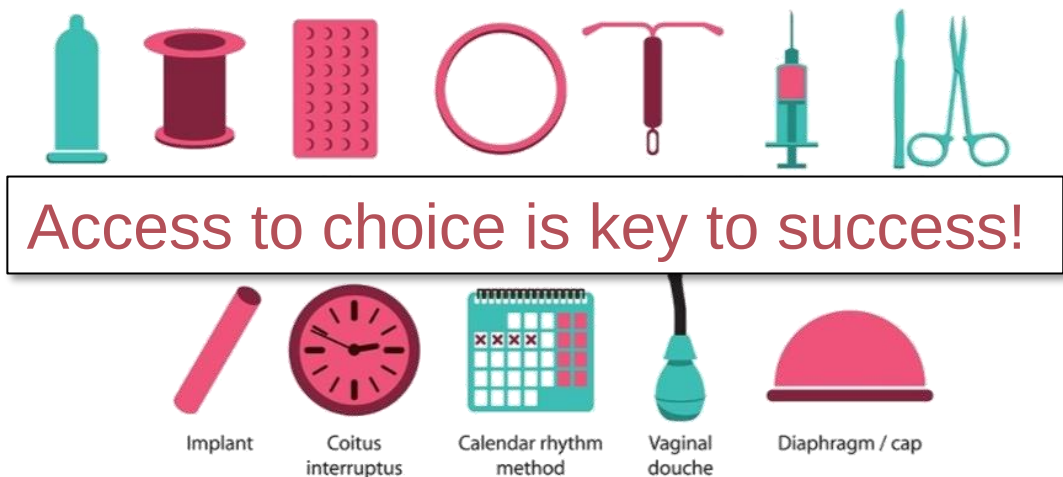
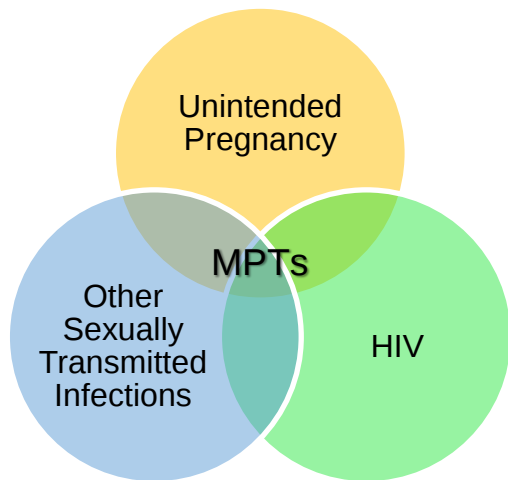


Long-acting multipurpose prevention technology (MPT) implants to prevent HIV & unintended pregnancy

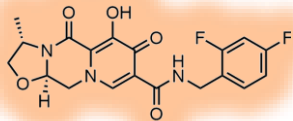
Archana Krovi, Ph.D.
RTI International

Need for multipurpose prevention technologies (MPTs)

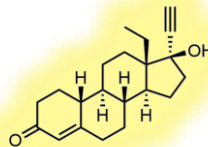
- 121 million unintended pregnancies reported worldwide each year
- Need for effective and easy-to-use platforms
- Long-acting (LA) options highly preferred over daily or on-demand regimens



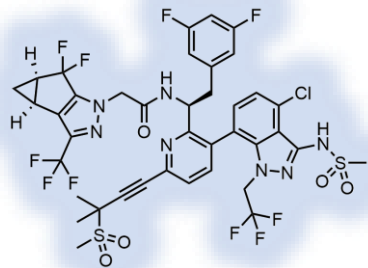
Current LA HIV PrEP and hormonal contraceptive landscape



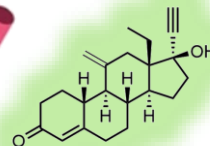
Cabotegravir
Apretude
Every 2 months



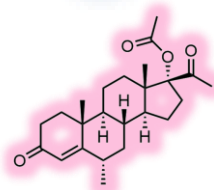
Levonorgestrel
Mirena, Liletta, Kyleena, Skyla
3-8 years



