

Microbiome Live Biotherapeutics as a Novel Approach to Treat Infectious and Inflammatory Diseases

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SERES
THERAPEUTICS™



Mission

To transform the lives of patients with revolutionary microbiome therapeutics

Location

Cambridge, MA

Clinical Assets

Advanced drug pipeline with Phase 3 & Phase 2 programs

Platform

Platforms enable early discovery through GMP manufacturing of microbiome therapeutics

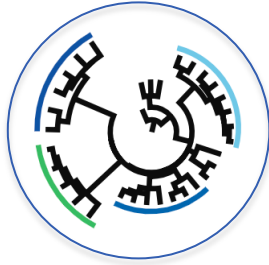
Employees

130+

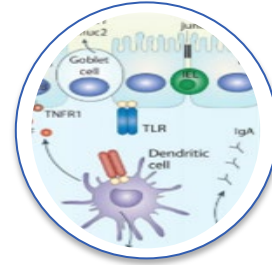
Seres is developing a novel drug modality that modulates the gut microbiome



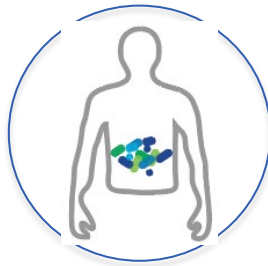
Ecobiotic® Live Microbiome Biotherapeutics are encapsulated consortia of commensal bacteria with specific pharmacologic properties



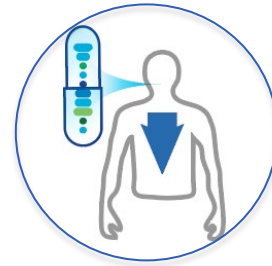
Consortia capture
**breadth of
phylogenetic
& functional
diversity** in gut



Designed to
**target
inflammatory
& immunological**
disease pathways
simultaneously

