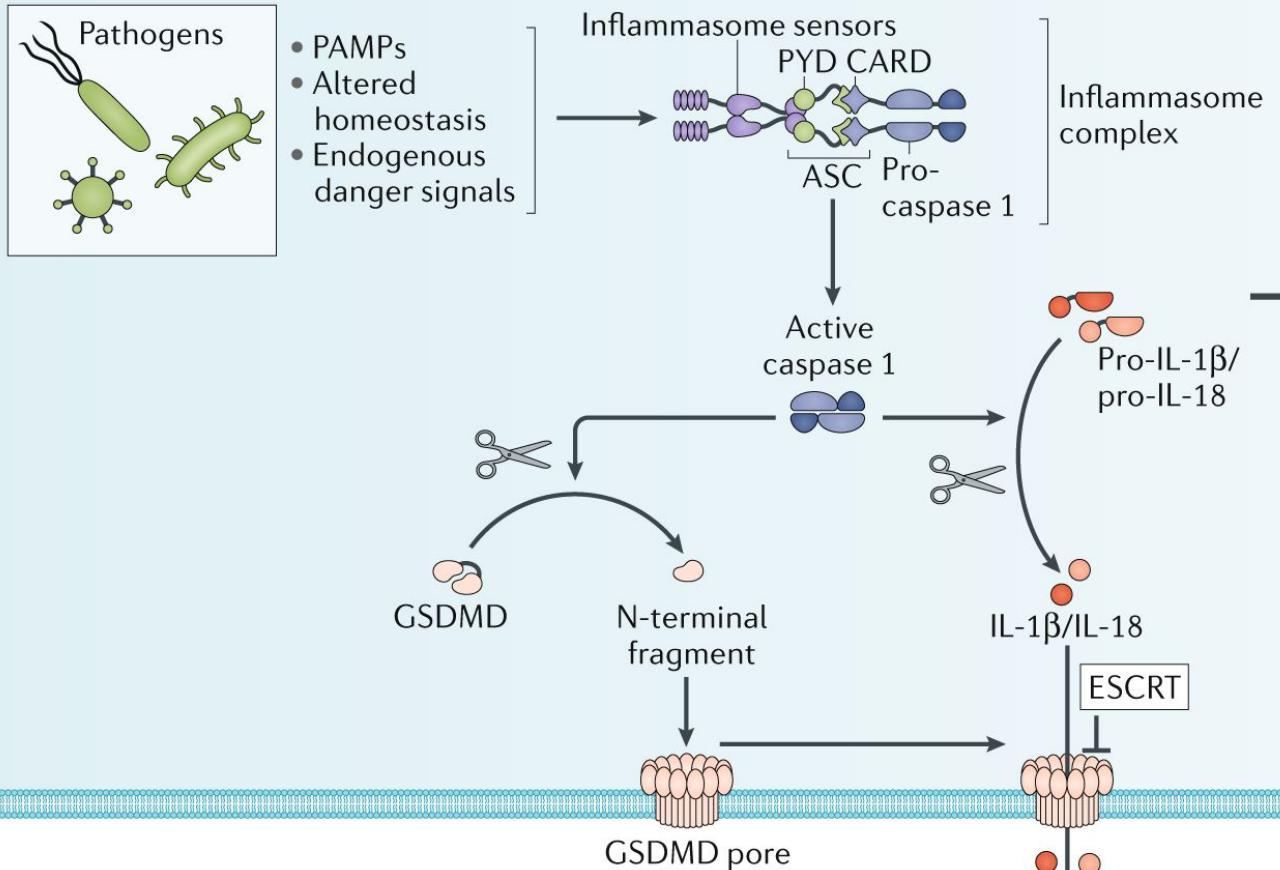
JULY 24-28, 2023

Paris Hotel » **Las Vegas, NV, USA**

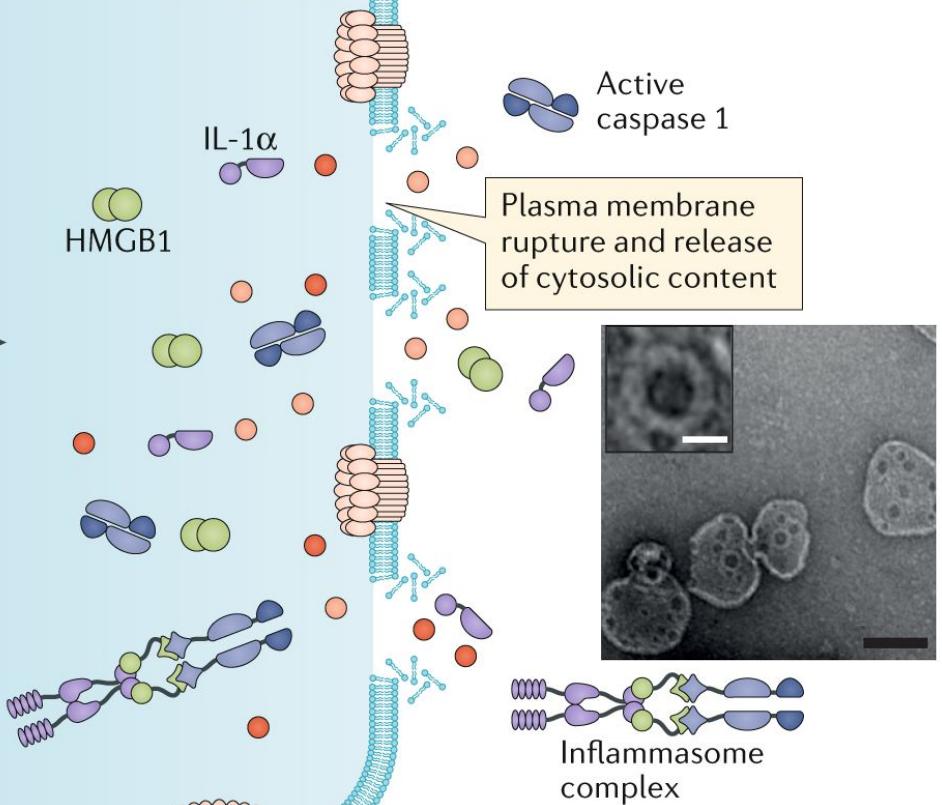
THE FUTURE OF DELIVERY SCIENCE

Bacteria & Pyroptosis

GSDMD activation and sublytic phase



Lytic phase (pyroptosis)



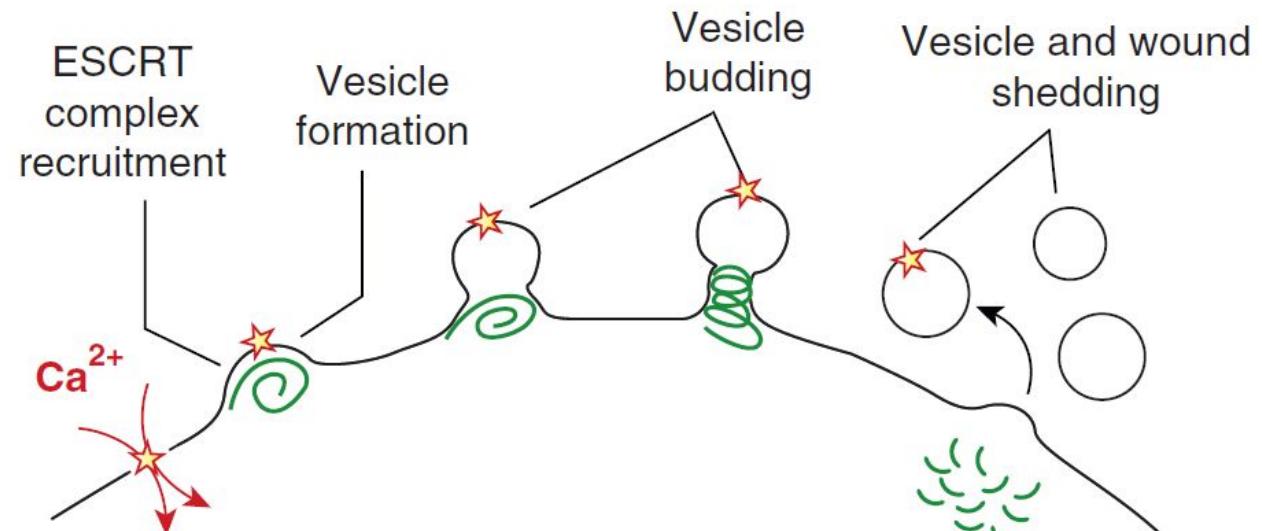
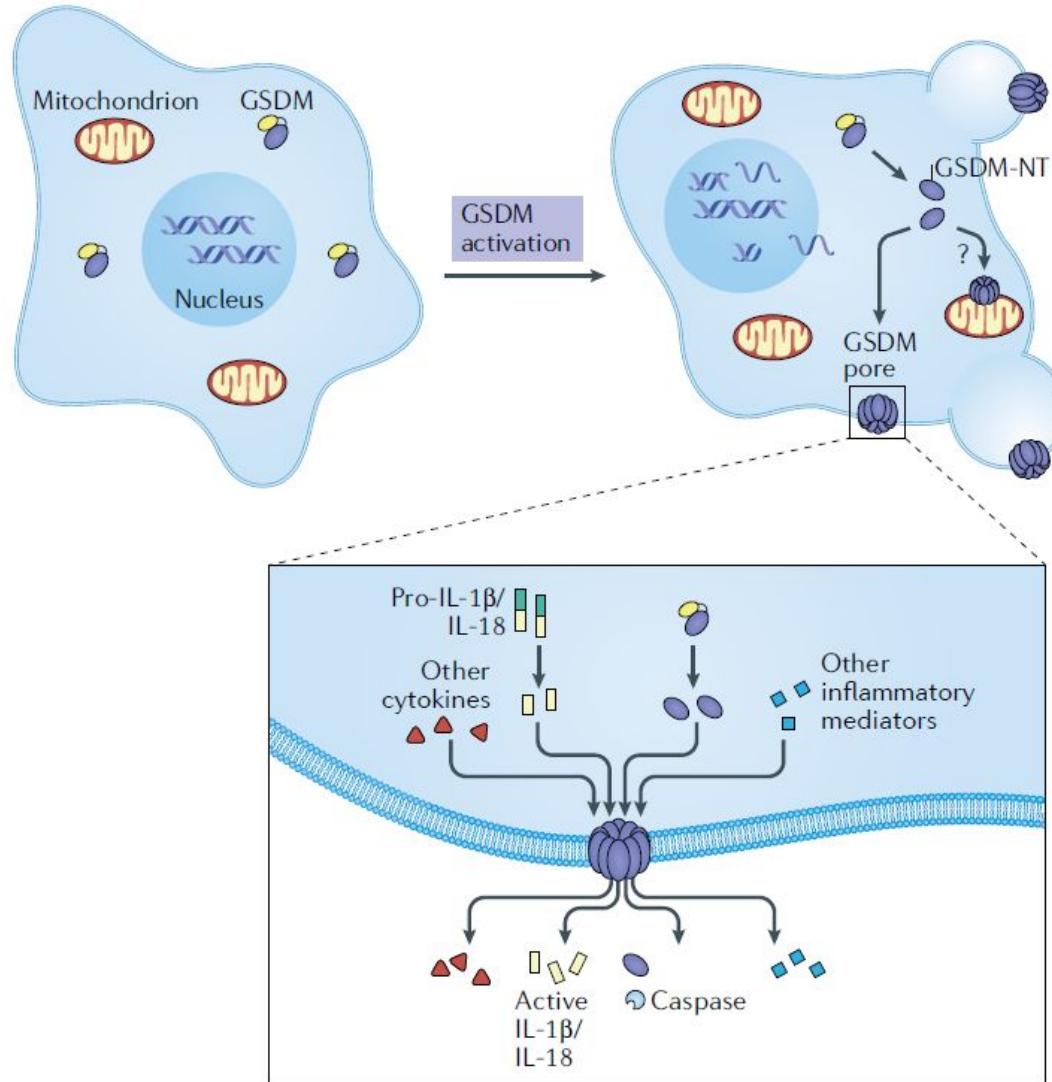
Nature, 2016. *Nature Reviews Immunology*, 2020.