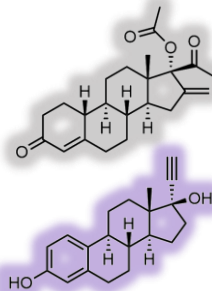
Lenacapavir
Approved on June 19th 2025
Every 6 months



Etonogestrel
Nexplanon
3 years



Medroxyprogesterone acetate
DepoProvera
Every 3 months

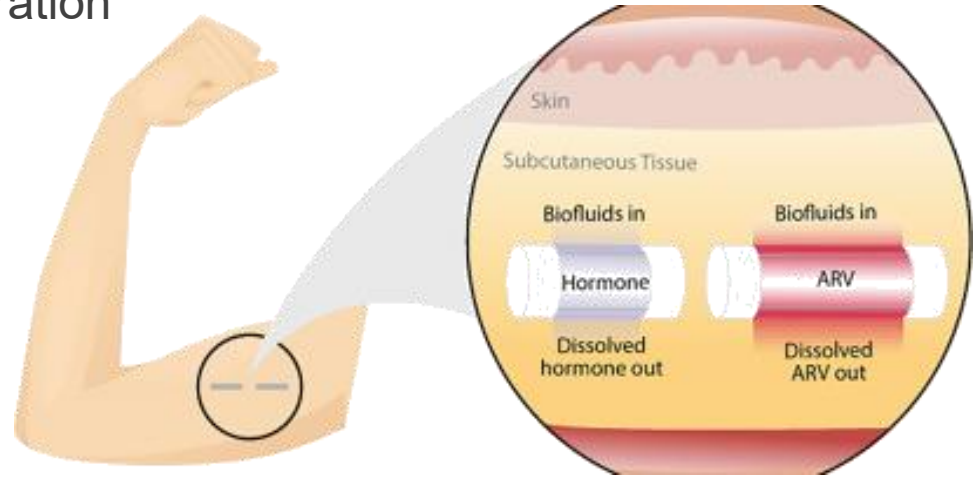


Etonogestrel or
Segesterone acetate + ethinylestradiol
NuvaRing (1 month)
Annovera (1 year)

Currently no long-acting MPT options available

Implants for long-acting MPT

- Sustained, ≥ 6 months therapeutic duration
 - Zero-order release kinetics
 - Capable of multidrug delivery
- Discreet (subcutaneous placement)
- Low burden, mistake-proof
- Trocar-compatible
- Biodegradable (after drug depletion)
- Reversible (during treatment period)



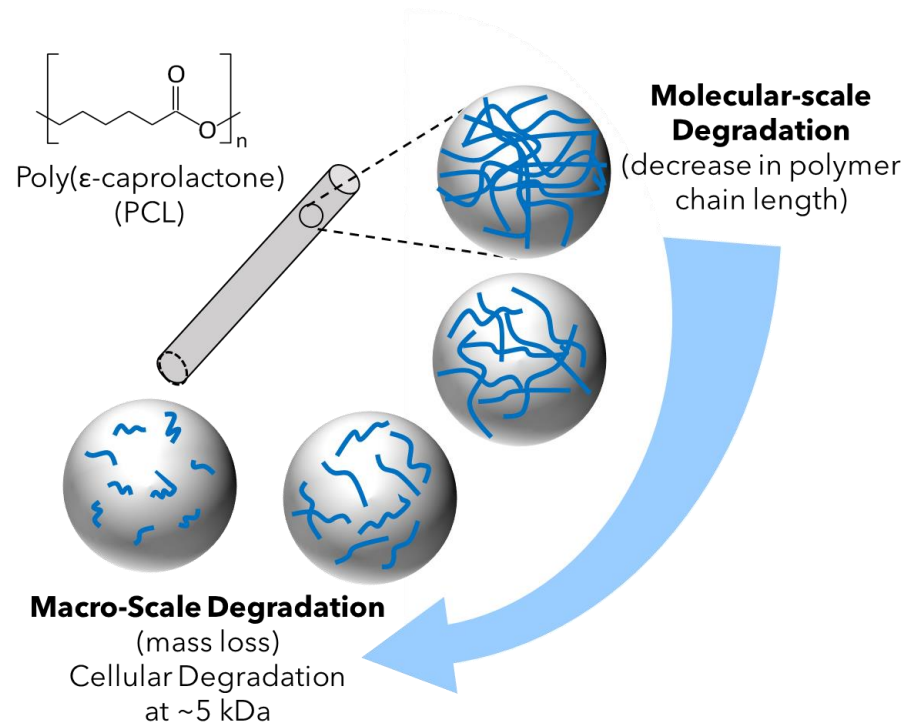
Li et al, *J. Controlled Rel.*, **2021**, 340, 188-199.

