

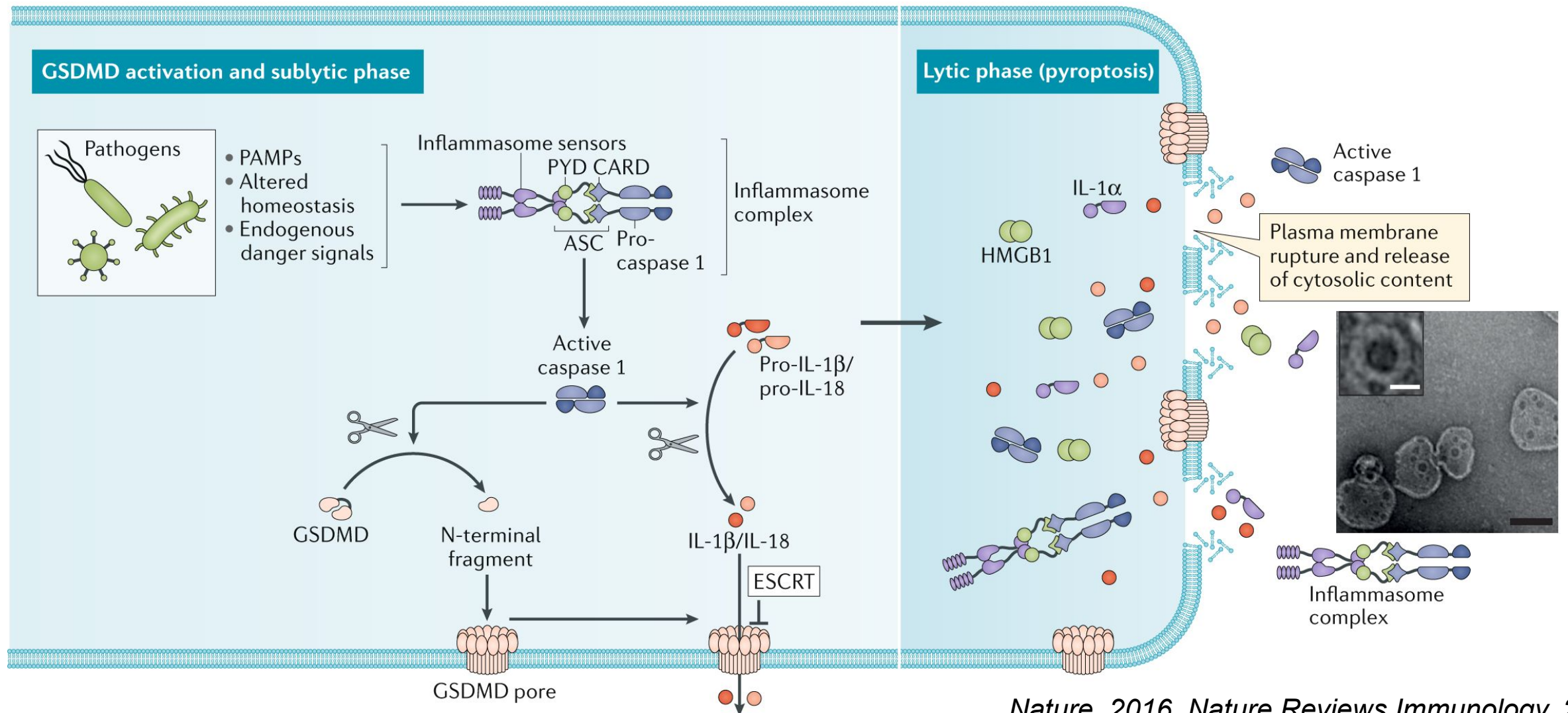
Bioengineered Bacteria Delivery System Enhances Tumor Pyroptosis Through Preventing ESCRT-Dependent Cell Membrane Repair

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University of Wisconsin-Madison

CONTROLLED RELEASE SOCIETY
CRS 2023 ANNUAL MEETING & EXPOSITION
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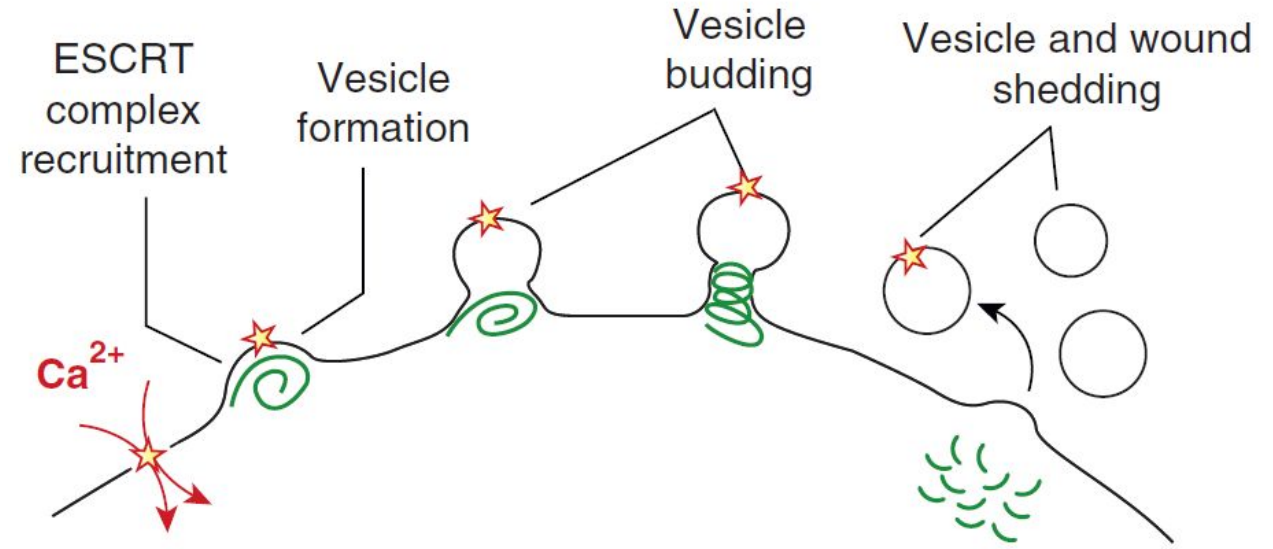
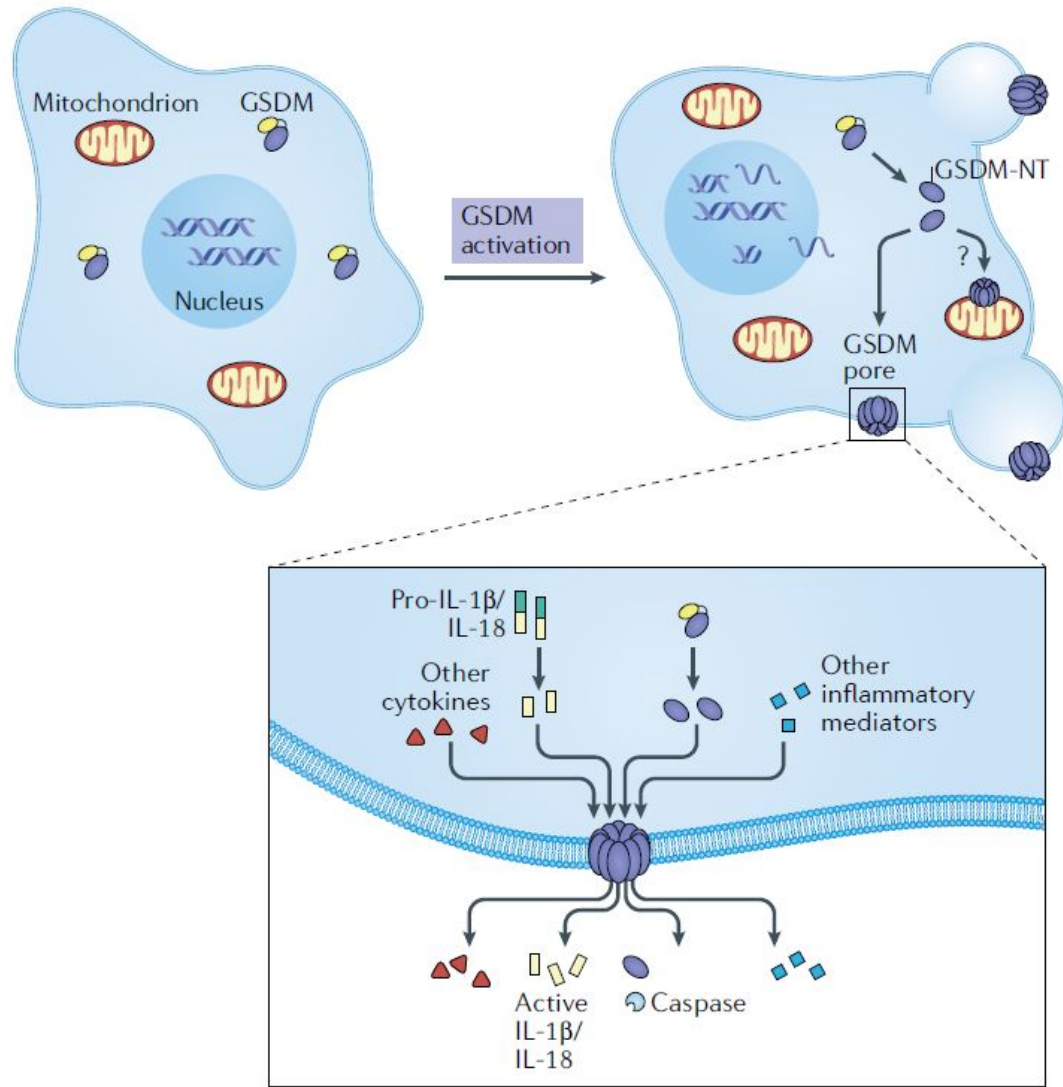
THE FUTURE OF DELIVERY SCIENCE

Bacteria & Pyroptosis



Nature, 2016. Nature Reviews Immunology, 2020.