CONTROLLED RELEASE SOCIETY

CRS2023 ANNUAL MEETING & EXPOSITION
JULY 24-28, 2023 **Paris Hotel » Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

ESCRT membrane repair & Pyroptosis



Calcium influx triggered
ESCRT-dependent cell membrane repair

Nature Reviews Drug Discovery, 2021.

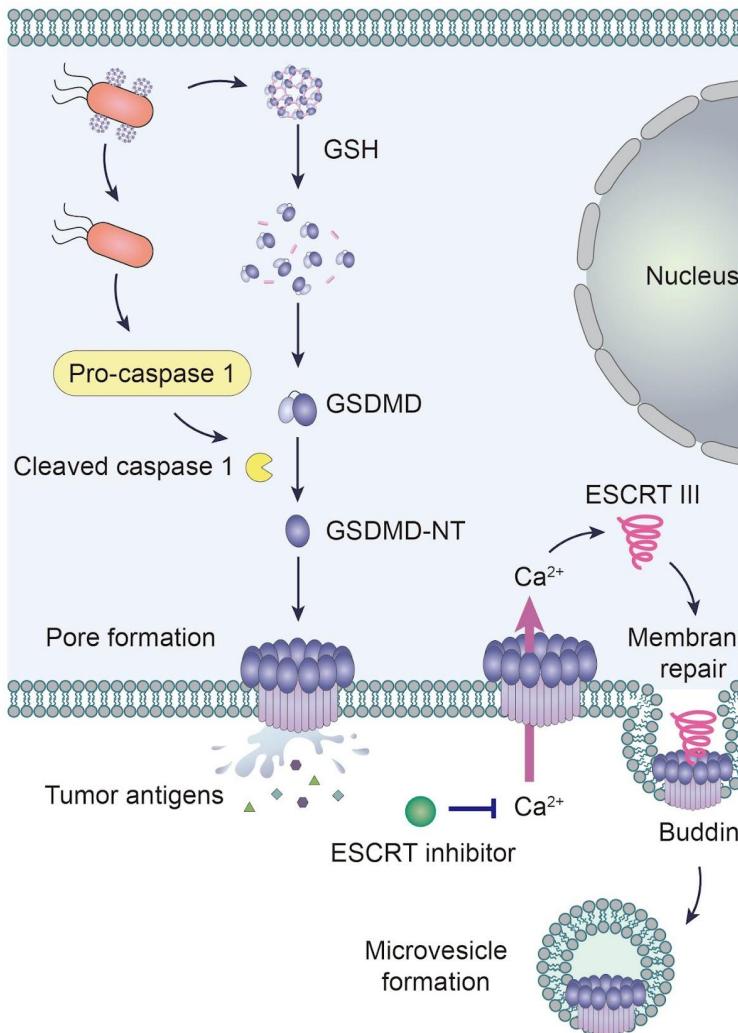
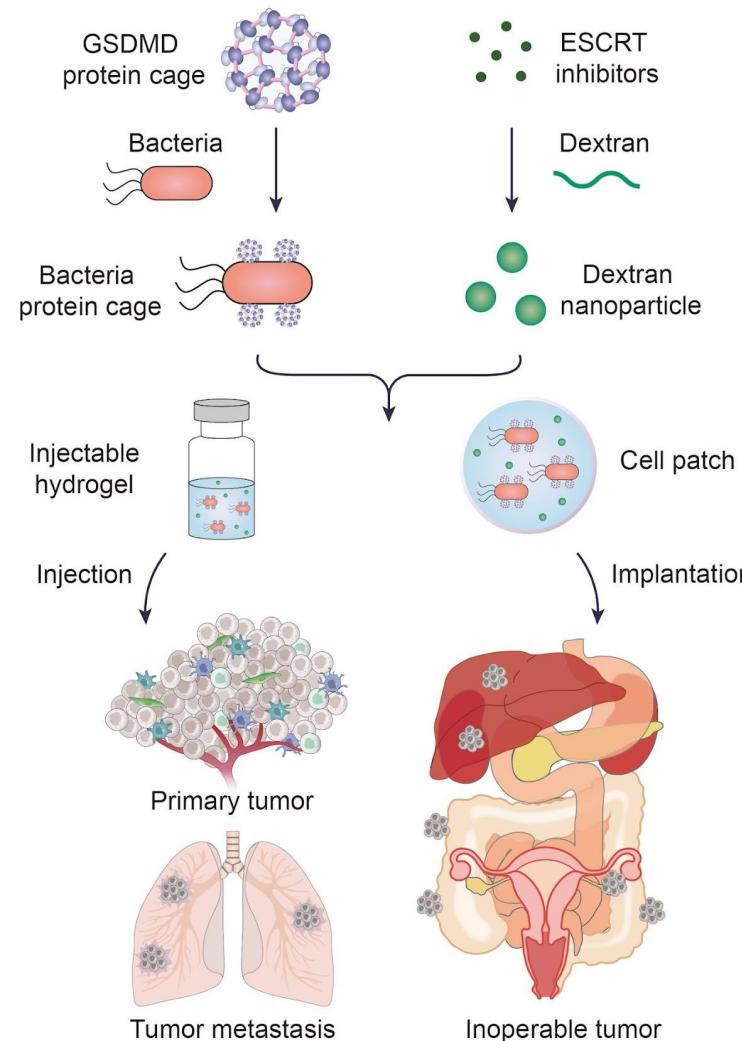
CONTROLLED RELEASE SOCIETY

CRS2023 ANNUAL MEETING & EXPOSITION

JULY 24-28, 2023 **Paris Hotel » Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