Biodegradable implants offer a long-acting alternative to conventional MPT option or technologies currently under development

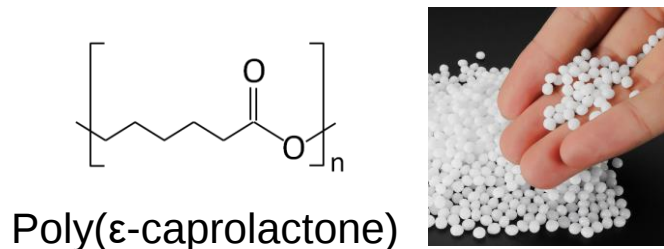
Biodegradable polymer candidate : Poly(ϵ -caprolactone)

- Flexible polyester
- T_m 60°C, T_g -60°C
- Biodegradable
 - Tunable by polymer chain length
 - Capable of >1 year lifetime
- FDA approved in applications
 - Medical sutures (monocryl, glycolon)
 - Root canal filling (resilon)

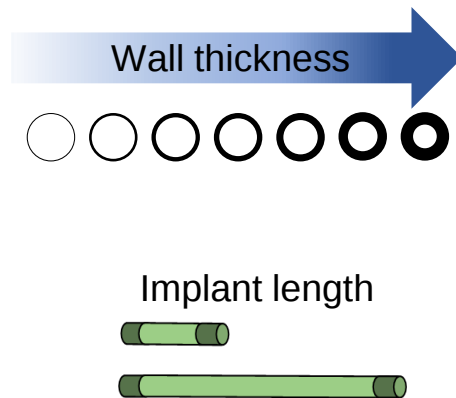
Semi-crystallinity and long-term degradation kinetics make PCL a promising choice



