

Refillable-nanofluidic implants for HIV PrEP

September 5th, 2018

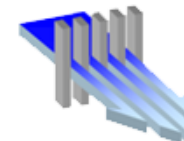
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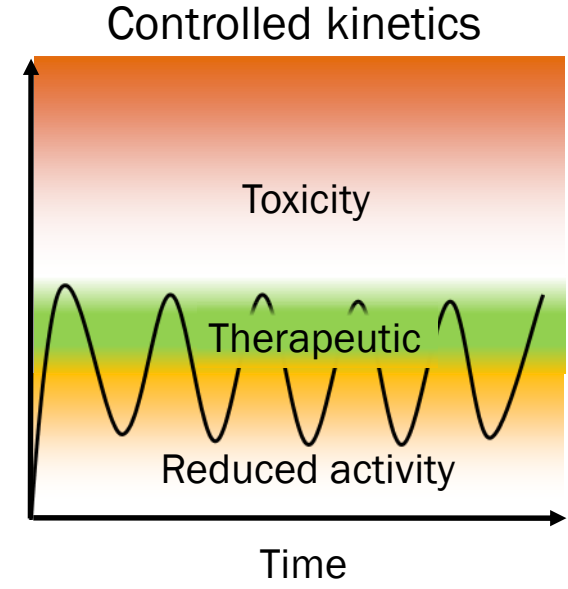
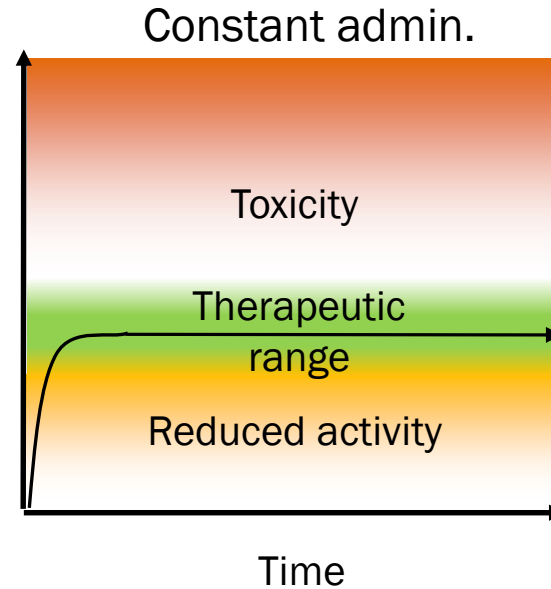
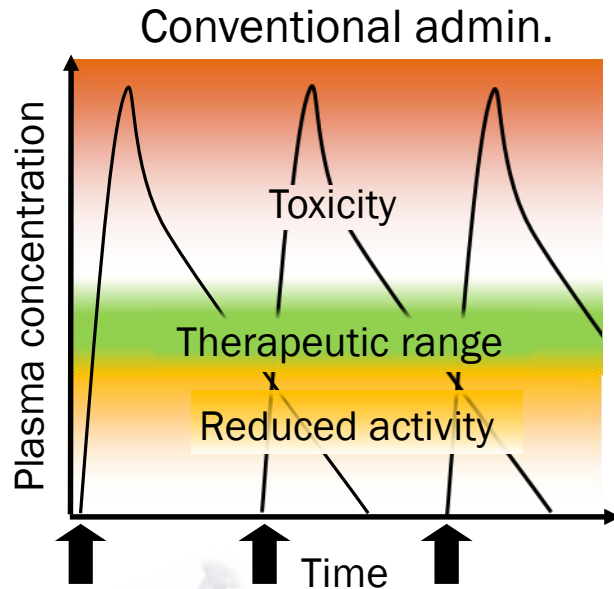
George and Angelina Kostas



Vivian L. Smith
Foundation



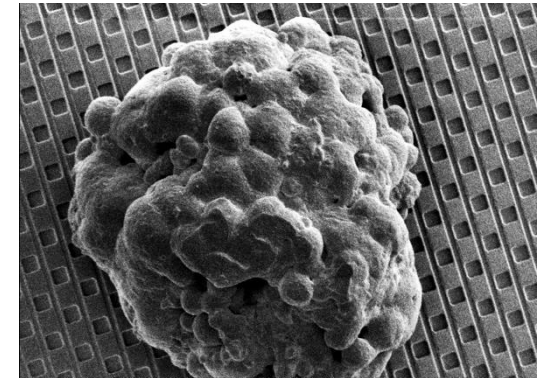
THE NEED FOR ALTERNATIVE DRUG DELIVERY STRATEGIES



- ✓ Repetitive admin.
- ✓ Large drug doses
- ✓ Adverse side effects
- ✓ Poor compliance



- ✓ Sustained release
- ✓ Minimization of drug dose
- ✓ Reduced side effects
- ✓ Assure compliance



