



EGFR-Targeted Nanocarriers Demonstrate Hormone-Responsive Uptake in an Endometrial Spheroid Model

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In collaboration with the Gnecco Lab, Tufts University

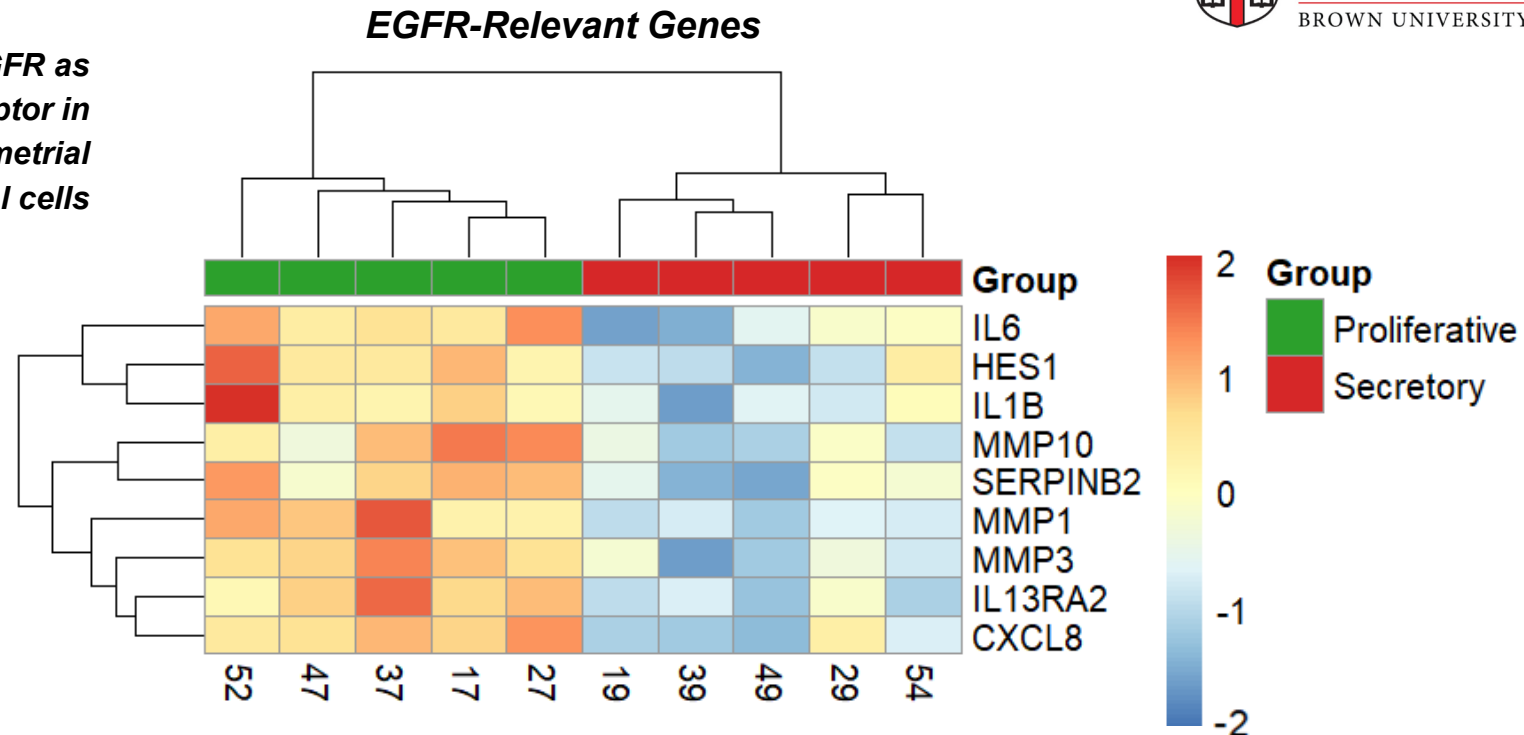
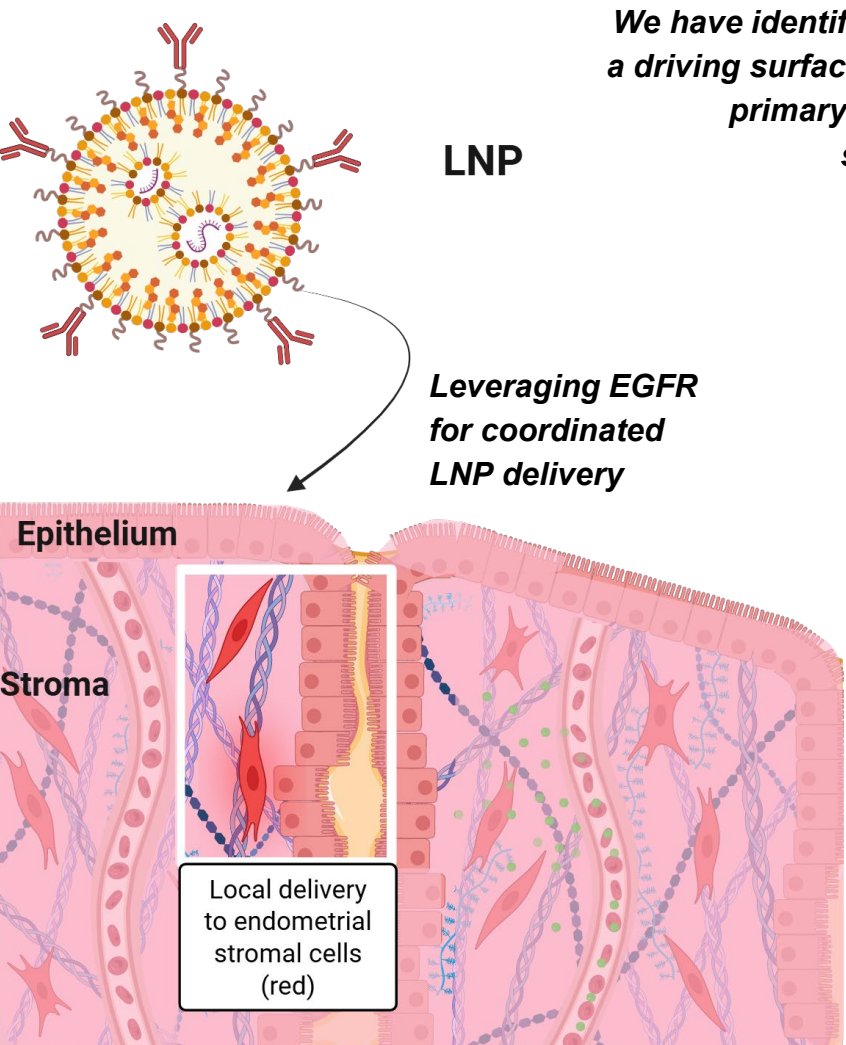
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MULTISECTOR
INNOVATION
for ADVANCING
DELIVERY SCIENCE
JULY 6-9, 2026