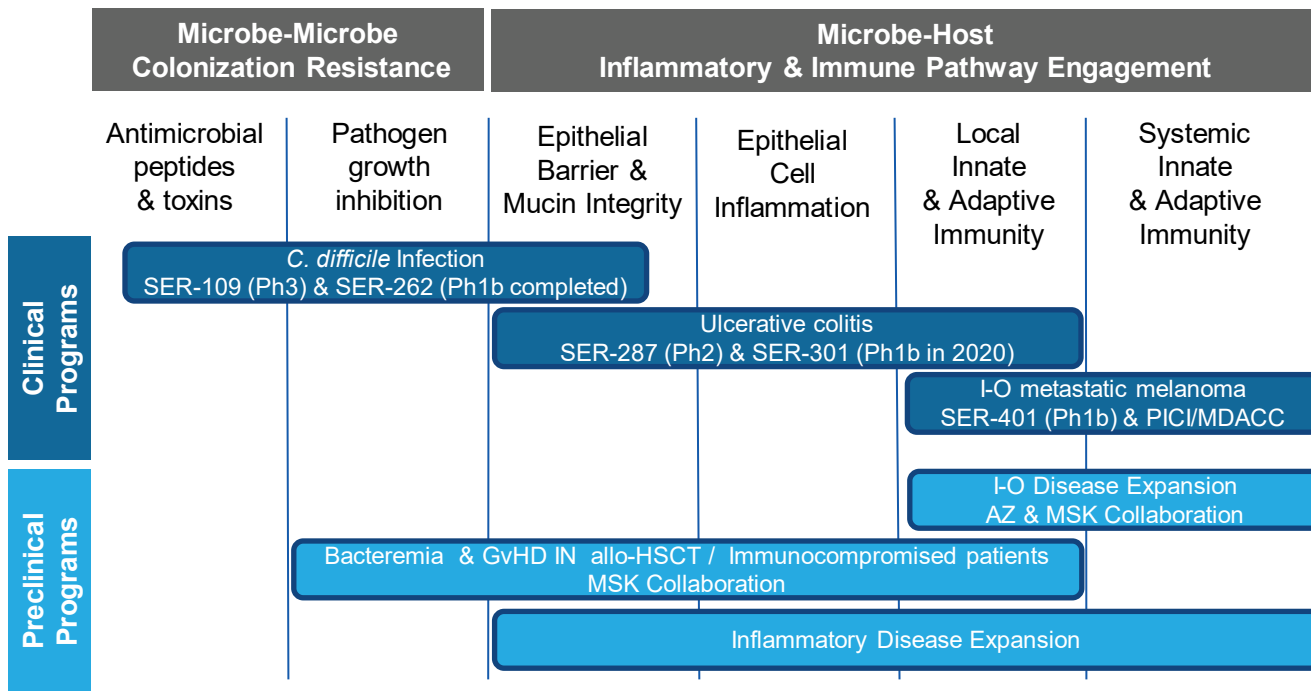


Mechanisms
includes microbial
**engraftment in
GI tract** to
restructure the
microbiome



Formulated for
oral delivery
using current
Good
Manufacturing
Practices (cGMP)

Drugs are designed to target therapeutic microbe-microbe & microbe-host functional interactions in the human gut

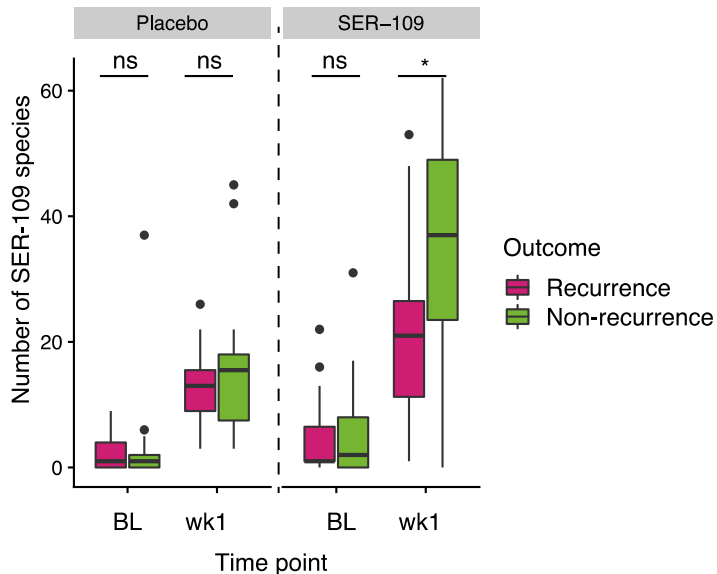


Reverse Translation Drug Discovery & Development Platform enables building of portfolio based on key learnings across programs

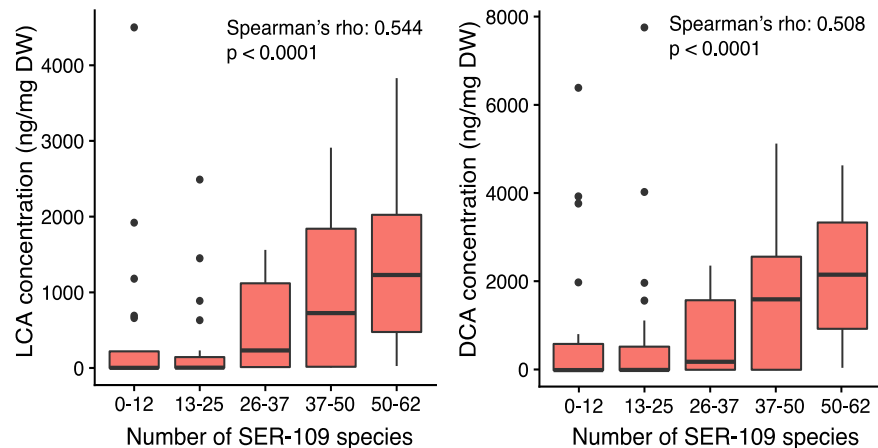
Human 'Proof of Concept' Phase 2: SER-109 for the reduction of *C. difficile* recurrence