- ✓ Bio-responsive
- ✓ *Ad hoc* delivery

SUSTAINED DRUG DELIVERY SYSTEMS

Reservoir-based
polymeric Implants



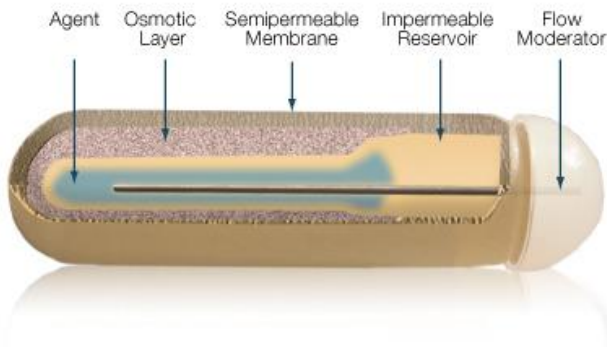
Biodegradable
polymeric rods



Long-acting depots



Osmotic pumps



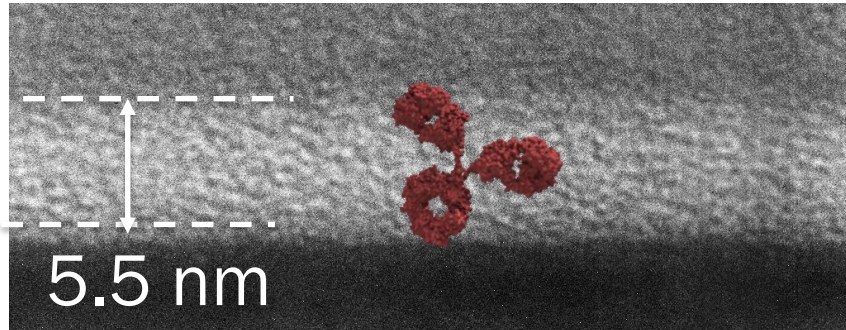
Wearable external pumps



MicroCHIP devices



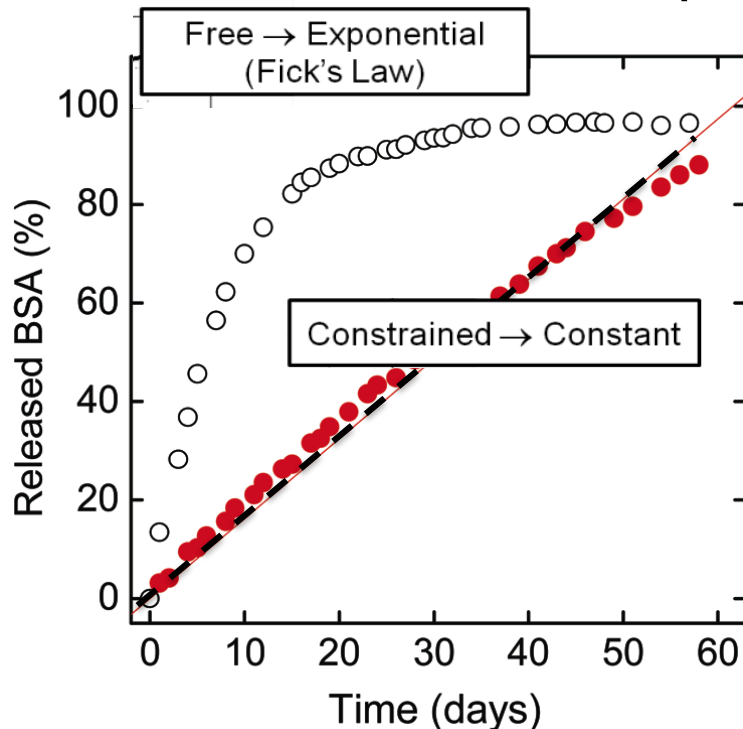
NANOFLUIDICS



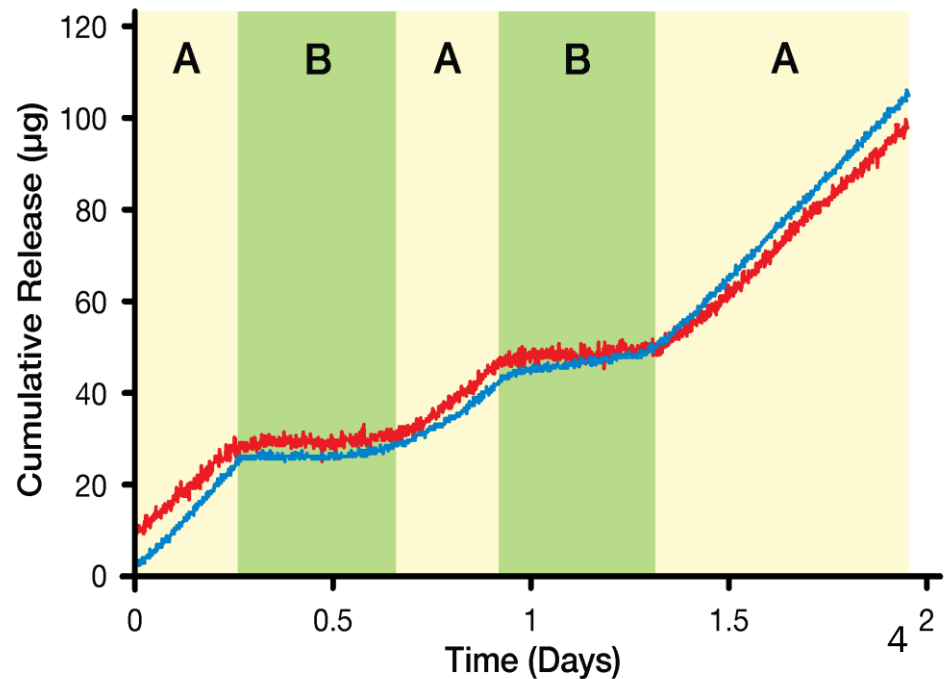
No pumps
No valves



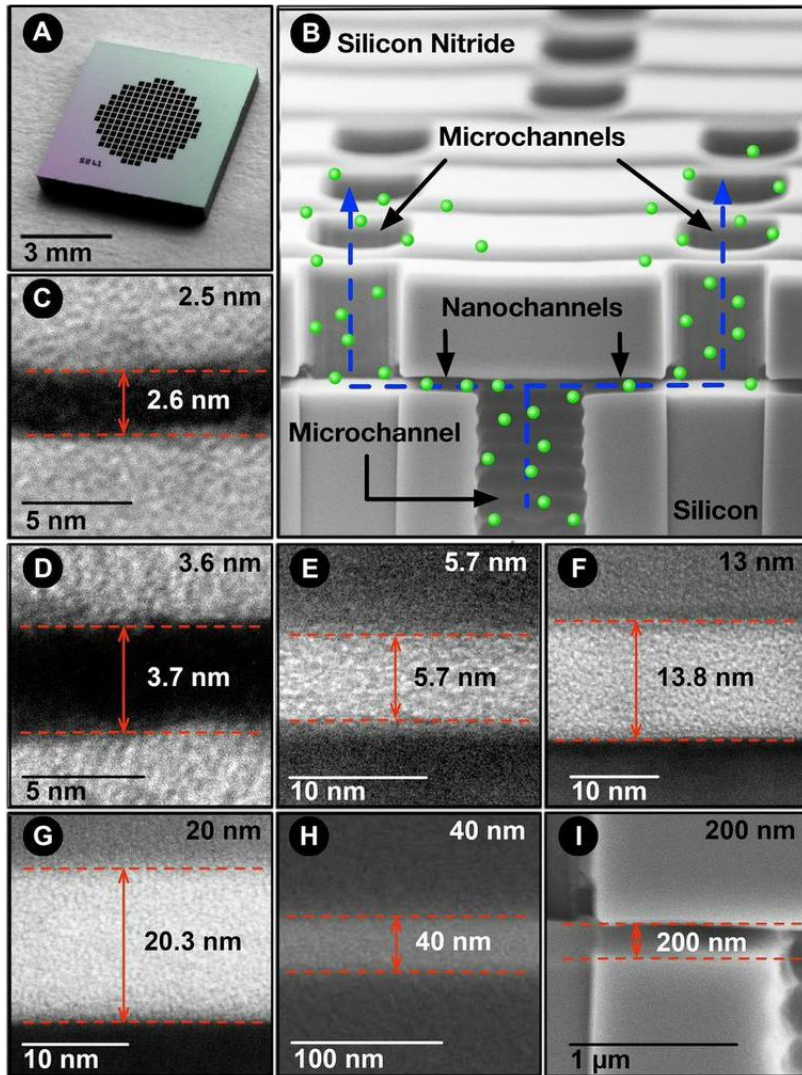