Targeted delivery to the endometrial stroma poses an opportunity in drug delivery



Bulk RNA-sequencing analysis of inflamed primary ESCs in Proliferative (E2+10ng/ml IL-1 β) and Secretory (E2+MPA+10ng/ml IL-1 β) samples. N=5 donors. E2 = 10 β -Estradiol; MPA = Medroxyprogesterone Acetate; IL-1 β =interleukin-1 β

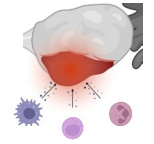
Tissue invasiveness



Drug resistance



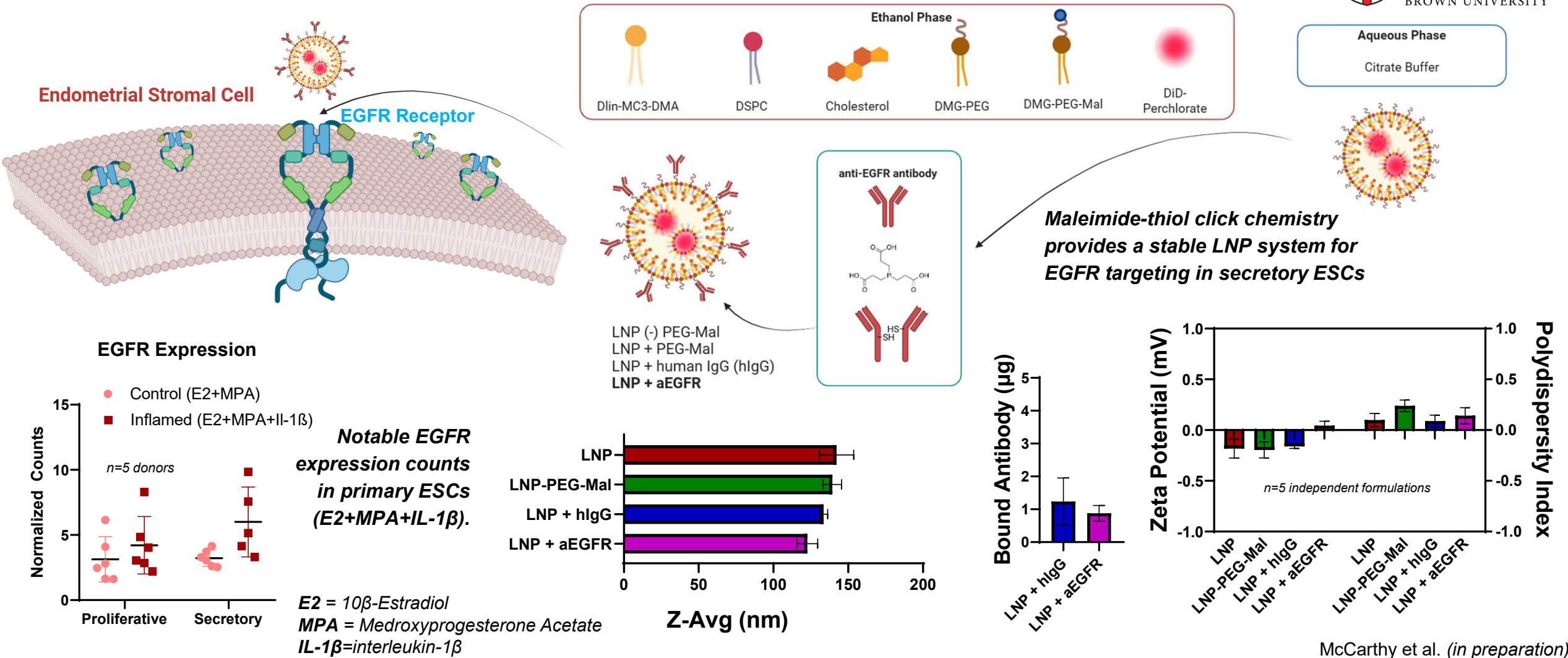
Immune evasion



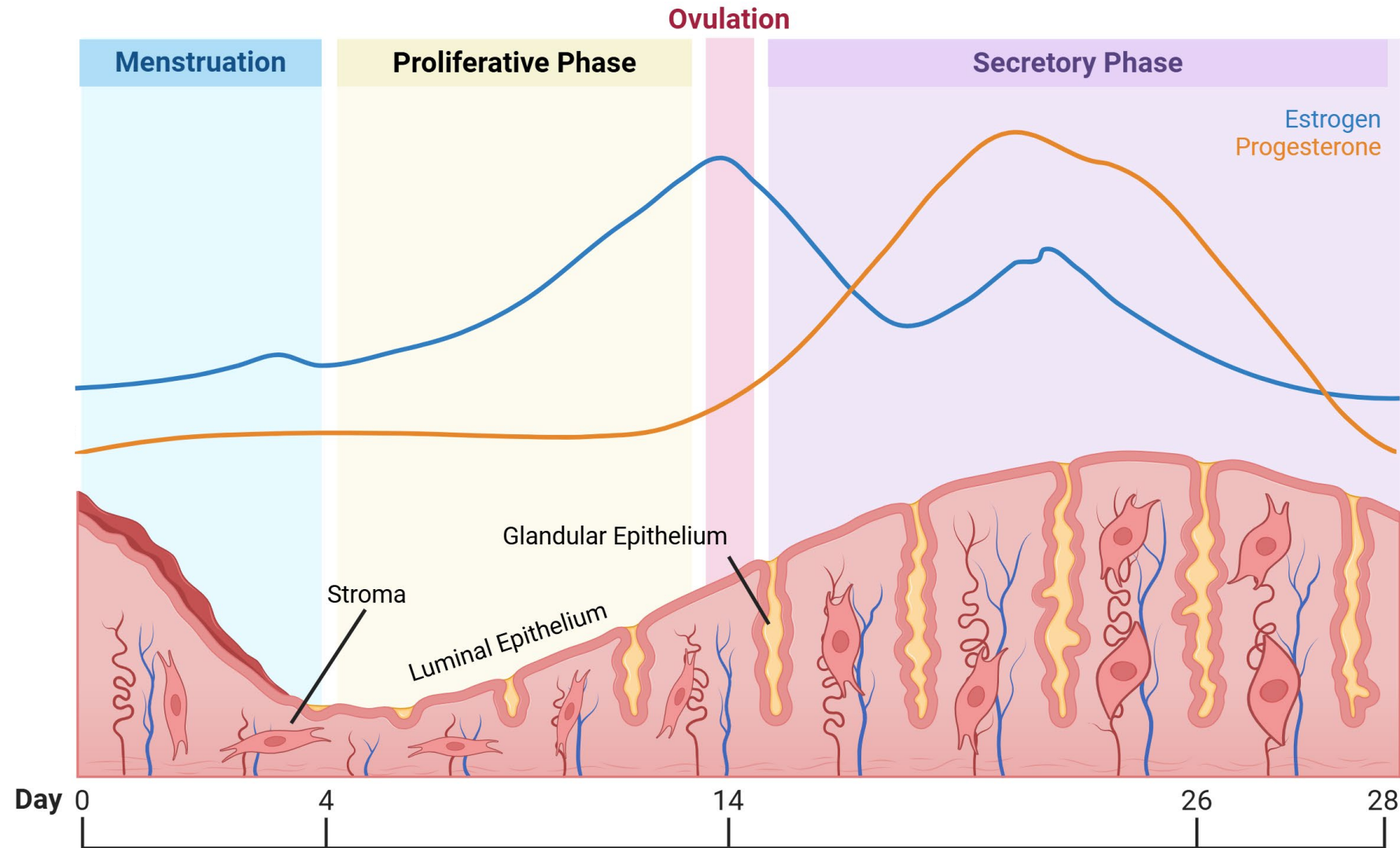
McCarthy et al. (in preparation)