Engineered bacteria system for enhanced tumor pyroptosis

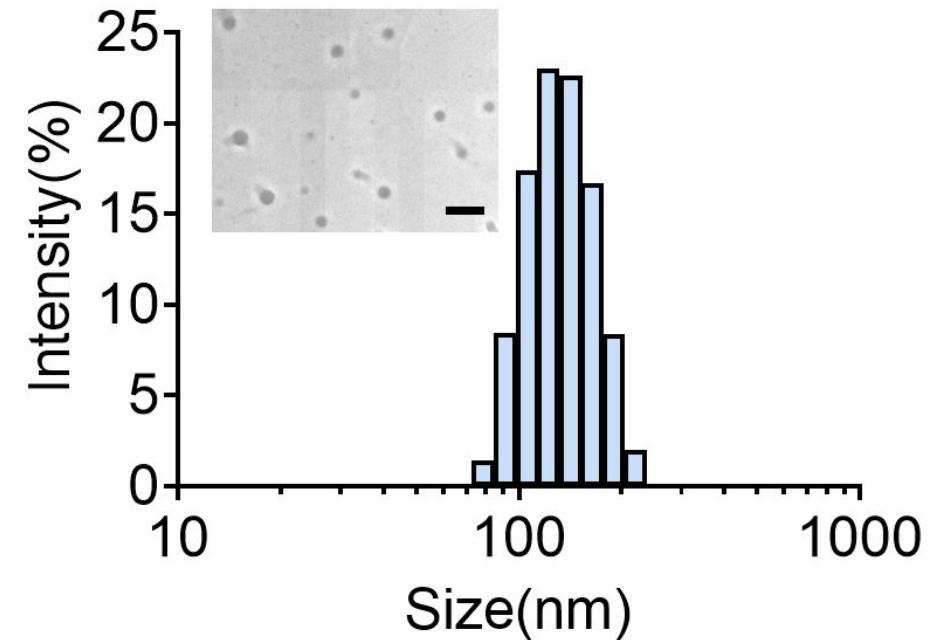
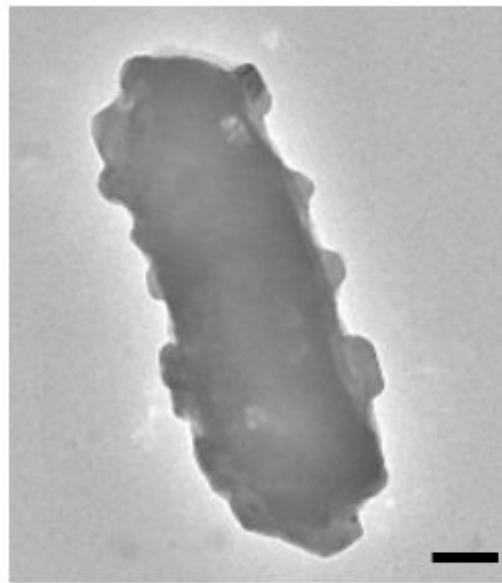
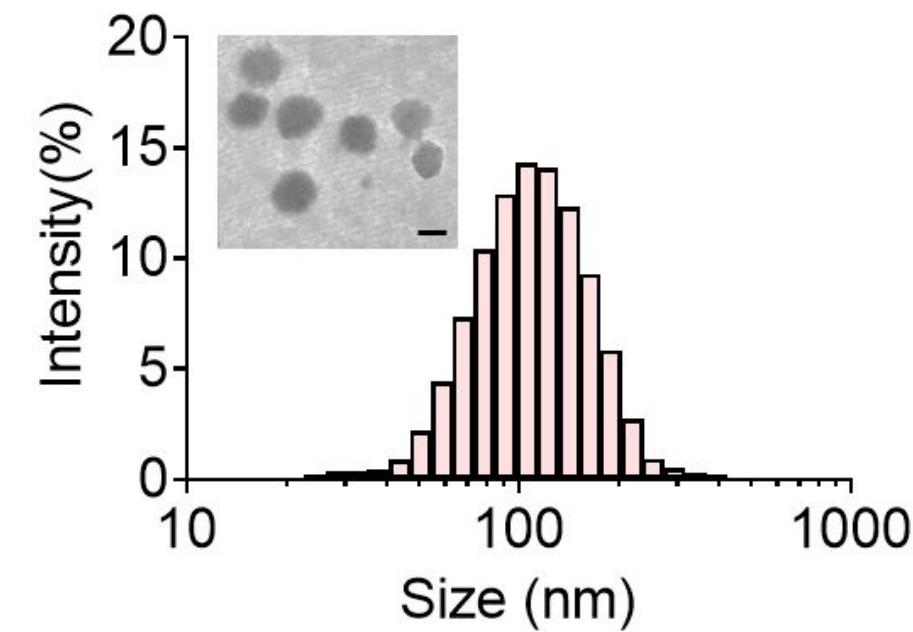


Key points:

1. **Bacteria & Protein delivery**
2. **Bacteria & Pyroptosis signaling pathway activation**
3. **Pyroptosis & ESCRT inhibition**