Trocar-compatible implant fabrication



Raw material
to
hollow tubes



1. Seal one end of hollow cylindrical PCL tube



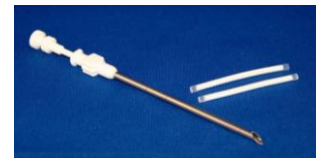
2. Fill with active formulation



3. Seal other end of tube

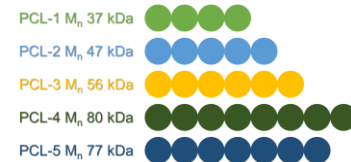


Final implant



Sino II trocar applicator

Polymer molecular weight



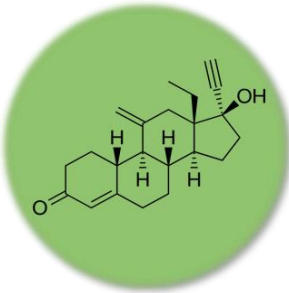
PCL implants are a versatile platform

Krovi et al, Poster presentation, Tech Connect **2022**, Abstract #649

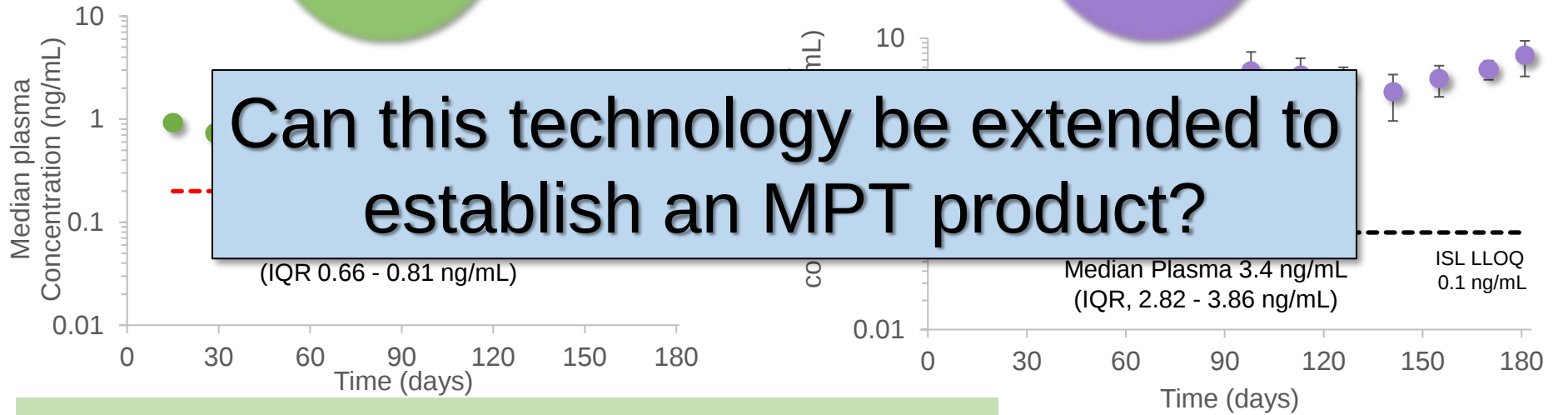
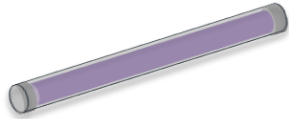
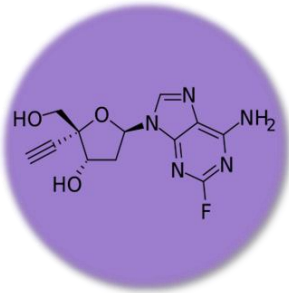
Individual implant performance in female Wistar rats



Etonogestrel
(ENG)



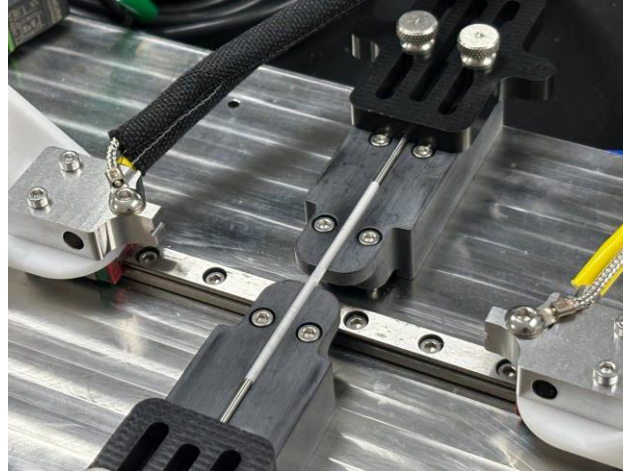
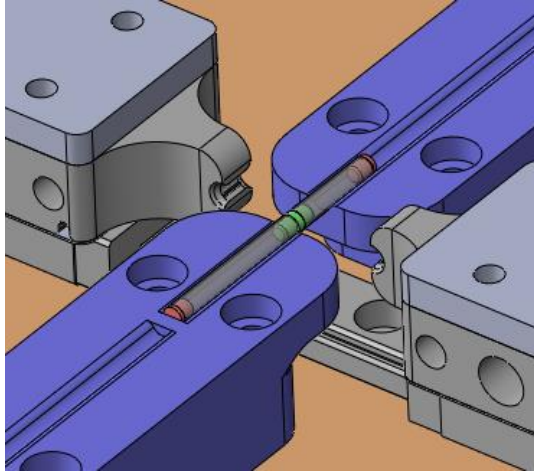
Islatravir
(ISL)



Sustained plasma release achieved from individual implants

Li et al, *J. Controlled Rel.*, **2021**, 340, 188-199.

