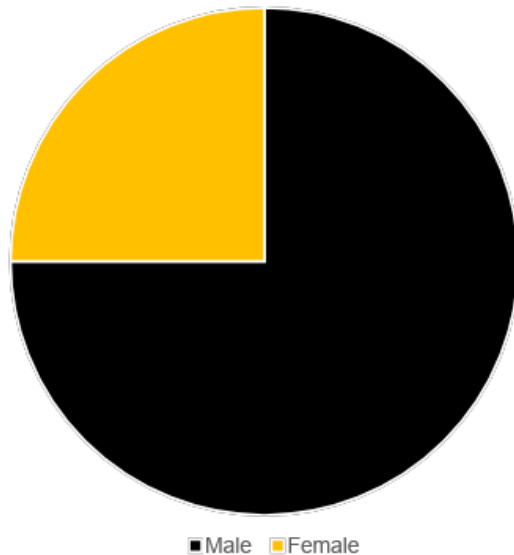


Bacterial extracellular vesicles as a tunable platform for vaginal drug delivery

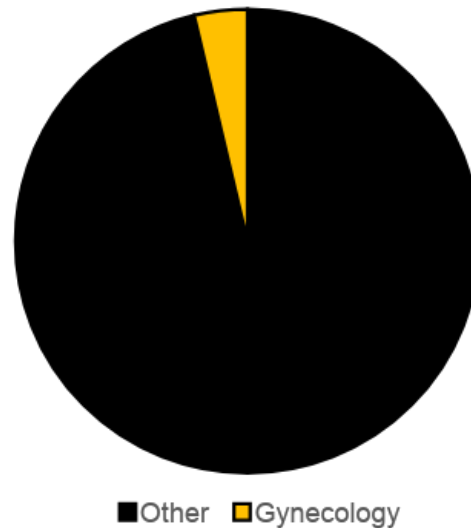
Varunaa Sri Hemanth Kumar
Living Material Design Lab

There is a desperate need for new therapies

Funding for Diseases
Primarily Affecting One Sex

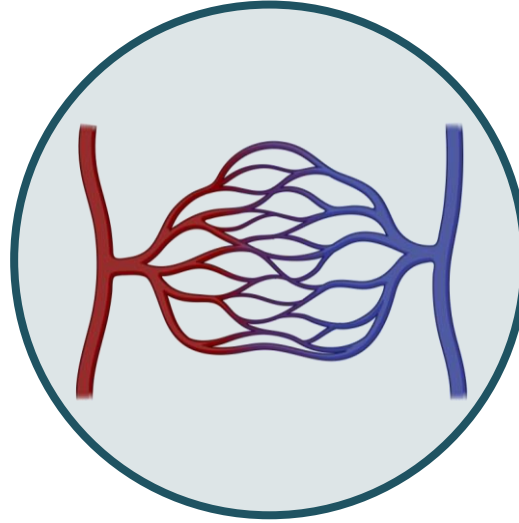
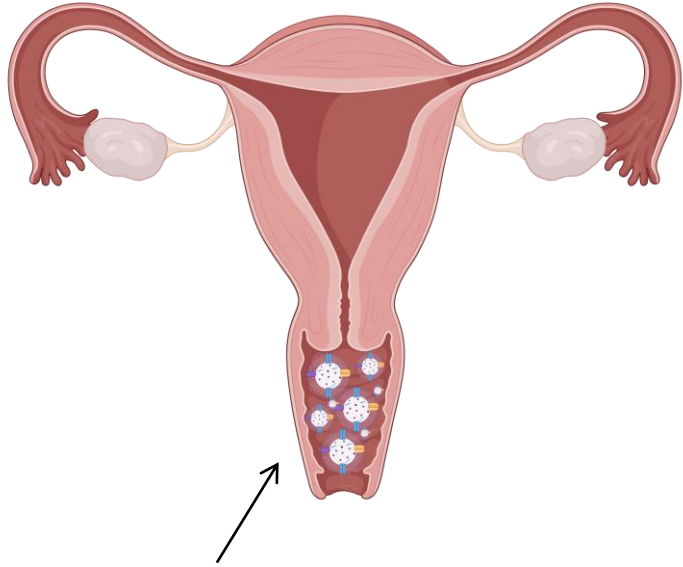


Clinical Trials
2007-2020

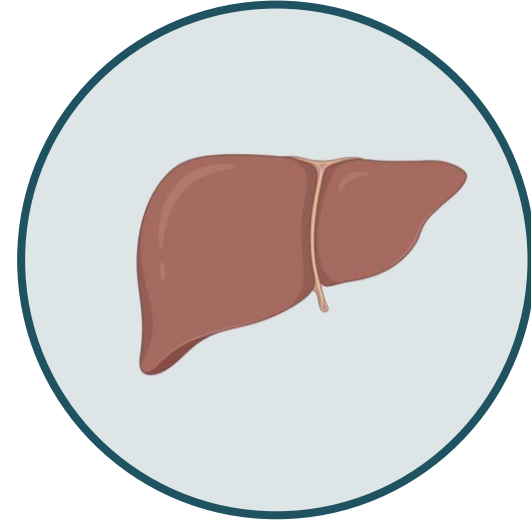


Mirin, A.A. *J Womens Health*. 2021
Steinberg, J.R., et al. *Obstet. Gynecol*. 2022

Local drug delivery improves therapeutic outcomes



**Extensive network
of blood arteries**



**Bypass first
hepatic filter**

Images created with Biorender.com
Adapted from Brako & Boateng. *Expert Opin. Drug Deliv.* 2025

Nanoparticles have limited transability

Enhanced drug delivery to the reproductive tract using Mucus-Penetrating Nanoparticles for Vaginal Drug nanomedicine reveals therapeutic options for prevention of preterm birth