Concentration-driven transport



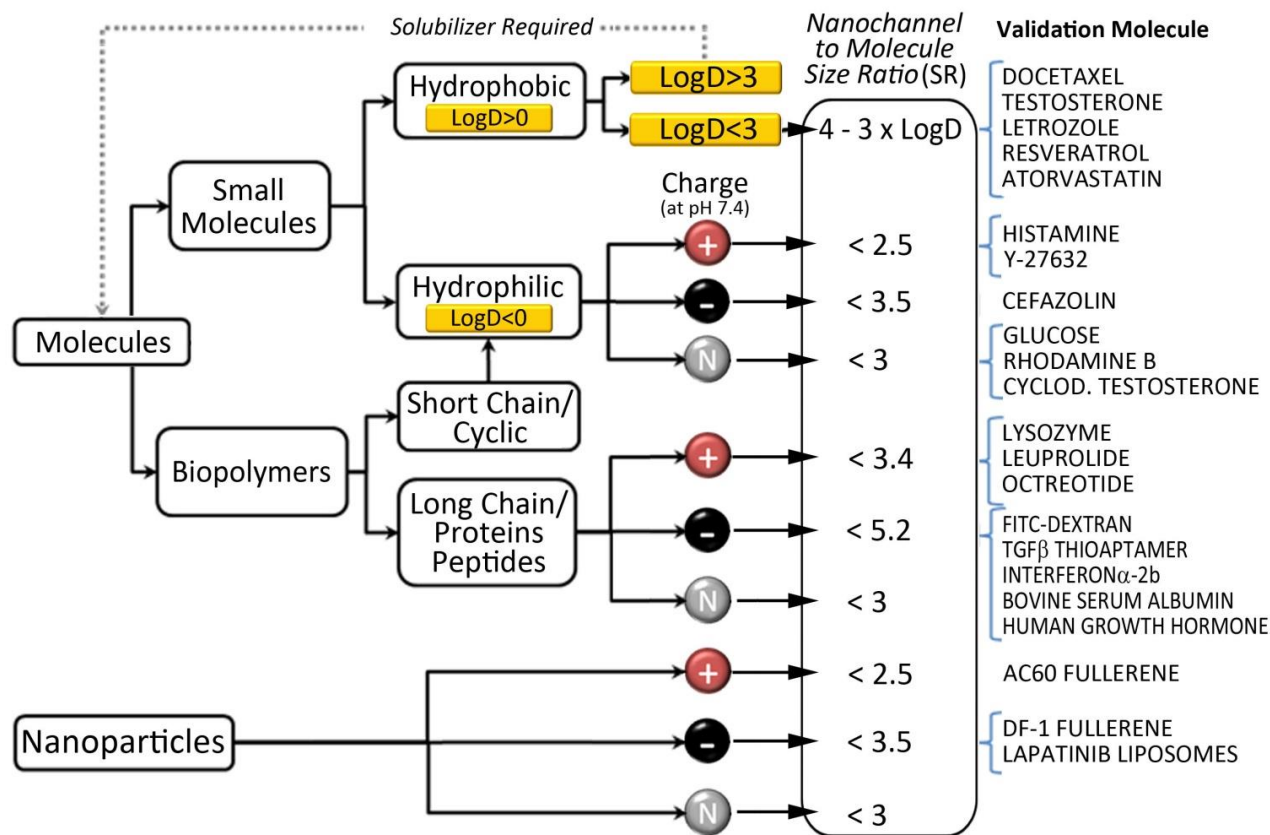
Electrokinetic transport



NANOCHANNEL MEMBRANE

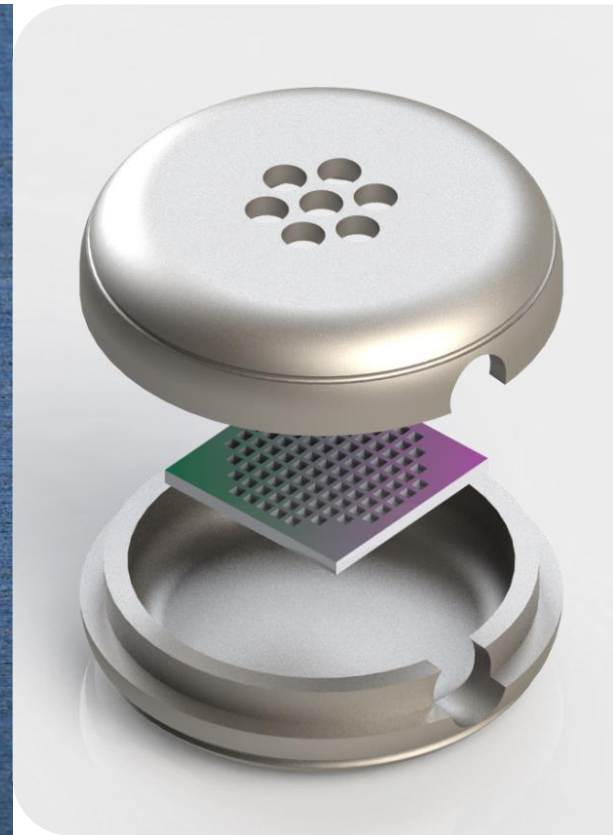
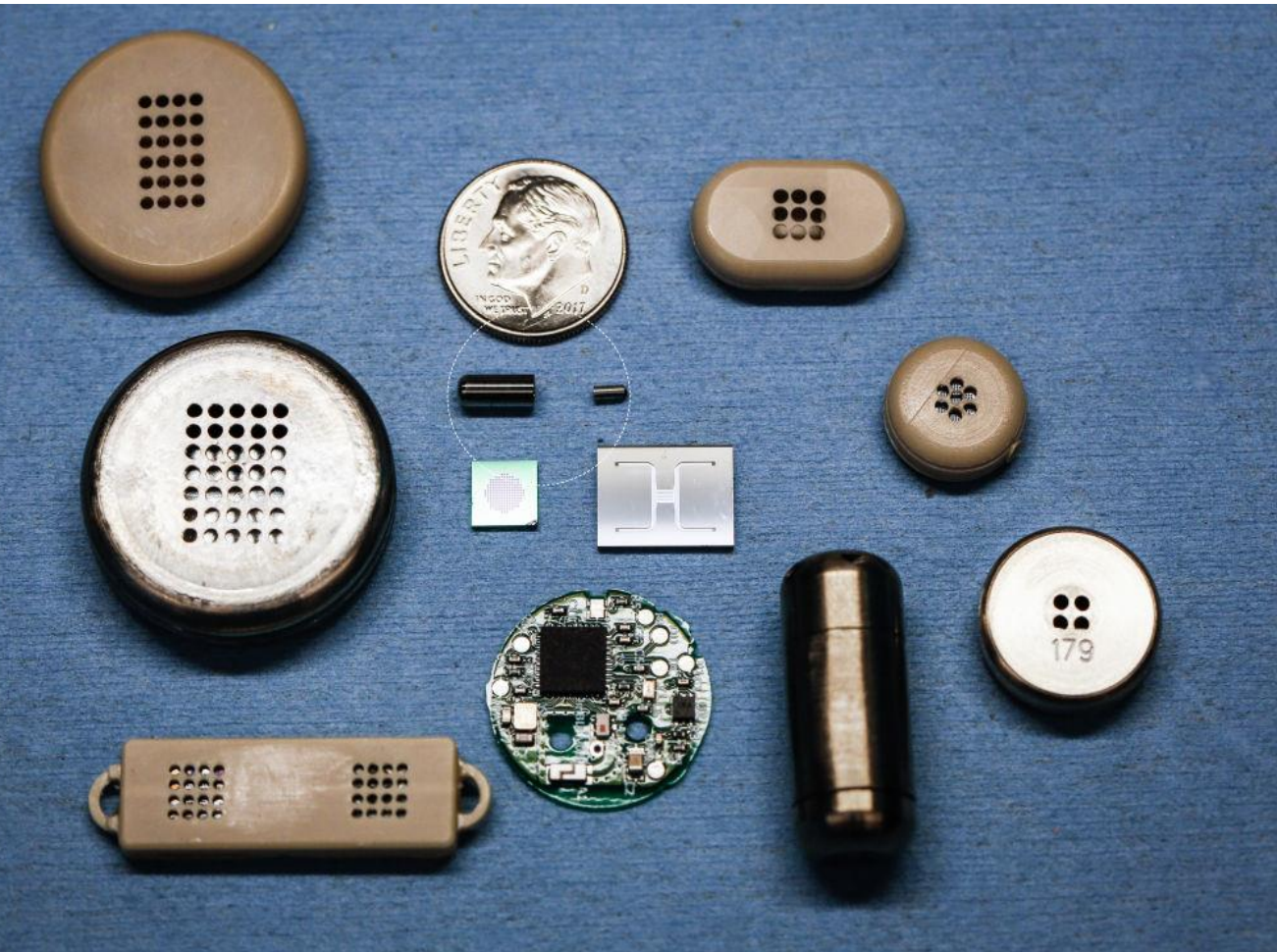