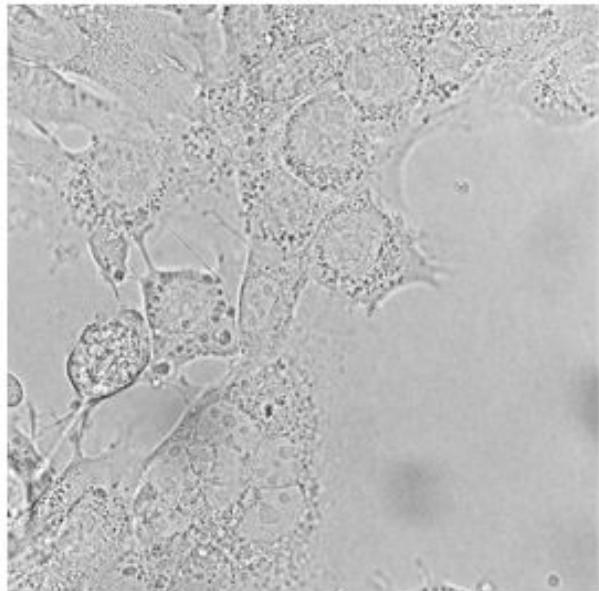
Nature Communications, 2022

Preparation and characterization

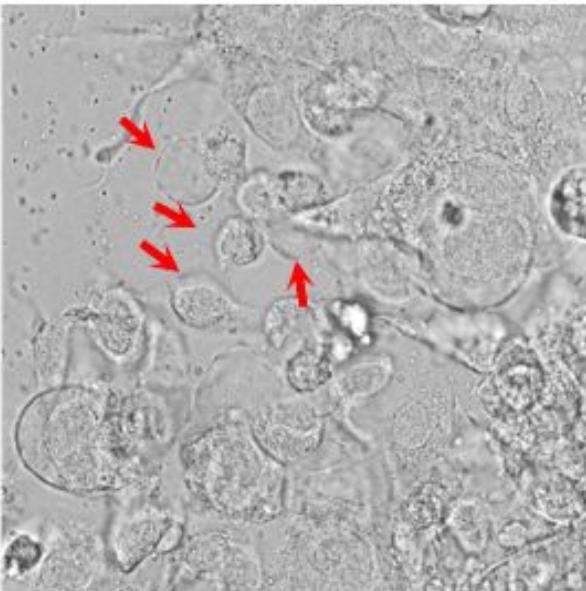


Pyroptosis verification

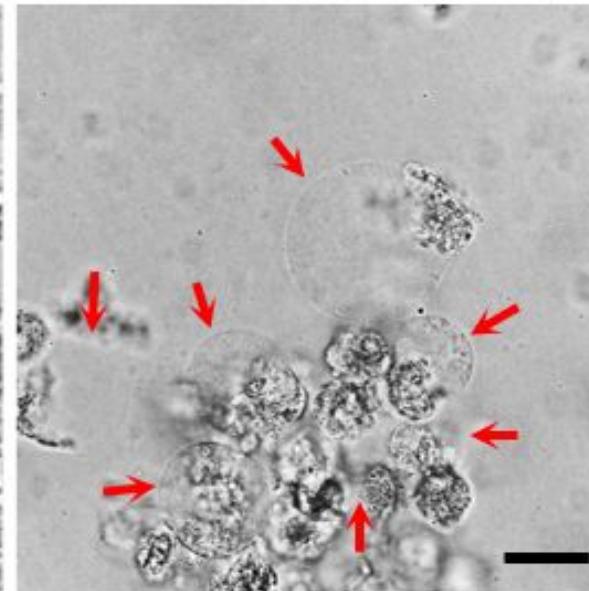
Control



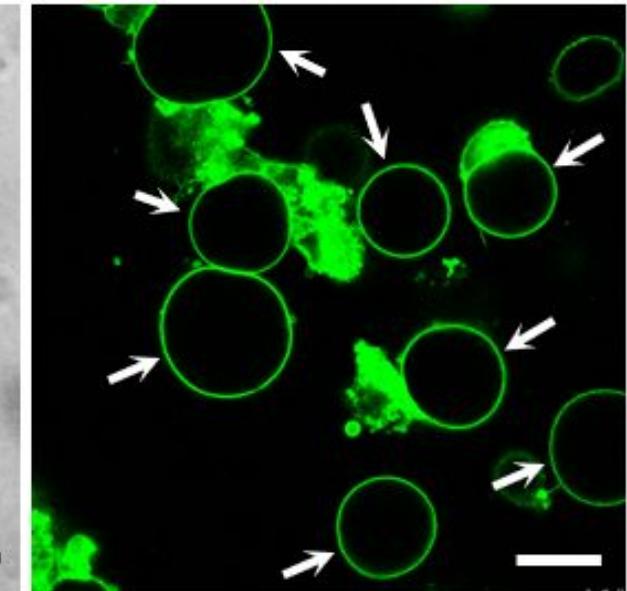
VNP-GD



VNP-GD+EI-NP



VNP-GD+EI-NP
Annexin V Staining



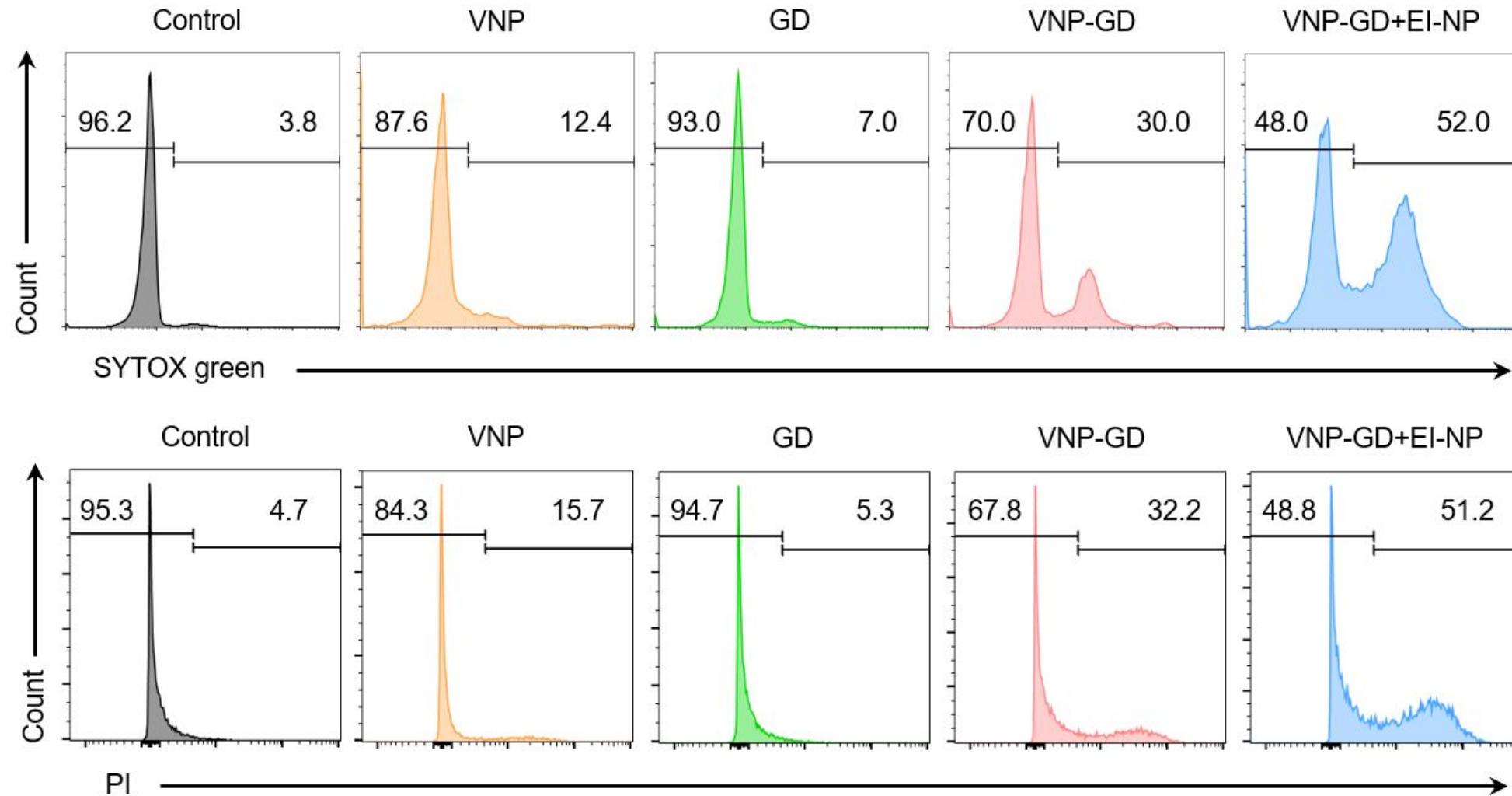
CONTROLLED RELEASE SOCIETY

CRS 2023 ANNUAL MEETING & EXPOSITION

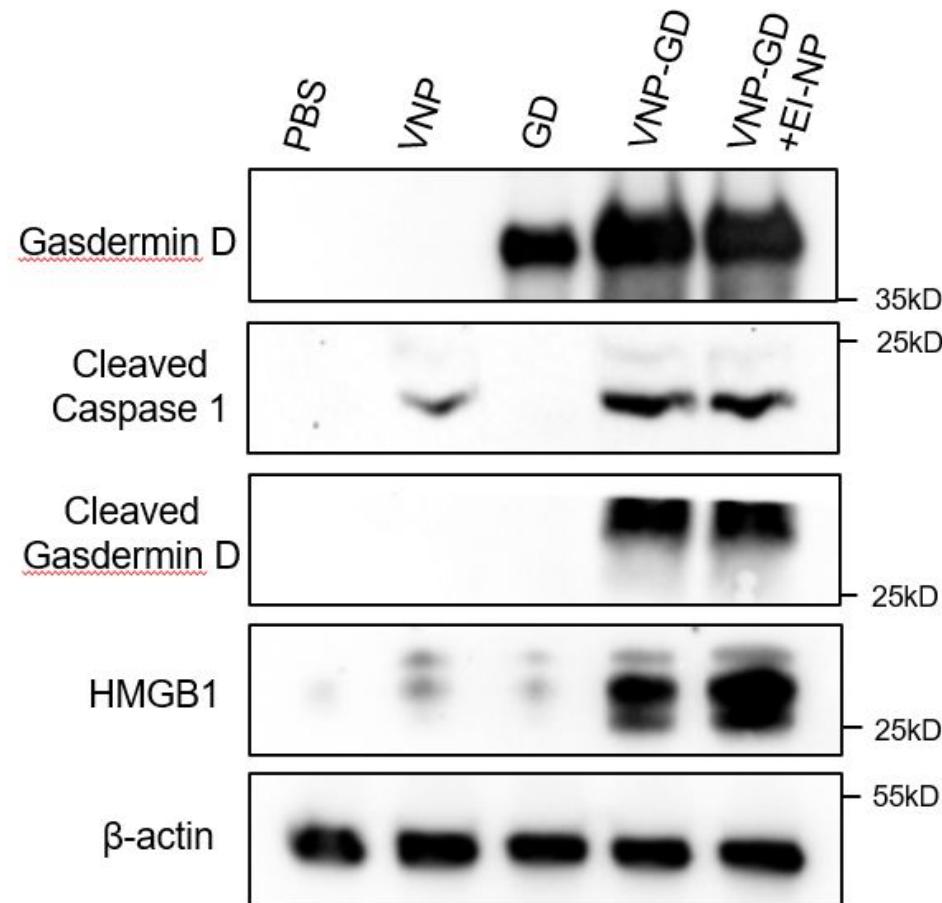
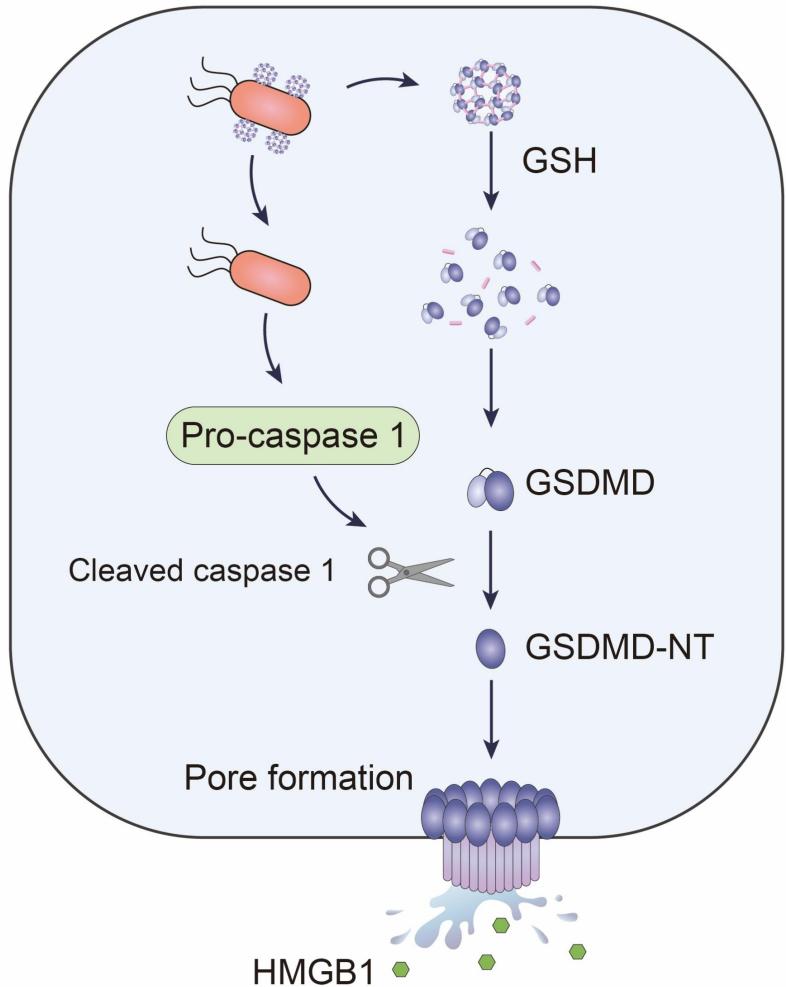
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