LAURA M. ENSIGN, BENJAMIN C. TANG, YING-YING WANG, TERENCE A. TSE, TIMOTHY HOEN, RICHARD CONE, AND JUSTIN HANES [Authors Info & Affiliations](#)

HANNAH C. ZIERDEN, JAIRO I. ORTIZ, KEVIN DELONG, JINGQI YU, GAOSHAN LI, PETER DIMITRIU, SABRINE BENSOUL

LAURA M. ENSIGN, +7 authors [Authors Info & Affiliations](#)

Nanoparticles-in-film for the combined vaginal delivery of anti-HIV microbicide drugs

Cassilda Cunha-Reis^a, Alexandra Machado^{b,c}, Luísa Barreiros^d, Francisca Araújo^{b,c,e}, Rute Nunes^{b,c,e}, Vítor Seabra^a, Domingos Ferreira^f, Marcela A. Segunda^d, Bruno Sarmento^{a,b,c}, José das Neves^{a,b,c}  

Locally administered increases delivery of treatment of vaginal

Original Article | Published: 15 May 2024

Efficacy of lipid nanoparticles-based vaccine to protect against vulvovaginal candidiasis (VVC): Implications for women's reproductive health

Masood Alam Khan^a , Ayman M. Mousa^a, Arwa Essa Alradhi^b, Khaled Allemailem^c

Vaginal drug delivery: strategies and concerns in polymeric nanoparticle development