NANOCHANNEL SELECTION



Molecule	MW (Da)	LogD (pH 7)	Charge (pH 7)	Mol Size (Å)	nCH size (nm)	SR
Interferonα-2b	19,200	-	-2	42	22	5.2
hGH	22,100	-	-5	52	20	3.8
Leuprolide	1,209	-	2.3	14	3.6	2.6
Octrotide	1,019	-	1.4	14	3.6	2.6
Letrozole	289	2.5	0	18	3.6	2.0
Y-27632	247	-1.2	1	15	3.6	2.4

NANOCHANNEL IMPLANTS



Ferrati et al. *J. Controlled Release*, 2013
Hood R.L. et al. *J. Biomedical Nanotechnology*, 2016
Ferrati et al. *Advanced Healthcare Materials*, 2014

HIV STATISTICS

Number of new HIV infections in 2016 and change since 2010

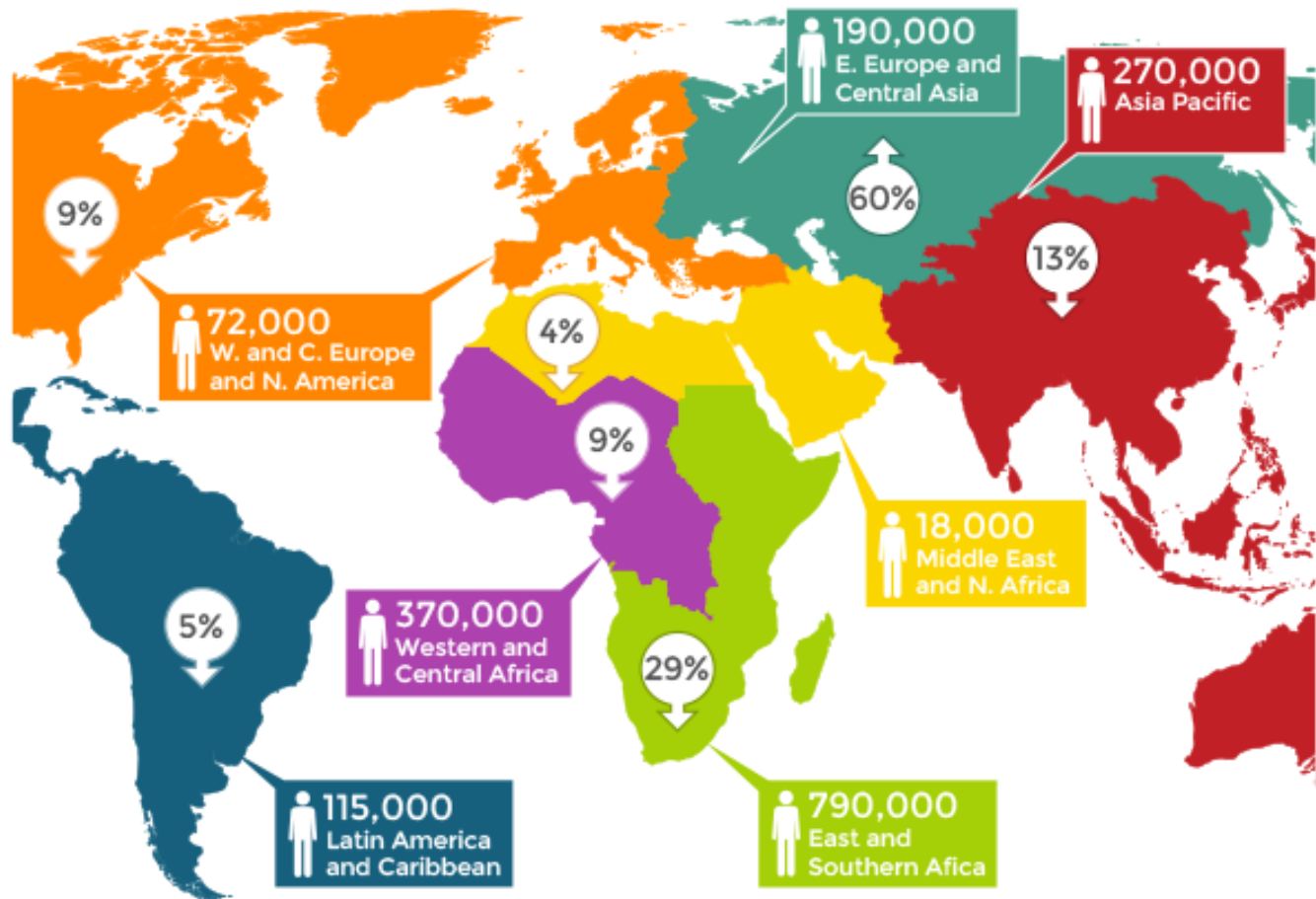
1.8 million
people newly
infected in
2016 globally

Decrease in
number of new
infections across
the global
population each
year since 2010

16%

AVERT.org

Source: UNAIDS Data 2017



HIV PrEP FACTS

PrEP Works...If You Take It

Trial	Efficacy	Adherence
CAPRISA 004 ⁶	1% tenofovir gel: 39%	51%
iPrEx ⁷	Oral daily Truvada: 42%	51%
Partners PrEP ⁸	Oral daily tenofovir: 67% Oral daily Truvada: 75%	83% 81%
TDF2 ⁹	Oral daily Truvada: 62%	81%



In iPrEx OLE,

PEOPLE WHO TOOK TRUVADA
4 TIMES A WEEK HAD
NO NEW INFECTIONS—

100% EFFICACY.