Design of anti-EGFR-LNP for endometrial stromal cell specific uptake



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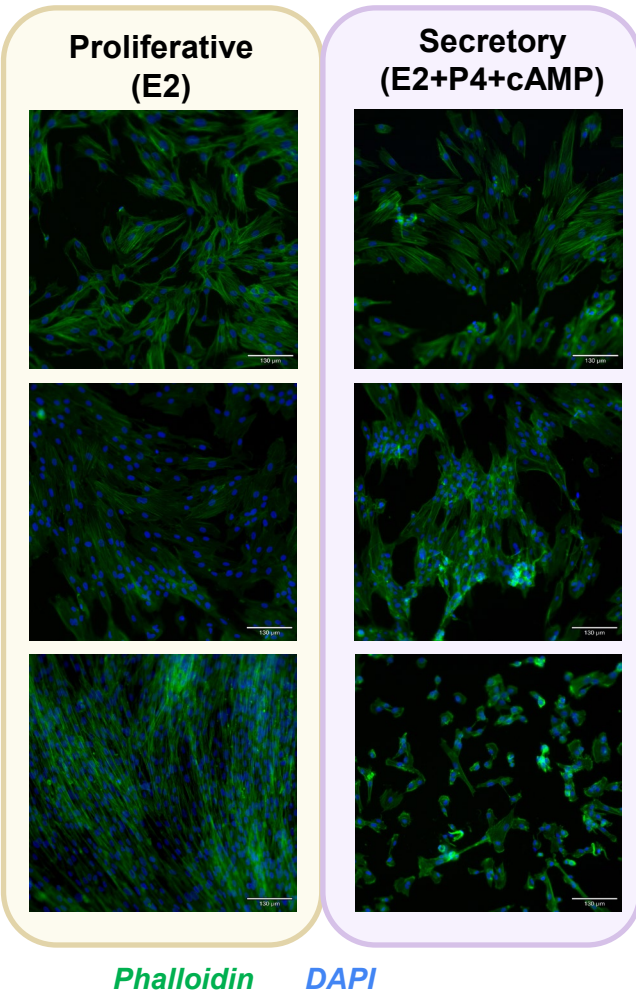
**Estrogen (E2)
dominates
proliferative phase**

**Estrogen (E2) +
Progesterone (P4) +
adenosine cyclic
monophosphate
(cAMP) dominate
secretory phase**

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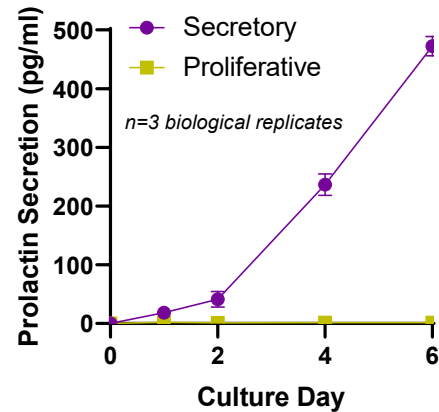


In vitro stimulation of secretory phase endometrium by stromal cell decidualization

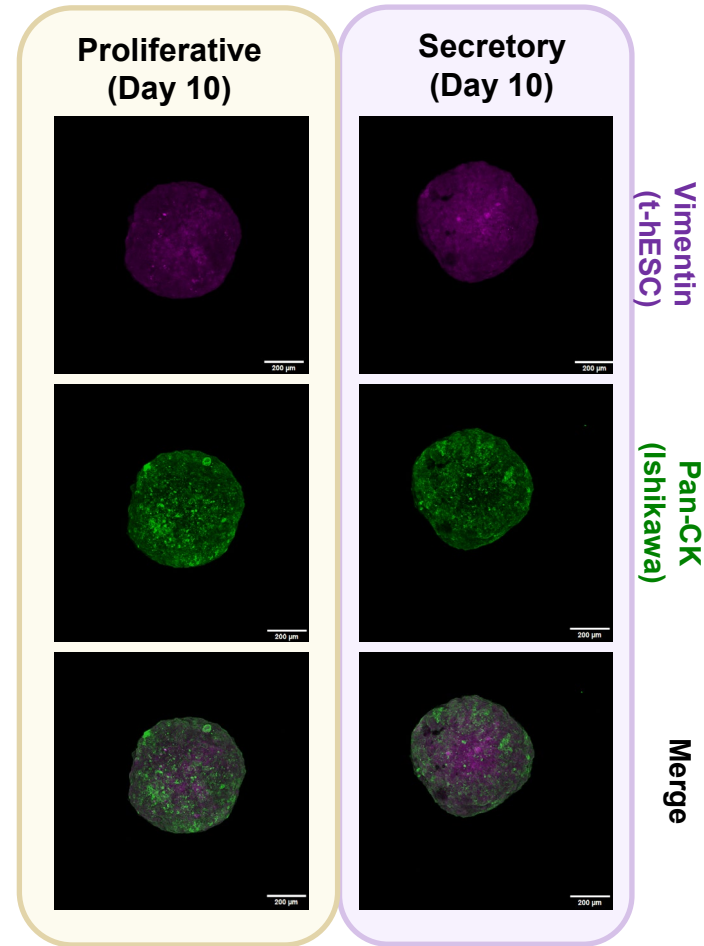


Stimulation of t-hESCs with E2 + P4 + cAMP results in cell differentiation into decidual phenotype