Tin Wui Wong, Meenakshi Dhanawat & Michael John Rathbone



Low-throughput



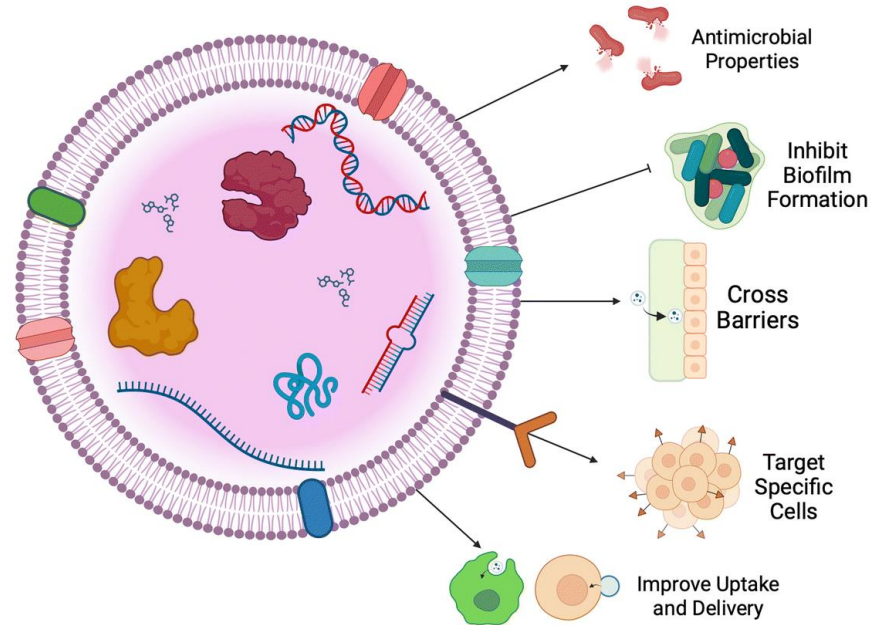
Time-consuming



Expensive

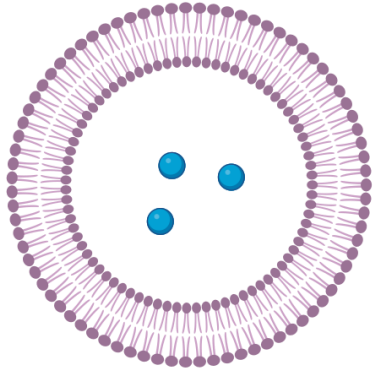
Feng et al. *J. Transl. Med.* 2019

Bacterial extracellular vesicles (bEVs) show potential as therapeutics

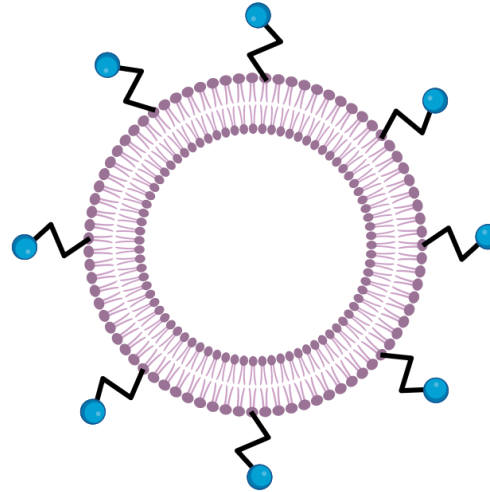


Adapted from Moore et al. *Nanoscale*. 2024

Genetic engineering allows for therapeutic modifications



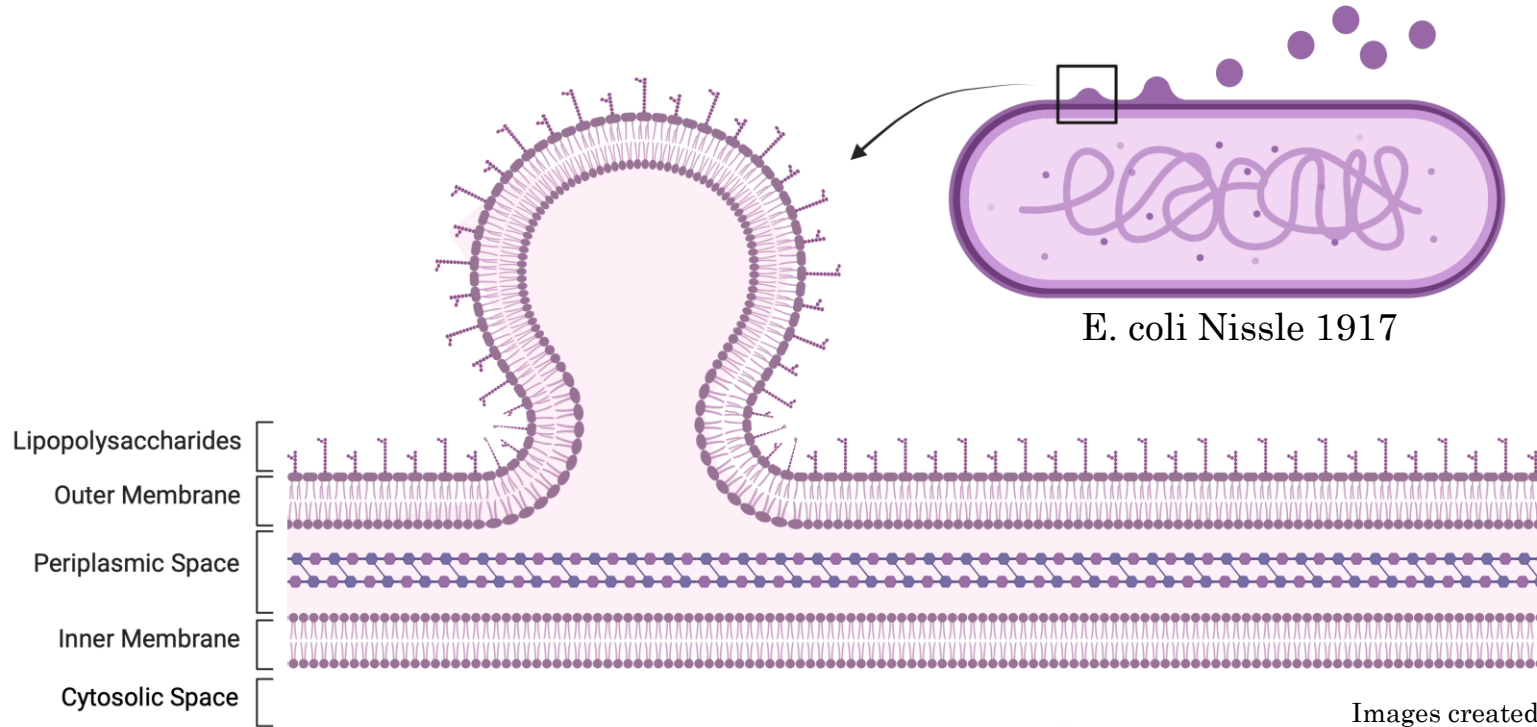
Loading



Surface Display

Images created with Biorender.com

E. coli Nissle 1917-derived bEVs for engineering



Images created with Biorender.com

bEV loading requires periplasmic translocation

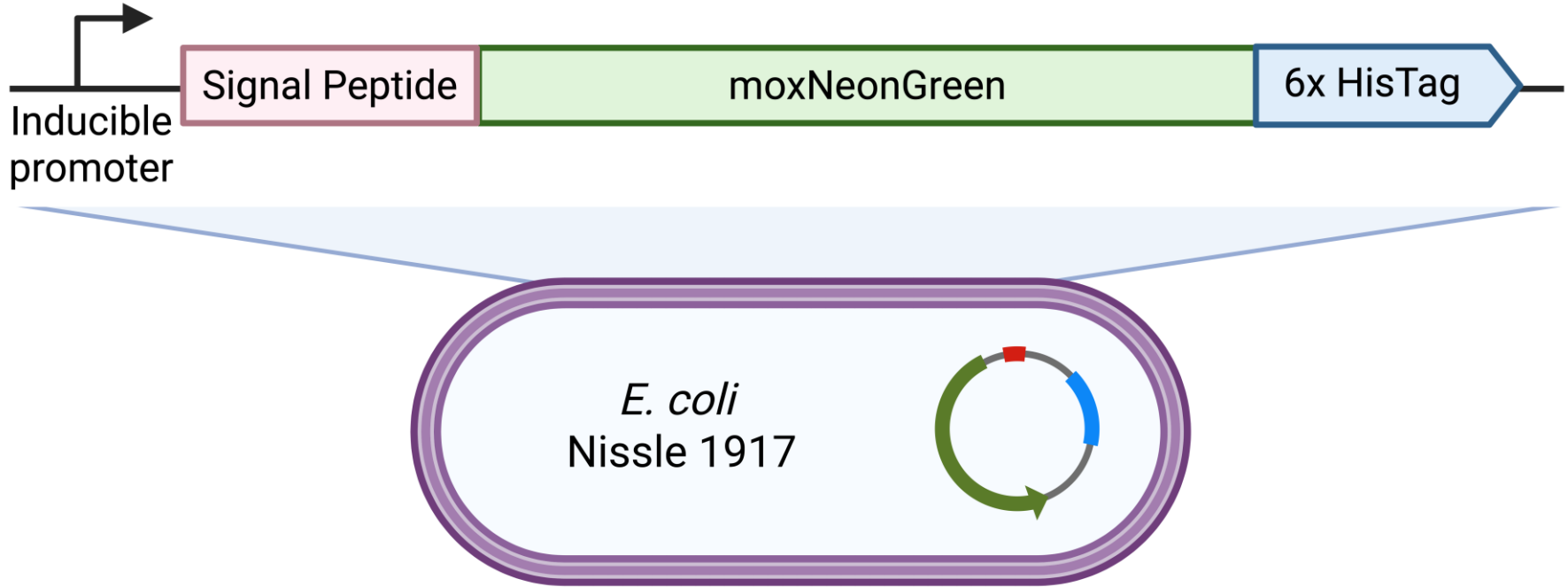
Factors that impact protein translocation/loading:

- Protein expression level
- Protein expression rate → cell metabolic rate

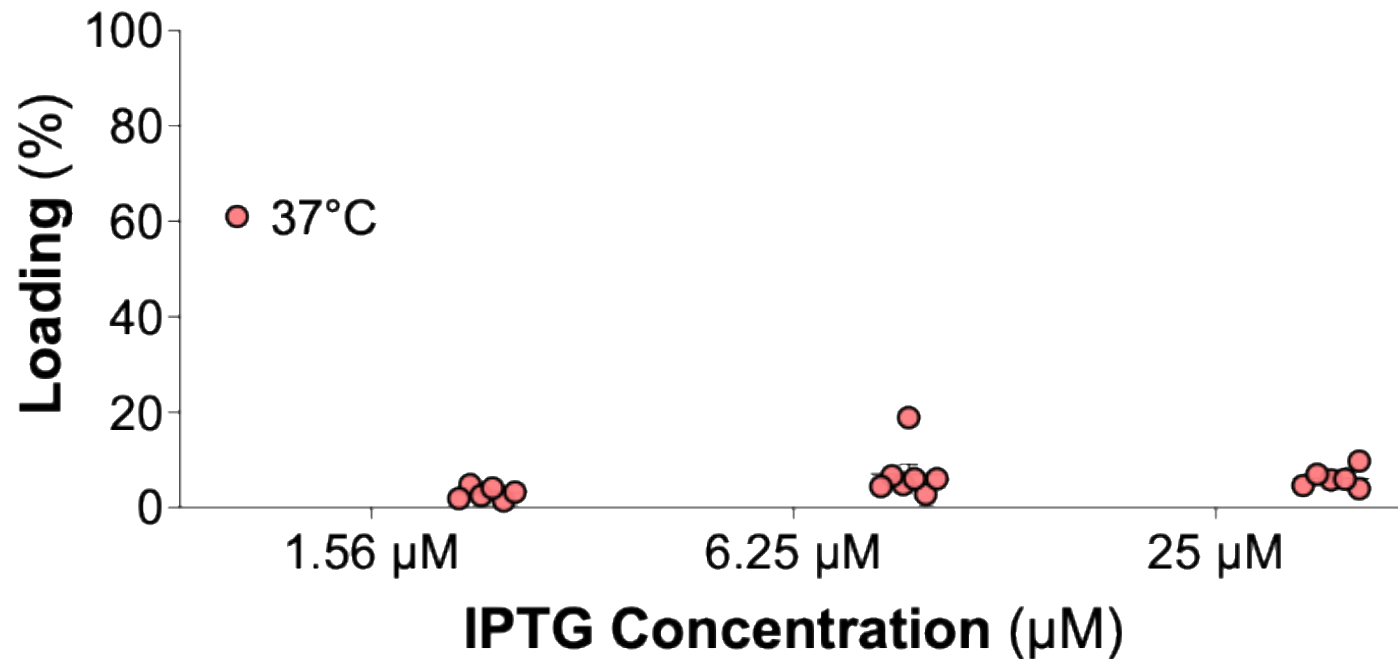


Images created with Biorender.com

Genetic cassette for protein loading

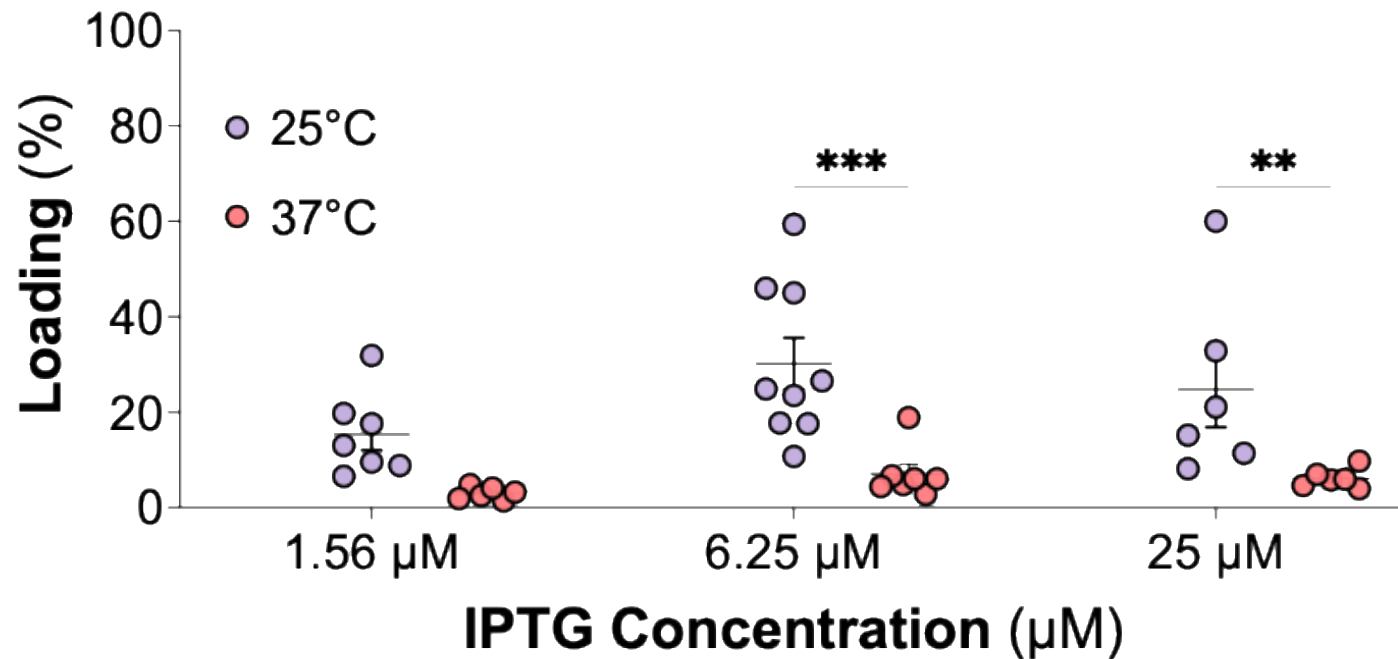


Investigating optimal conditions for loaded bEVs