Early engraftment of SER-109 strains was associated with non-recurrence



Increased engraftment was associated with increased production of secondary bile acids

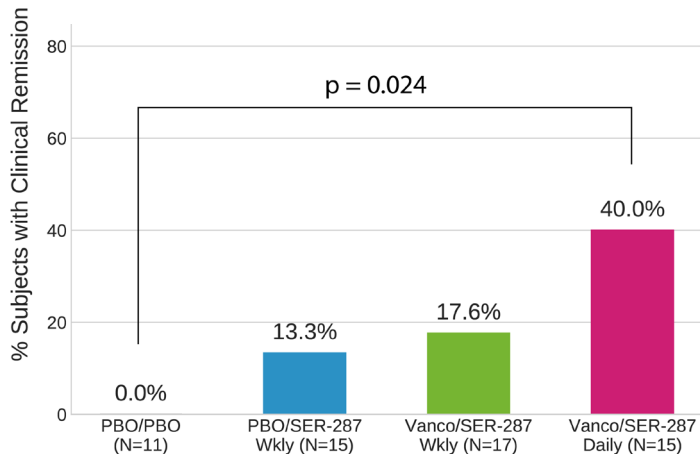


McGovern, Ford, Henn et al. (in revision)

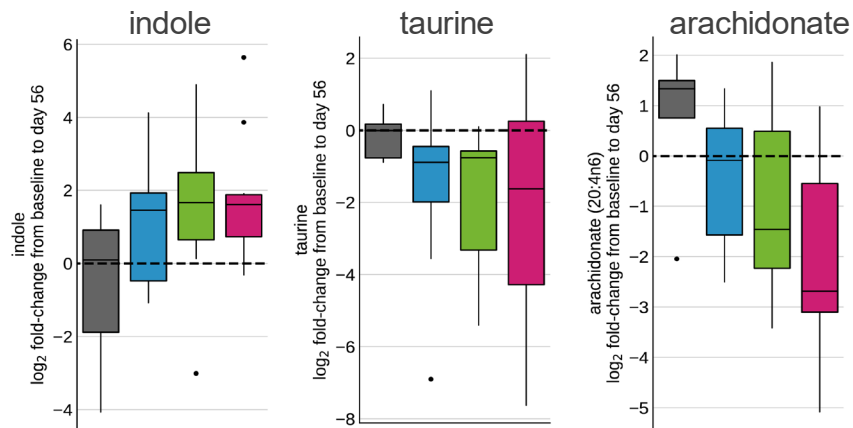
Human 'Proof of Concept' Phase 1b: SER-287 for the treatment of mild-moderate ulcerative colitis



Preconditioning with vancomycin followed by daily dosing of SER-287 was associated with clinical remission



Microbially-mediated metabolites that modulate host inflammation & barrier integrity are associated with SER-287 treatment and clinical outcome



Henn et al. (in revision)

How does the gastrointestinal (GI) microbiome impact antibiotic resistant infection?