Single-rod segmented fabrication of MPT implant (trocar-compatible)



Fabrication Method A



Fabrication Method B

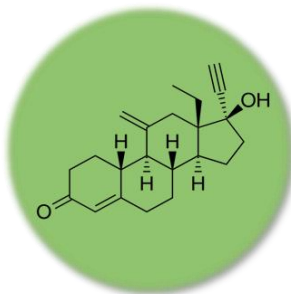
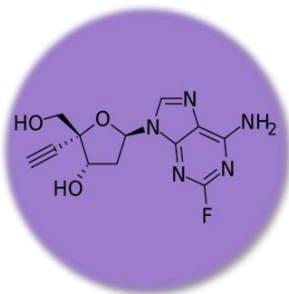


Single rod capable of co-delivery of therapeutics can simplify administration and reduce number of overall implants

Formulation optimization and advancement of lead configurations to preclinical studies

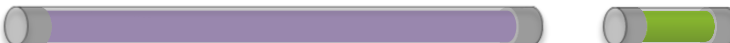
Islatravir
(ISL)

ISL : glycerol (1:1 w/w%)
30 mm implant segment length

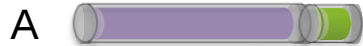


Etonogestrel
(ENG)

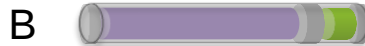
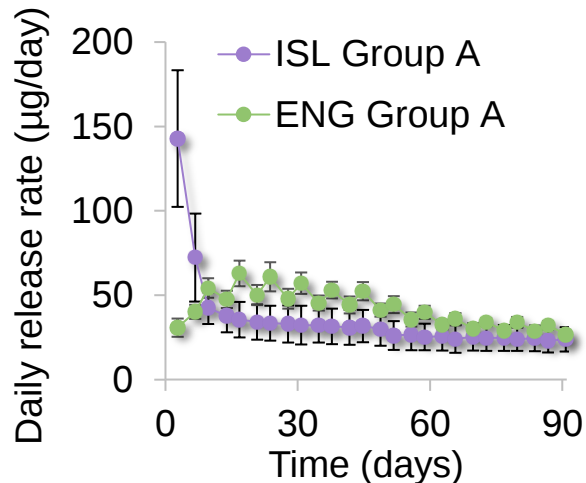
ENG : PEG40 castor oil (2:1 w/w%)
5 mm implant segment length

- Group A  Separate tubes joined with PCL spacer
- Group B  Single tube with PCL spacer
- Group C  Individual implants

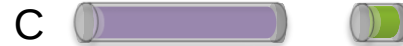
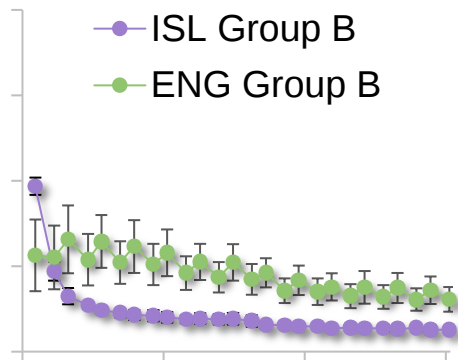
In vitro release profiles of lead MPT implant configurations



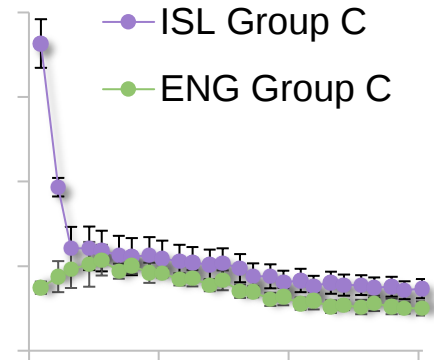
ISL release rate : 27 ± 3 $\mu\text{g/day}$
ENG release rate : 39 ± 9 $\mu\text{g/day}$



ISL release rate : 16 ± 3 $\mu\text{g/day}$
ENG release rate : 41 ± 8 $\mu\text{g/day}$



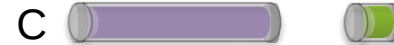
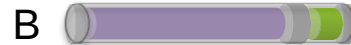
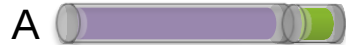
ISL release rate : 44 ± 7 $\mu\text{g/day}$
ENG release rate : 33 ± 7 $\mu\text{g/day}$



