

Nanomedicine approaches for Women's Health

Laura Ensign, Ph.D.
CRS 2025

Tech Session V: Women's Health II



PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**

Reproductive rights?

- Access to birth control and abortion care has been politically weaponized
- Disparities in access to fertility support and assisted reproductive technologies exist among people of color, low income people, people with disabilities, and LGBTQ communities
- Significantly higher rates of preterm birth and maternal mortality exist in the US among black women compared to white women, in part due to differences in access to healthcare
- There is little to no data on the fetal safety of 90% of prescription medications, as pregnant women are often left out of clinical trials (including COVID-19 vaccines)

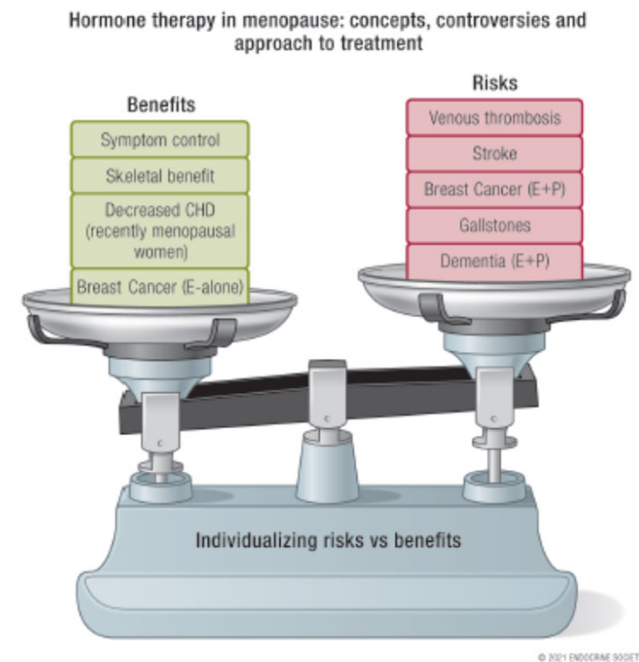
Options for preterm birth are limited

- The only drug approved for prevention of preterm birth (Makena) was pulled from the market in 2023 due to lack of clinical benefit in a confirmatory study
- Currently, our ability to identify women at risk for preterm birth is very limited, with only a few phenotypic characteristics that identify a small percentage of women at risk
- Women in preterm labor are given tocolytics to try to stop contractions, but these drugs are used entirely off-label and generally only work long enough to dose antenatal corticosteroids to accelerate fetal lung development.



Controversy over hormone replacement therapy

- The first HRT drugs were approved by the FDA in 1942, and became more widely used in the 1960's and 1970's
- Sensationalized results of the Women's Health Initiative (WHI) hormone trials grabbed headlines in 2002, claiming increased risks of blood clots, strokes, and breast cancer, leading to a drastic decline in use of HRT
- The study is now seen as flawed, and secondary analyses of the data from the WHI study and others has identified nuanced benefits and risks depending on the situation



Flores et al., (2021), *Endocrine Reviews*

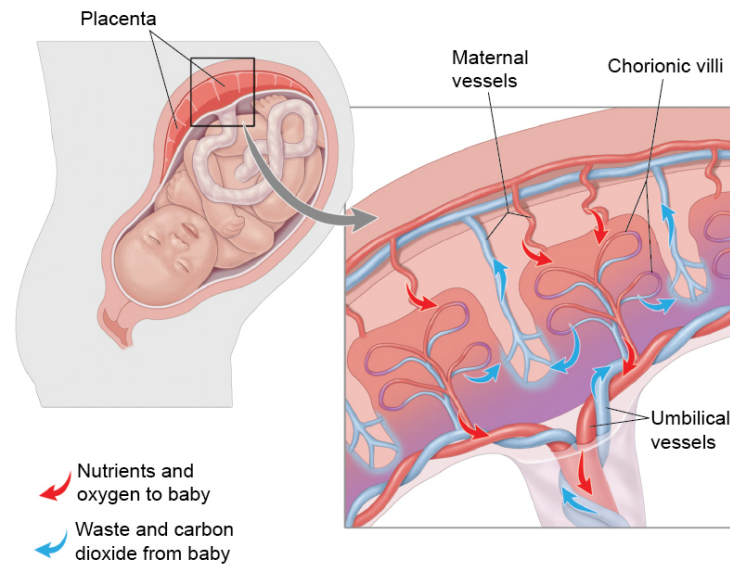
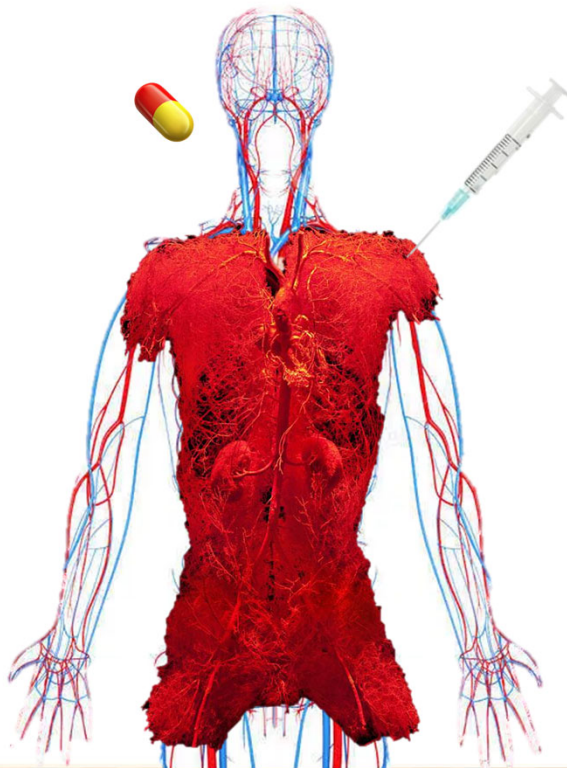
**There is tremendous opportunity for
nanomedicine to address unmet needs in
Women's Health**



