Gastrointestinal Devices for Long-Term In Situ Delivery of Therapeutic Microbes

Miguel Jimenez

Postdoctoral Associate
Langer Lab

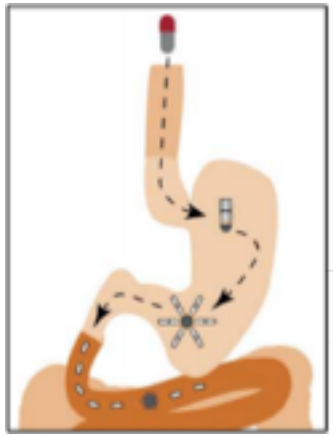
Koch Institute

MIT

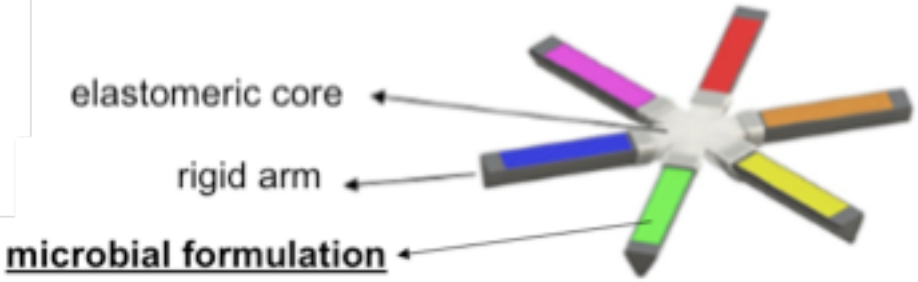
TRISH Virtual Forum, May 23, 2018

team & project overview

gastric residence



microbial delivery



stomach injury model

Aim 1. **Microbe formulations compatible with gastric residence.**

Aim 2. **Device safety for spaceflight and in vivo validation.**

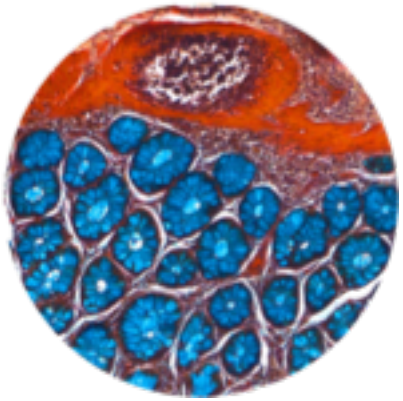
Robert Langer
PI – *biotechnology, materials, drug delivery*

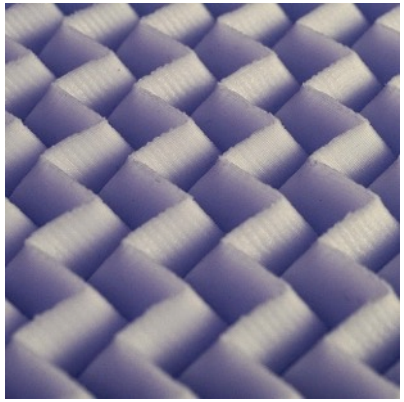
Giovanni Traverso
Collaborator - *gastroenterologist, devices, drug delivery*

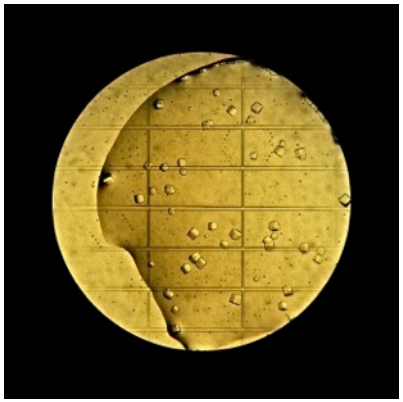
Alison Hayward
Veterinarian - *animal models, drug delivery*

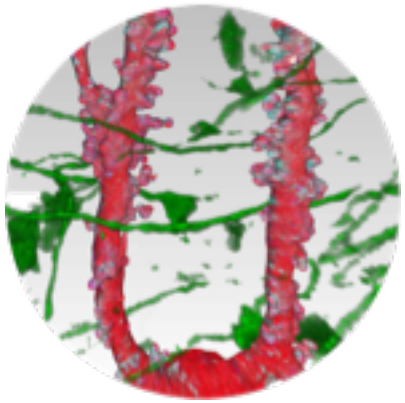
Miguel Jimenez
Postdoc – *synthetic and chemical biology, microbiology*

Koch Institute of Integrative Cancer Research









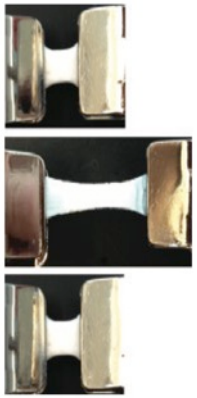
KOCH INSTITUTE
for Integrative Cancer Research at MIT

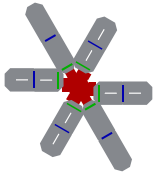
The Langer Lab @ MIT

Massachusetts Institute of Technology

LANGER LAB

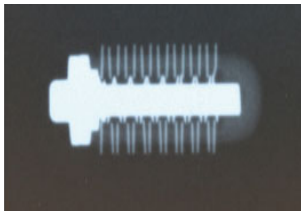
gastrointestinal delivery “GI group” @ Langer Lab



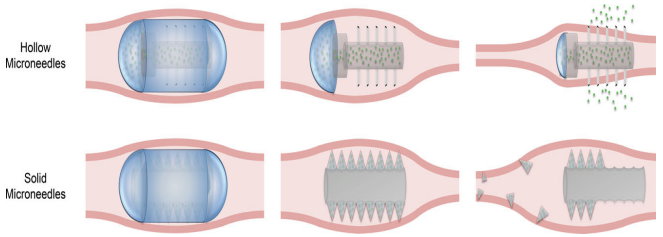


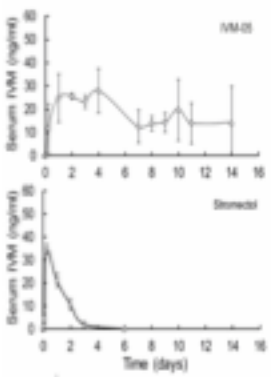
Adherence Solutions

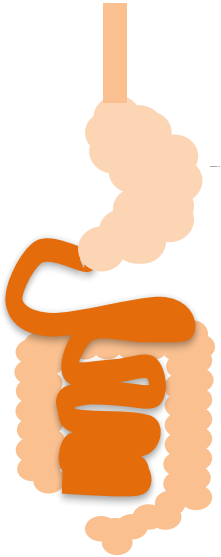
Physical Modes of Delivery



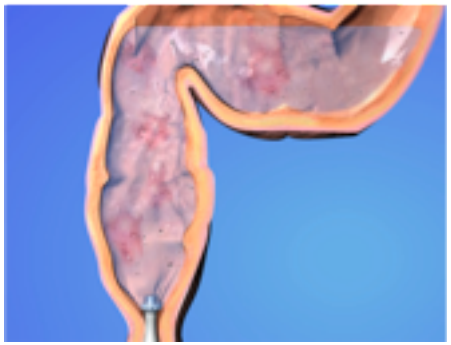
Microneedle systems



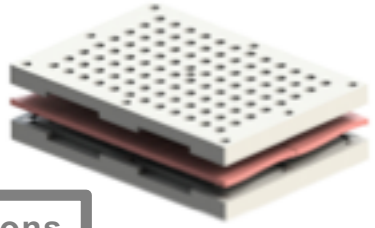


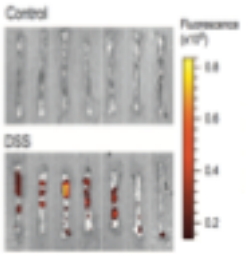


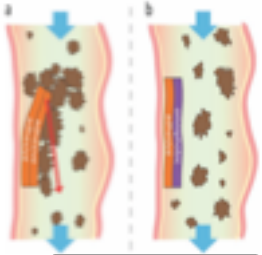
Ultrasound-based systems



High-throughput formulation dev







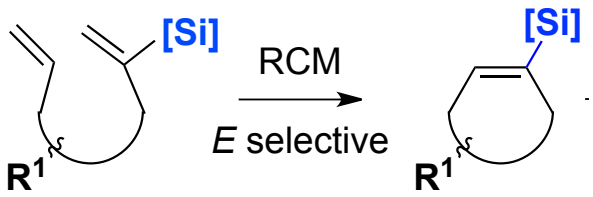
Dosage form Texturing

Inflammation targeting

Novel Formulations

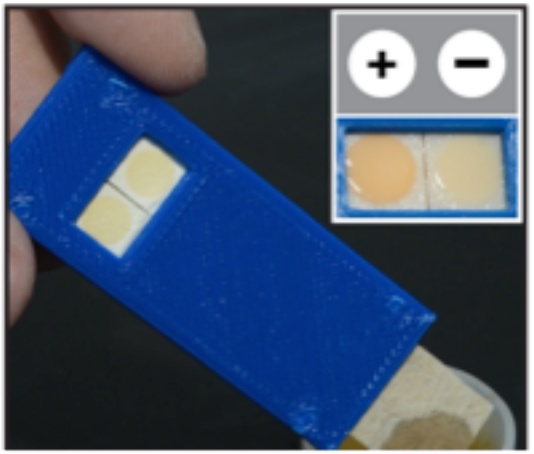
Undergraduate
2007 - 2011
Stuart Schreiber
Damian Young
Harvard University

macrocyclic
ring-closing metathesis
of vinylsilanes



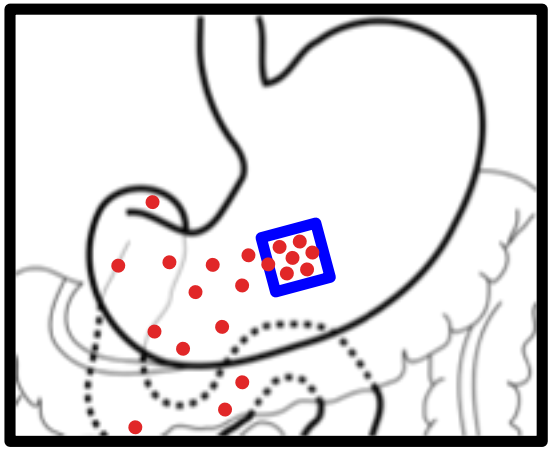
Ph.D.
2011 - 2017
Virginia Cornish
Columbia University

yeast sensor for
low-cost point-of-care
pathogen detection

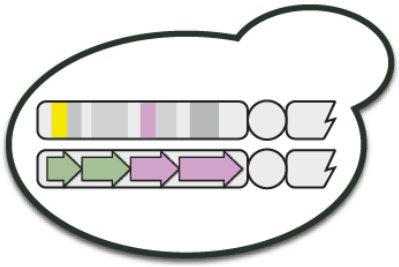


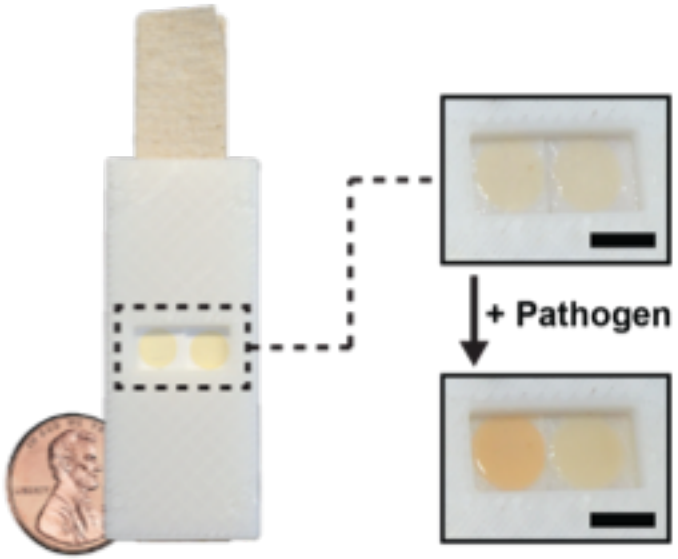
Postdoctoral
2017 – current
Robert Langer
MIT

microbiome
drug delivery
in the GI tract



The Cornish Group





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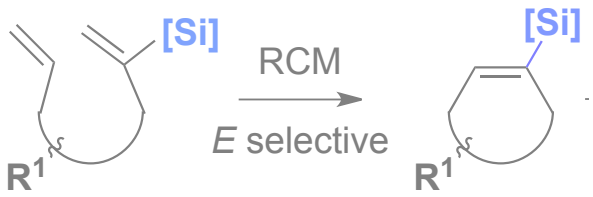

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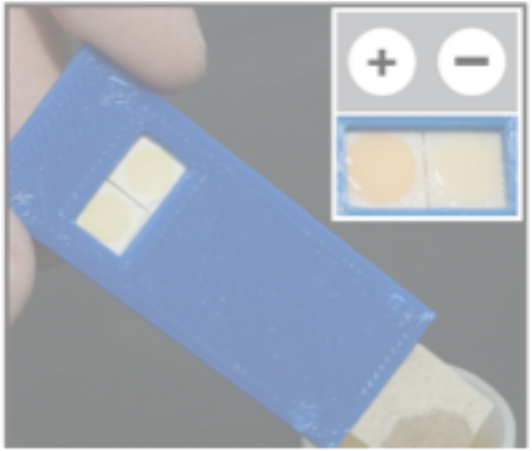

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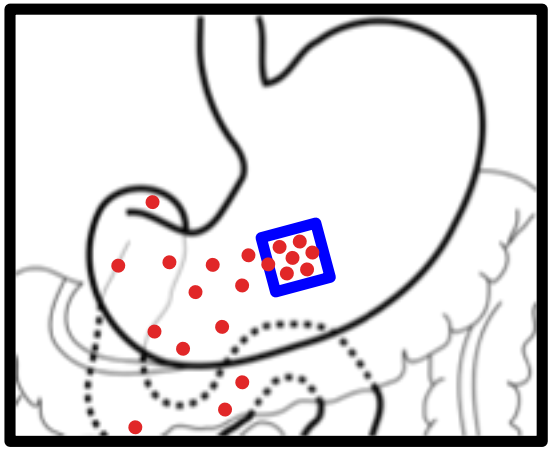
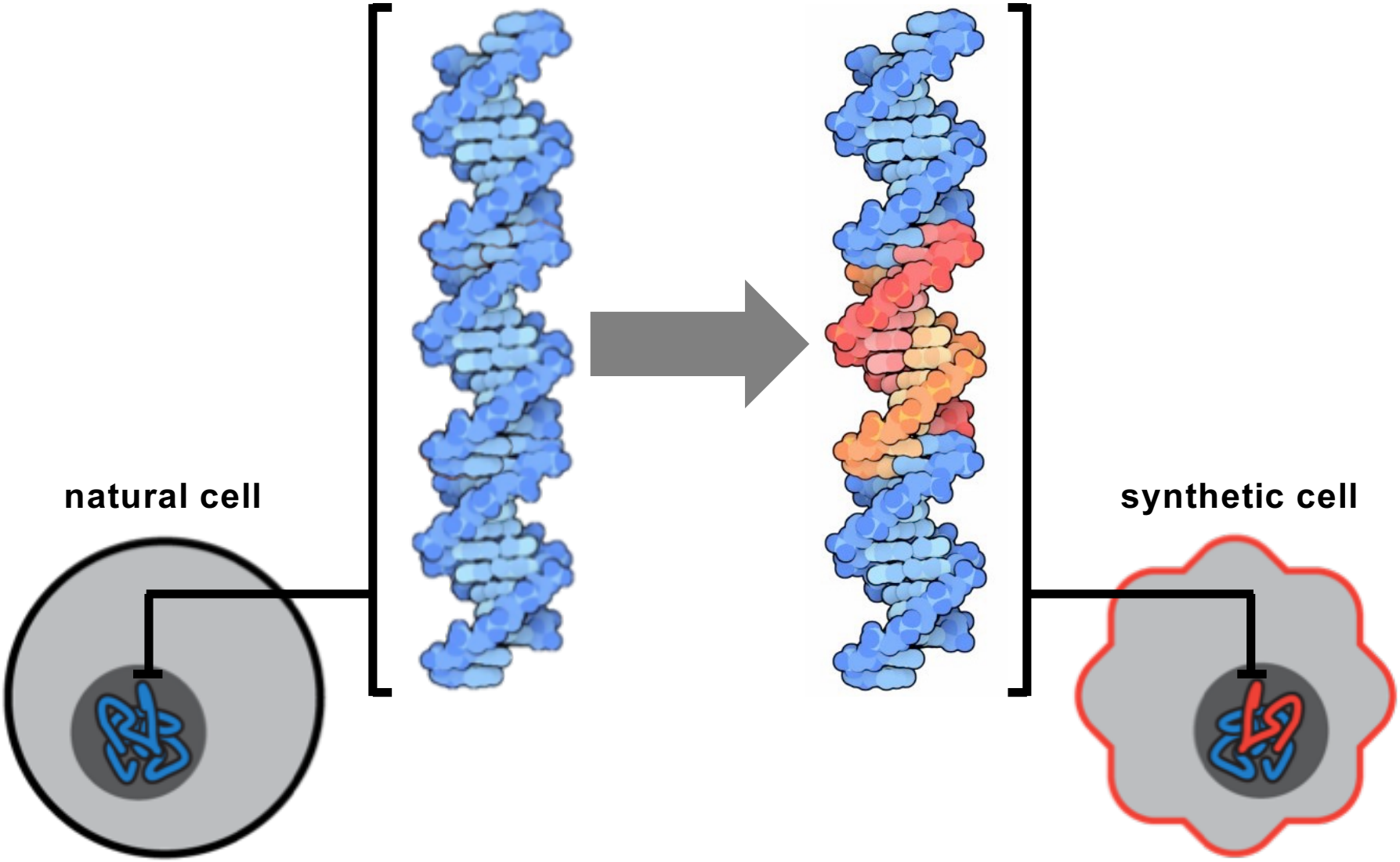
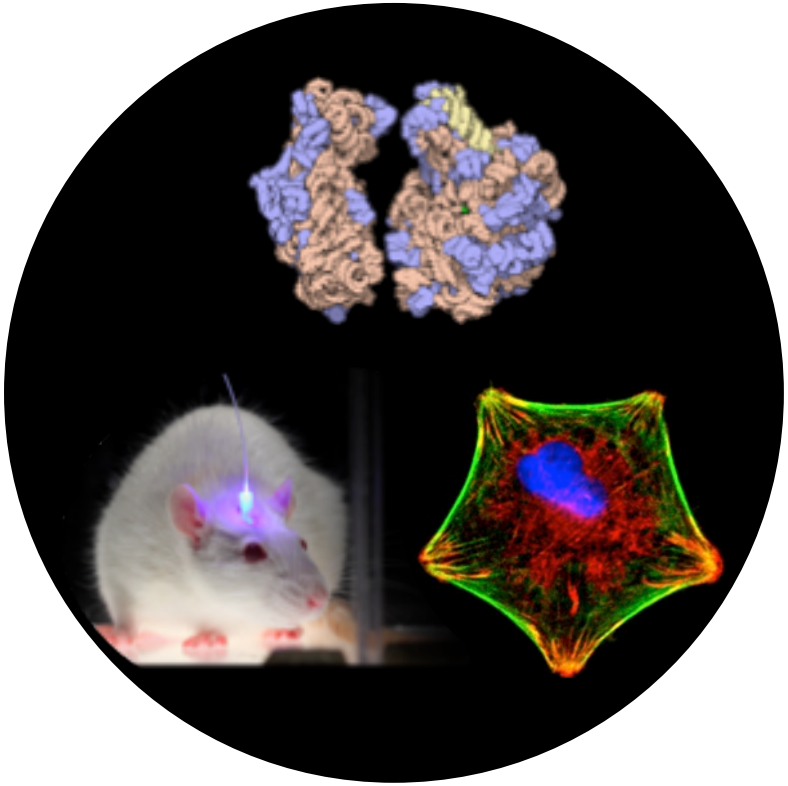


Synthetic biology means building with **DNA**



synthetic biological systems are used for **basic research** and practical **applications**

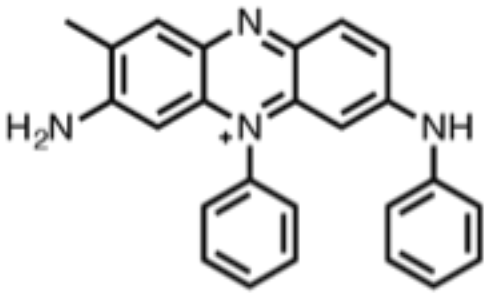
basic research



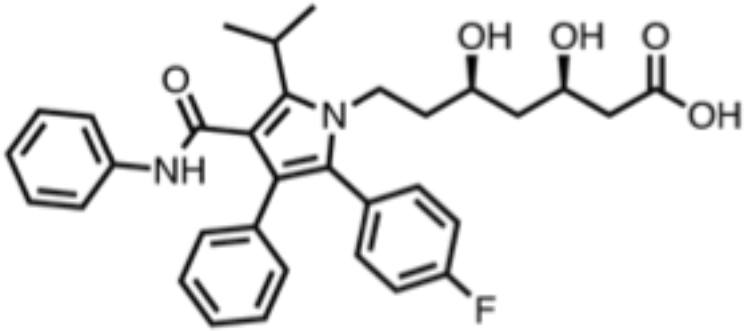
applications

powerful applications of synthesis have been **practical**

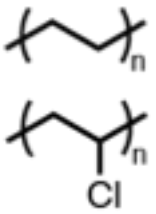
dyes



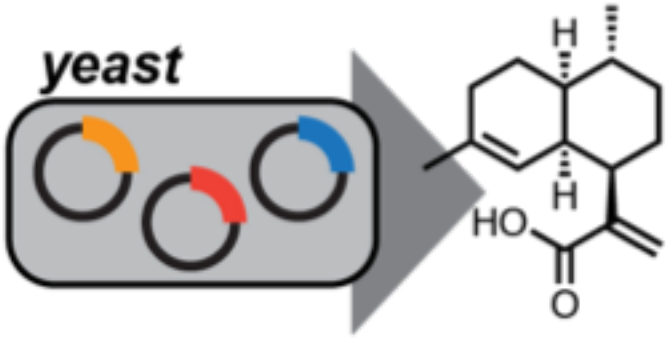
drugs



plastics



therapeutic antibodies

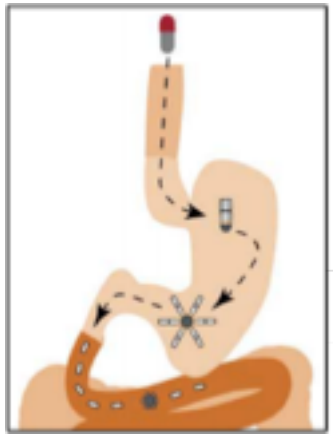


yeast-made drugs

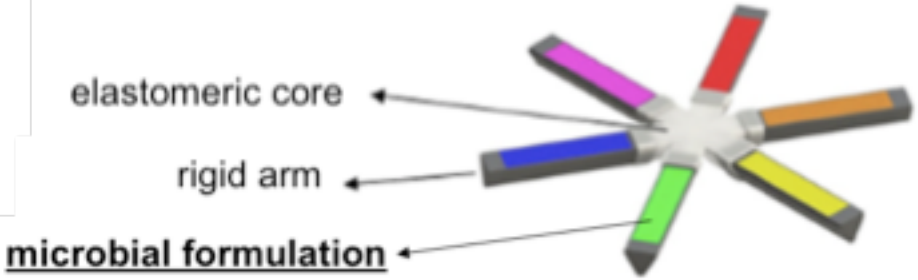
chimeric antigen receptor (CAR-T cells)

team & project overview

gastric residence



microbial delivery



stomach injury model

Aim 1. **Microbe formulations compatible with gastric residence.**

Aim 2. **Device safety for spaceflight and in vivo validation.**

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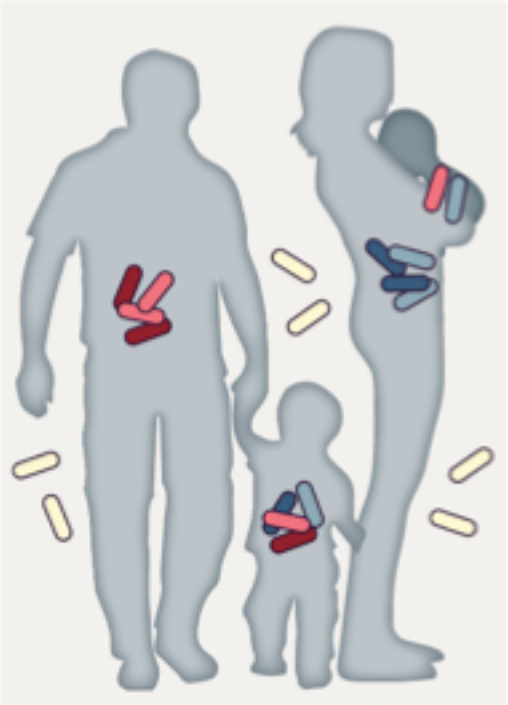
Veterinarian - *animal models, drug delivery*

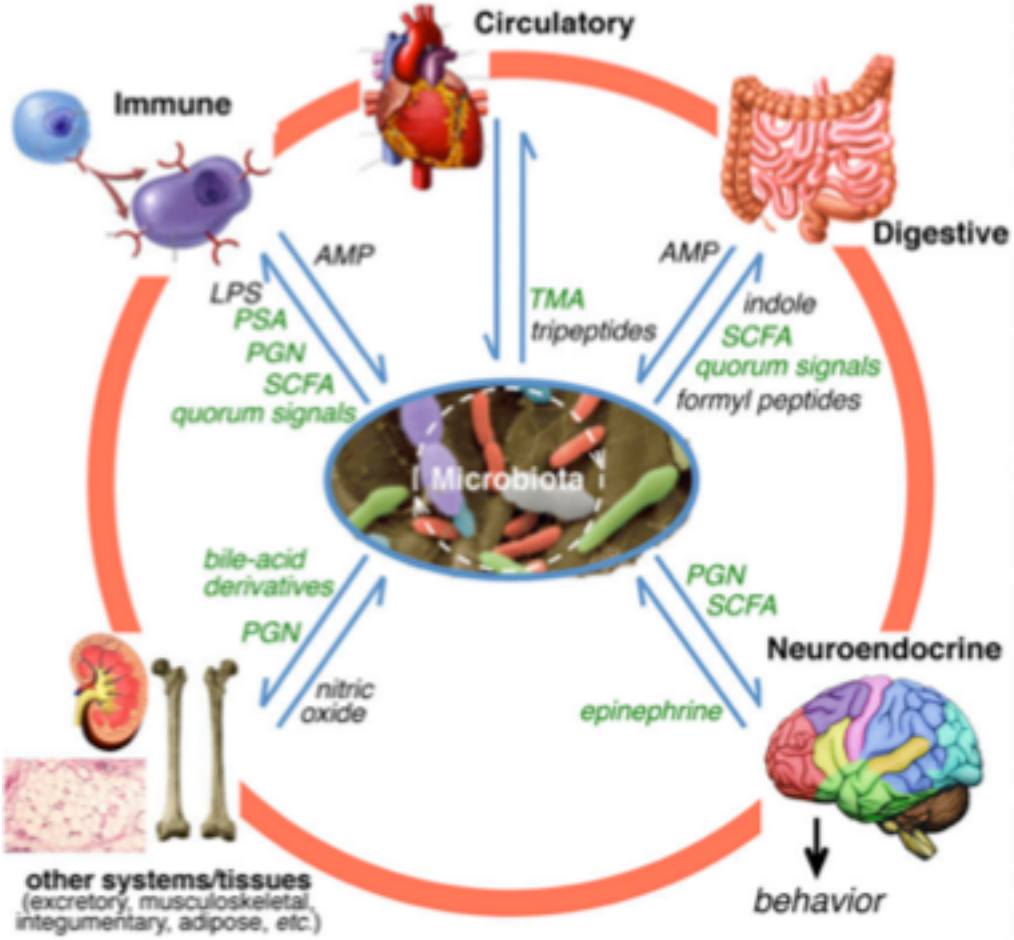
Miguel Jimenez
Postdoc – *synthetic and chemical biology, microbiology*

microbes in the GI tract affect human health and development

microbiome



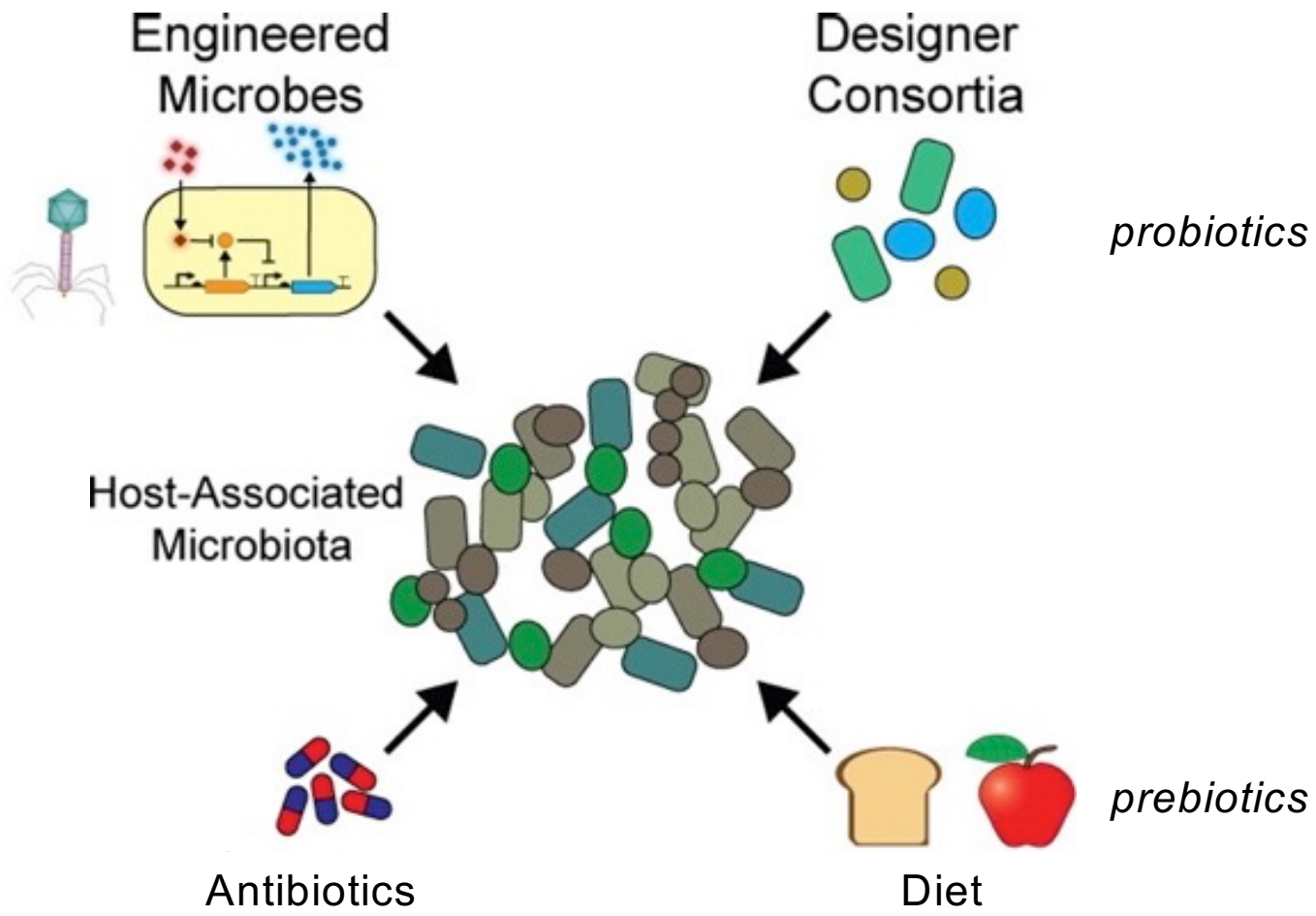
	human	microbe
cells	$3x10^{13}$	**$4x10^{13}$**
genes	$2x10^{4}$	**10^{5}-10^{6}**



Fischbach, M. A. & Segre, J. A. Signaling in Host-Associated Microbial Communities. Cell 164, 1288–1300 (2016).

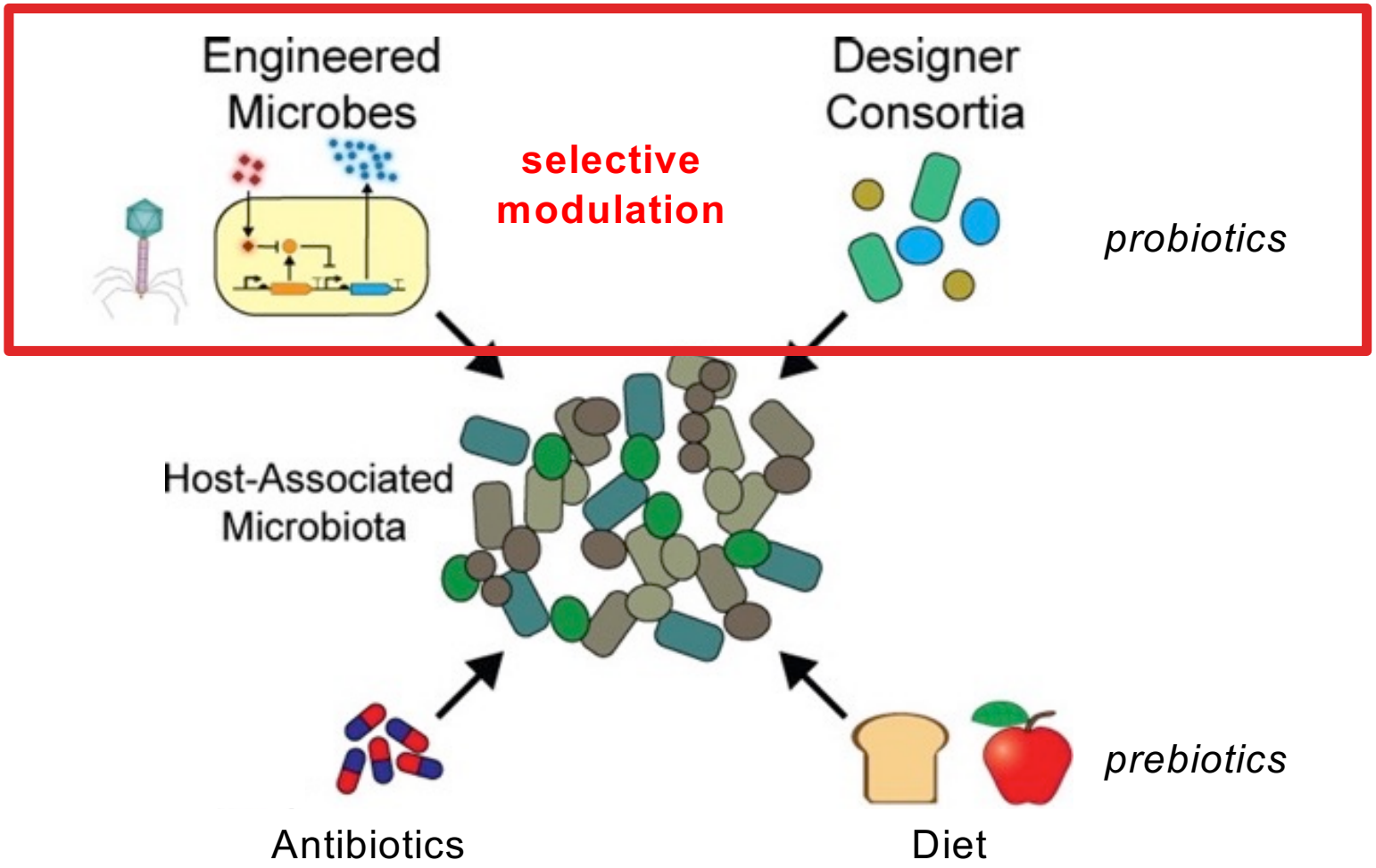
McFall-Ngai, M. *et al.* Animals in a bacterial world, a new imperative for the life sciences. *PNAS* **110,** 3229–3236 (2013).
Qin, J. *et al.* A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* **464,** 59–65 (2010).

how can we modulate the microbiome?



Mimee, M., Citorik, R. J. & Lu, T. K. Microbiome therapeutics — Advances and challenges. *Advanced Drug Delivery Reviews* **105, Part A,** 44–54 (2016).

engineered microbes enable **selective modulation**



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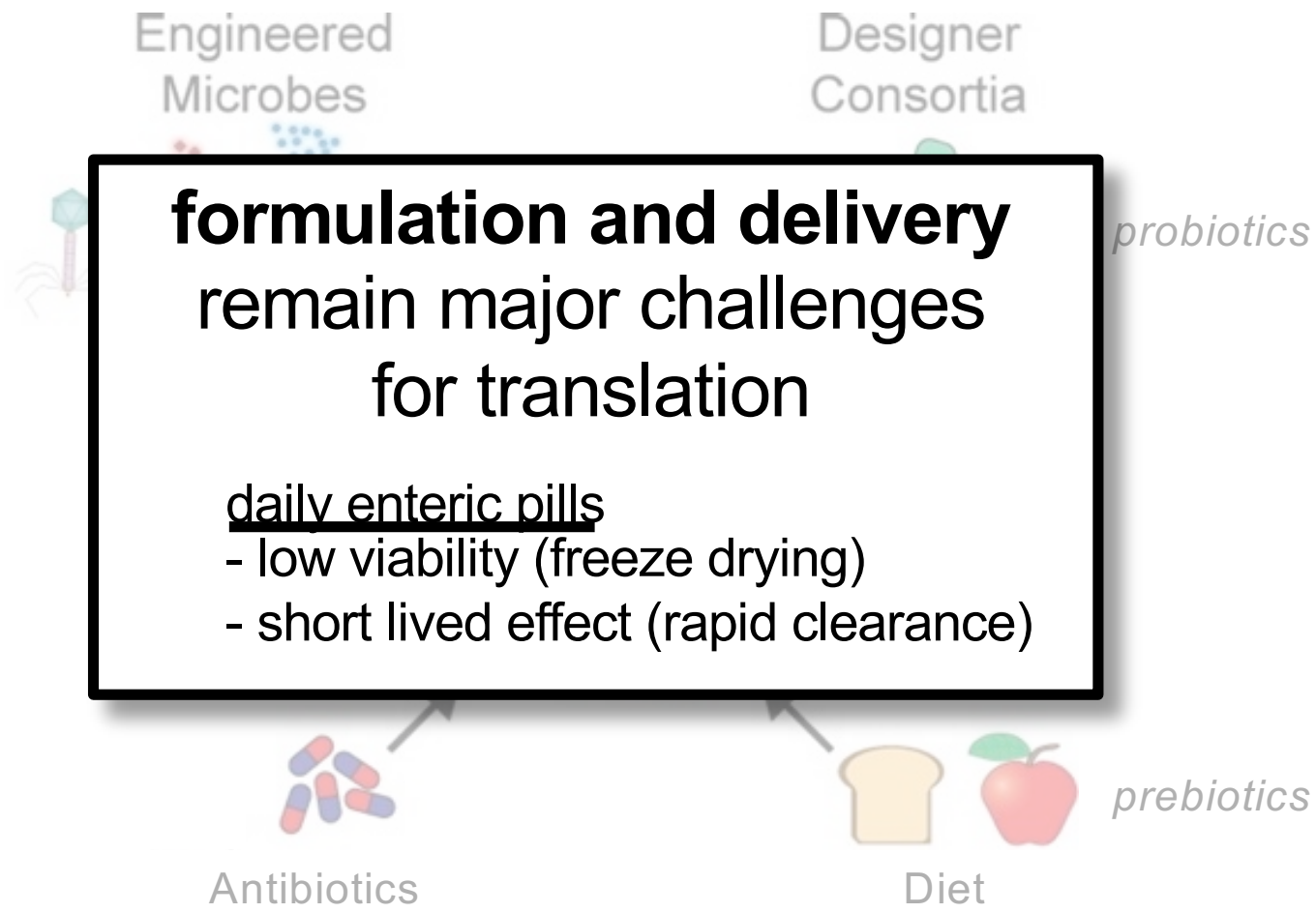
delivery remains a major challenge to translation



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AIM 1: develop formulations of live microbes compatible with gastric residence

microbe

+

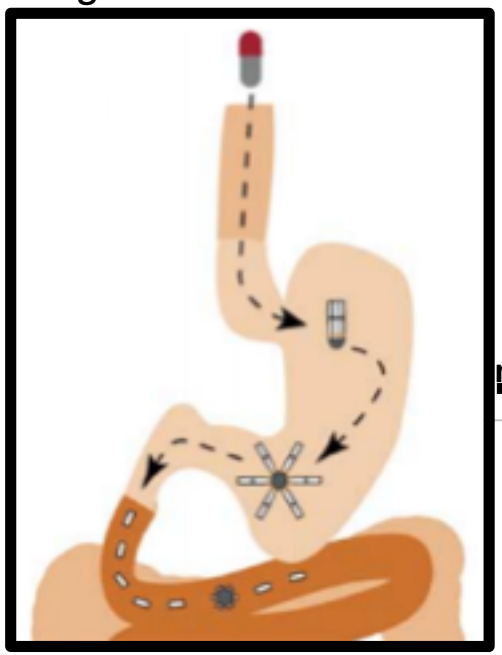
formulation

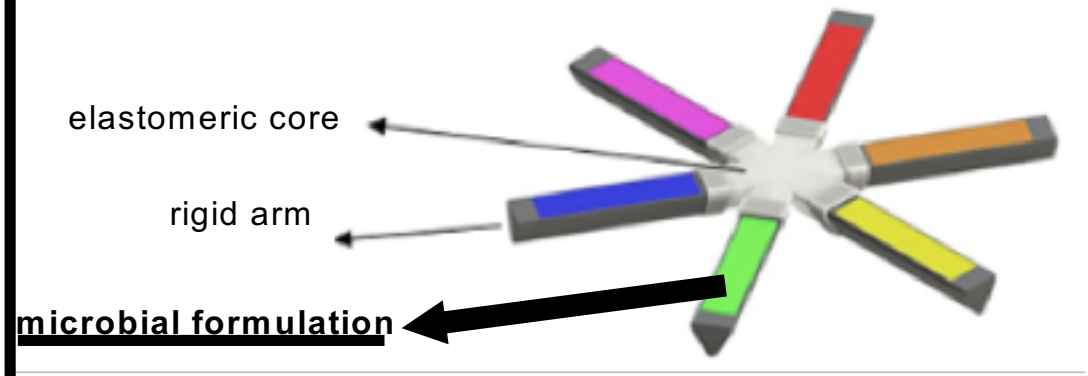
+

dosage form

GI-resident devices for long-term microbiome modulation

gastric residence

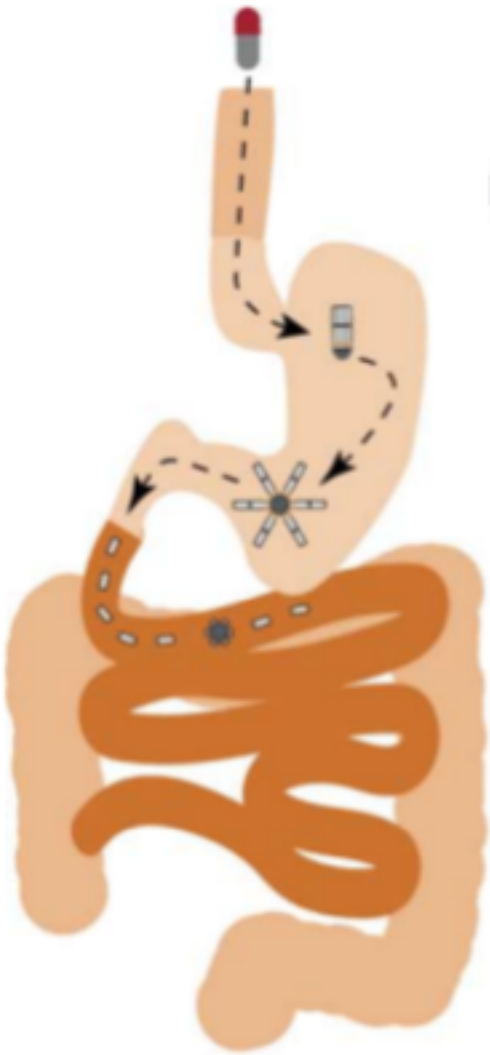


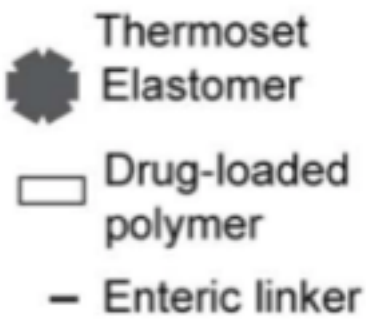


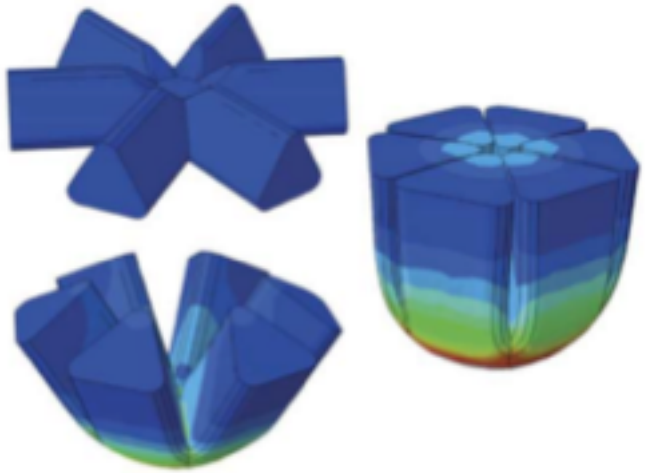
Bellinger, A. M., Jafari, M., Grant, T. M., Zhang, S., Slater, H. C., Wenger, E. A., Mo, S., Lee, Y.-A. L., Mazdiyasni, H., Kogan, L., Barman, R., Cleveland, C., Booth, L., Bensel, T., Minahan, D., Hurowitz, H. M., Tai, T., Daily, J., Nikolic, B., Wood, L., Eckhoff, P. A., Langer, R. & Traverso, G.*Science Translational Medicine* **8**, 365ra157-36

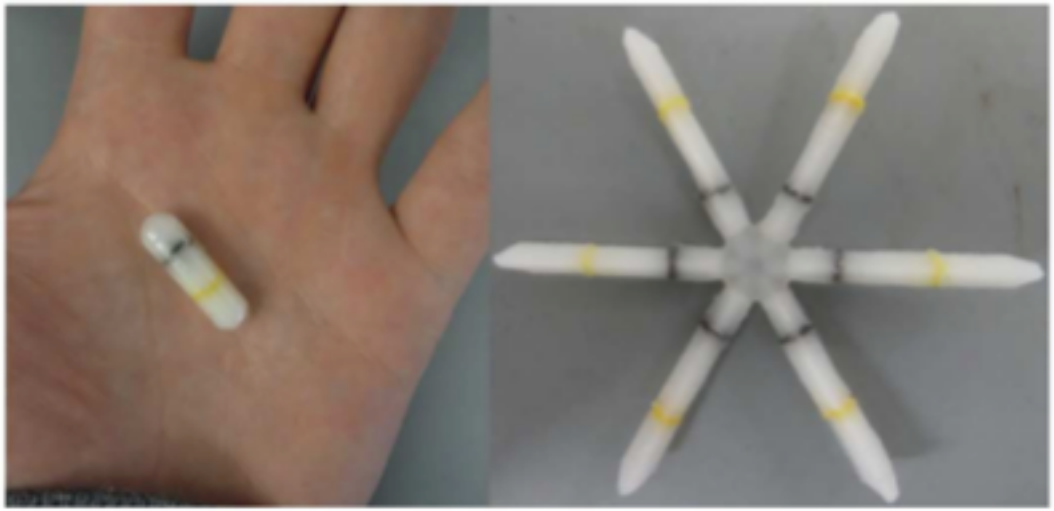
Kirtane, A. R., Abouzid, O., Minahan, D., Bensel, T., Hill, A. L., Selinger, C., Bershteyn, A., Craig, M., Mo, S. S., Mazdiyasni, H., Cleveland, C., Rogner, J., Lee, Y.-A. L., Booth, L., Javid, F., Wu, S. J., Grant, T., Bellinger, A. M., Nikolic, B., Hayward, A., Wood, L., Eckhoff, P. A., Nowak, M. A., Langer, R. & Traverso, G. *Nature Communications* **9**, 2 (2018).

gastric resident platform for delivery









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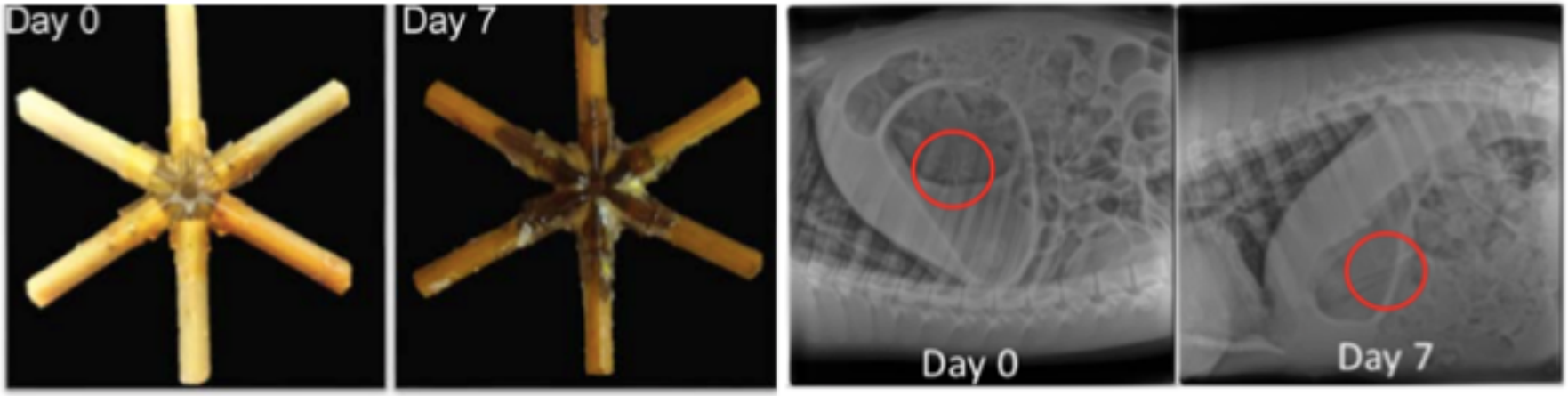
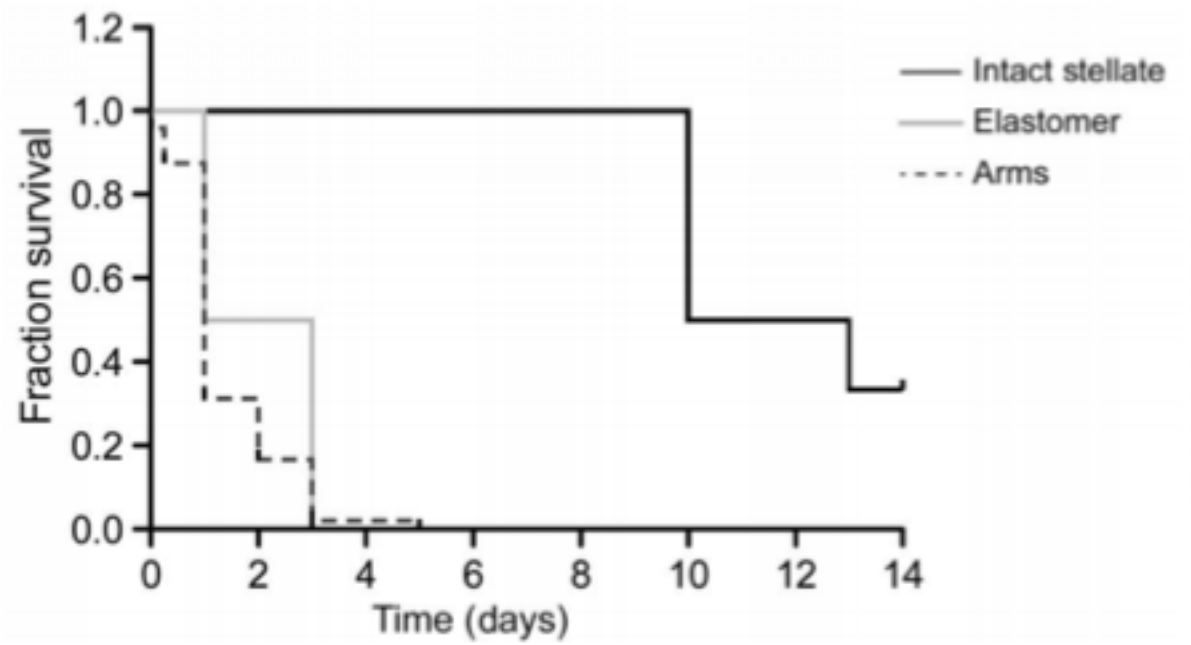
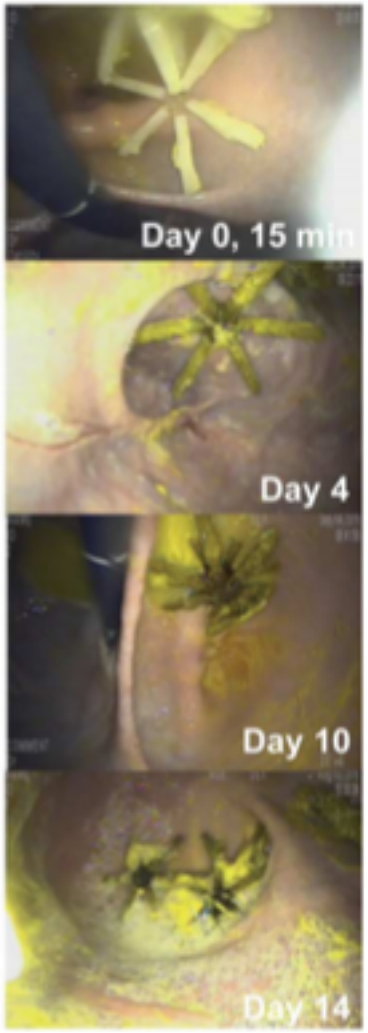
validated in vivo large animal model



Bellinger, A. M. et al. (Langer & Traverso). Science Translational Medicine 8, 365ra157-365ra157 (2016).
Kirtane, A. R. et al. (Langer & Traverso). Nature Communications 9, 2 (2018).

current platform persists multiple weeks





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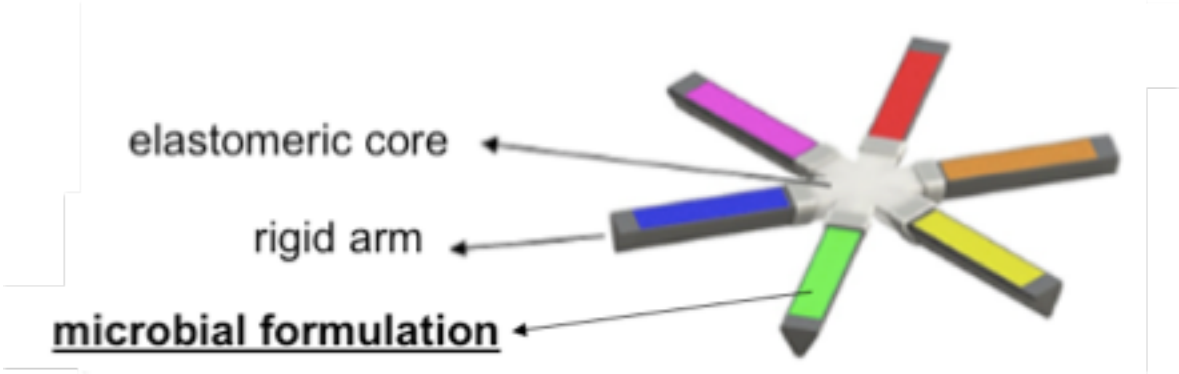
hollow arms can be loaded with formulation of choice



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AIM 1: develop formulations of live microbes compatible with gastric residence

microbe

+

formulation

+

dosage form

high throughput formulation screening pipeline

microbe culture

+

compound library

high throughput screening

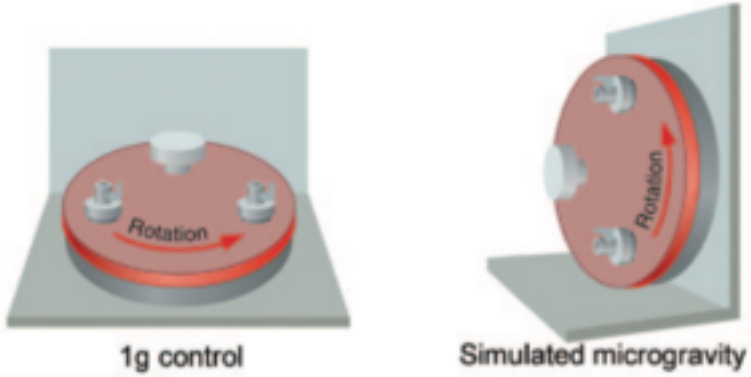
alive ?
or
dead ?

AIM 2: device safety for spaceflight and in vivo validation.

stomach injury model

during launch

microbe formulation viability in simulated microgravity



during microgravity

Lynch, S. V., Mukundakrishnan, K., Benoit, M. R., Ayyaswamy, P. S. & Matin, A. Appl. Environ. Microbiol. 72, 7701–7710 (2006).

what are good analogues for defining potential risk from gastric resident systems?

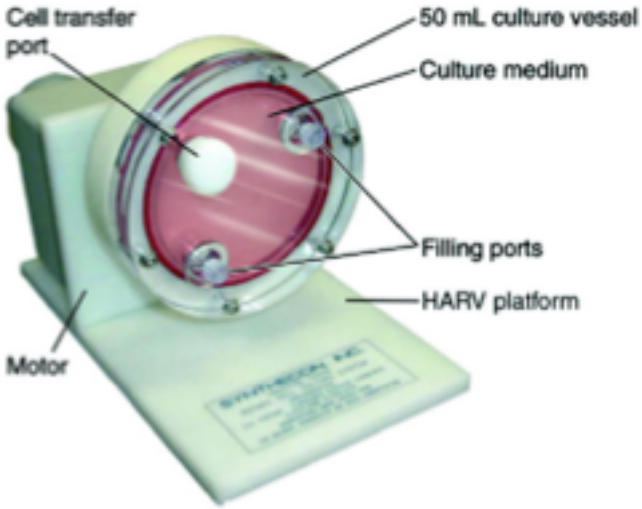
stomach injury model

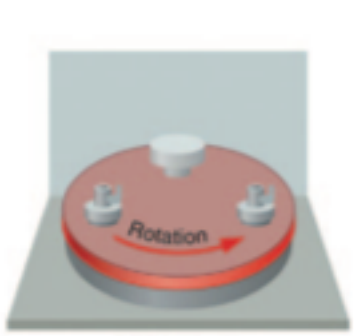
What force levels?

Other tests?

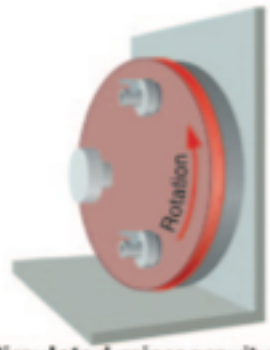
Equipment availability?

what are good analogues for defining microbial formulation efficacy?





1g control



Simulated microgravity

Collaborators with previous experience?

How to validate?

Equipment availability?

Compatibility with gastric-resident system?

science challenges: what is the roadmap to implementation in astronauts?

translational medicine pipeline

earth-based	**space-based**
design	
in vitro (chemical)	
in vitro (cells)	ground analogue
in vivo (animal)	???
in vivo (human healthy)	parabolic flight
in vivo (human patient)	space station

career challenges: what is the roadmap to research at intersection of basic + applied research?

Synthetic chemistry

Genetic engineering

Human health

Space health

Thank you!

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