Sustained co-delivery of ISL and ENG achieved from a segmented form factor

Krovi *et al*, manuscript in preparation

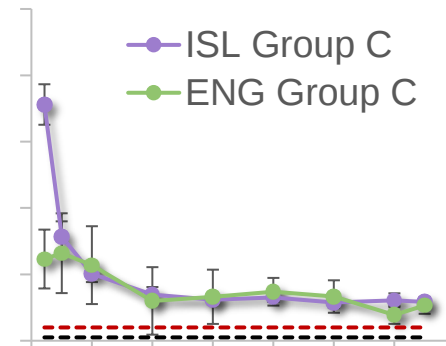
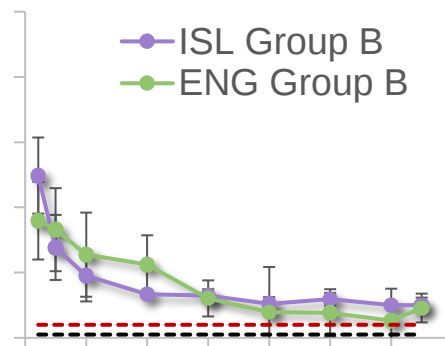
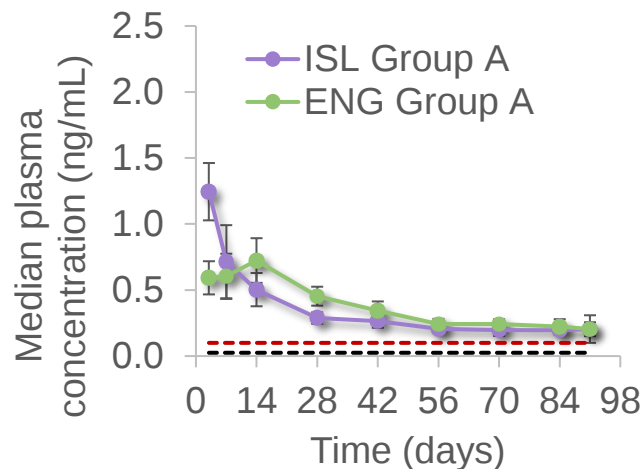
Safety and PK evaluation in NZW rabbit model



ISL median 0.21 (0.19-0.24) ng/mL
ENG median 0.25 (0.22-0.27) ng/mL

ISL median 0.26 (0.25-0.28) ng/mL
ENG median 0.22 (0.20-0.30) ng/mL

ISL median 0.31 (0.29-0.33) ng/mL
ENG median 0.32 (0.28-0.36) ng/mL



Implants were well-tolerated with sustained plasma profiles for 90 days

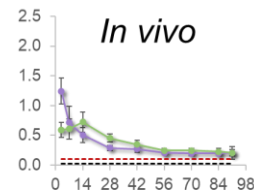
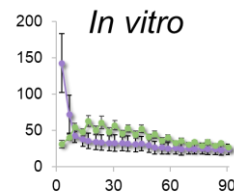
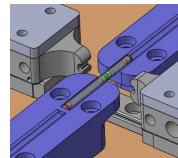
----- ISL LLOQ 0.025 ng/mL
----- ENG LLOQ 0.1 ng/mL

Krovi et al, manuscript in preparation

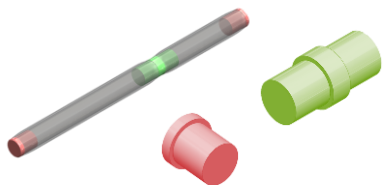
Conclusions and Future Directions

Conclusions

- Fabricated single-rod, trocar-compatible MPT implant configurations with lead ENG and ISL formulations
- Achieved sustained and simultaneous release *in vitro* and *in vivo* of both contraceptive and antiretroviral from a single-rod implant



Future Directions



- Optimize formulation to achieve co-depletion of both therapeutics and polymer selection to tailor biodegradation timeline
- Improve assembly process development by using molded plug designs and automated implant filling approaches (pneumatic filling, hydraulic press, arbor press)

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