PHILADELPHIA, PA
JULY 13-18, 2025

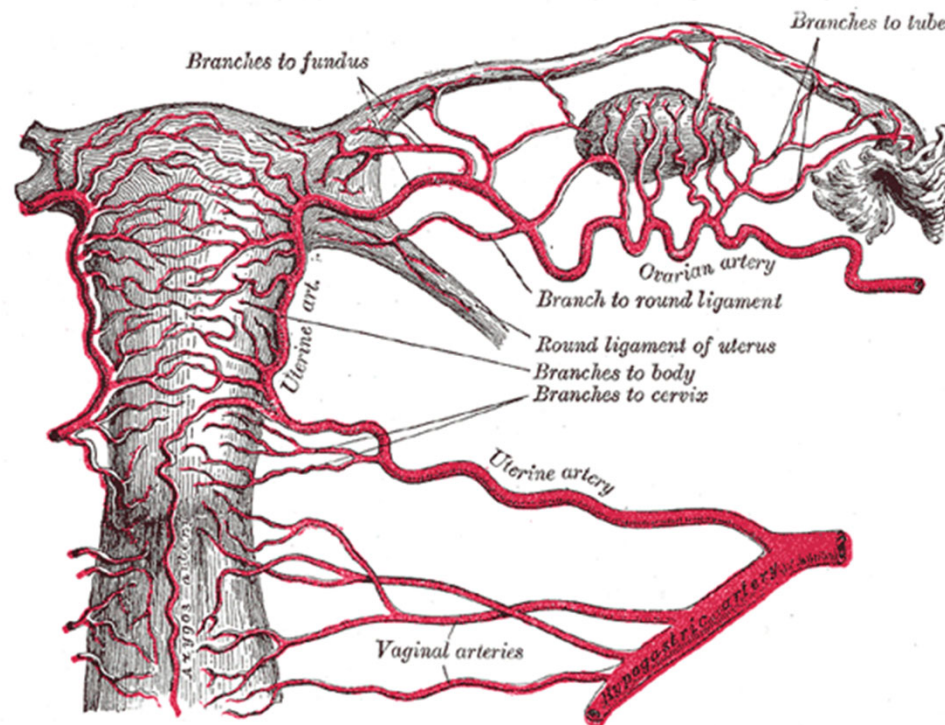
**NEXT-GENERATION
DELIVERY INNOVATIONS**