Pyroptosis verification



Mechanism exploration



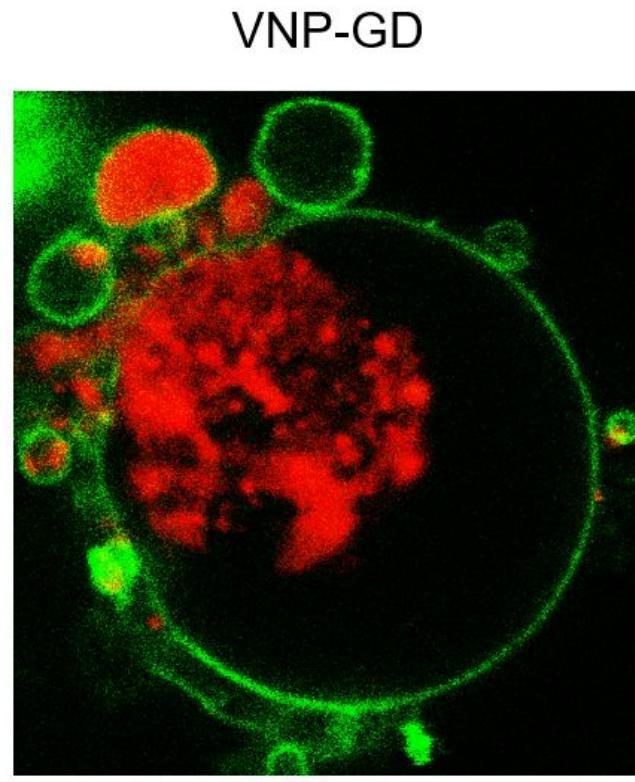
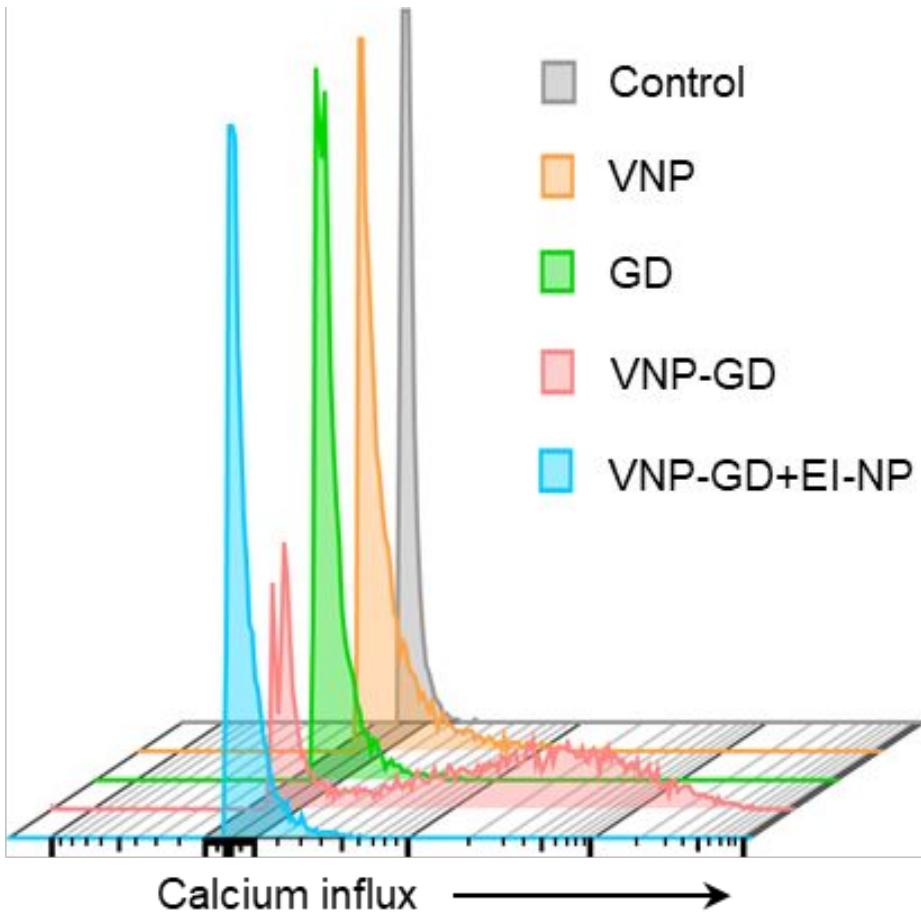
CONTROLLED RELEASE SOCIETY

CRS 2023 ANNUAL MEETING & EXPOSITION

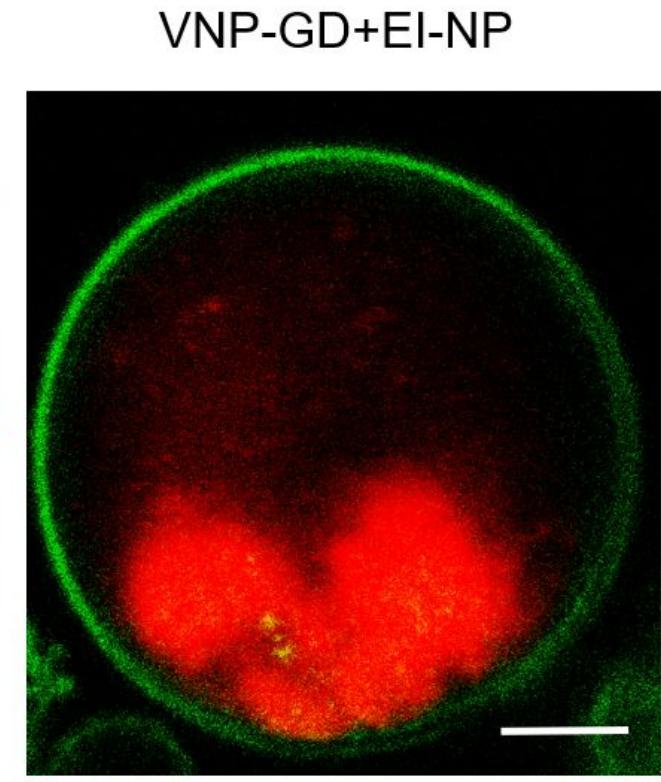
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

Mechanism exploration

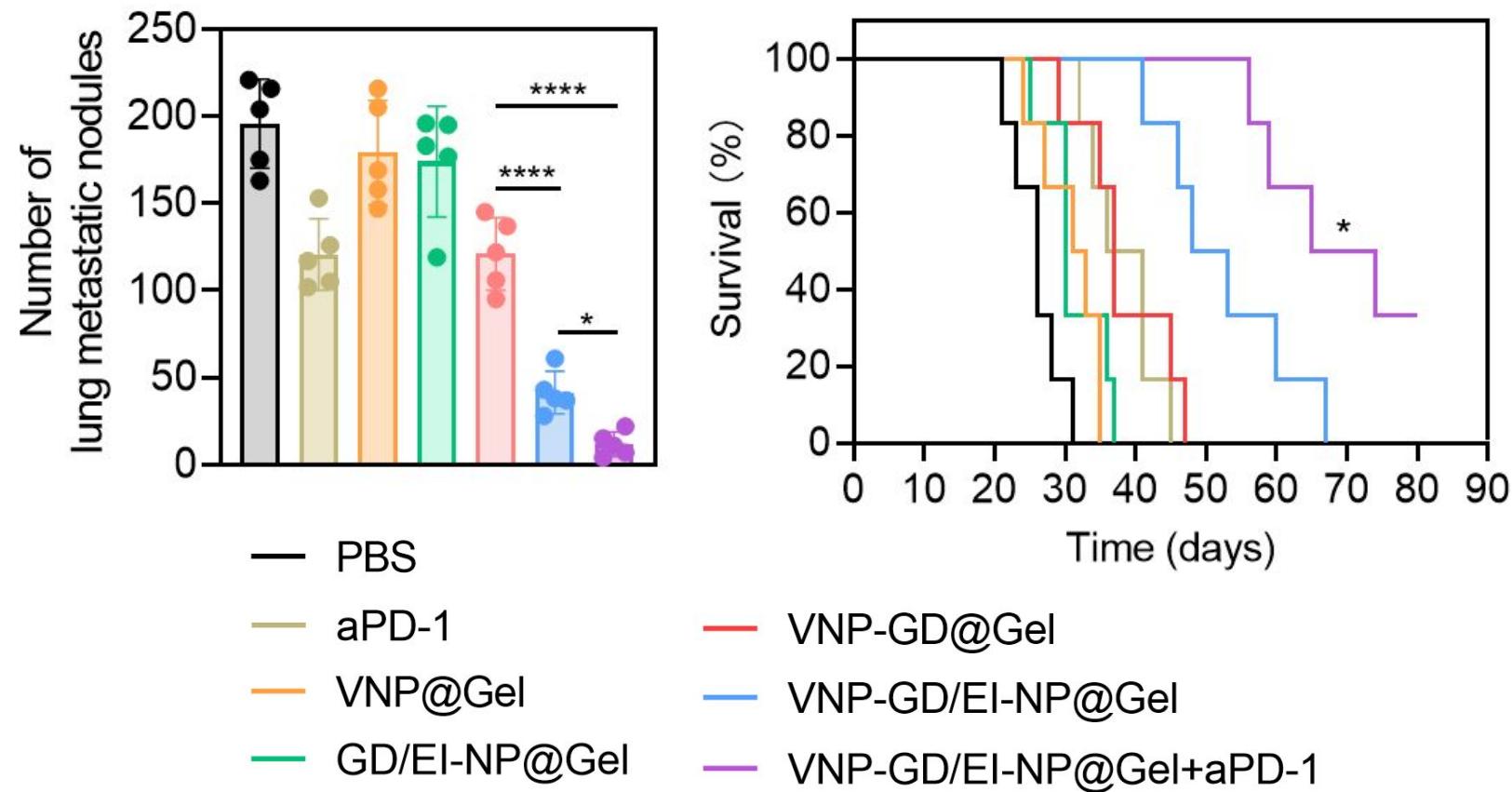
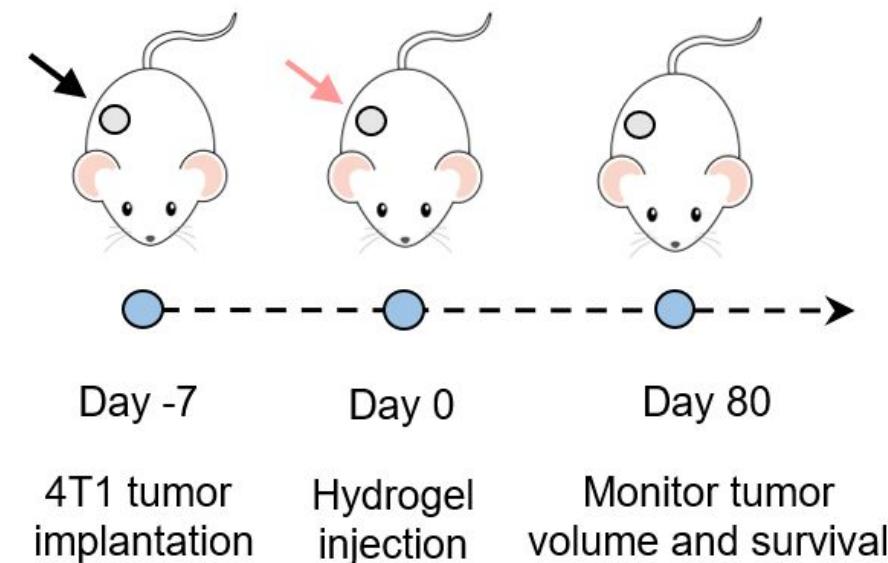