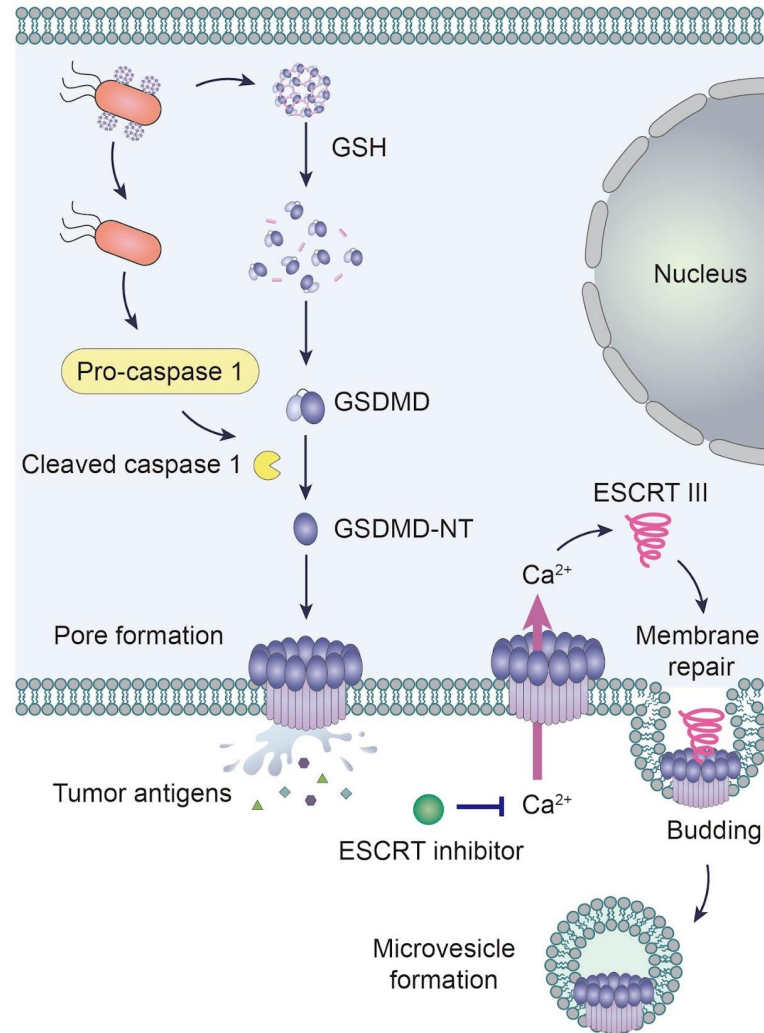
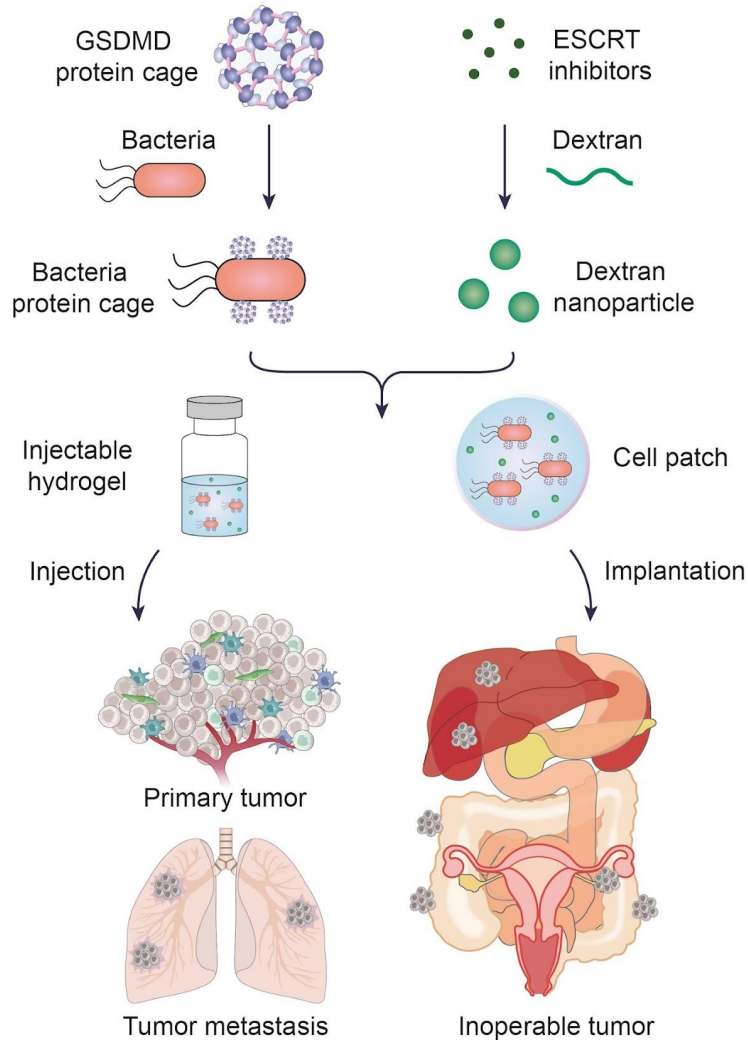
ESCRT membrane repair & Pyroptosis



Calcium influx triggered
ESCRT-dependent cell membrane repair

Nature Reviews Drug Discovery, 2021.

Engineered bacteria system for enhanced tumor pyroptosis

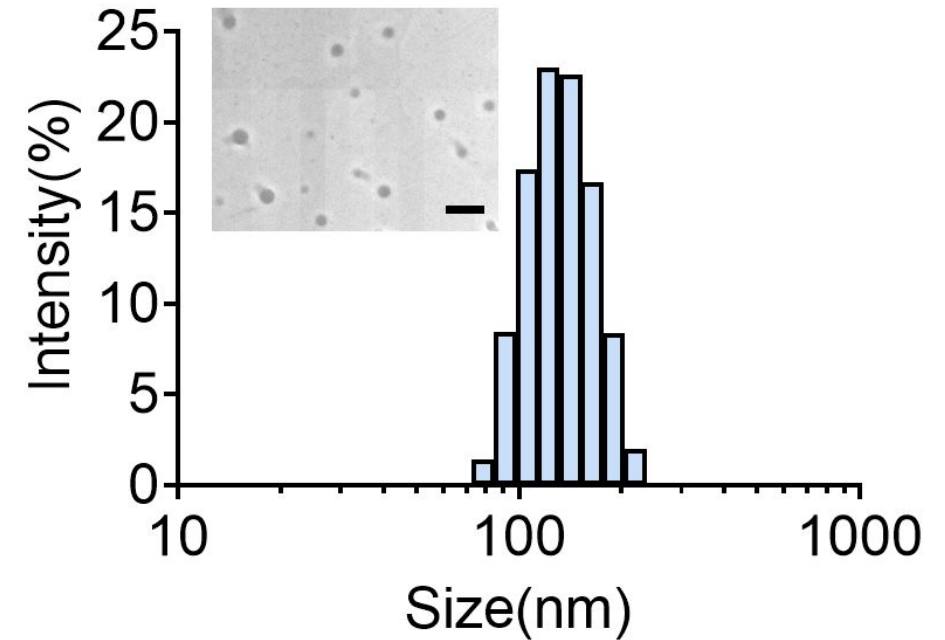
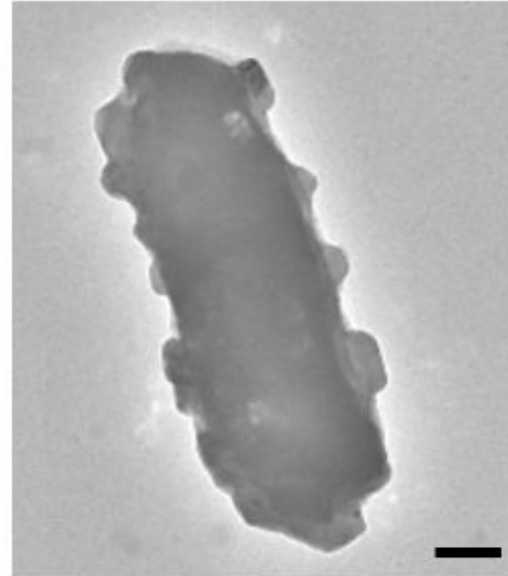
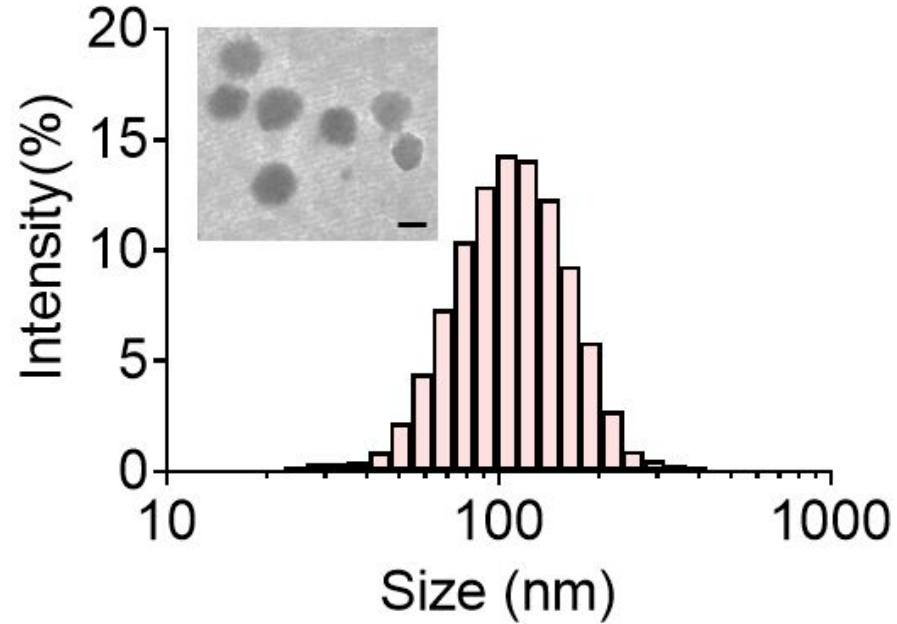