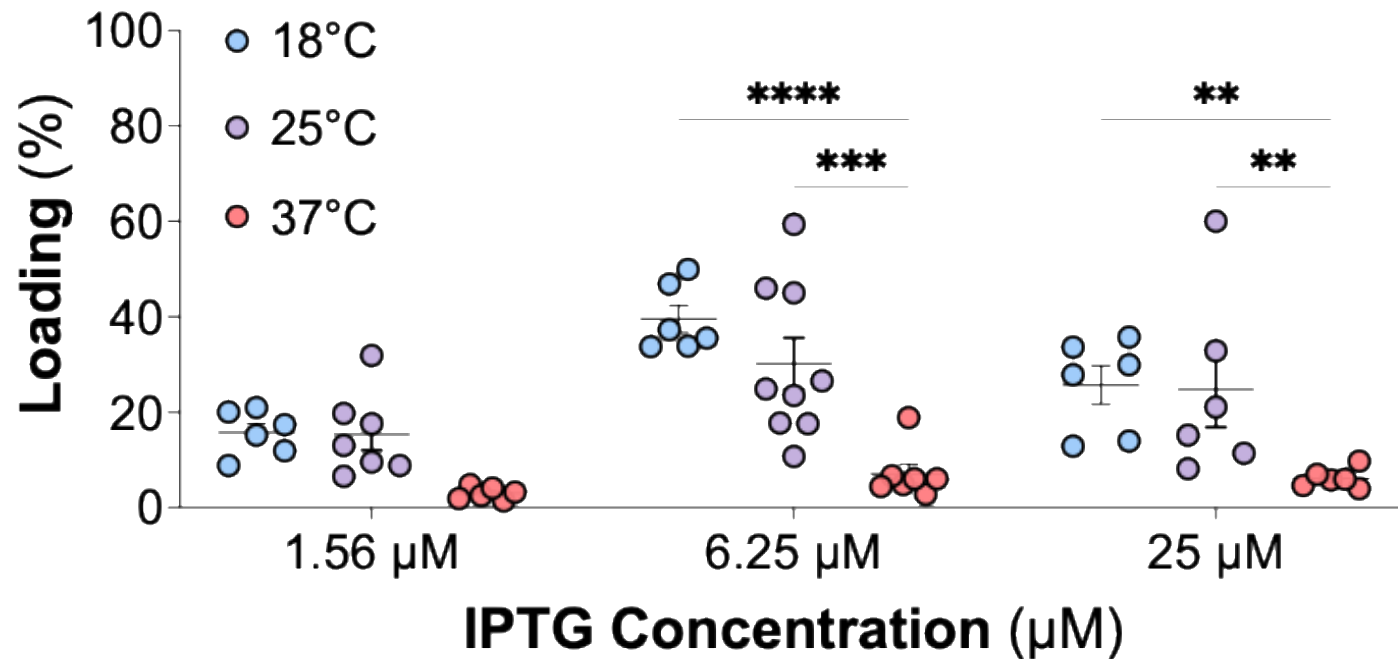
Darby Steinman
Zierden Lab

Investigating optimal conditions for loaded bEVs



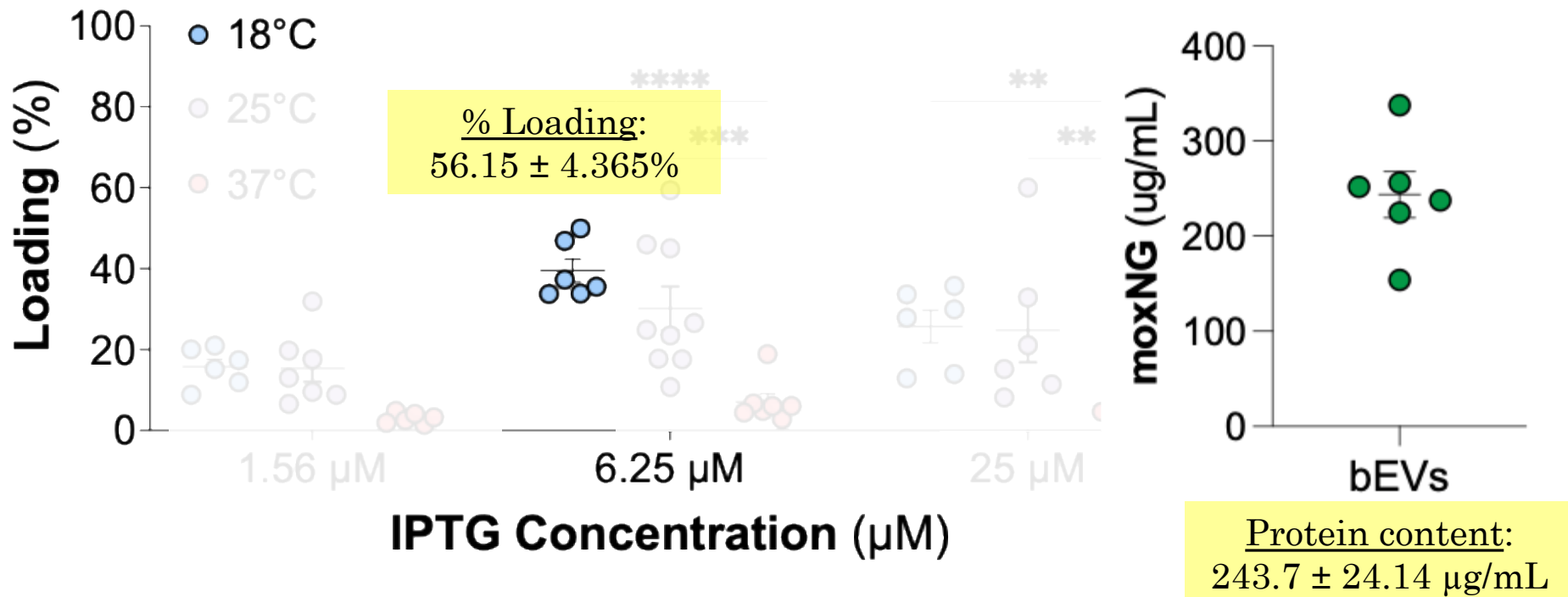
Darby Steinman
Zierden Lab

Investigating optimal conditions for loaded bEVs

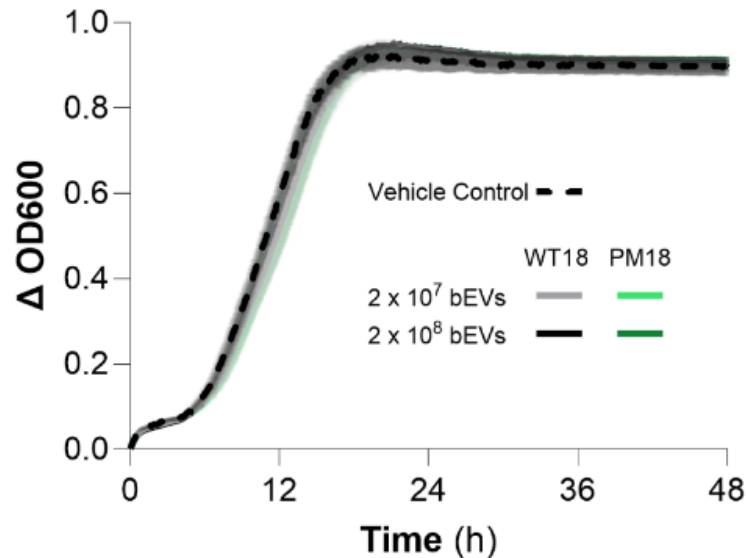
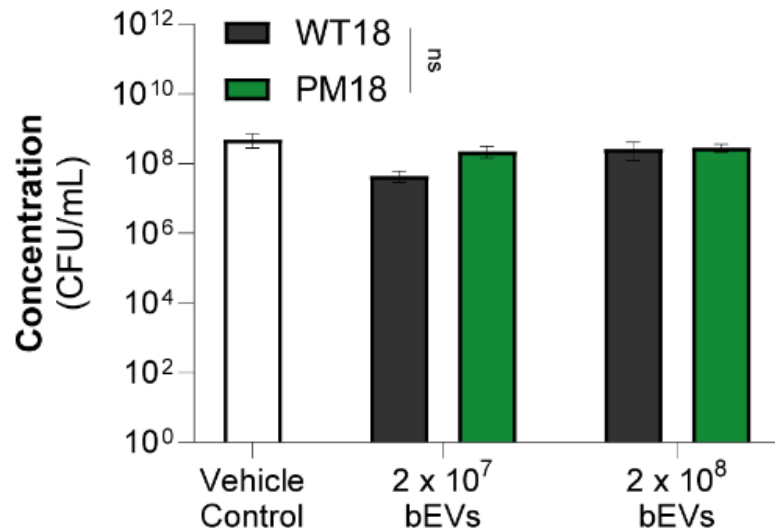