PEOPLE WHO TOOK TRUVADA
2 OR 3 TIMES A WEEK HAD AN
84% LOWER RISK
OF INFECTION.

BUT THOSE WHO TOOK
FEWER THAN 2 DOSES SAW
NO SIGNIFICANT
PROTECTION.

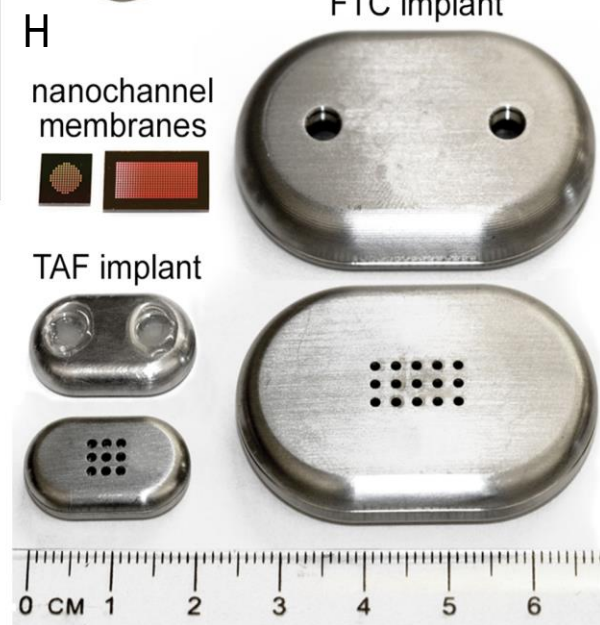
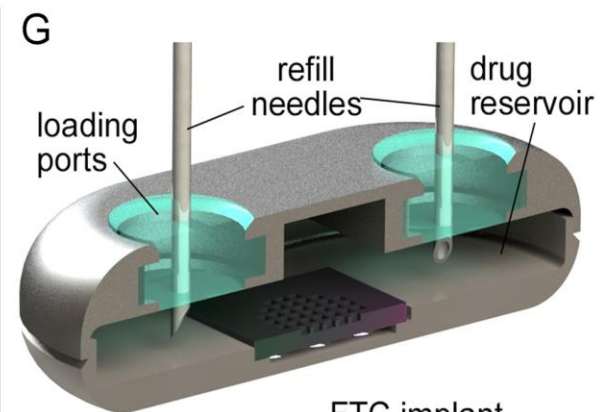
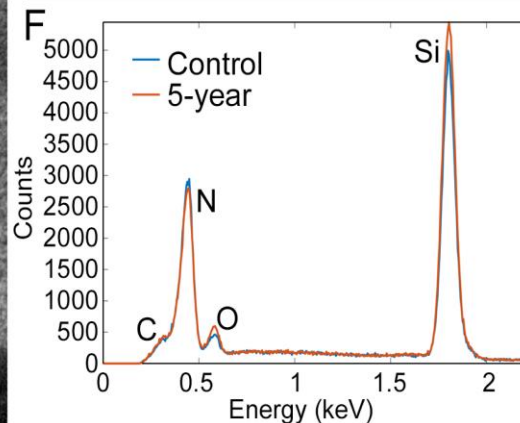
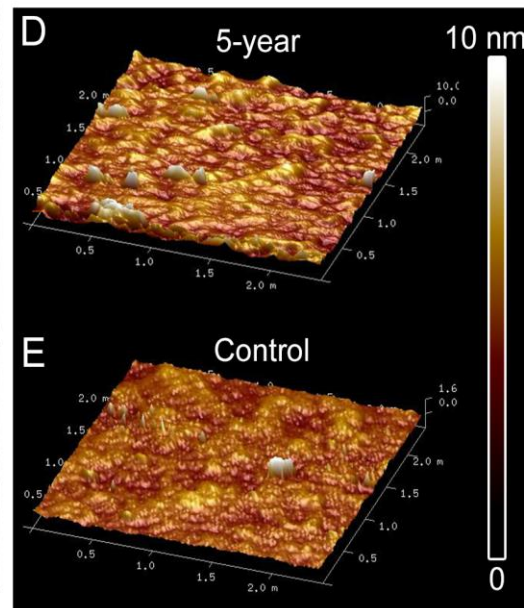
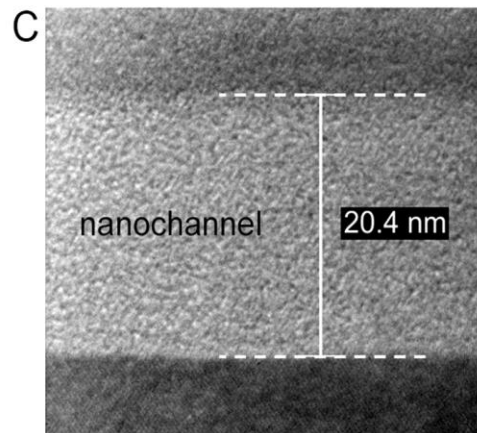
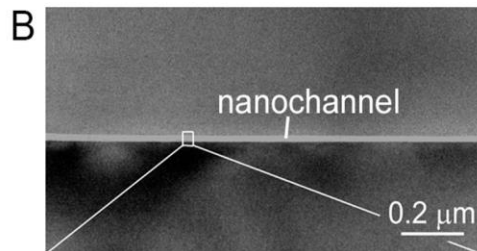
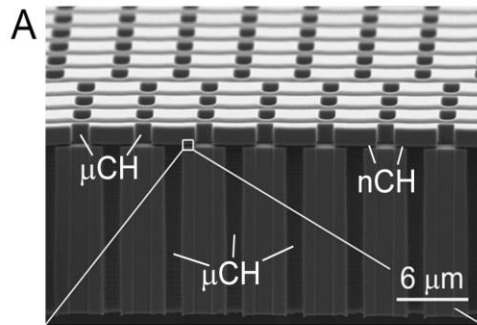
TRUVADA (Gilead) = TDF + FTC