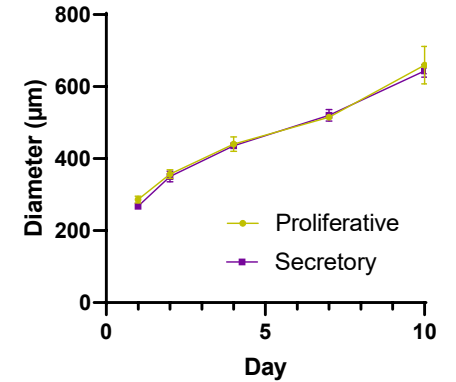
t-hESC Decidualization



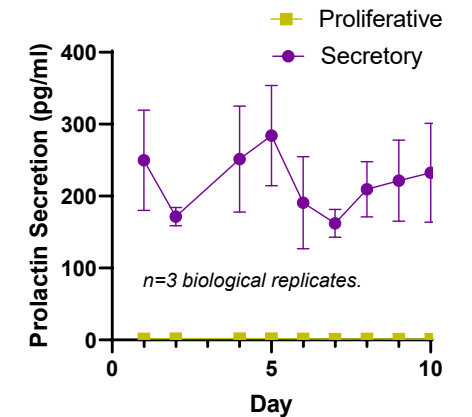
E2 = 10 β -Estradiol
P4 = Progesterone
cAMP = Adenosine cyclic monophosphate



Coculture Spheroids



Coculture Decidualization

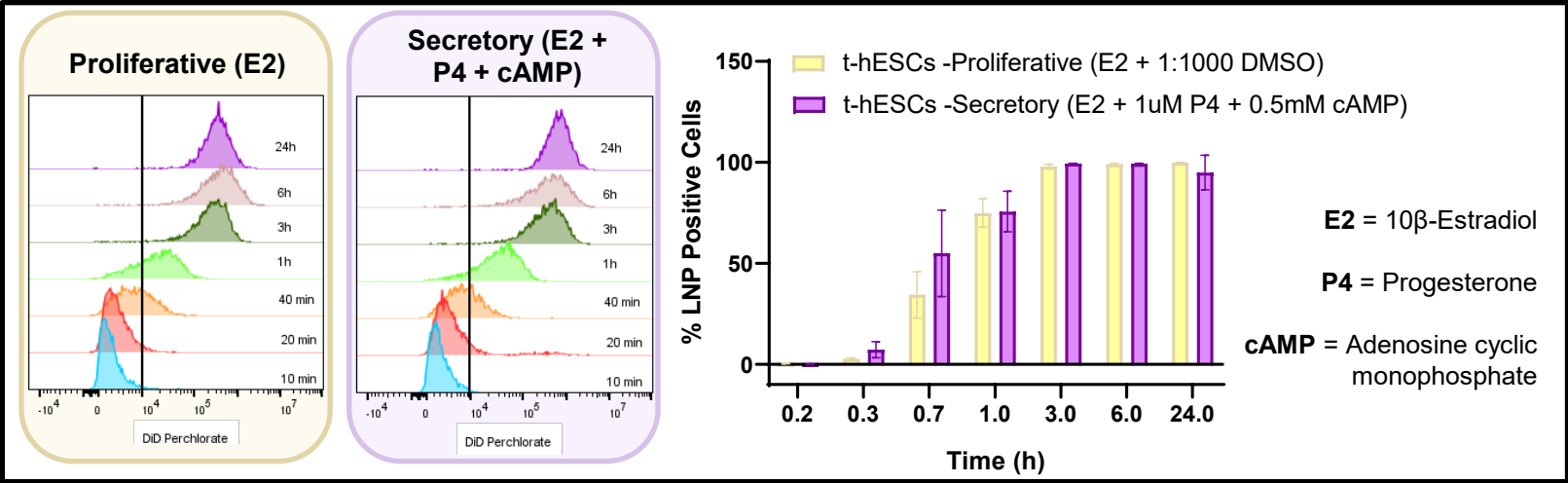


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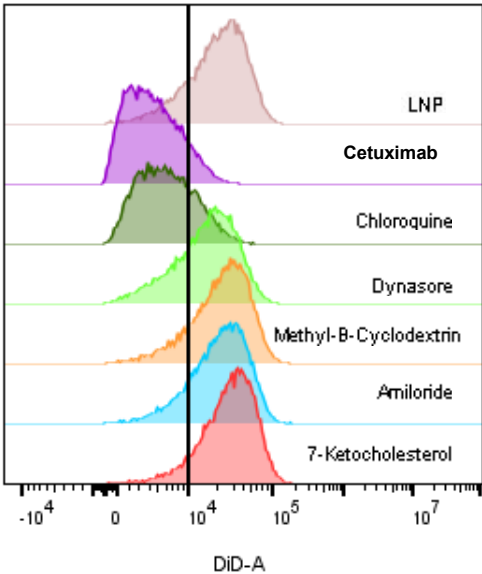