Darby Steinman
Zierden Lab

Investigating optimal conditions for loaded bEVs



bEVs are compatible with key vaginal microbiota: *L. crispatus*

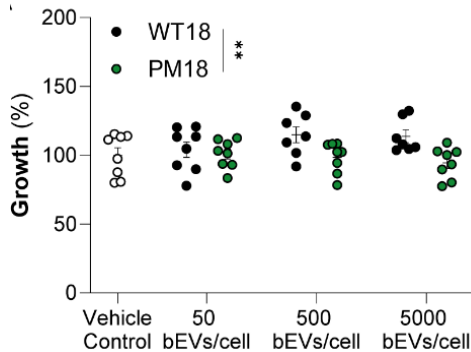


Darby Steinman
Zierden Lab

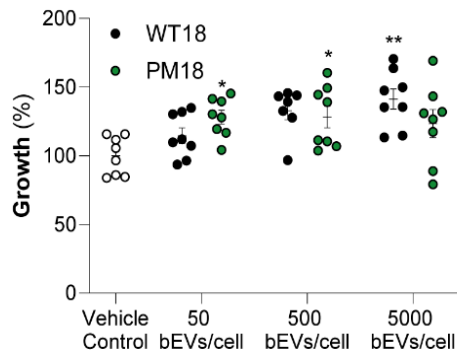
bEVs are compatible with reproductive tract cells