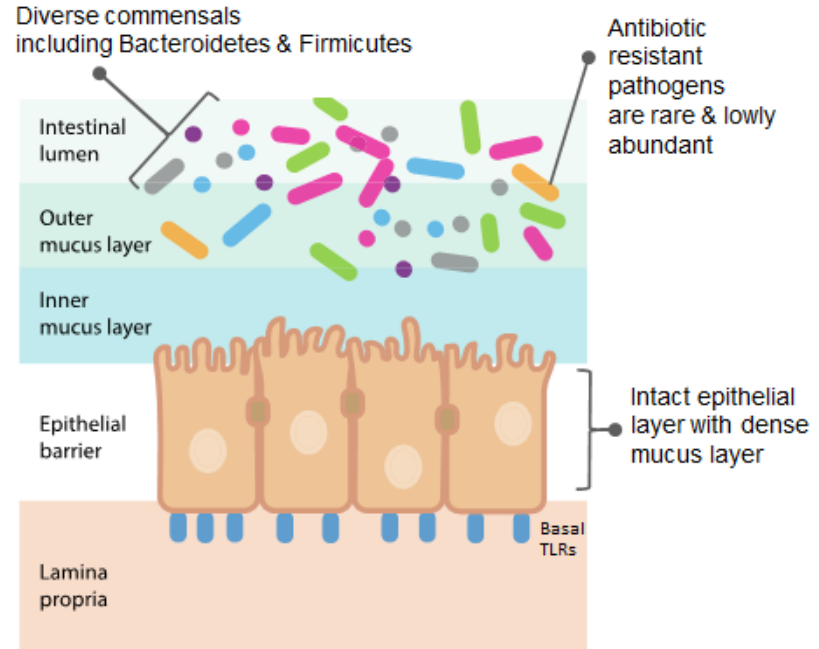
- (1) The GI tract is home to trillions of bacterial cells; a healthy intact microbiome is essential to preventing colonization with pathogens.

Suau et al, Appl Environ Microbiol. 1999

Kim et al, Nature, 2019

Caballero et al, Cell Host & Microbe, 2017

Pamer, E., Science 2016

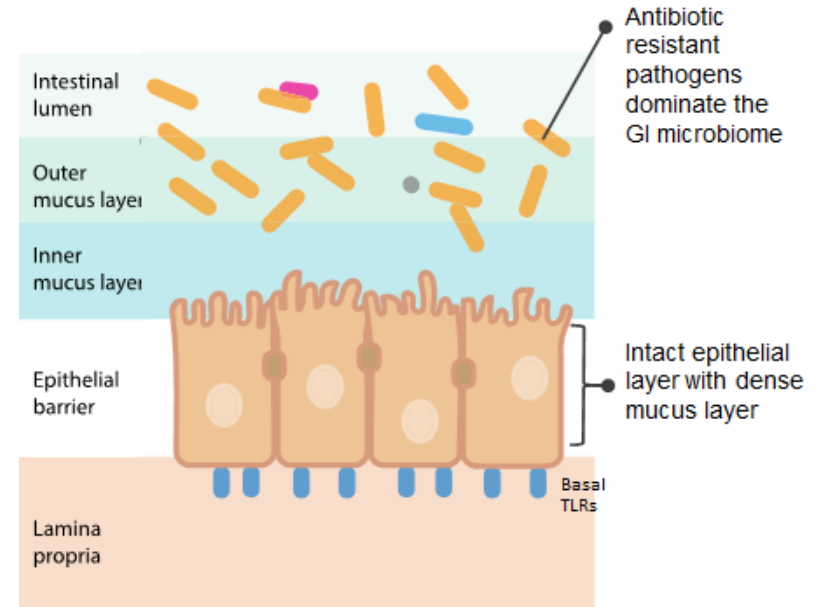


How does the gastrointestinal (GI) microbiome impact antibiotic resistant infection?

- (1) The GI tract is home to trillions of bacterial cells; a healthy intact microbiome is essential to preventing colonization with pathogens.
- (2) **Antibiotic resistant & tolerant bacteria rapidly expand in the absence of commensals resulting in domination by a few species.**