TDF = Tenofovir Disoproxil Fumarate (nucleoside reverse transcriptase inhibitor)

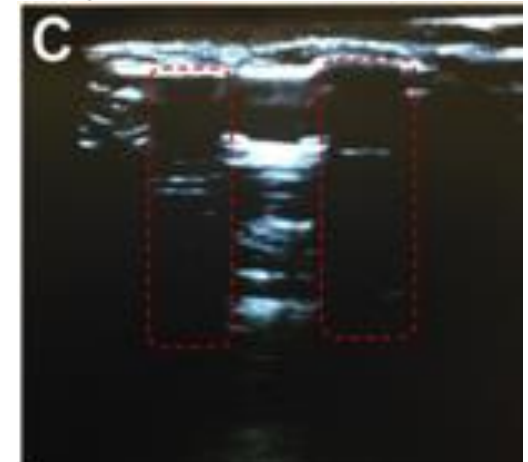
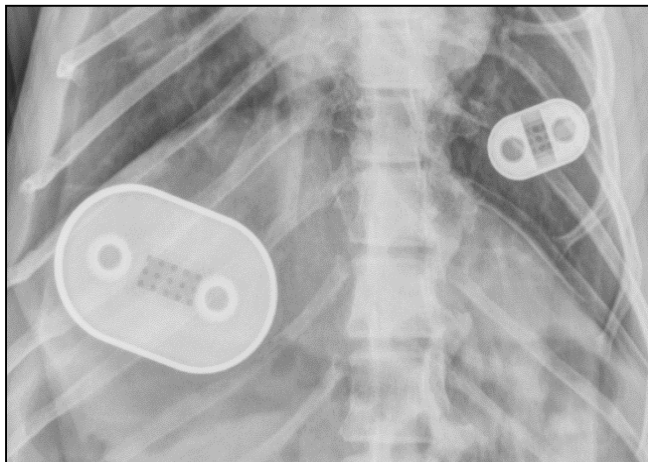
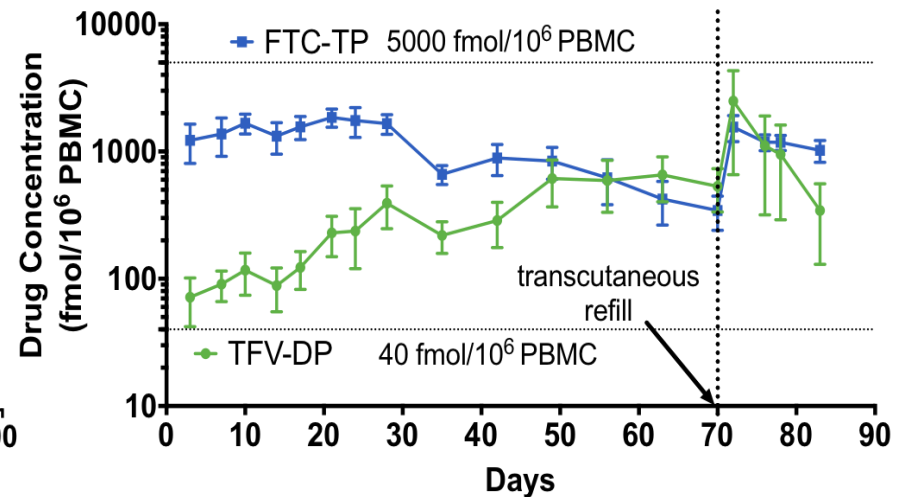
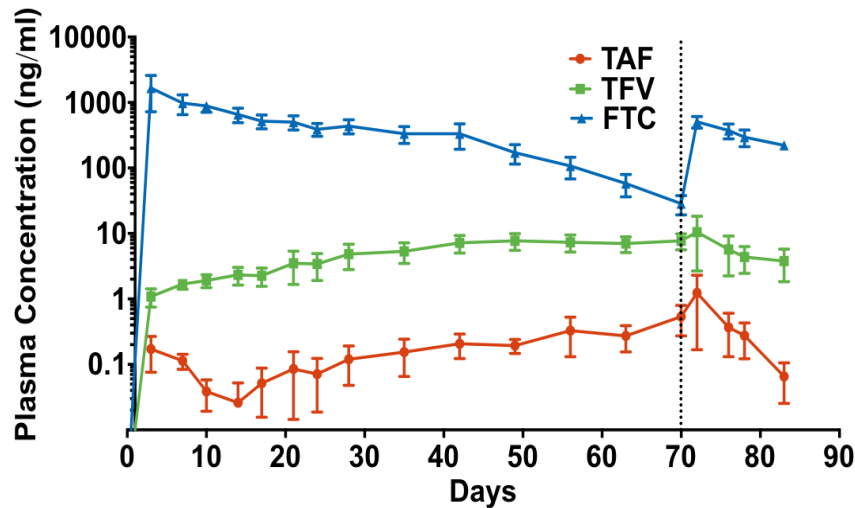
FTC = Emtricitabine (NRTI)

TAF = Tenofovir Alafenamide Fumarate (nucleotide reverse transcriptase inhibitor)

NANOFLUIDIC IMPLANT FOR HIV PREVENTION



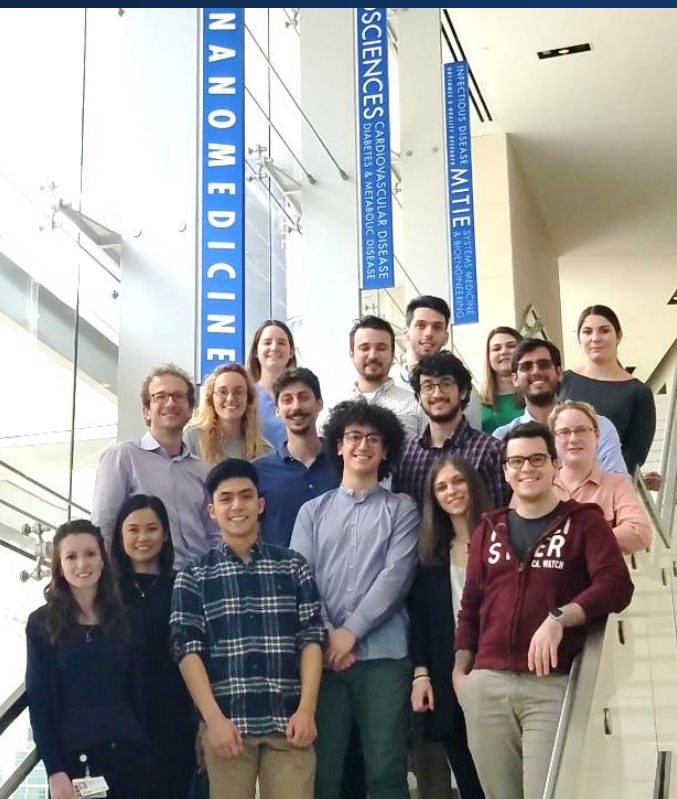
NANOFLUIDIC IMPLANT FOR HIV PREVENTION TAF+FTC



The TEAM

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- Roberto Arduino, M.D. UTHSC Medical School
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ACKNOWLEDGEMENTS



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- Nicola Di Trani, M.S. student
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Collaborators

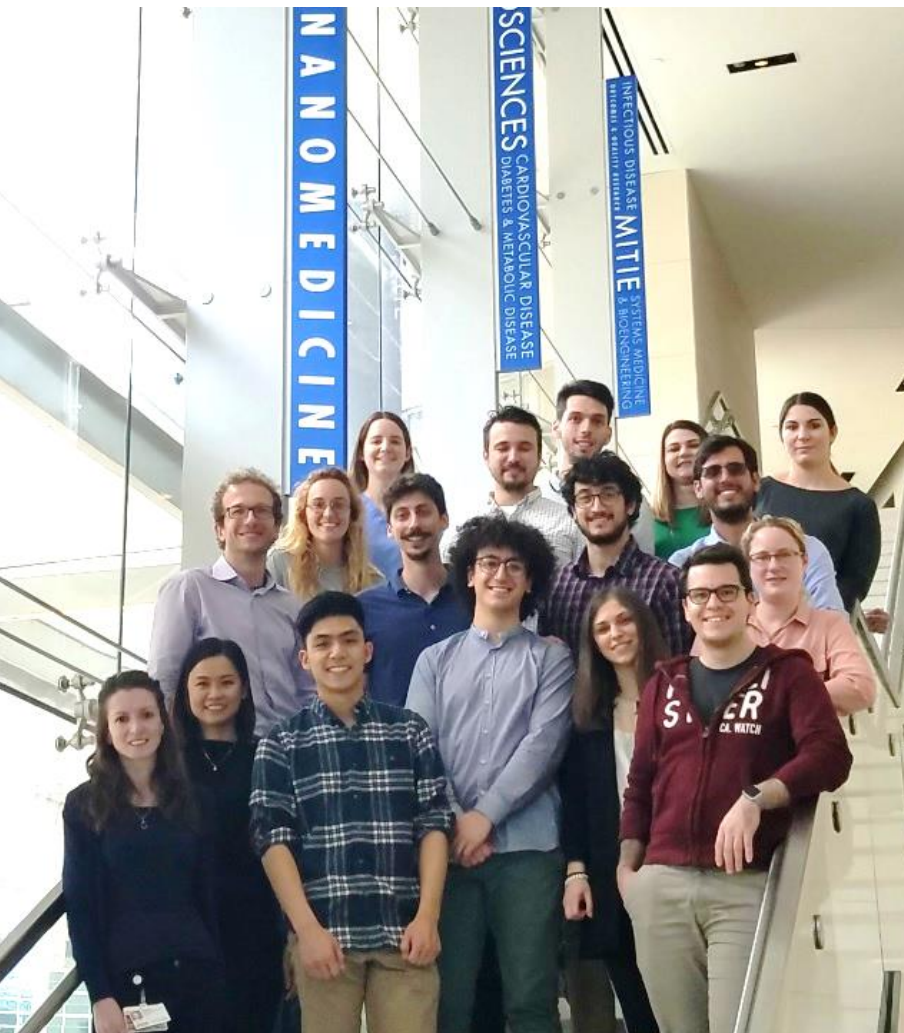
- Alberto Pimpinelli, Ph.D.
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- Peter Anderson, Ph.D.
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