Vaginal
epithelial cells

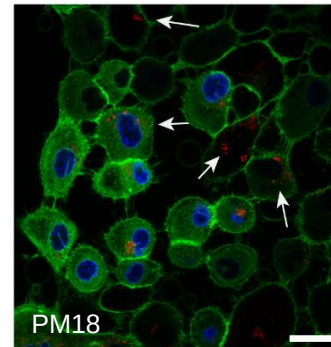
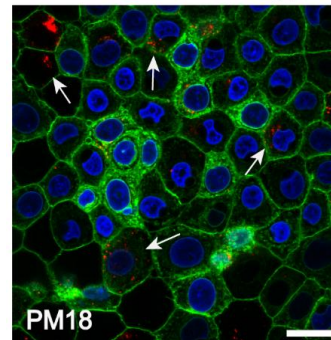
Viability



Endocervical
cells

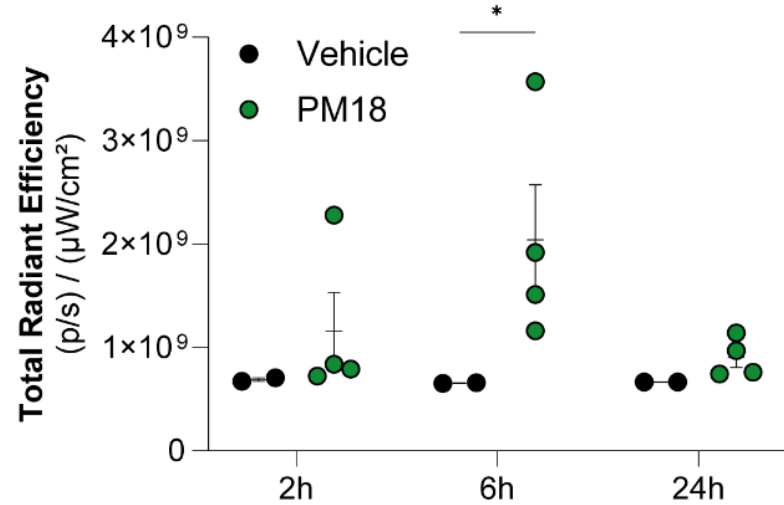
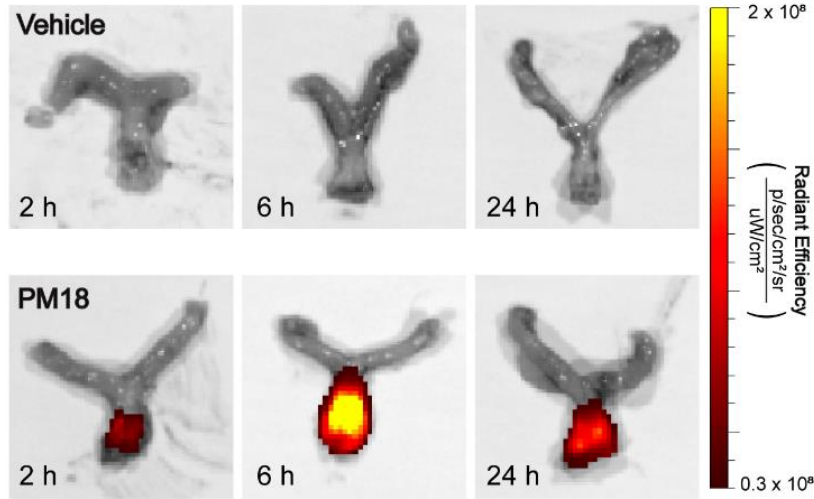


Cellular Uptake



Darby Steinman
Zierden Lab

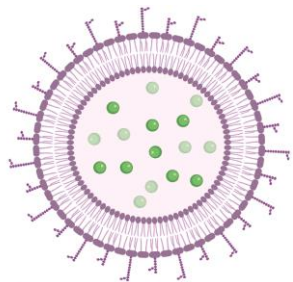
Engineered bEVs are retained in the vagina



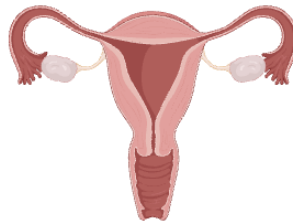
Darby Steinman
Zierden Lab

Vehicle: PBS PM18: Engineered bEV

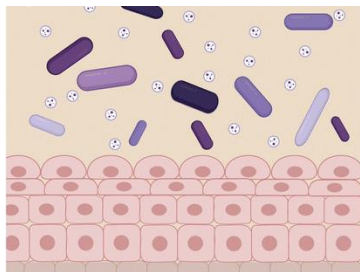
Bacterial extracellular vesicles as a tunable platform for vaginal drug delivery