Ubeda et al, J.Clin Invest 2010

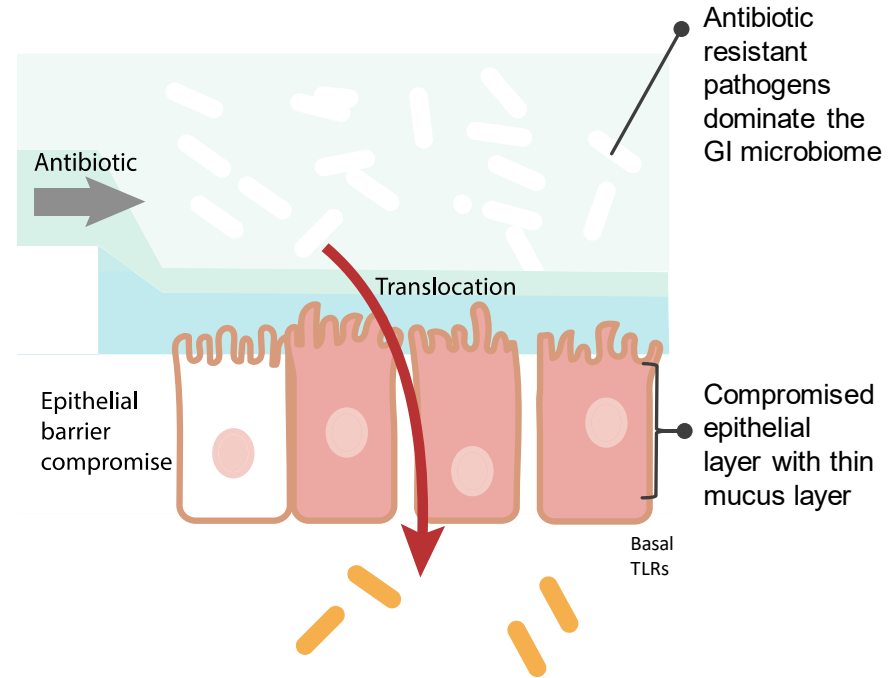
Taur et al, Clin Infect Dis, 2012



How does the gastrointestinal (GI) microbiome impact antibiotic resistant infection?

- (1) The GI tract is home to trillions of bacterial cells; a healthy intact microbiome is essential to preventing colonization with pathogens.
- (2) Antibiotic resistant & tolerant bacteria rapidly expand in the absence of commensals resulting in domination by a few species.
- (3) **Domination with multidrug resistant organisms (MDRO) in populations with increased intestinal permeability has been associated with increased risk of bacteremia.**

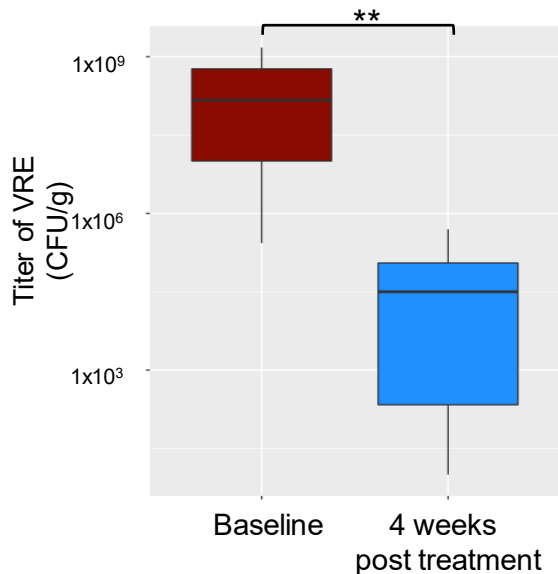
Tamburini et al, Nat Med 2018



Ecobiotic[®] live biotherapeutics may disrupt this path and represent a novel approach to combating antibiotic resistance