Drugs suffer from a delivery problem



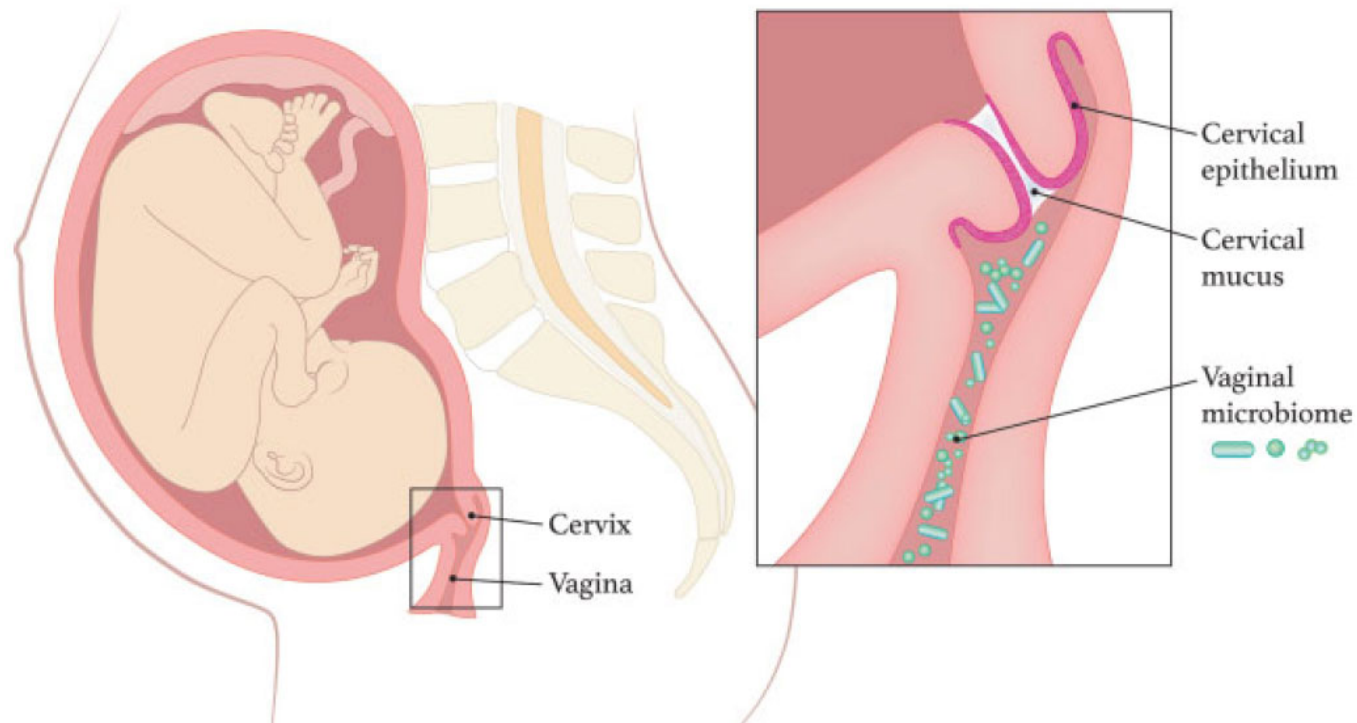
<https://s-media-cache-ak0.pinimg.com/736x/ca/81/85/ca8185982ed7b42c562072e14384310a.jp>;
<https://twsmassage.wordpress.com/2016/01/11/benefits-for-the-circulatory-system/>;
https://www.babycenter.com/pregnancy/your-baby/the-placenta-what-it-is-and-how-it-works_40005564

Local drug delivery to the FRT



De Ziegler et al, Annals NY Acad Sci, 1997 Sep 26; 828:291-9

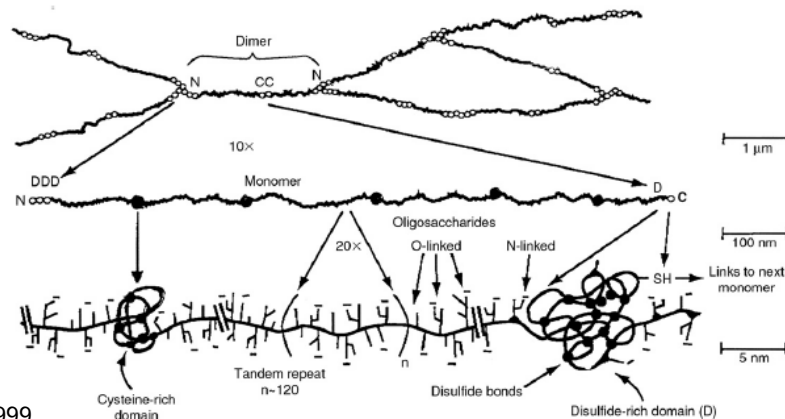
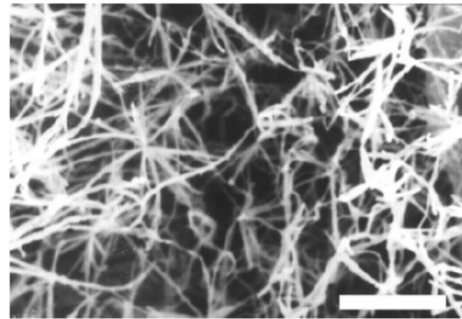
Mucus is a protective barrier in pregnancy



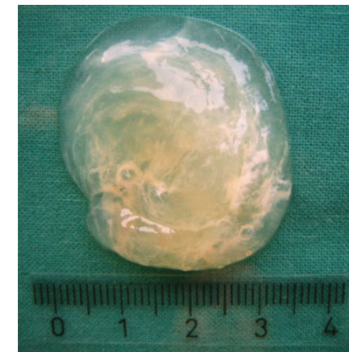
Nallasamy, S., Mahendroo, M. *Semin Reprod Med* 2017; 35:190-200

How does mucus act as a barrier?

SEM of midcycle human cervical mucus
Ceric, et al. *Jap Soc Microscopy*, 2005

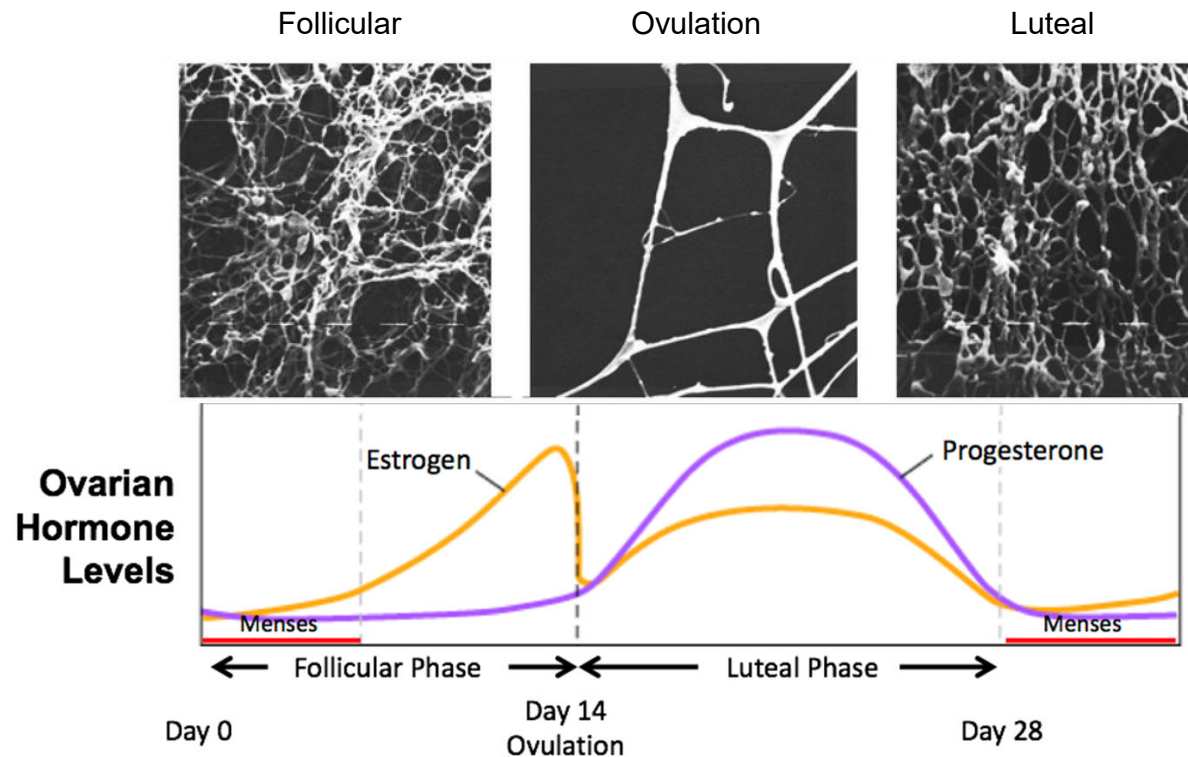


Photograph of a cervical mucus plug shed spontaneous during term labor
Becher, et al. *Acta Obstet Gynec Scand*, 2009



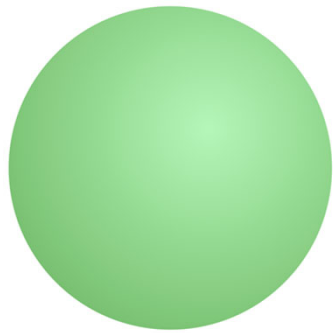
Mucin proteins are physicochemically complex, facilitating interactions with a wide range of chemical functionalities

Hormones affect mucus properties

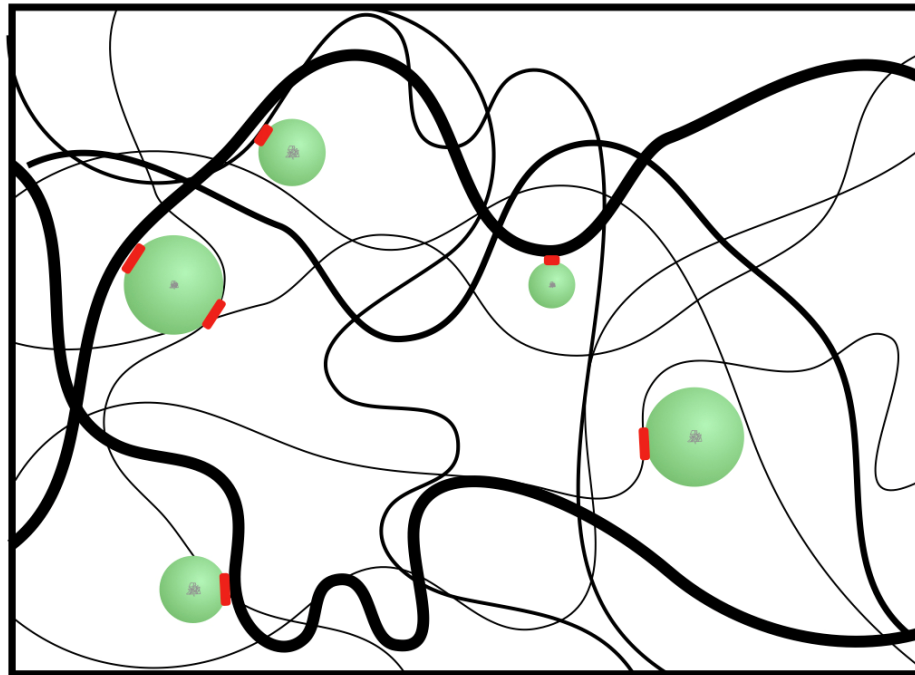


Moreno-Escalón B, Chappel S, Blasco L. Fertil Steril. 1982 Apr;37(4):536-41.

Characterizing the mucus barrier

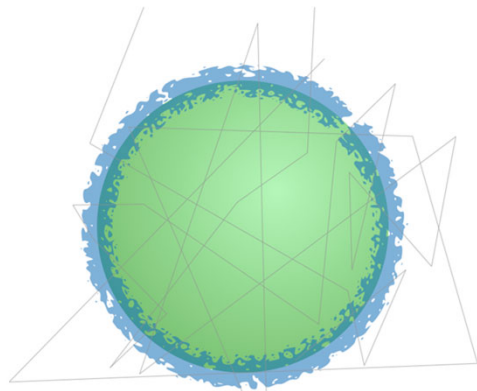


Conventional
Particles (CPs)

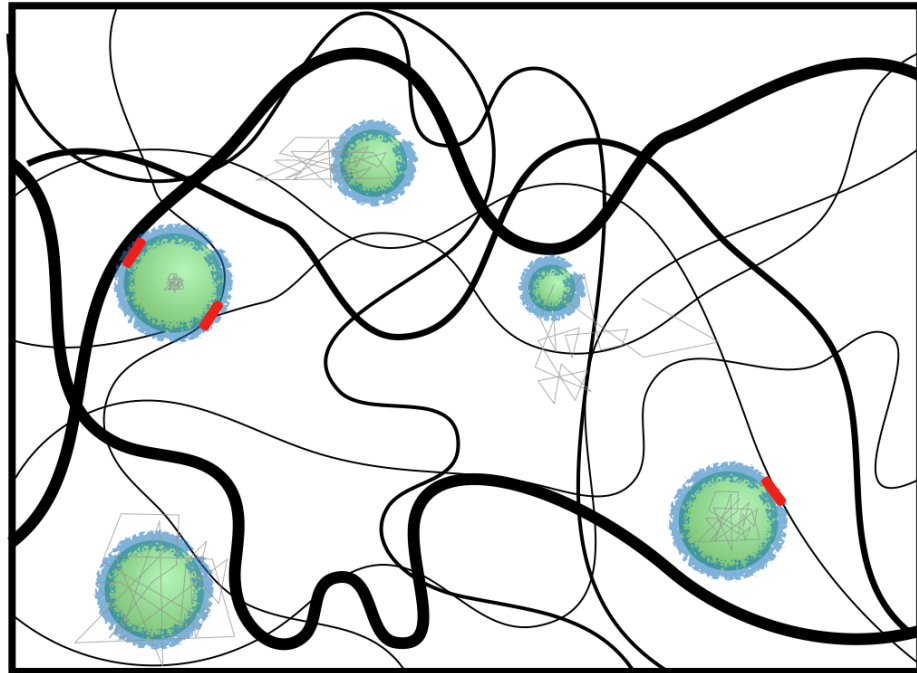


Lai, et al., *PNAS*, 2007; Lai, et al., *ADDR*, 2009; Suh, et al., *ADDR*, 2005; Wang, et al., *Ang Chem*, 2008; and others

Characterizing the mucus barrier

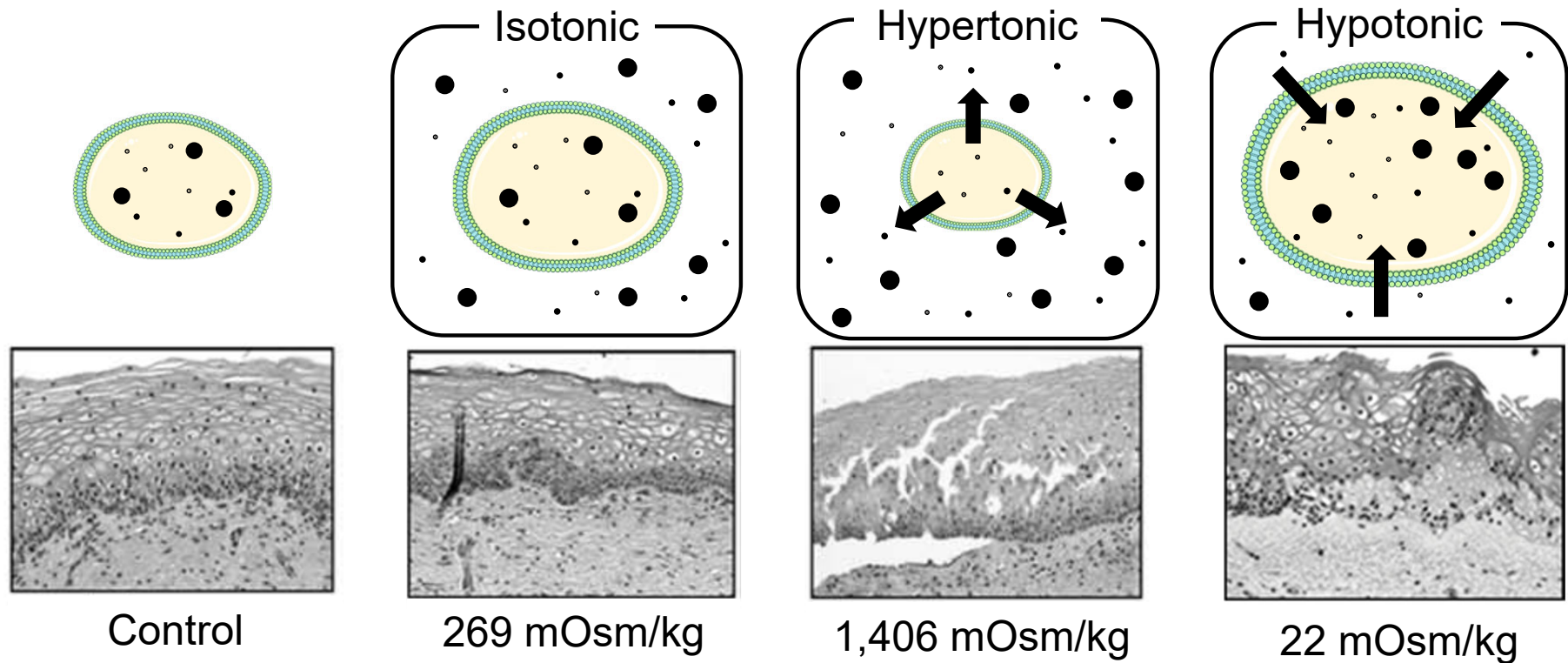


Mucoinert
Particles (MIPs)



Lai, et al., *PNAS*, 2007; Lai, et al., *ADDR*, 2009; Suh, et al., *ADDR*, 2005; Wang, et al., *Ang Chem*, 2008; and others

The vehicle also matters



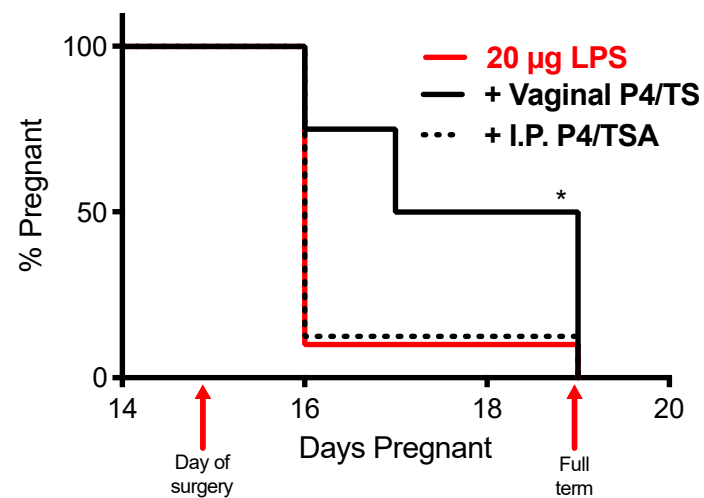
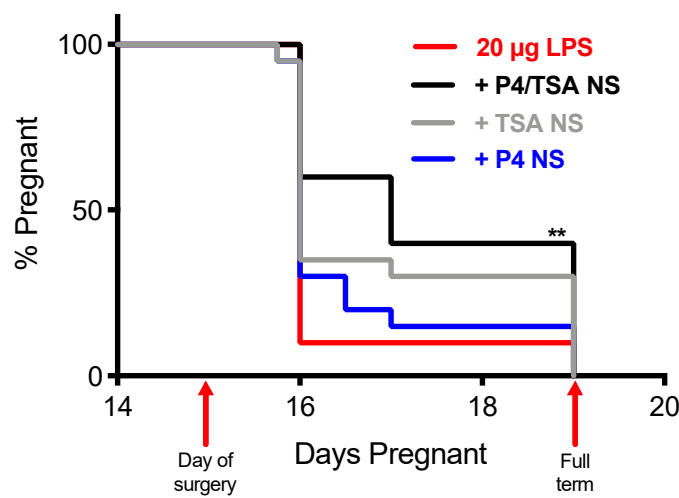
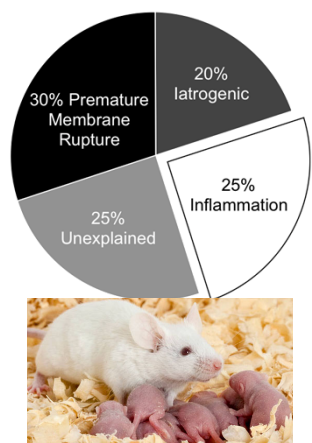
Ensign, et al., *Sci Transl Med*, 2012 Moench, et al., *BMC Infect Dis*, 2010 Dezzutti, et al., *PLoS One*, 2012 Ensign, et al., *Biomaterials*, 2013

CRS 2025
ANNUAL MEETING
& EXPOSITION

PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**

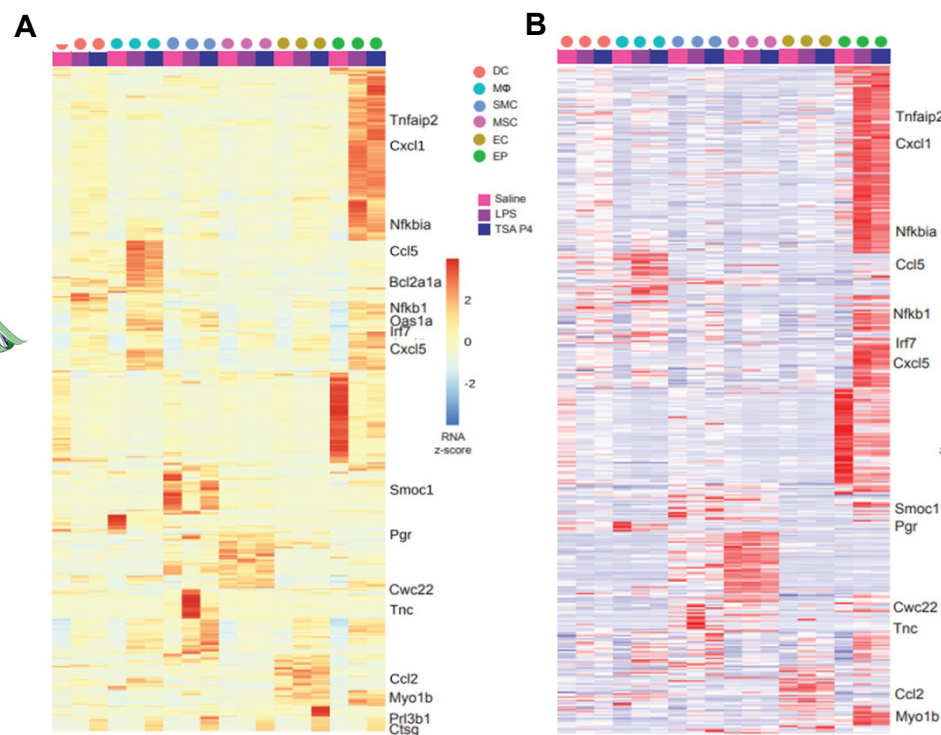
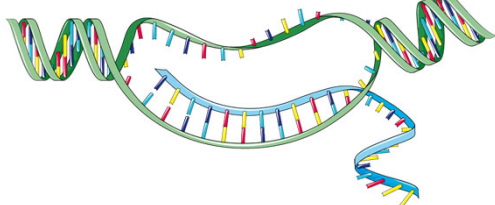
Vaginal delivery is more effective in PTB prevention



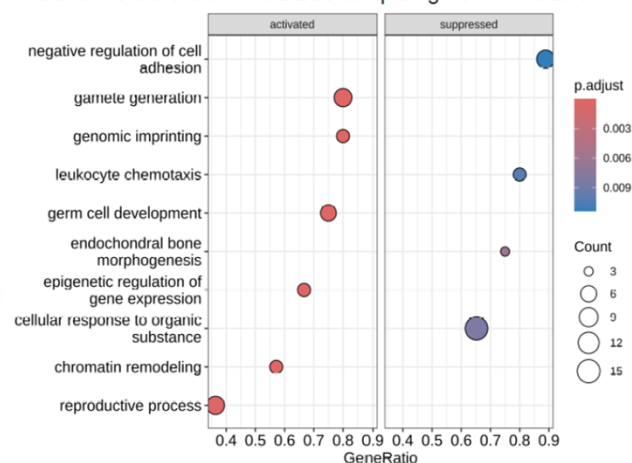
Local delivery more effective

Nanomedicine for probing the biology of PTB

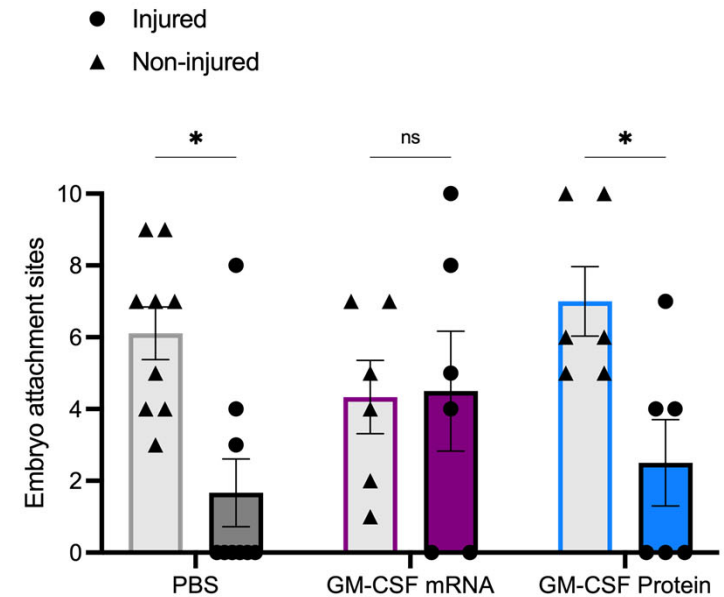
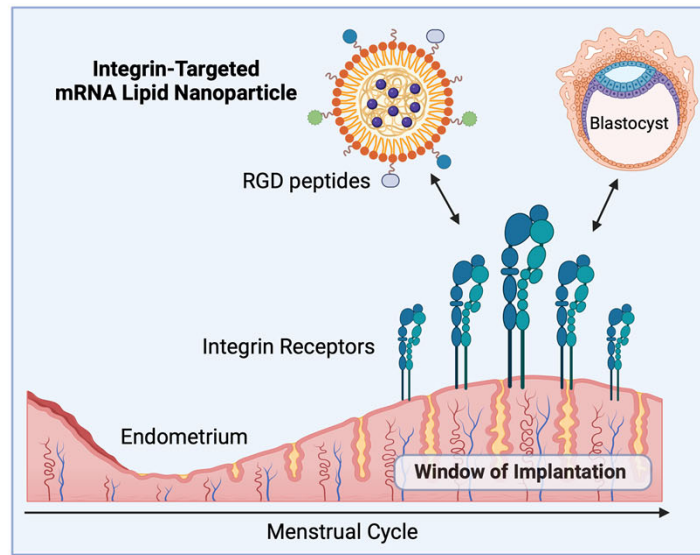
HDAC inhibitor



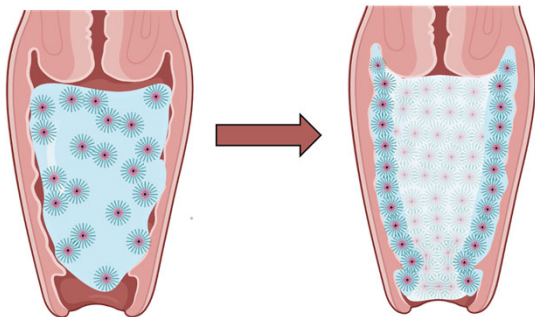
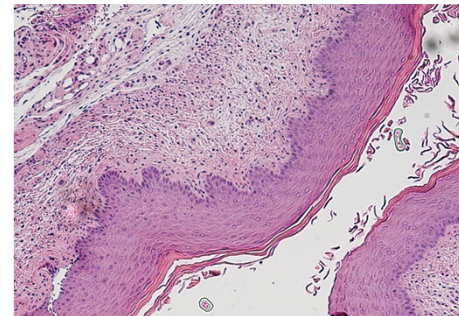
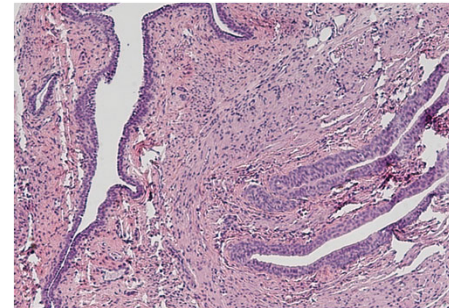
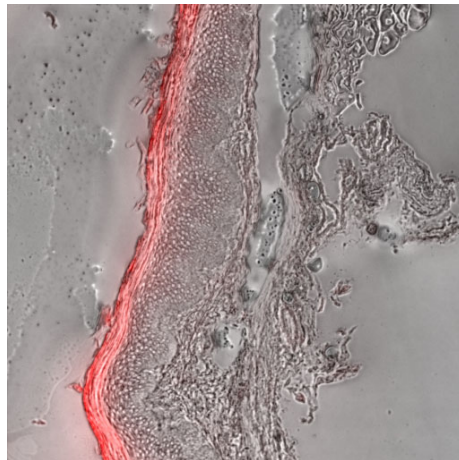
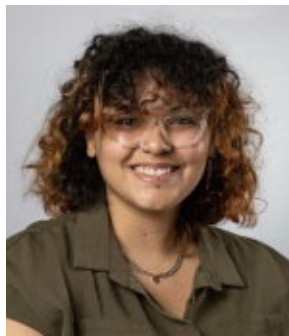
GO terms enriched in the DEGs comparing TSA P4 vs LPS



Spatiotemporal Targeting of mRNA LNPs to the Endometrium for the Treatment of Infertility



Development of a gel-forming vaginal estradiol formulation for treatment of post-menopausal atrophy

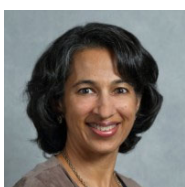


CRS 2025
ANNUAL MEETING
& EXPOSITION

PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**

Acknowledgements



BURROUGHS
WELLCOME
FUND 

THE HARTWELL FOUNDATION
 



CRS **2025**
ANNUAL MEETING
& EXPOSITION

PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**