EGFR-driven internalization of targeted LNPs in endometrial stromal cells

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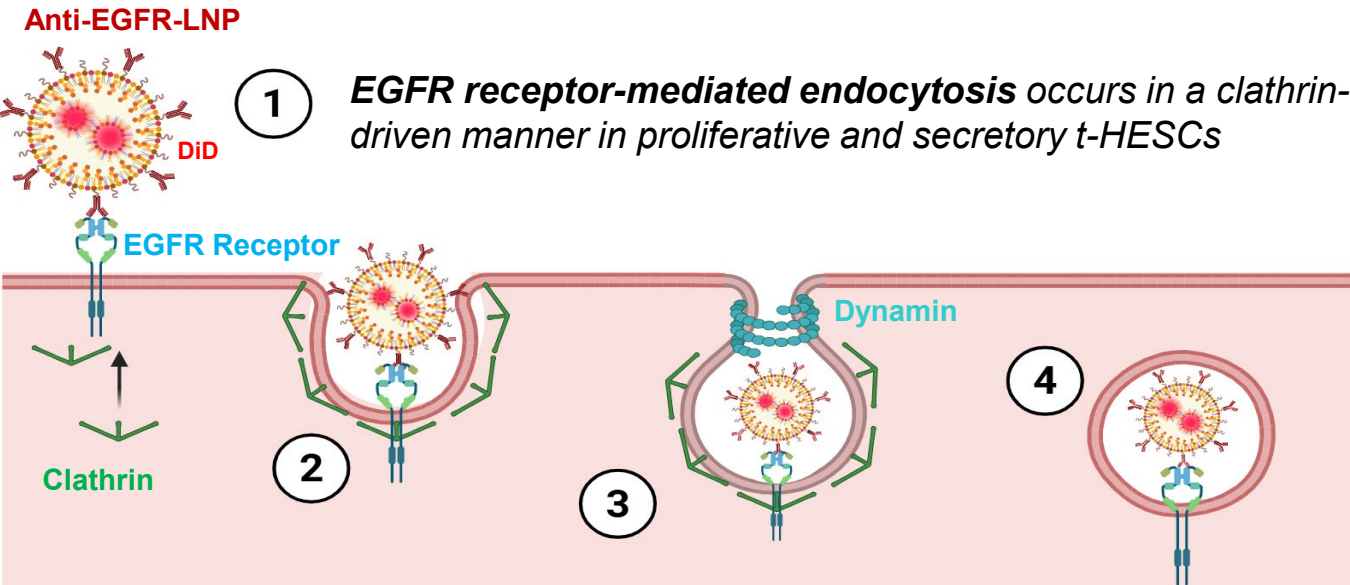
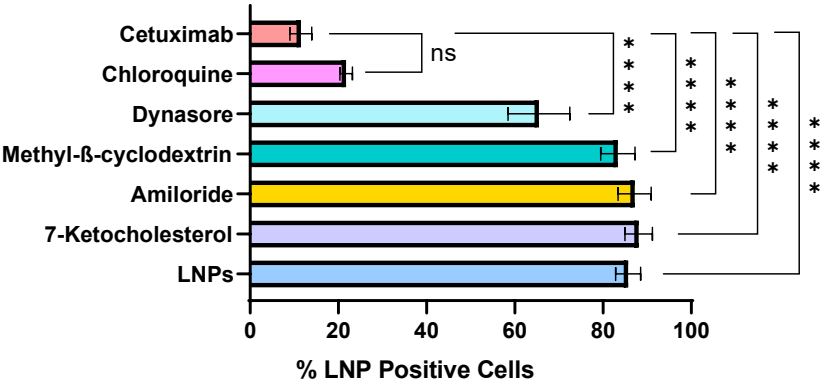


Flow cytometry results of DiD-LNP fluorescence intensity in t-hESCs after 1h of anti-EGFR LNP incubation.



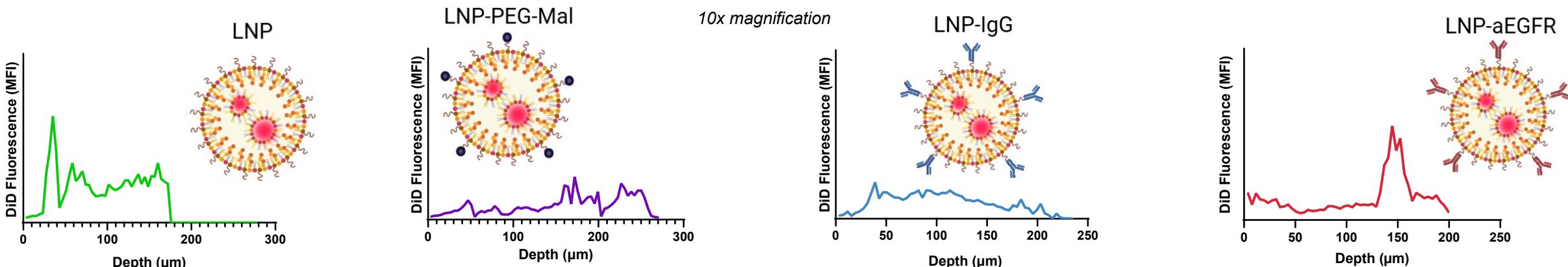
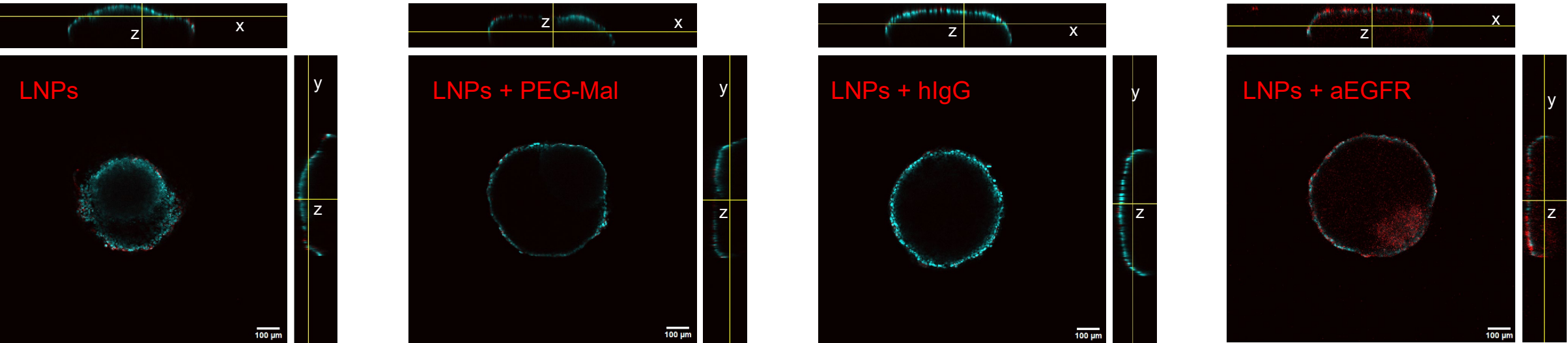
Test: one-way ANOVA + Tukey's, n=3 replicates

Quantification of %DiD(+) Cells after 1h anti-EGFR-LNP



ESC-specific uptake of targeted LNPs in 3D endometrial coculture constructs

Confocal imaging of *t*-hESC/Ishikawa spheroids across z-slices reveal DiD accumulation in the stromal core @ 4h

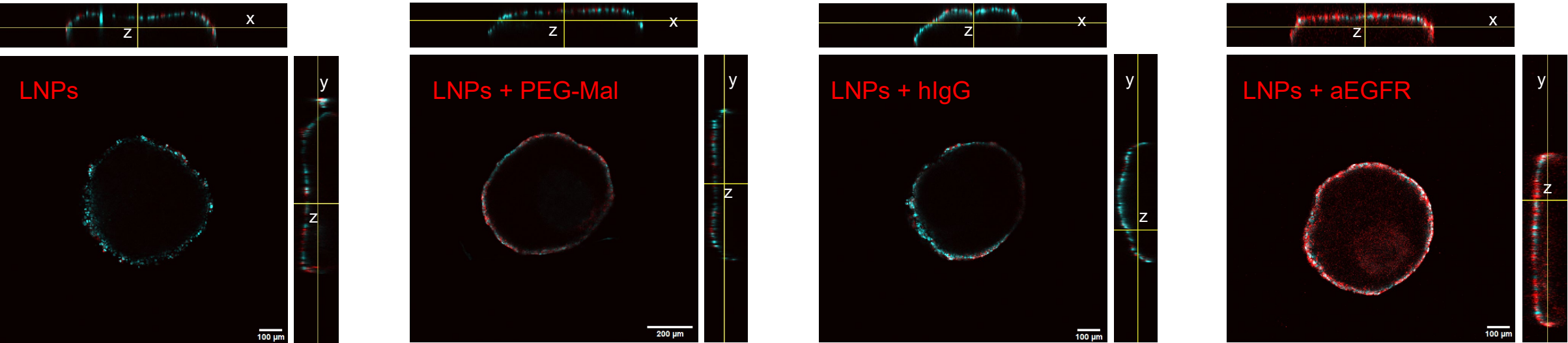


Corrected total cell fluorescence of each confocal slice as a function of spheroid depth (3.91μm per slice)