Annexin V-stained cell membrane

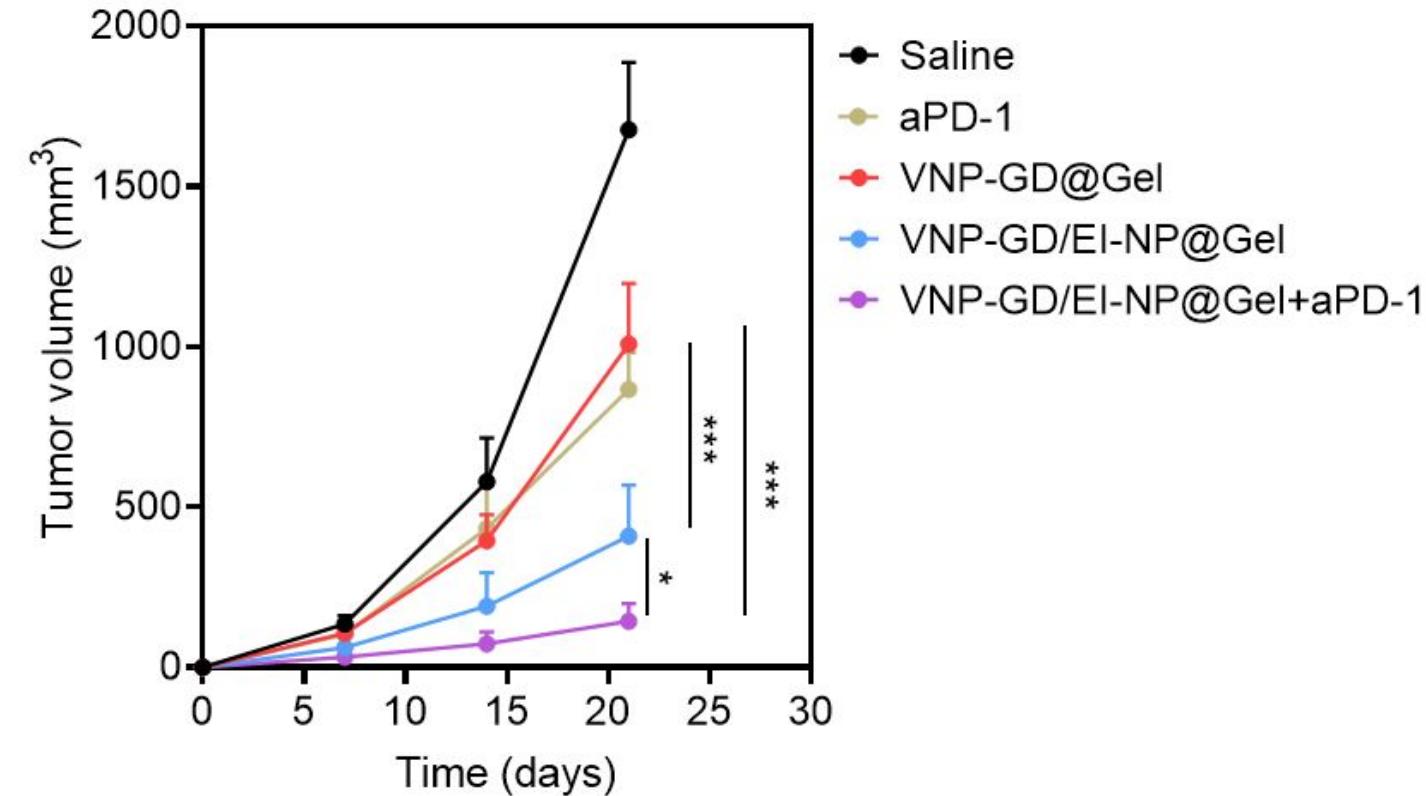
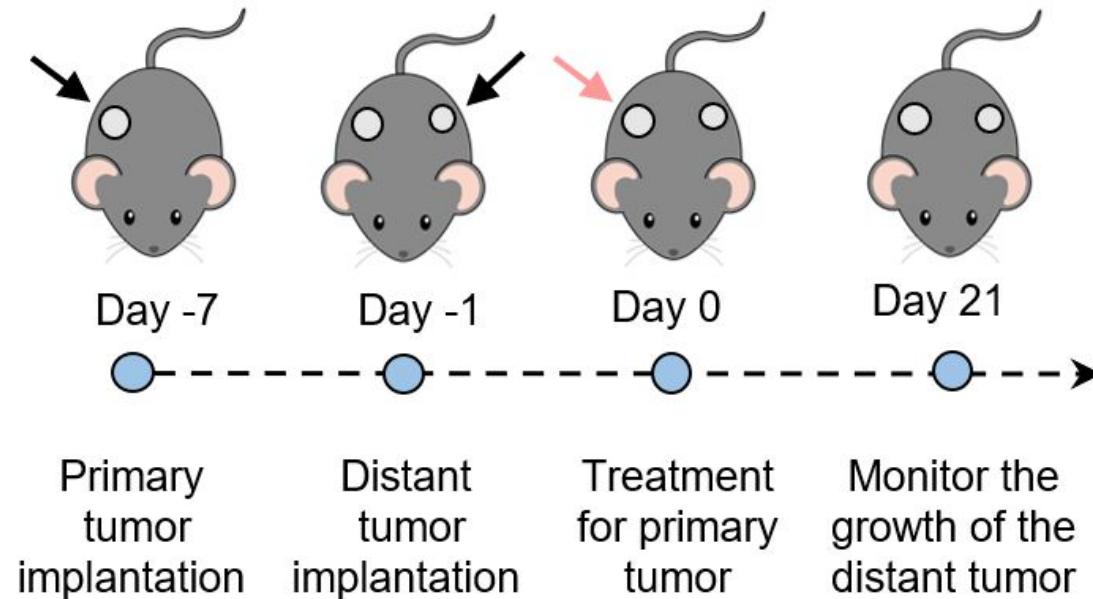


mCherry-labeled CHMP3

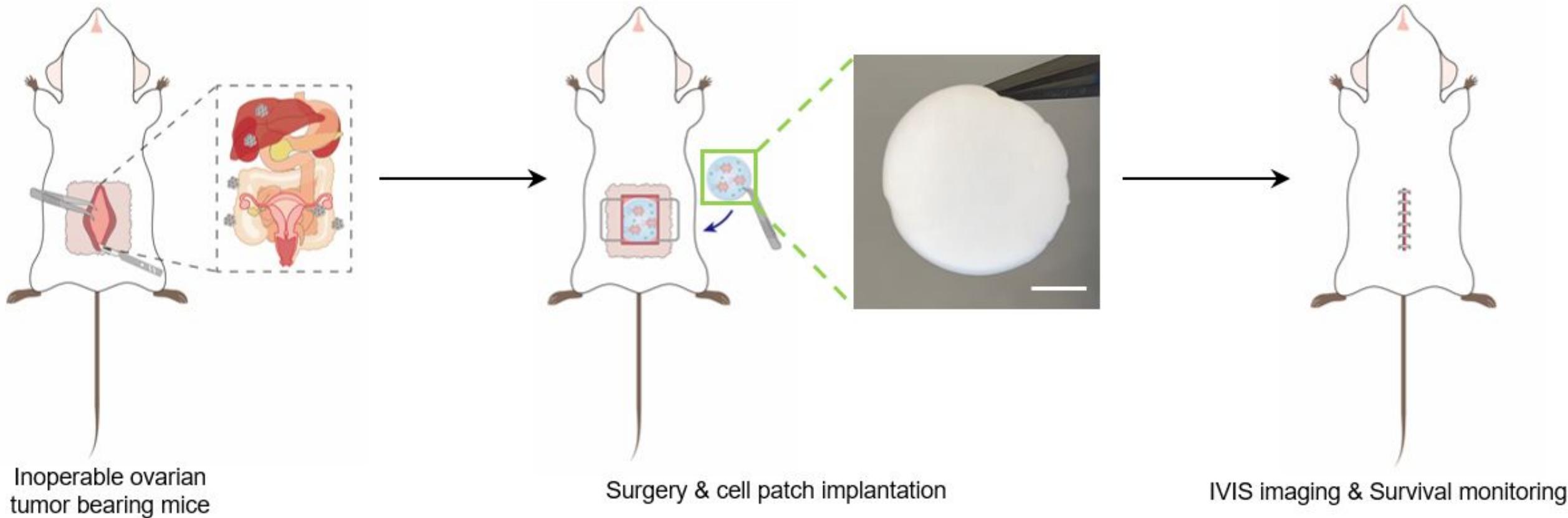
In vivo anti-tumor efficacy (Breast cancer)