Key points:

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

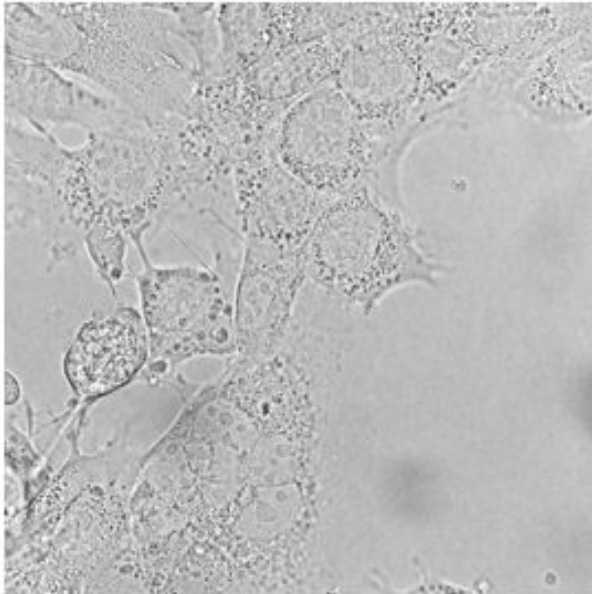
Nature Communications, 2022

Preparation and characterization

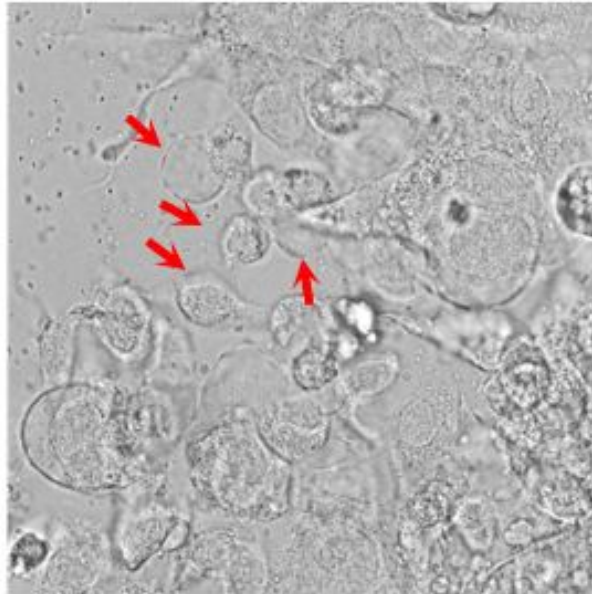


Pyroptosis verification