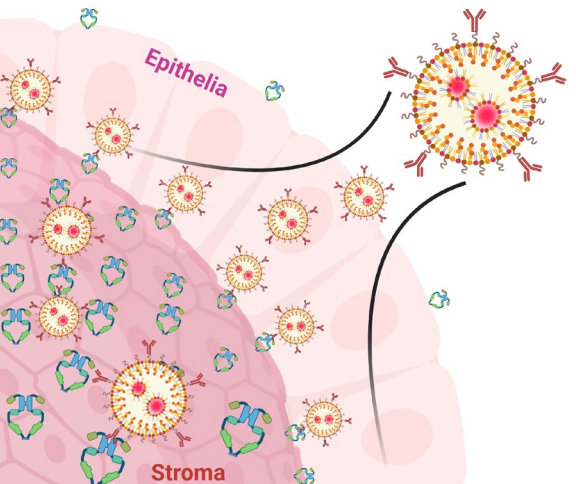
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ESC core penetration of targeted LNPs in 3D endometrial coculture constructs

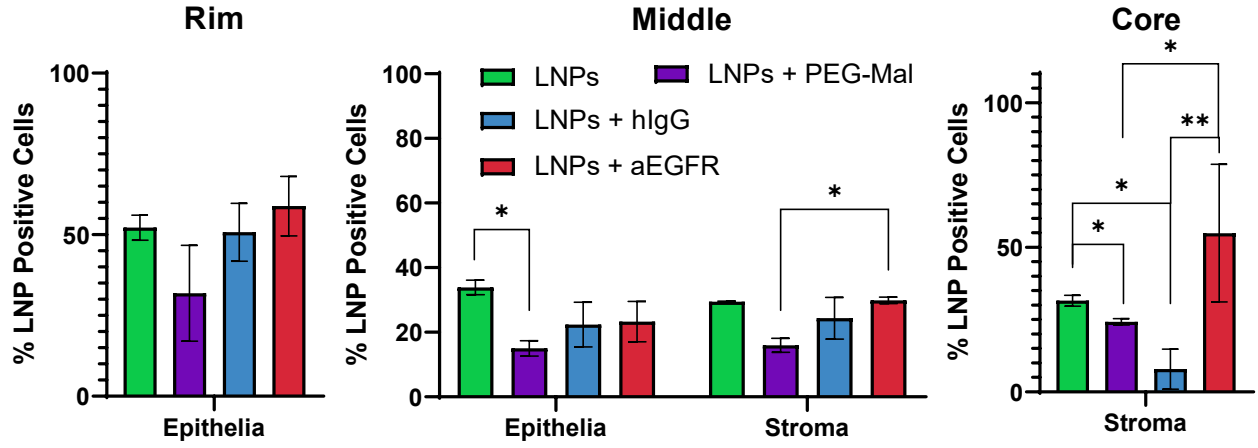
Confocal imaging of t-hESC/Ishikawa spheroids across z-slices reveal DiD accumulation in the stromal core @ 24h



Test: one-way ANOVA + Tukey's, n=3 replicates



Flow cytometry results of DiD fluorescence across spheroid radial segments



anti-EGFR-LNP demonstrated significant uptake in the stromal core compared to nontarget LNP controls

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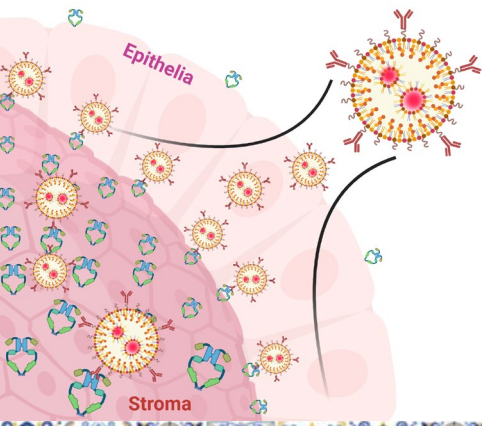
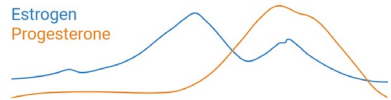
Endometrial stromal-targeted LNPs for therapeutic potential in endometriosis

EGFR-triggered endocytosis of LNPs into defective endometrial stromal cells –particularly in secretory phase endometrium for modulating...