Optimized model protein loading into bEVs



Internalized by vaginal epithelial cells and endocervical cells *in vitro*

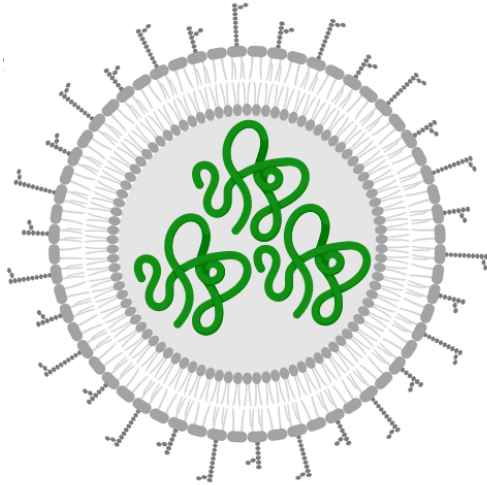


Compatible with key vaginal microbiota

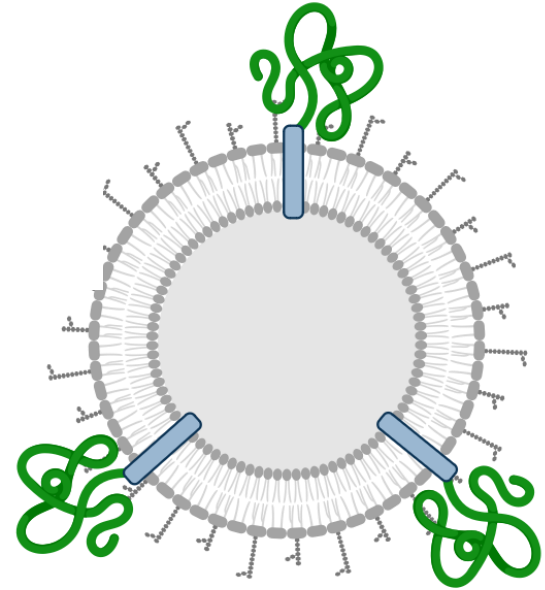


Retained in the vagina for 6 h after administration

Future Work



Loading relevant proteins



Engineering the surface
with cell targeting peptides

Acknowledgements

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Sara Molinari, PhD

Faculty Assistant

Sarah Browning

Graduate Students

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Andy Ng

Past Graduate Students

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Daniele Pastorelli

Undergraduate Students

Hahnbit Kang

Adib Khan

Shiv Anderson

Talia Levine

Past Undergraduate Students

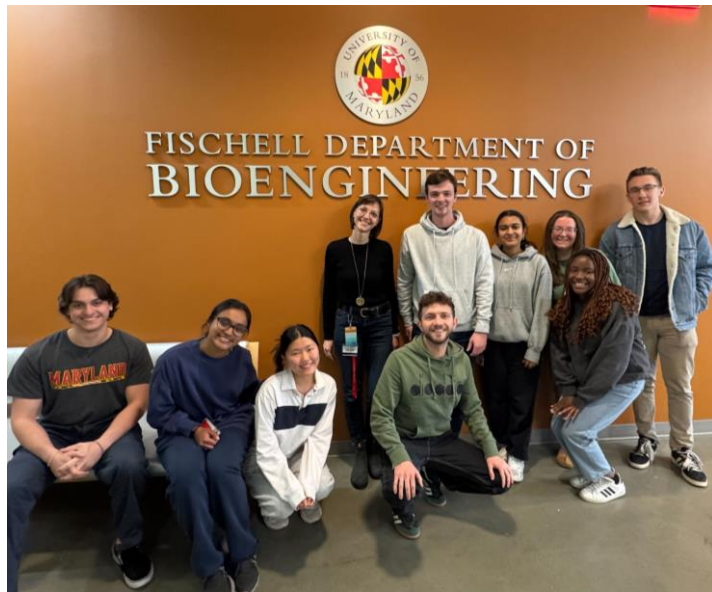
Raifah Alam

UMD Collaborations

Hannah Zierden, PhD

Darby Steinman

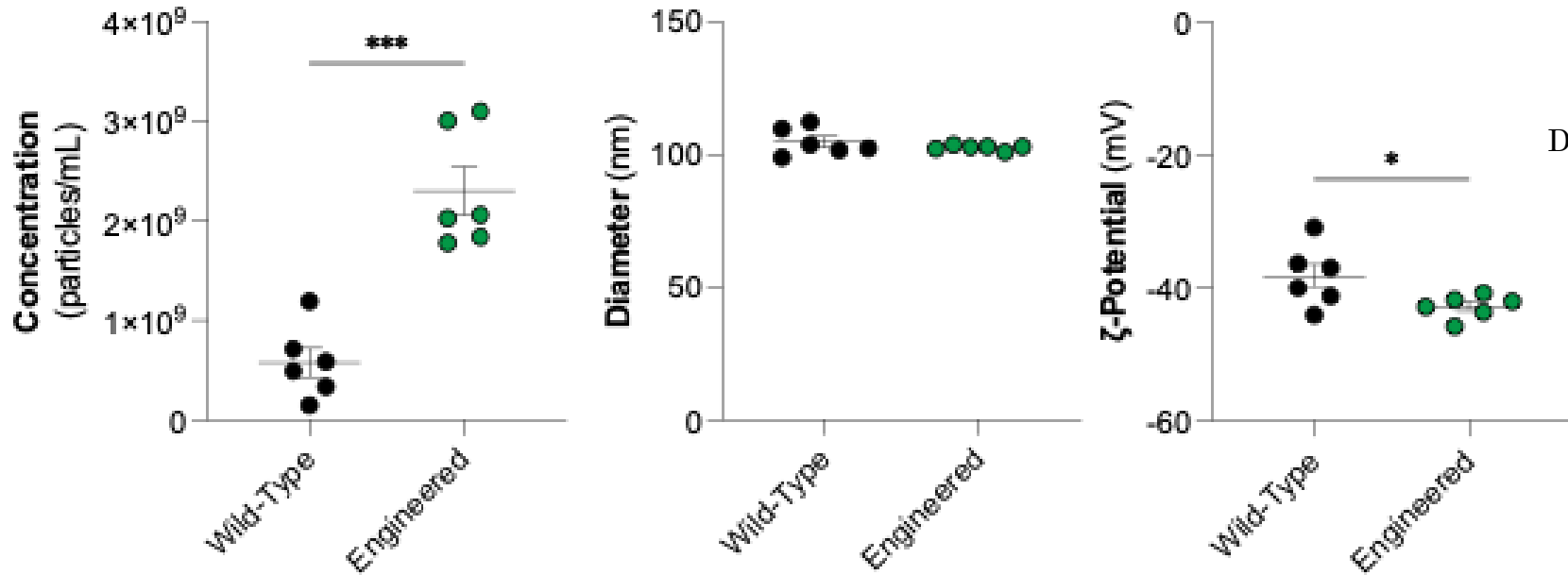
Pranshu Tyagi



Periplasmic loading increases bEV concentration



Darby Steinman
Zierden Lab



Steinman et al. Journal, Under Review