In vivo anti-tumor efficacy (Melanoma)



In vivo anti-tumor efficacy (Ovarian cancer)



Inoperable ovarian tumor bearing mice

Surgery & cell patch implantation

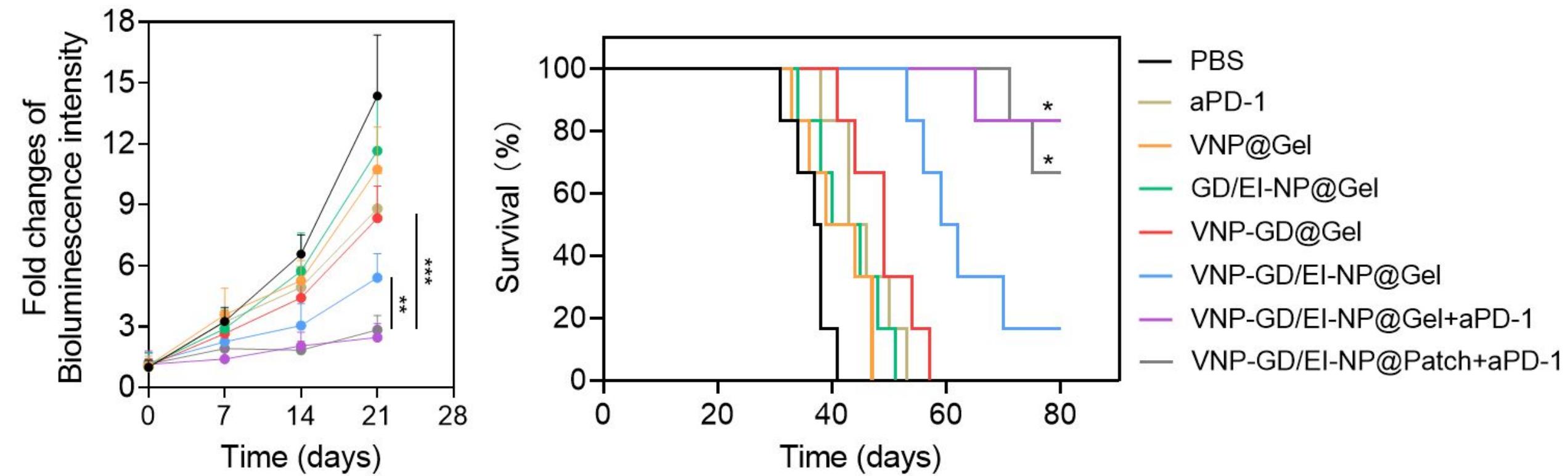
IVIS imaging & Survival monitoring



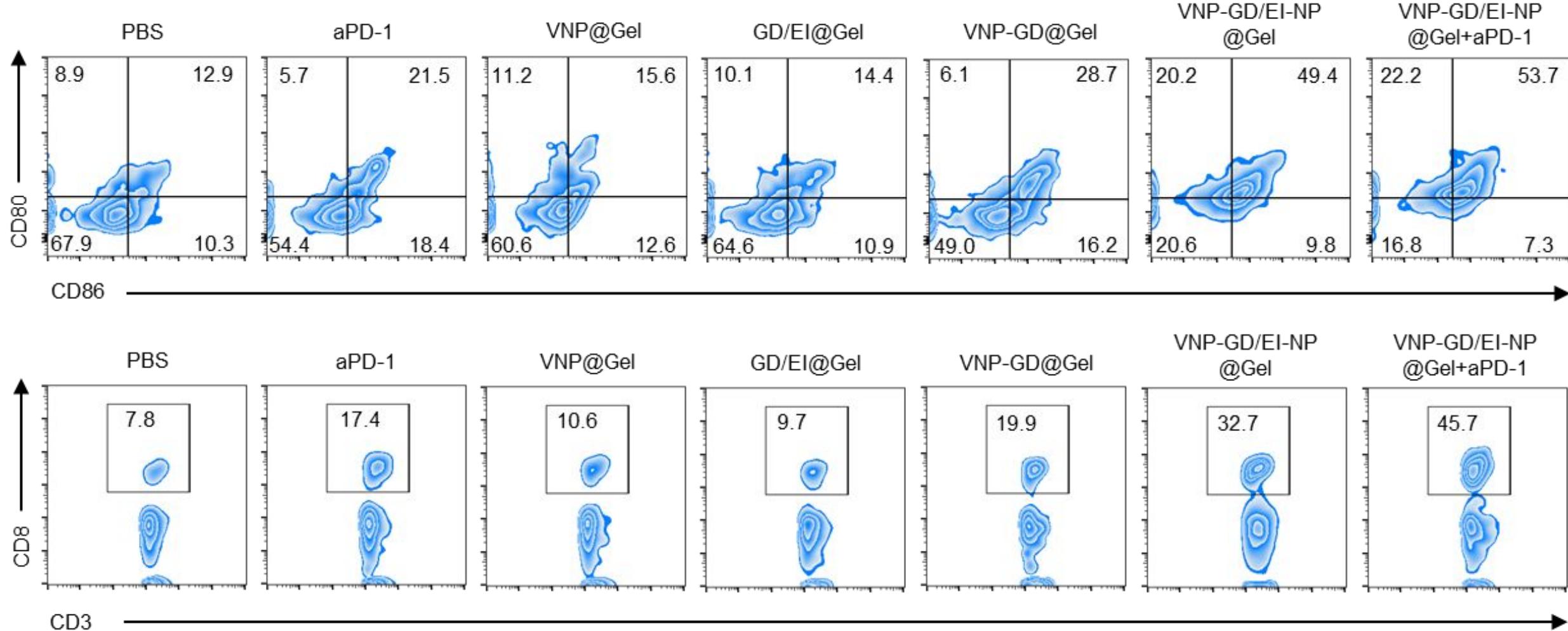
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

In vivo anti-tumor efficacy (Ovarian cancer)