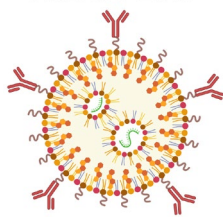
immune-coordination

chemotactic signaling

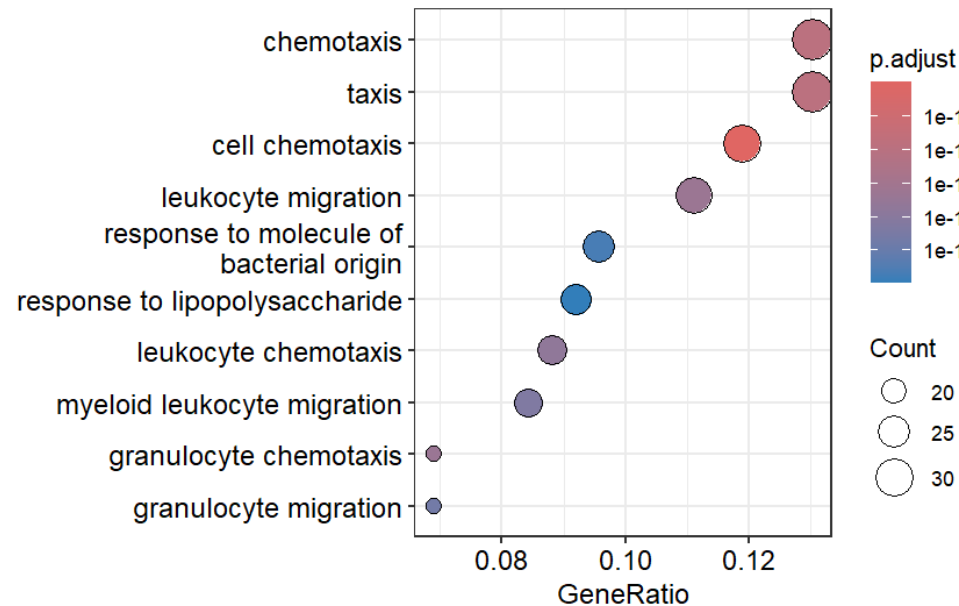
hormone responsiveness



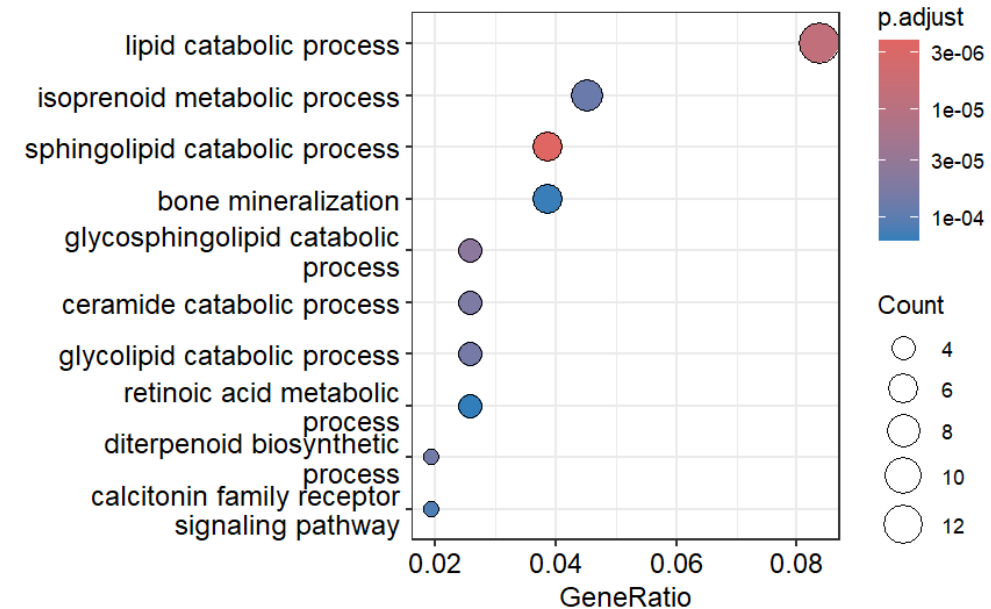
siRNA-LNP



Upregulated (Inflamed relative to Control)



Downregulated (Inflamed relative to Control)



Gene Ontology analysis of primary ESCs in control (E2+MPA) and inflamed (E2+MPA+10ng/ml IL-1 β) samples.
Control: E2 + MPA; Inflamed: E2 + MPA + 1L-1 β (10ng/ml). N=5 donors. E2 = 10 β -Estradiol;
MPA = Medroxyprogesterone Acetate; IL-1 β =interleukin-1 β

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Acknowledgements

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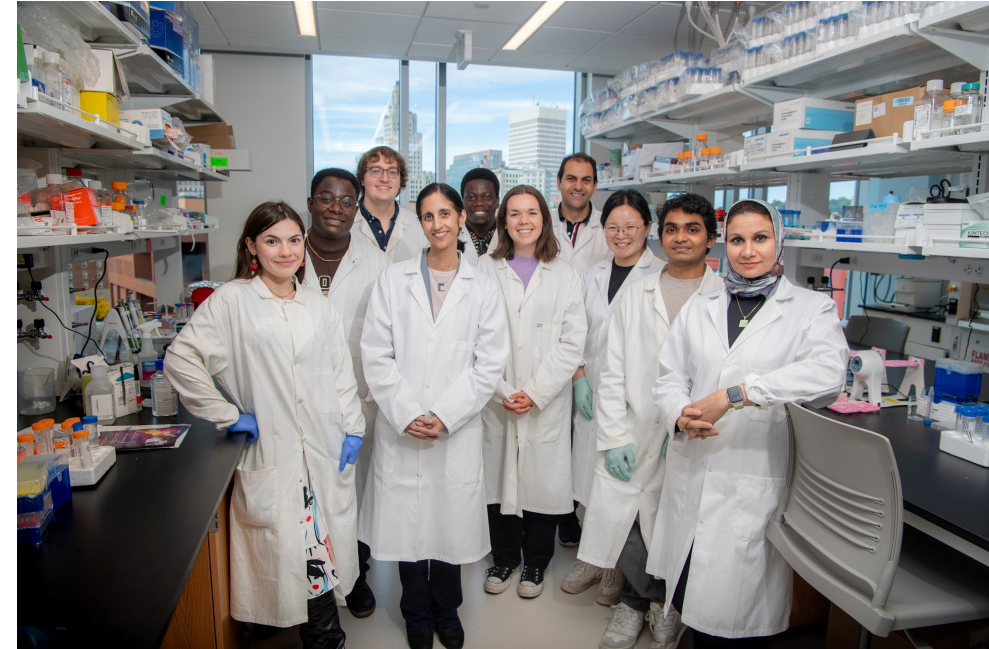
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Advisory Committee:

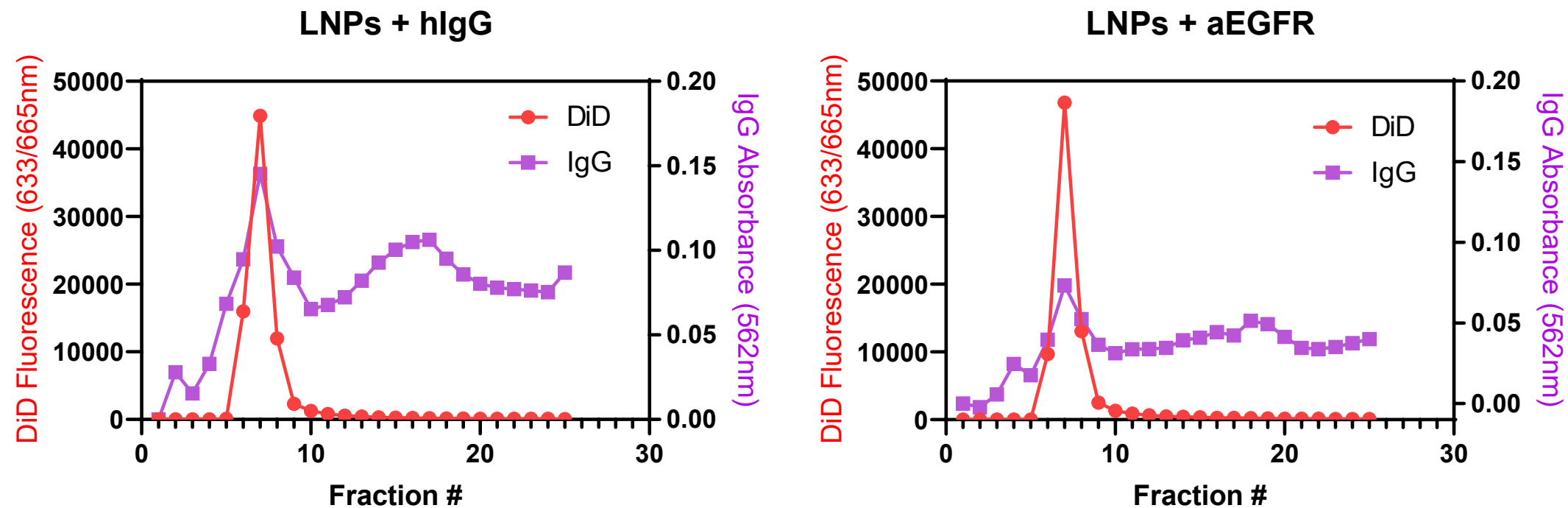
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Core Facilities:

Kevin Carlson, Flow Cytometry Core
Christoph Schorl, Genomics Core



Design of anti-EGFR-LNP for endometrial stromal cell specific uptake

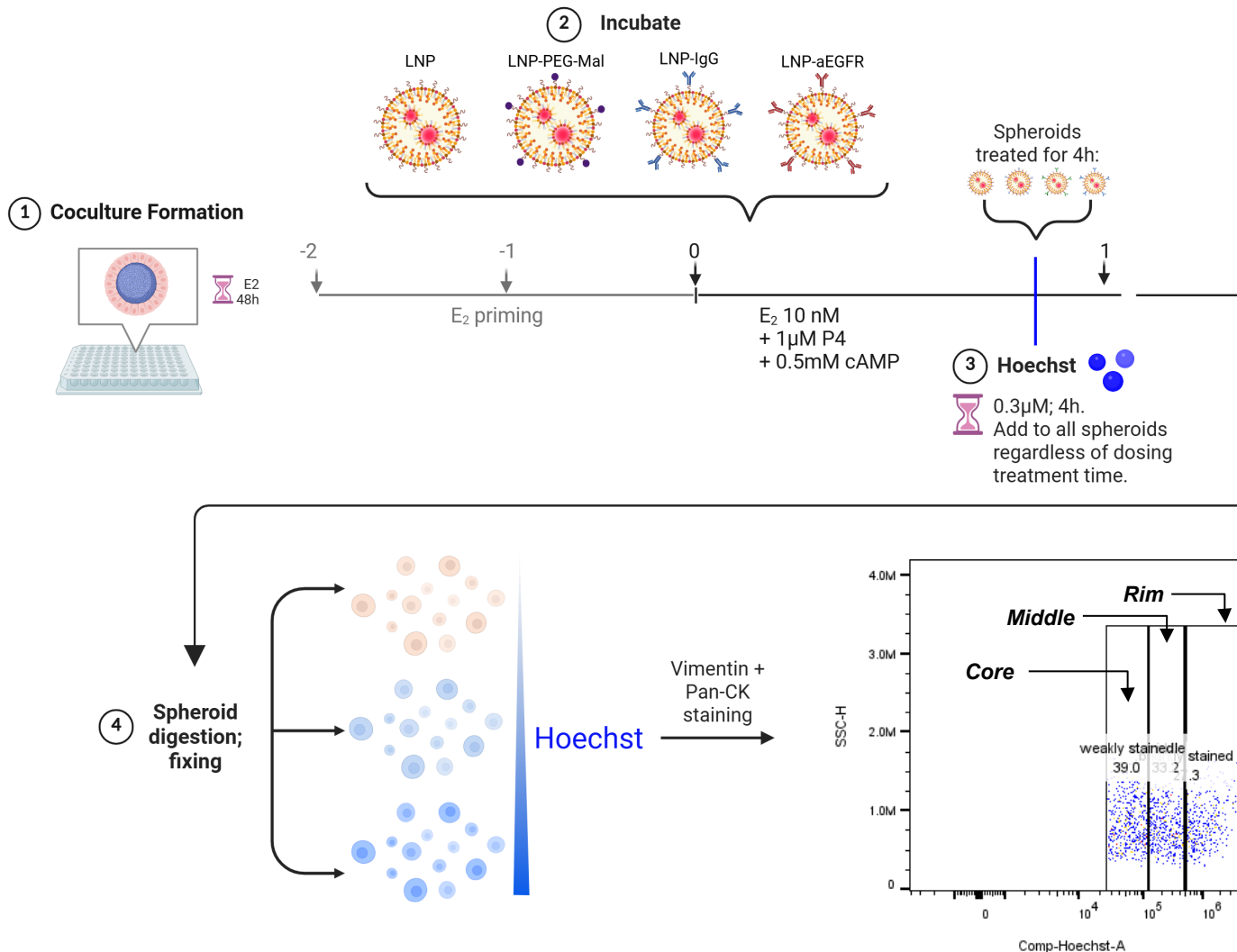


Dual spectroscopic evaluation of antibody conjugation by DiD fluorescence (red) and IgG absorbance (purple)

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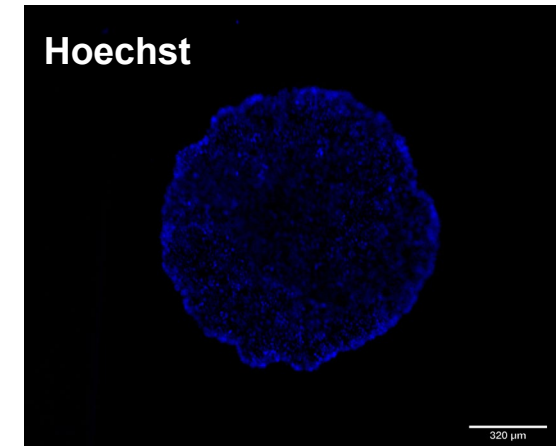


Hoechst Assay for Flow Cytometry Evaluation of Spheroidal Segments



- Precondition Spheroids with E2 (48h)
- Add LNP panel at t=24 hours before harvest. Add secretory hormones (E2+P4+cAMP)
- Add LNP panel at t= 4 hours before harvest. At the same time, **incubate with 0.3 μ M Hoechst.**

Hoechst dye forms a diffusion gradient in spheroids that can be divided into core, middle, and rim segments.



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