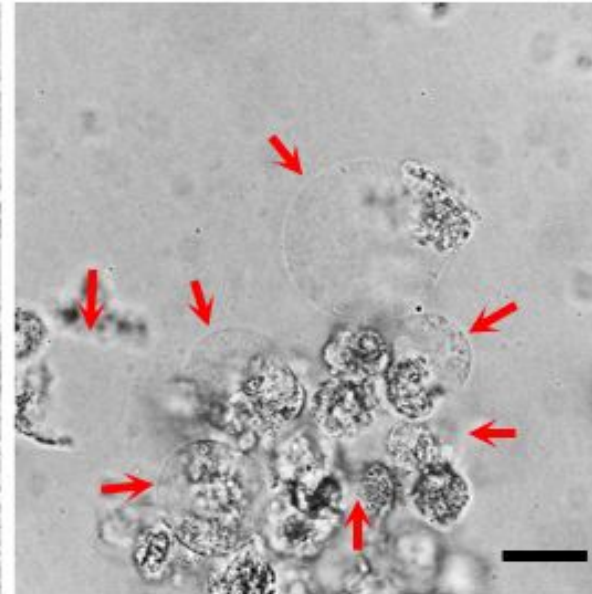
Control



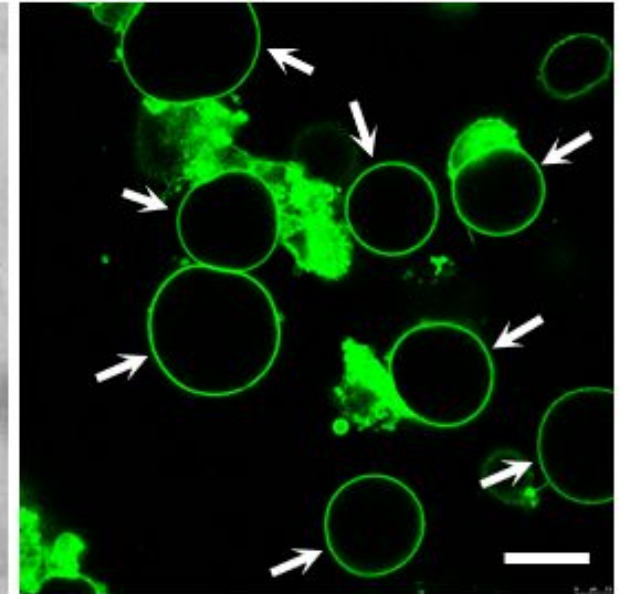
VNP-GD



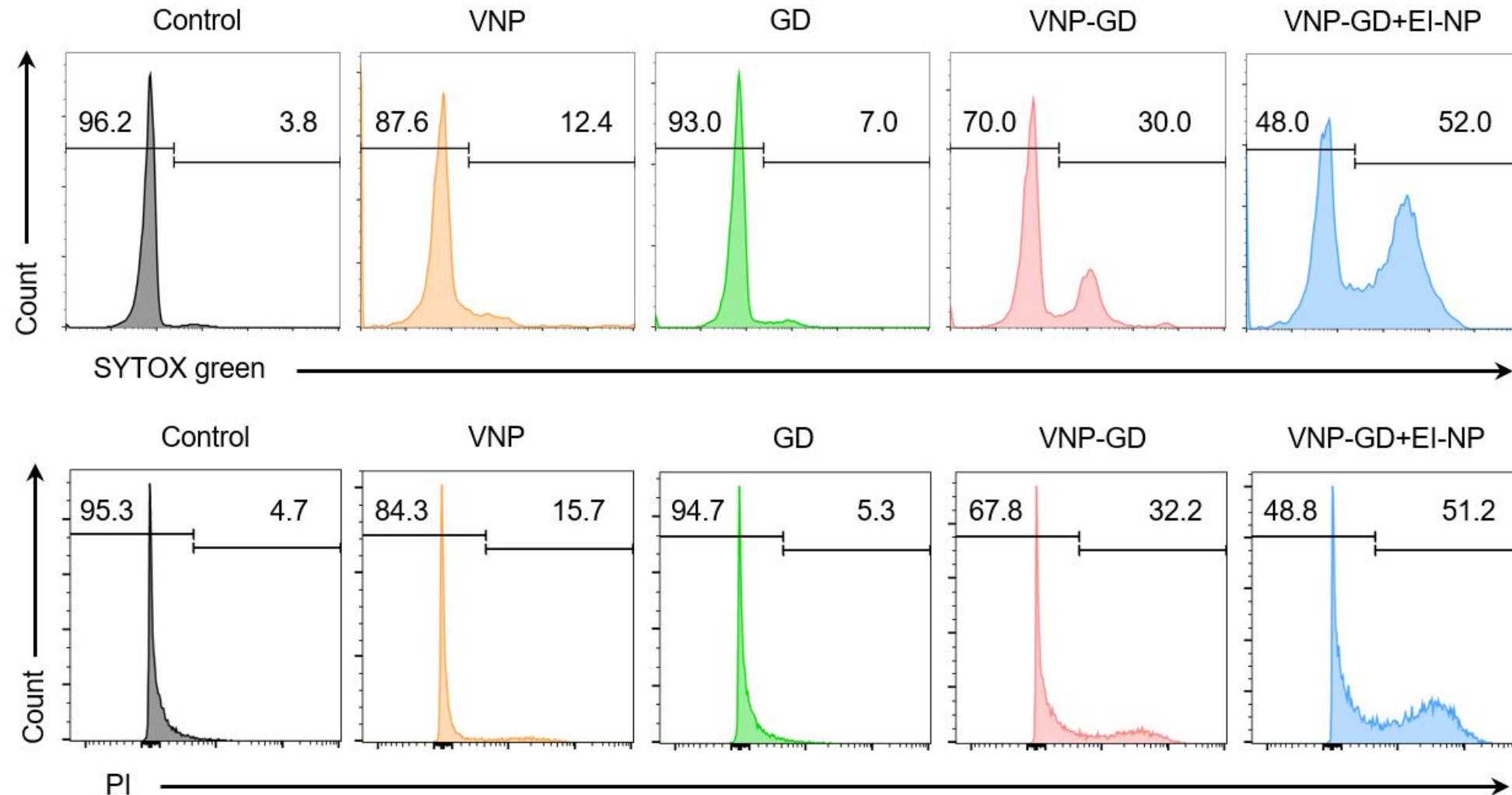
VNP-GD+EI-NP



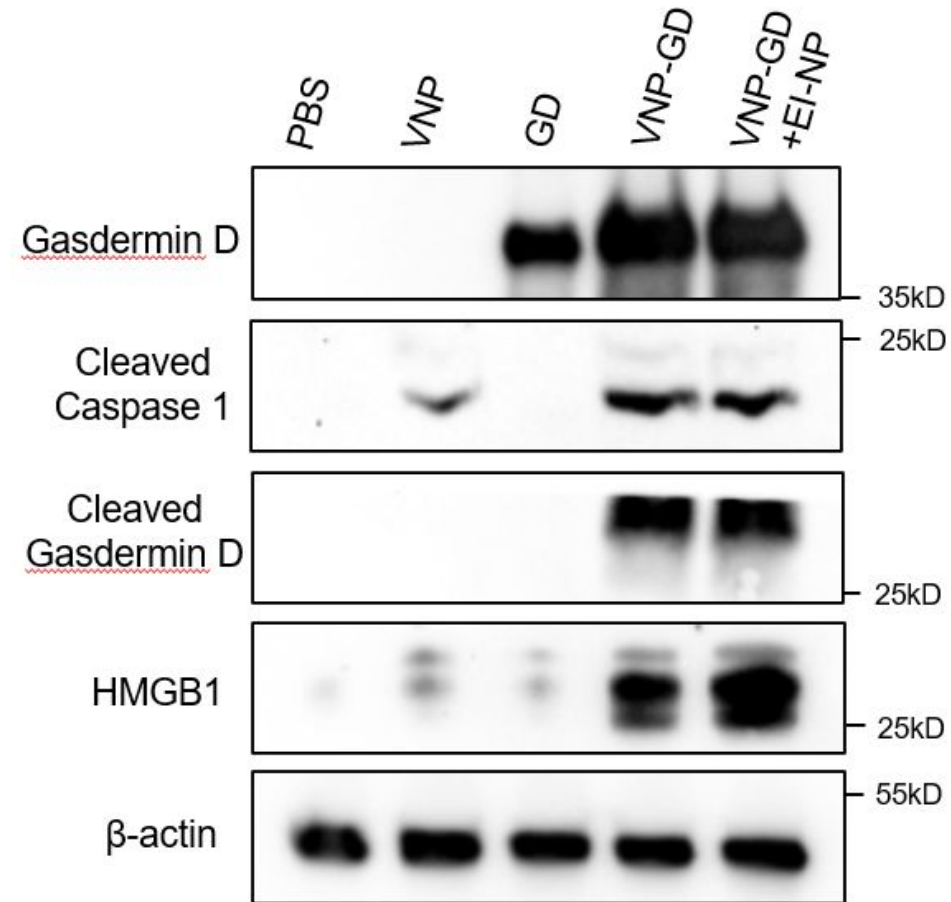
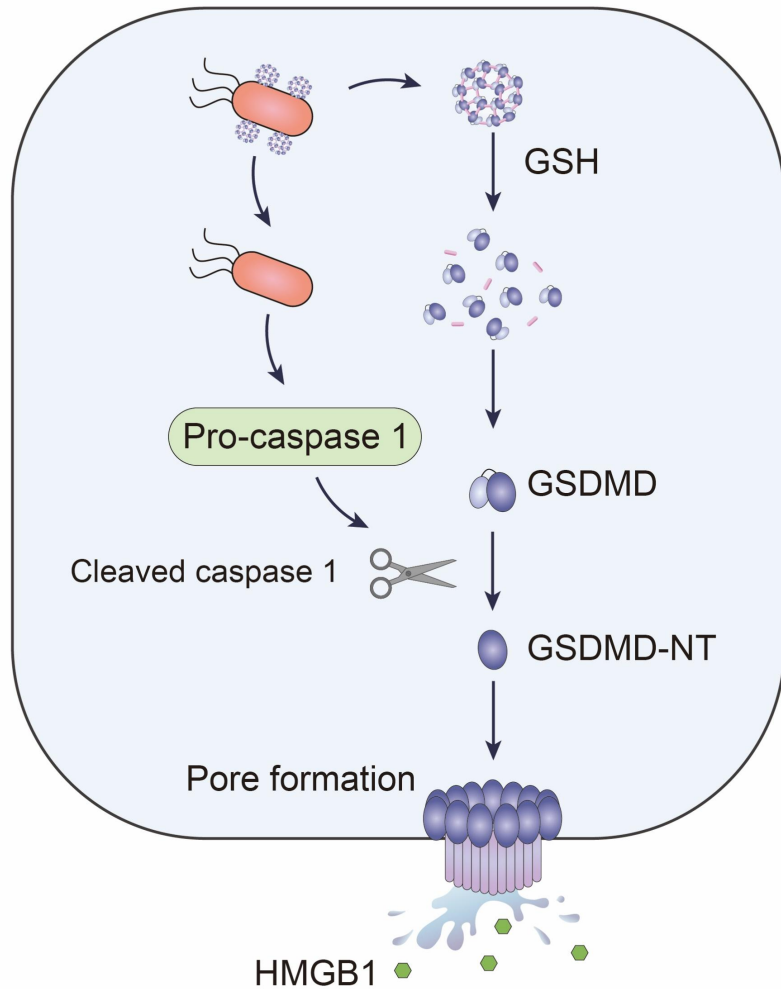
VNP-GD+EI-NP
Annexin V Staining



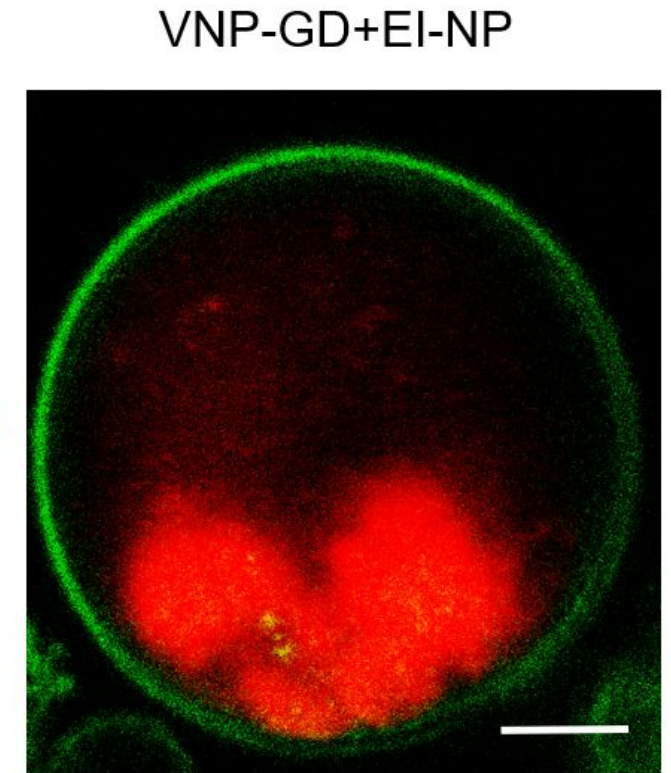
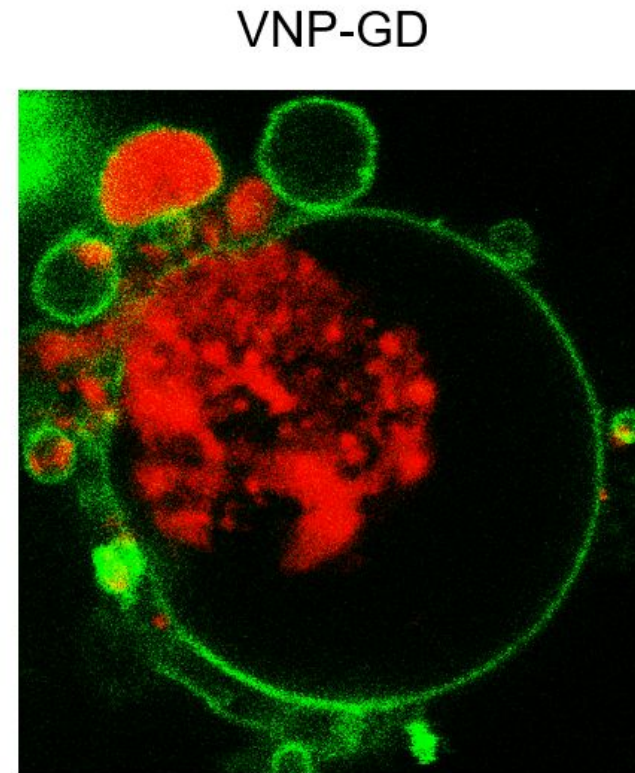
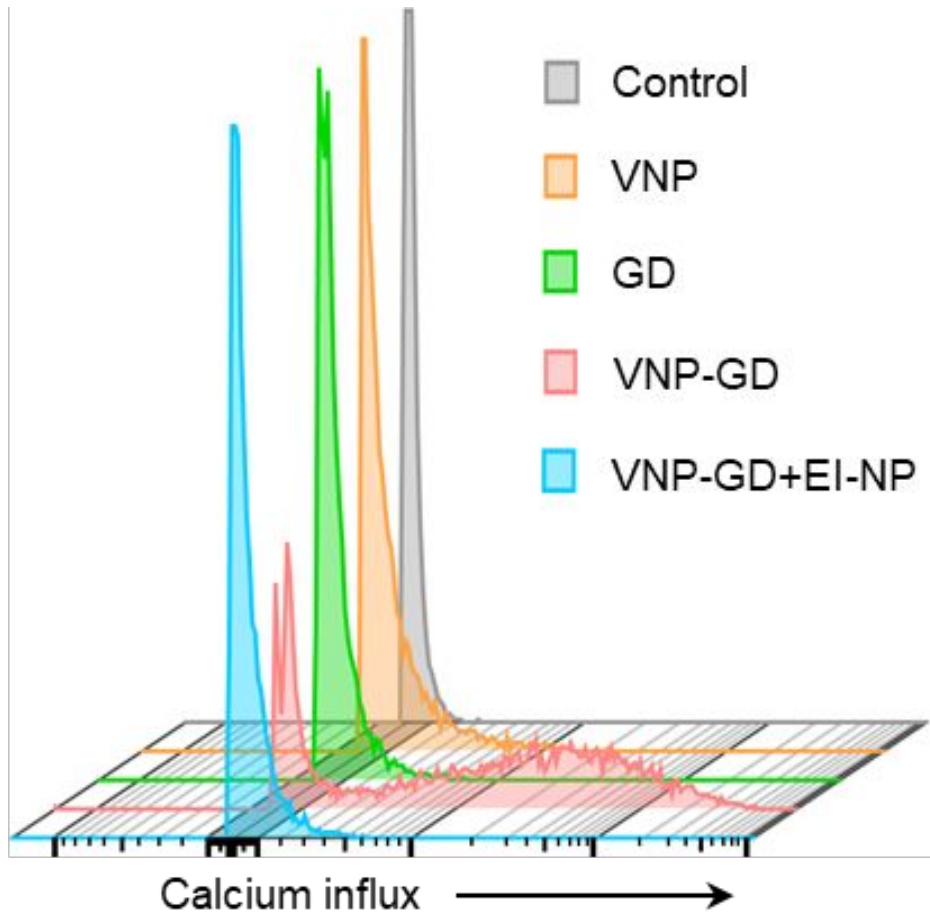
Pyroptosis verification



Mechanism exploration



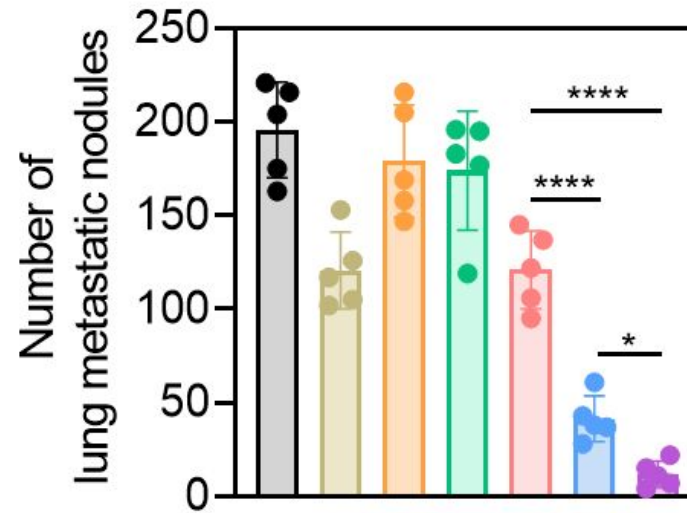
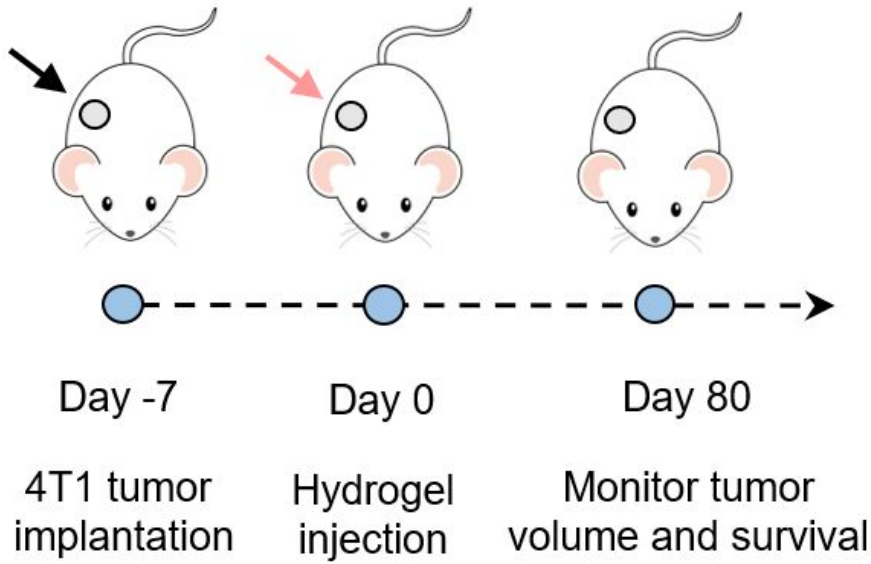
Mechanism exploration



Annexin V-stained cell membrane

mCherry-labeled CHMP3

In vivo anti-tumor efficacy (Breast cancer)



— PBS

— aPD-1

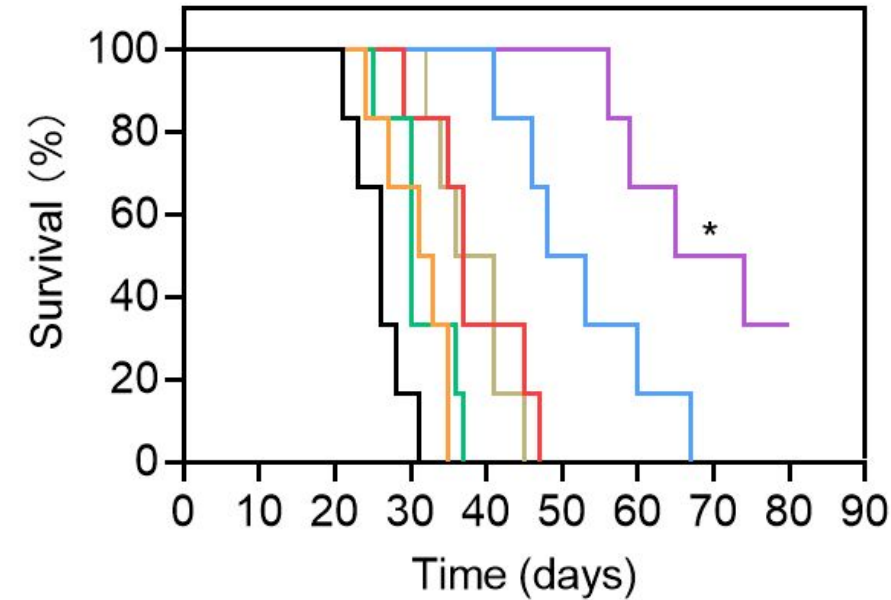
— VNP@Gel

— GD/EI-NP@Gel

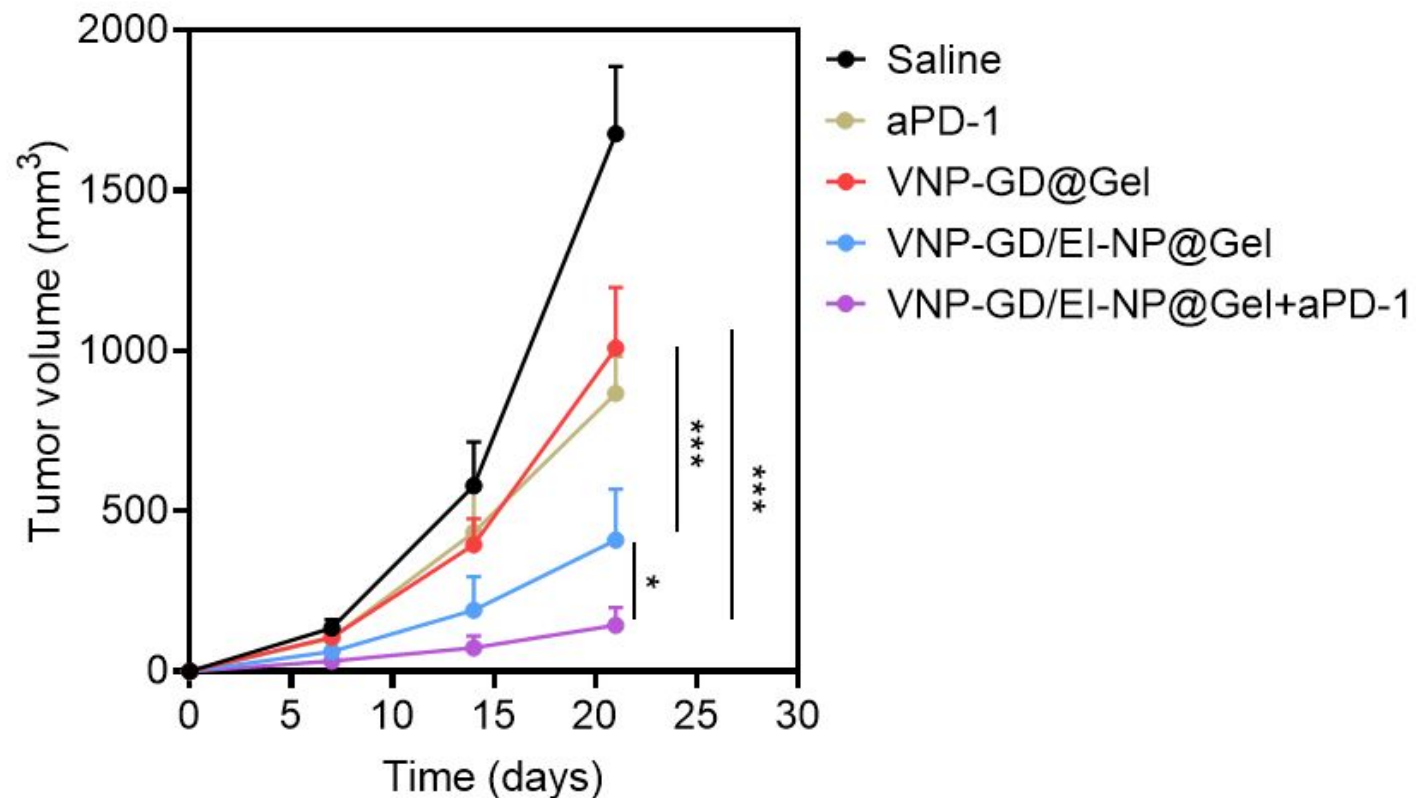
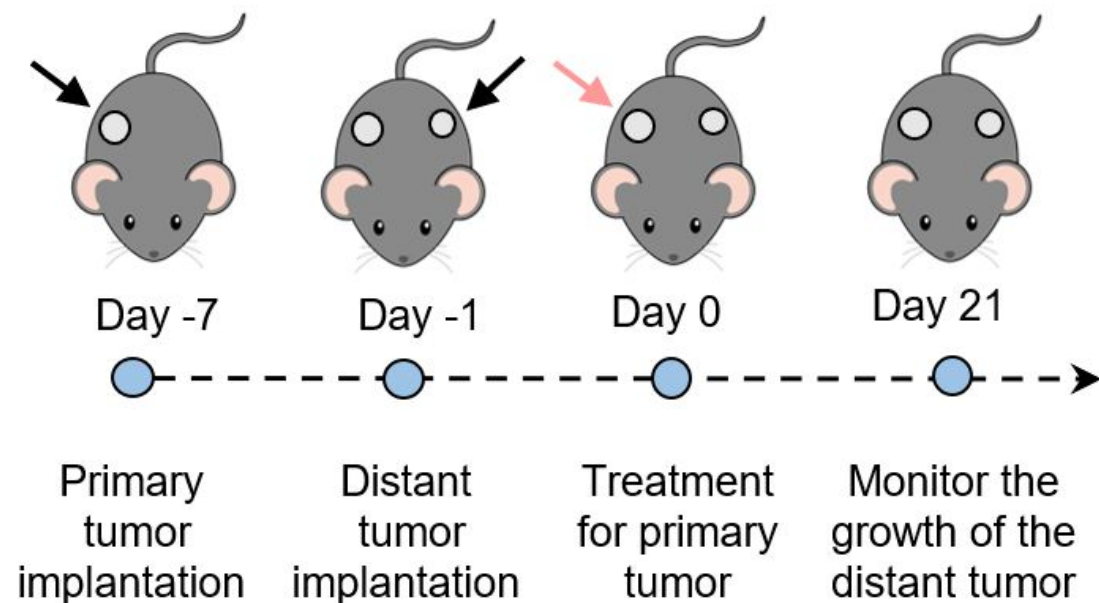
— VNP-GD@Gel

— VNP-GD/EI-NP@Gel

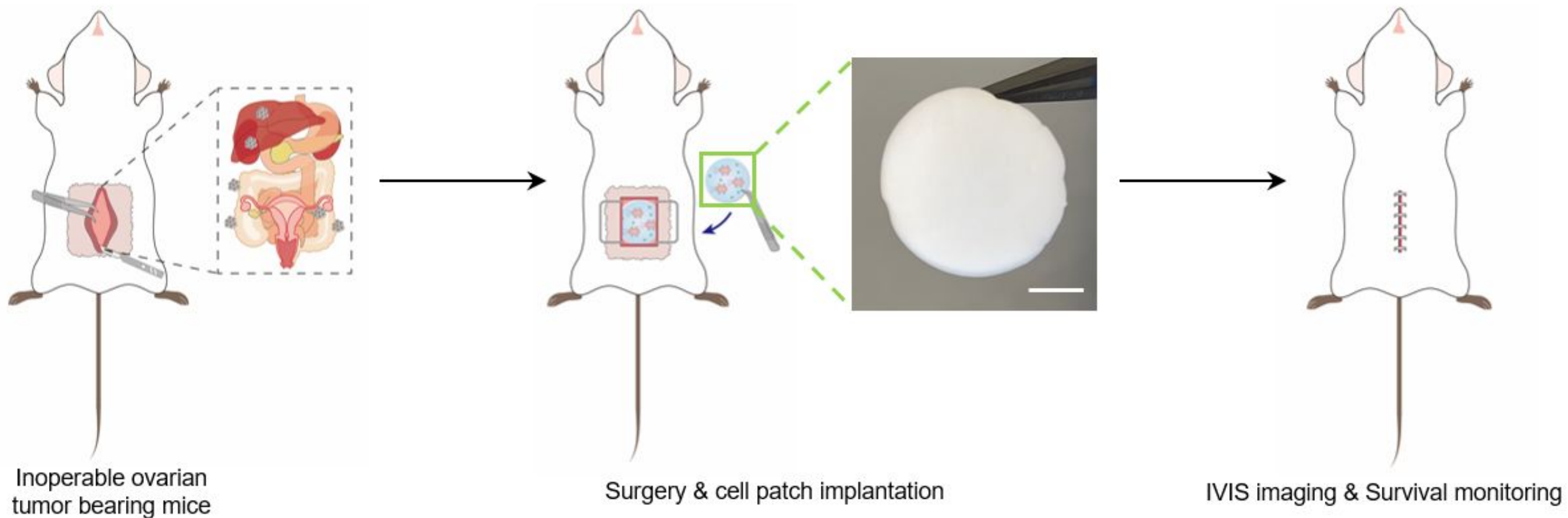
— VNP-GD/EI-NP@Gel+aPD-1



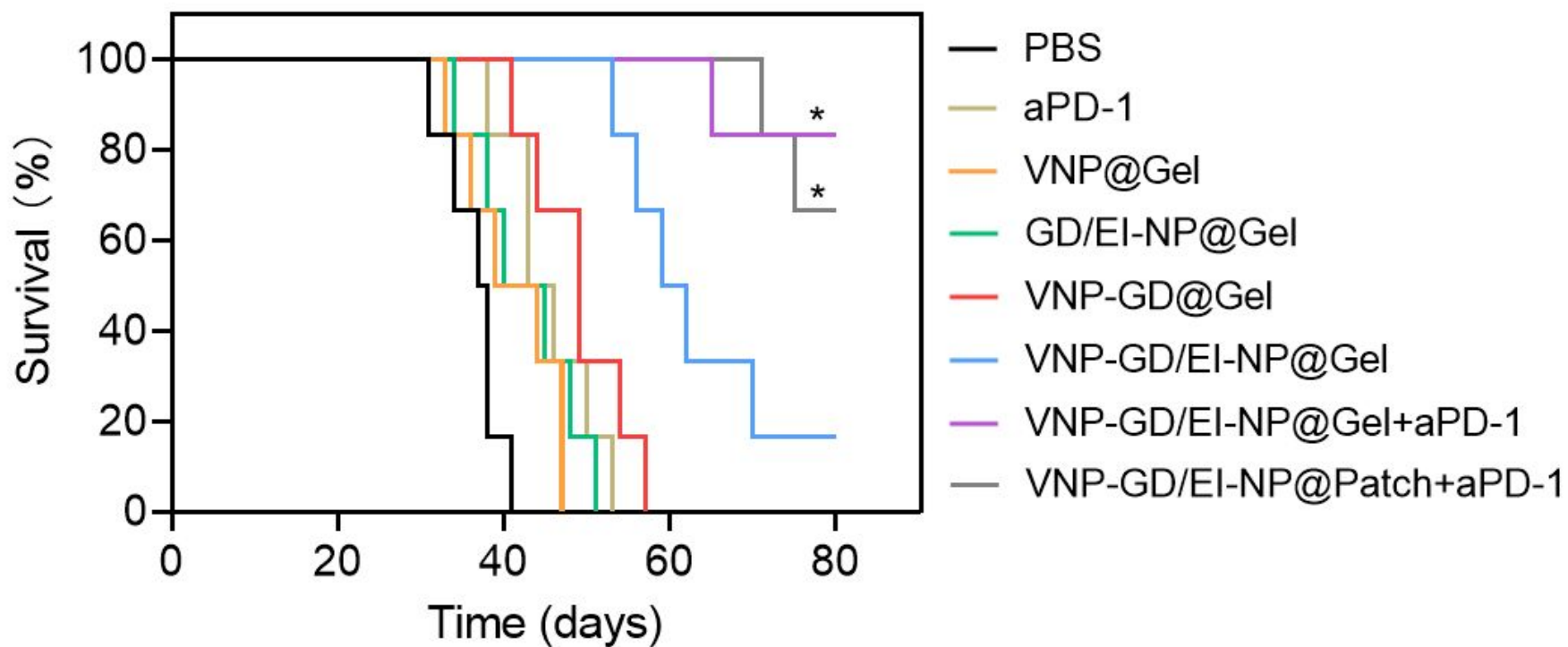
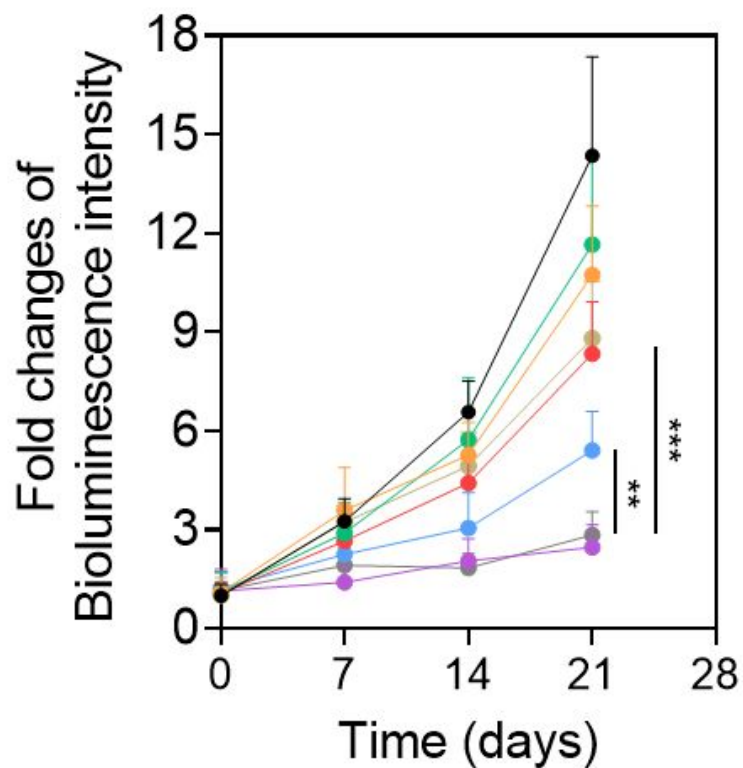
In vivo anti-tumor efficacy (Melanoma)



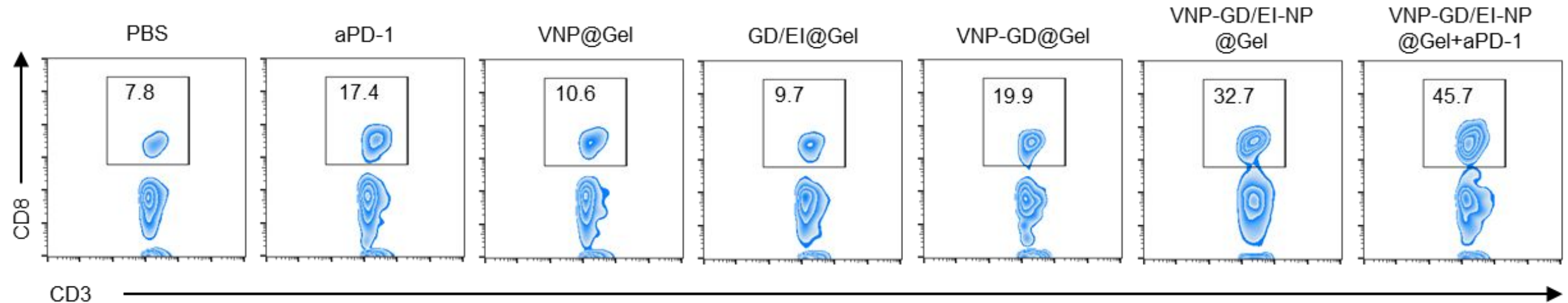
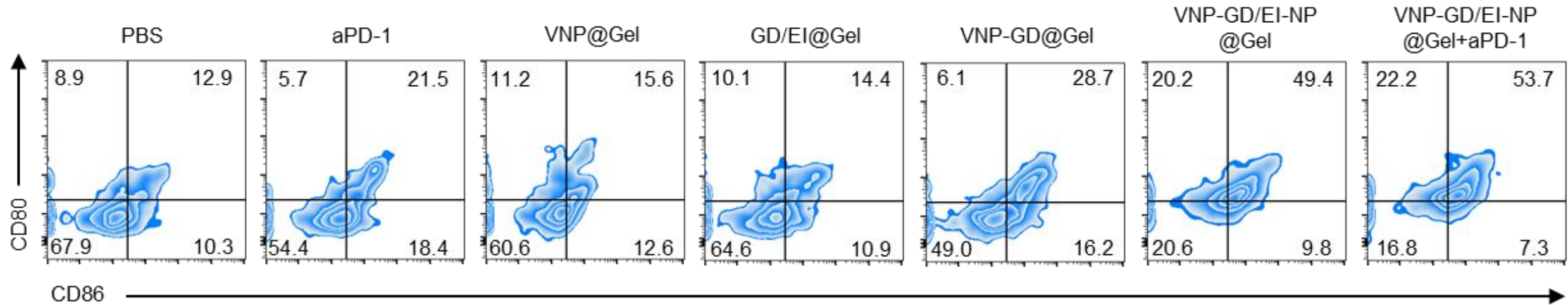
In vivo anti-tumor efficacy (Ovarian cancer)



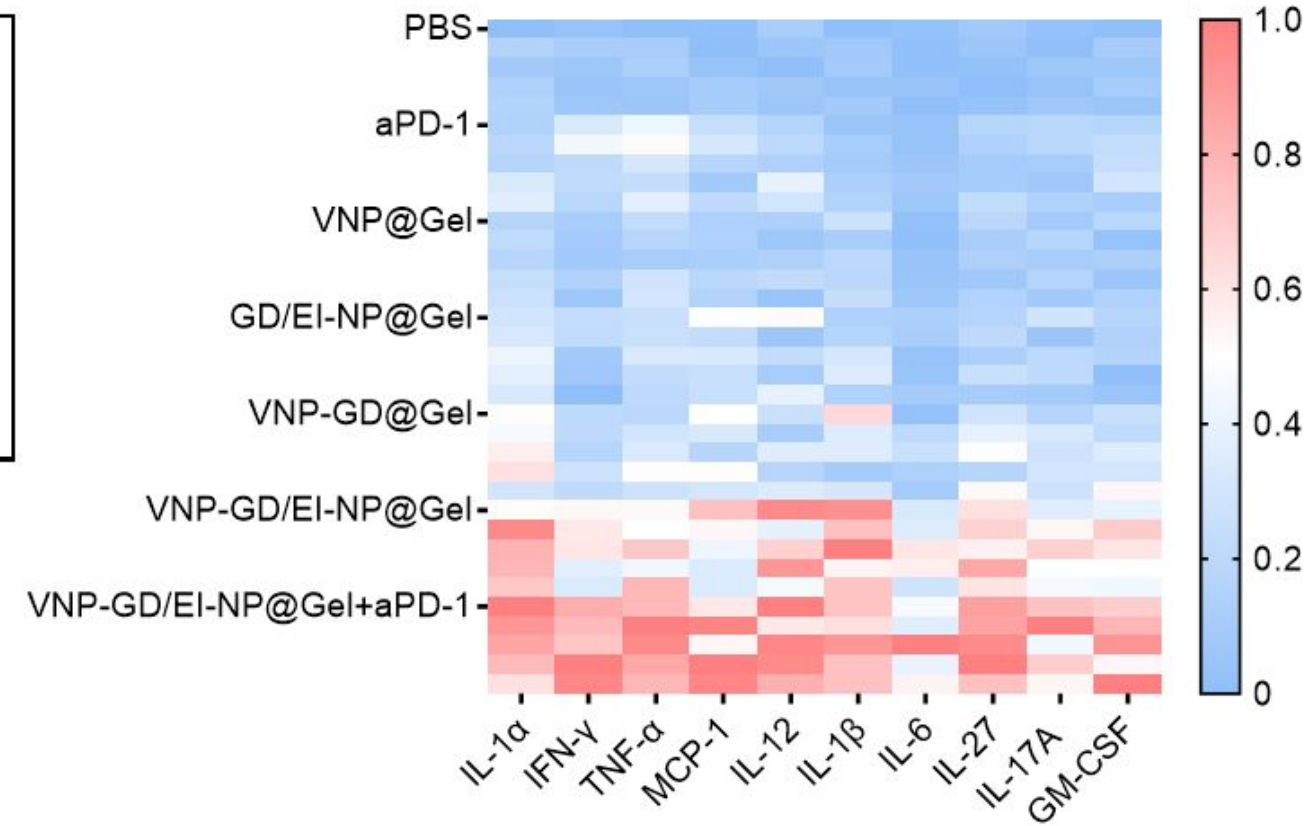
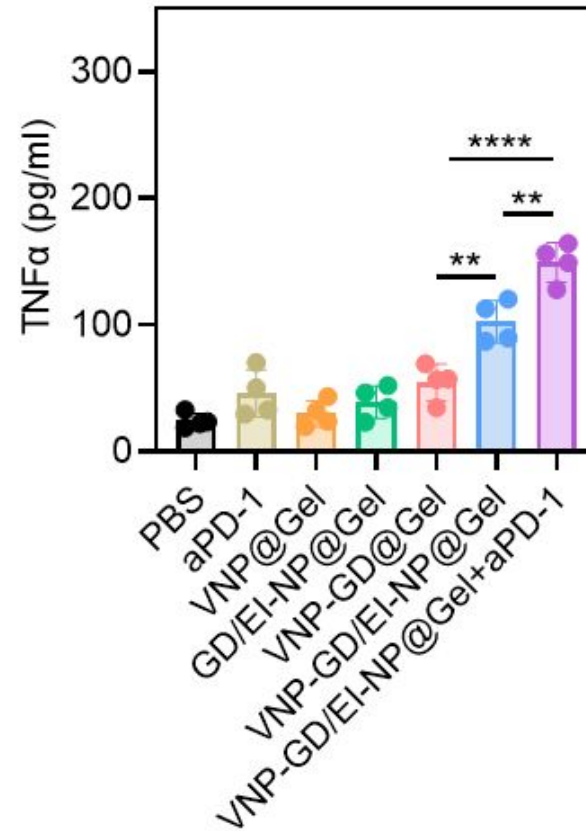
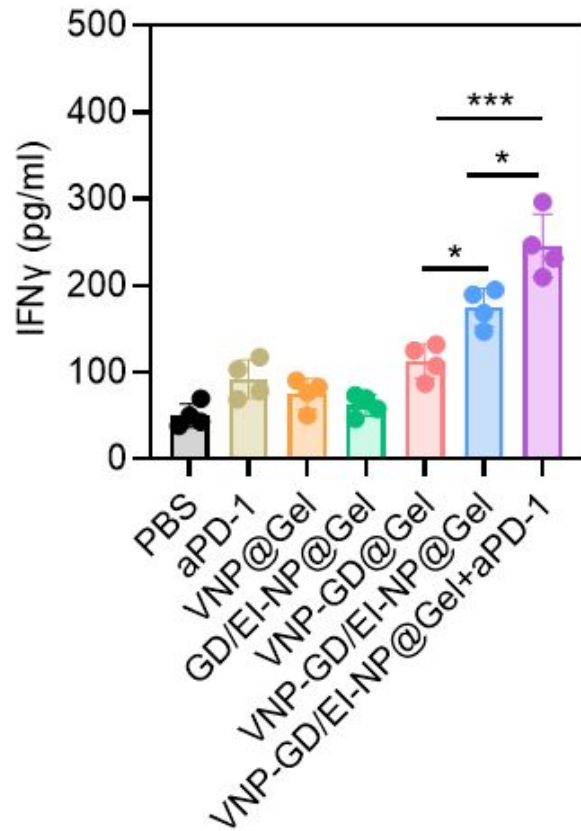
In vivo anti-tumor efficacy (Ovarian cancer)



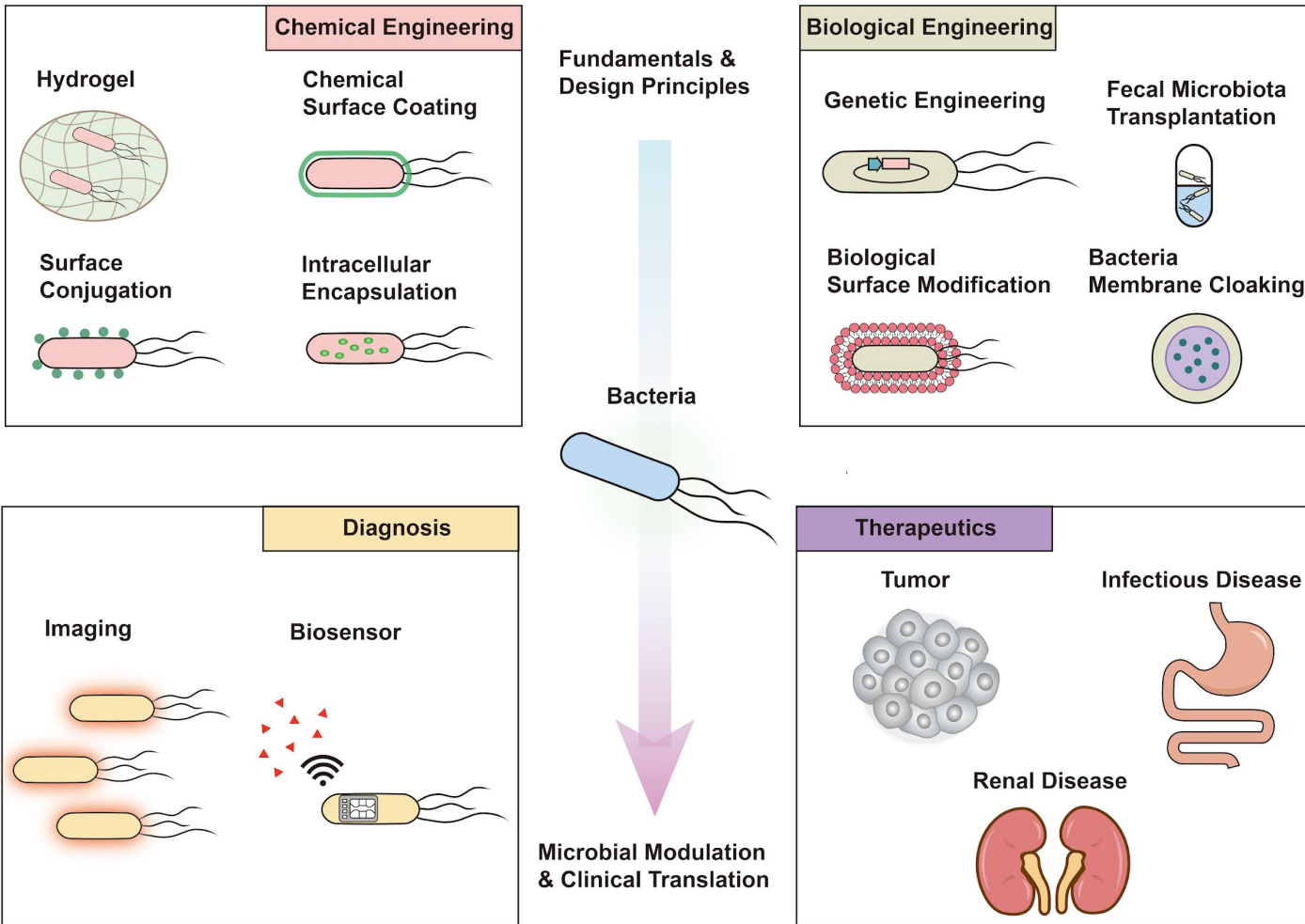
In vivo immune activation



In vivo immune activation



Conclusion



Surface conjugation & tumor pyroptosis



Chemically & biologically engineered bacteria delivery systems

Acknowledgment



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Lauren Dempsey, Aryan Saini, Ting-Jing Chen-Mayfield

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