In vivo immune activation



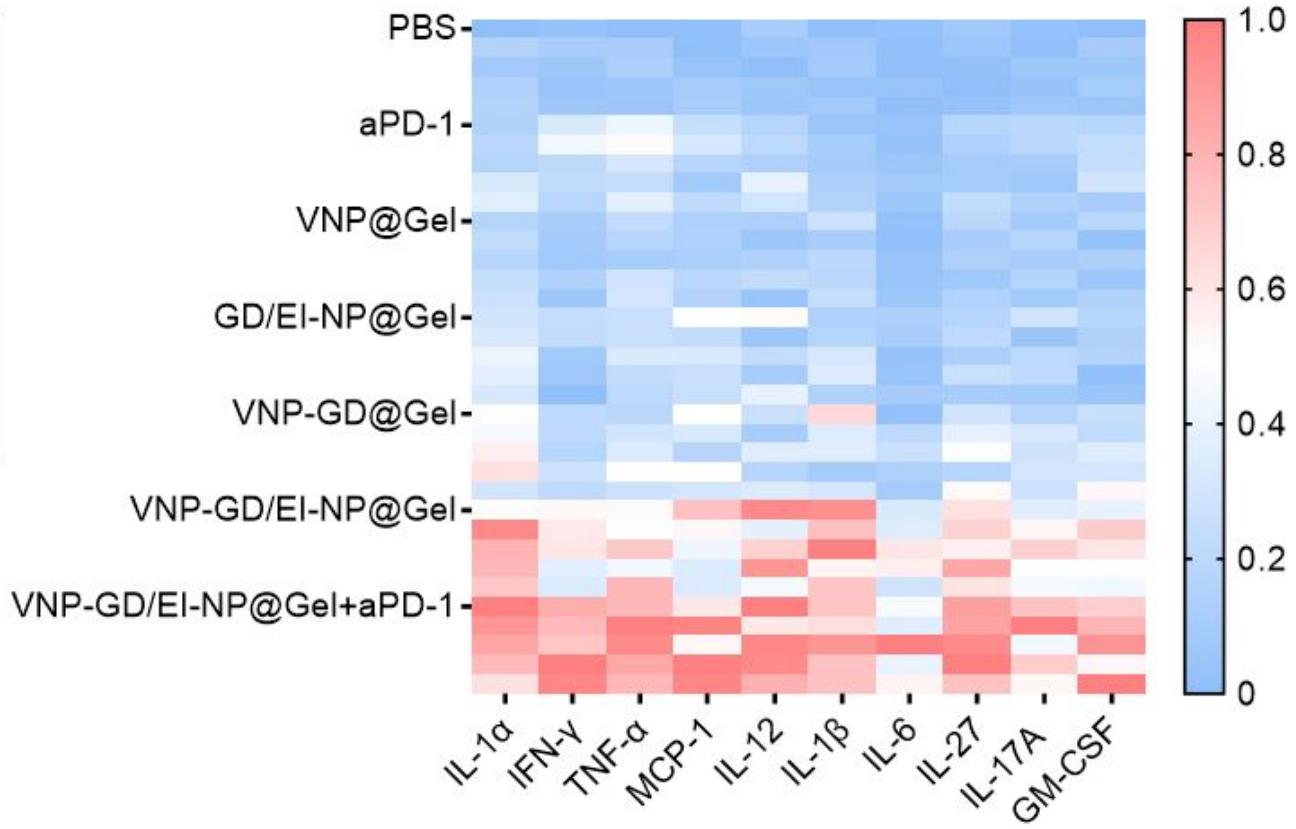
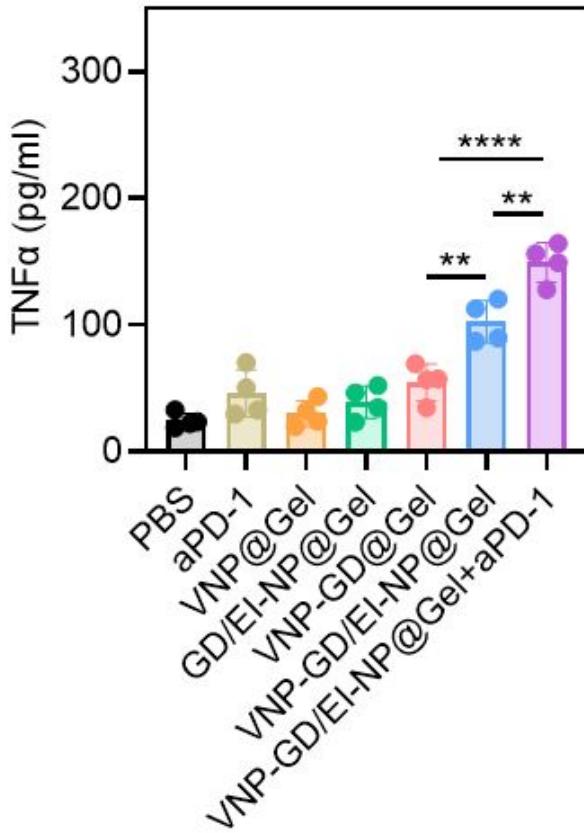
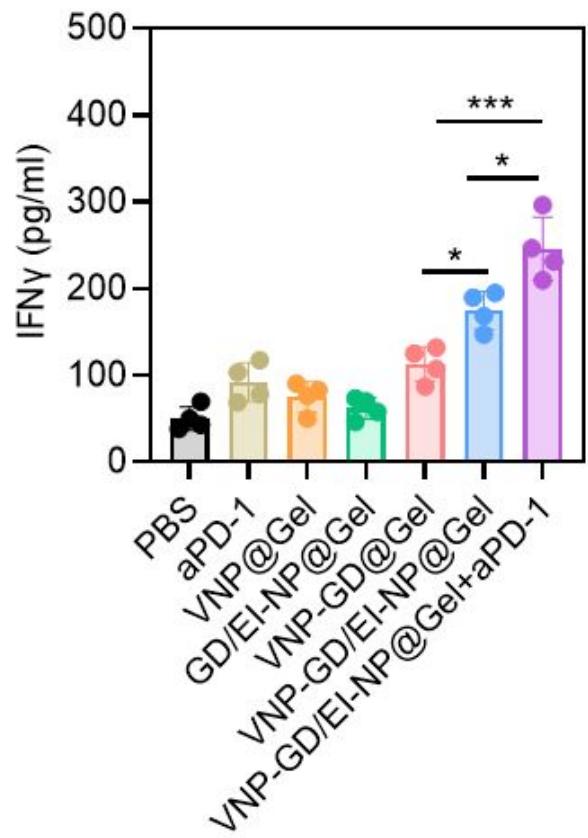
CONTROLLED RELEASE SOCIETY

CRS 2023 ANNUAL MEETING & EXPOSITION

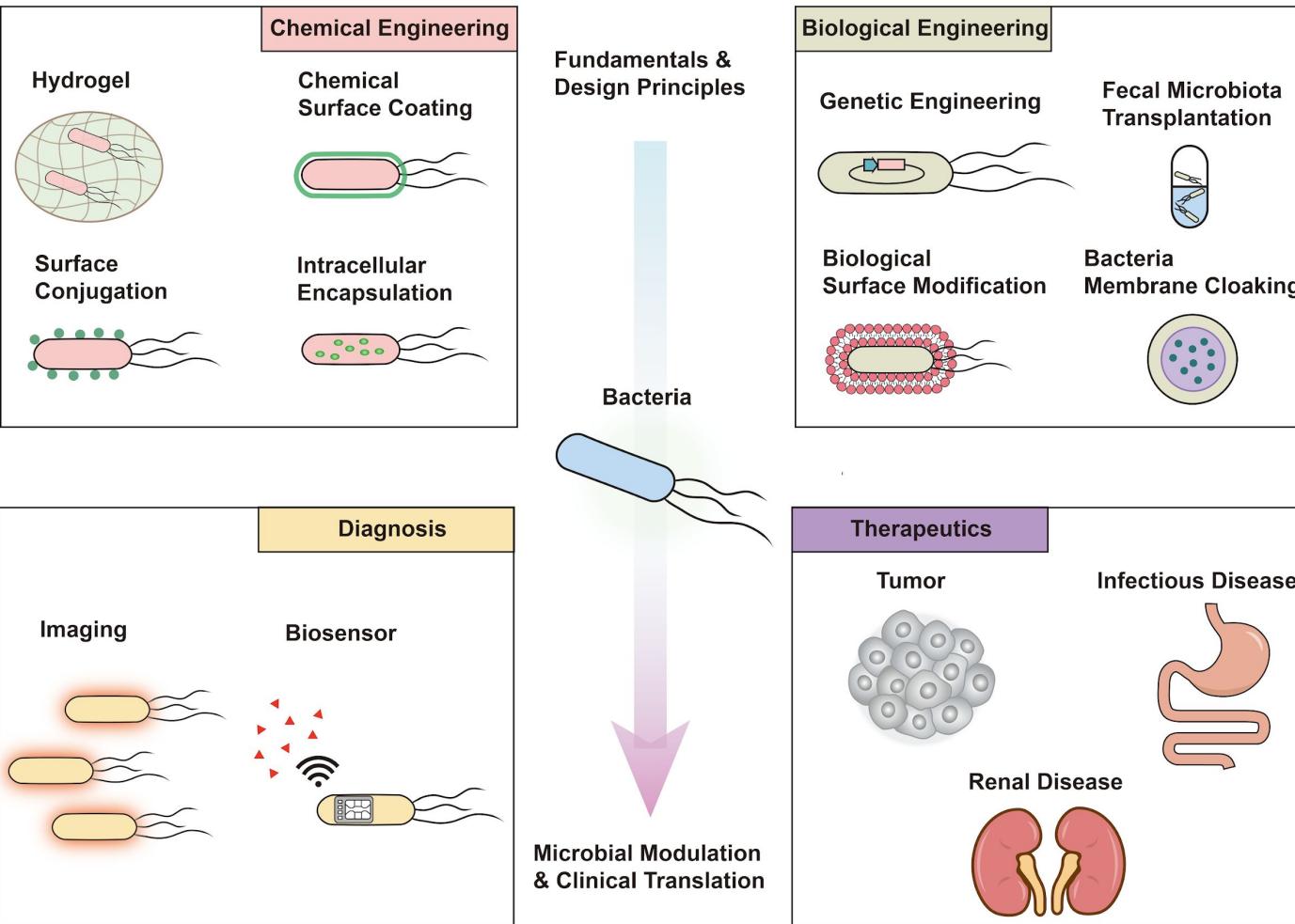
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

In vivo immune activation



Conclusion



Surface conjugation & tumor pyroptosis



Chemically & biologically engineered
bacteria delivery systems

Acknowledgment



School of Pharmacy
UNIVERSITY OF WISCONSIN-MADISON



Carbone Cancer Center
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

PI: Dr. Quanyin Hu

Lab Members: Dr. Yu Chen, Dr. Yawen You, Yixin Wang, Sichen Yuan

**My Undergraduates: Fanyi Mo, Nathaniel Richmond, Jerry Liu,
Lauren Dempsey, Aryan Saini, Ting-Jing Chen-Mayfield**

Contact:

- zli2443@wisc.edu
- Twitter: [@zhaoting_li](https://twitter.com/zhaoting_li)

CONTROLLED RELEASE SOCIETY

CRS 2023 ANNUAL MEETING & EXPOSITION
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE