

Spatiotemporal targeting of mRNA LNPs to the endometrium for the treatment of infertility

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Infertility

- Failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse.
- 1 in 6 people of reproductive age worldwide experience infertility
- Many causes, both male and female originating
 - Female: Hormonal, abnormal anatomy, and thin endometrium



Thin endometrium

- <6 mm is associated with lower probability of pregnancy due to poor receptivity
- There are limited treatment options for thin endometrium.
 - Cell therapies, Intrauterine administration of growth hormones and cytokines
- Challenges: targeting, systemic exposure, and the inability to sustain adequate therapeutic protein levels



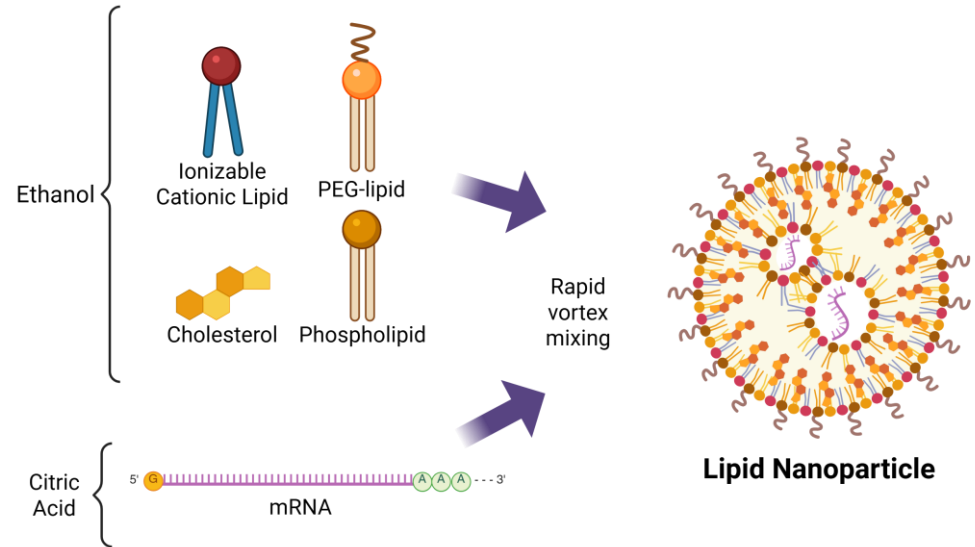
Thin Endometrium
(Non receptive)



Thick Endometrium
(Receptive)

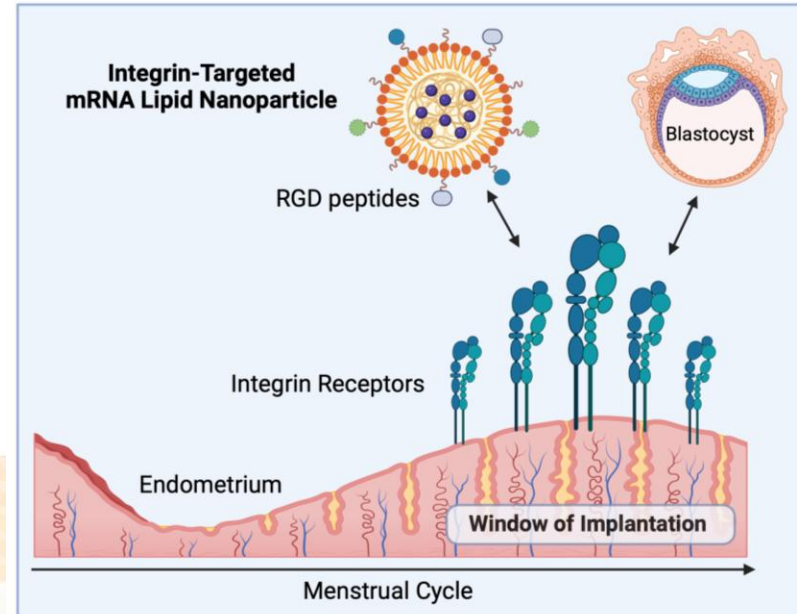
LNPs are effective delivery vehicles

- LNPs have already been approved in several FDA treatments
- The composition of LNPs can be modified to alter their characteristics, biodistribution, tissue specificity and off-target effects.

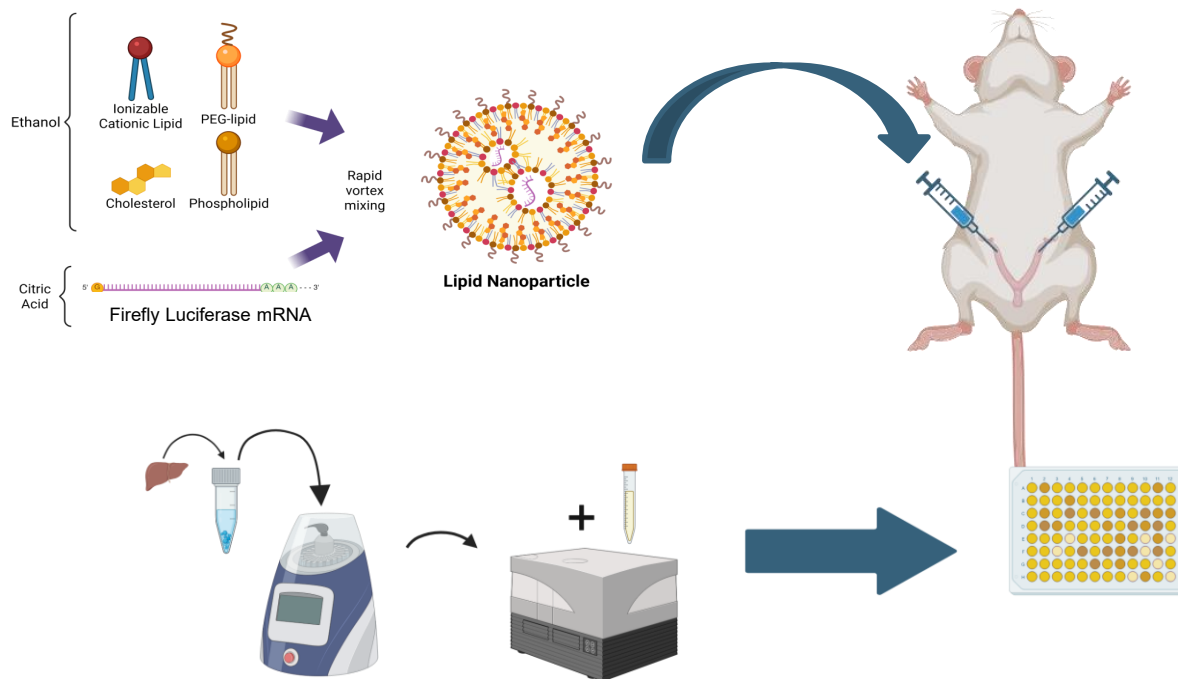


Targeting the Endometrium

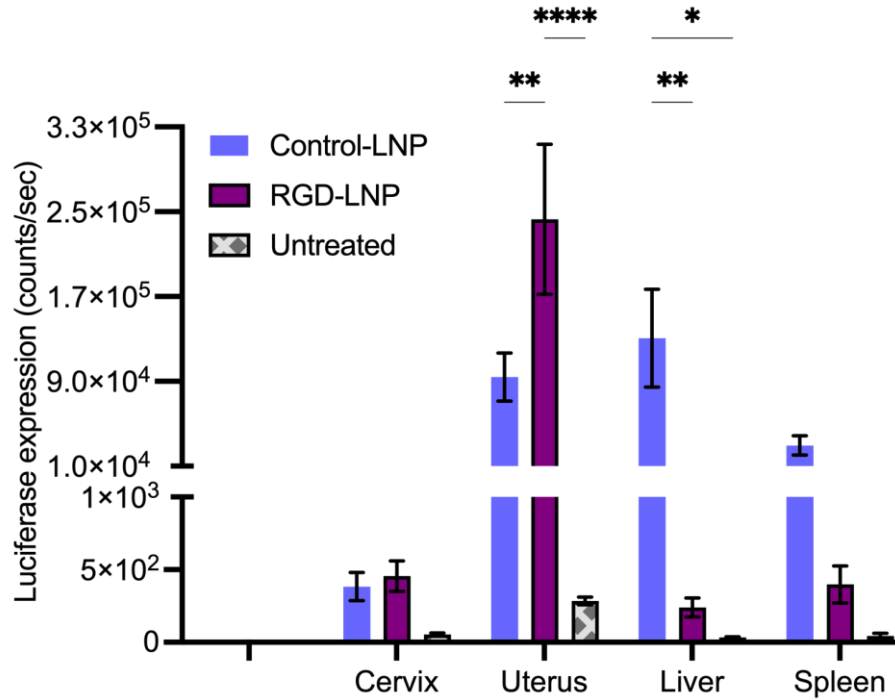
- The uterus prepares for embryo attachment by upregulating cell adhesion molecules on the endometrial surface
- We took advantage of this to increase on target RNA delivery
- By functionalizing LNPs with arginylglycylaspartic acid (RGD) peptides we can enhance integrin receptor-mediated uptake



Intrauterine administration



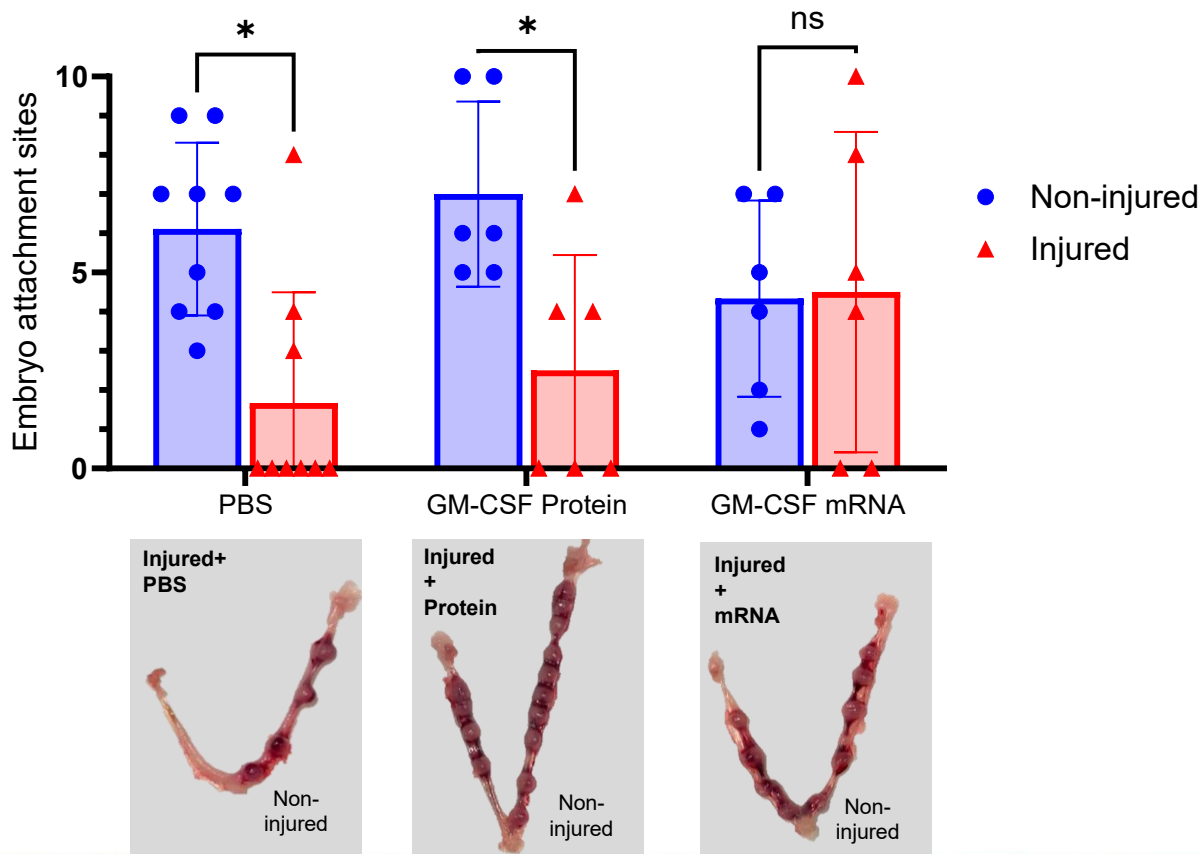
RGD increases expression in the uterus



Thin Endometrium Model and Treatment



Therapeutic efficacy



Conclusion and Next steps

- First mRNA-based approach for female infertility treatment
- We plan to further investigate the health of the full pregnancy and pups as well as any potential toxicities.
- Going forward, our integrin-targeted LNP can be used to encapsulate other therapies to treat a variety of disorders that affect the endometrium.

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