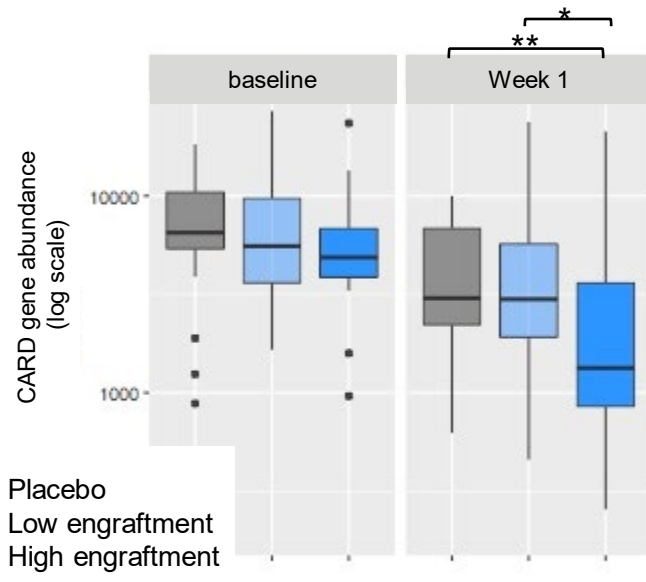


Treatment with SER-109 reduced VRE Carriage



Results from Seres SER-109 Phase 1 trial

SER-109 engraftment resulted in reduction of carriage of antibiotic resistance genes



Results from Seres SER-109 Phase 2 trial

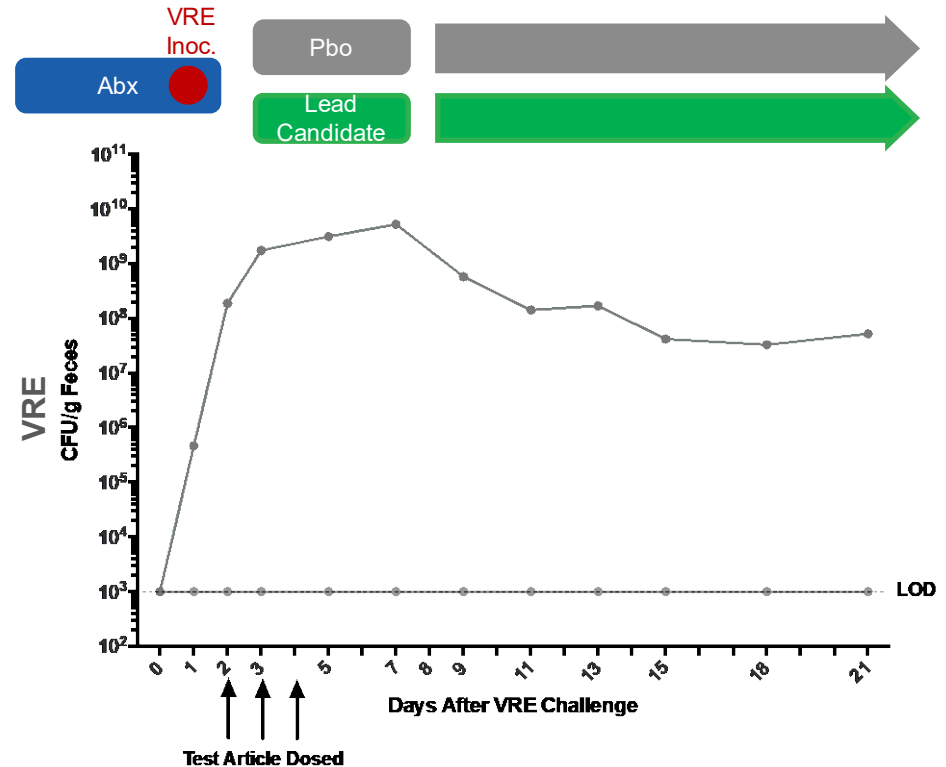
Seres is leveraging clinical insights to design Ecobiotic[®] live biotherapeutics as a novel solution to MDRO infection



Designed to prevent infection through decolonization & barrier restoration

- Defined consortia of laboratory-grown bacteria
- **Consortia Design:** Leverages insights on species and target pathways from SER-109 & SER-287 trials to define compositions of interest
- **Consortia Screening:** *in vivo* & *in vitro* models of VRE (shown), CRE, epithelial barrier integrity, & host immunity

Program supported by CARB-X



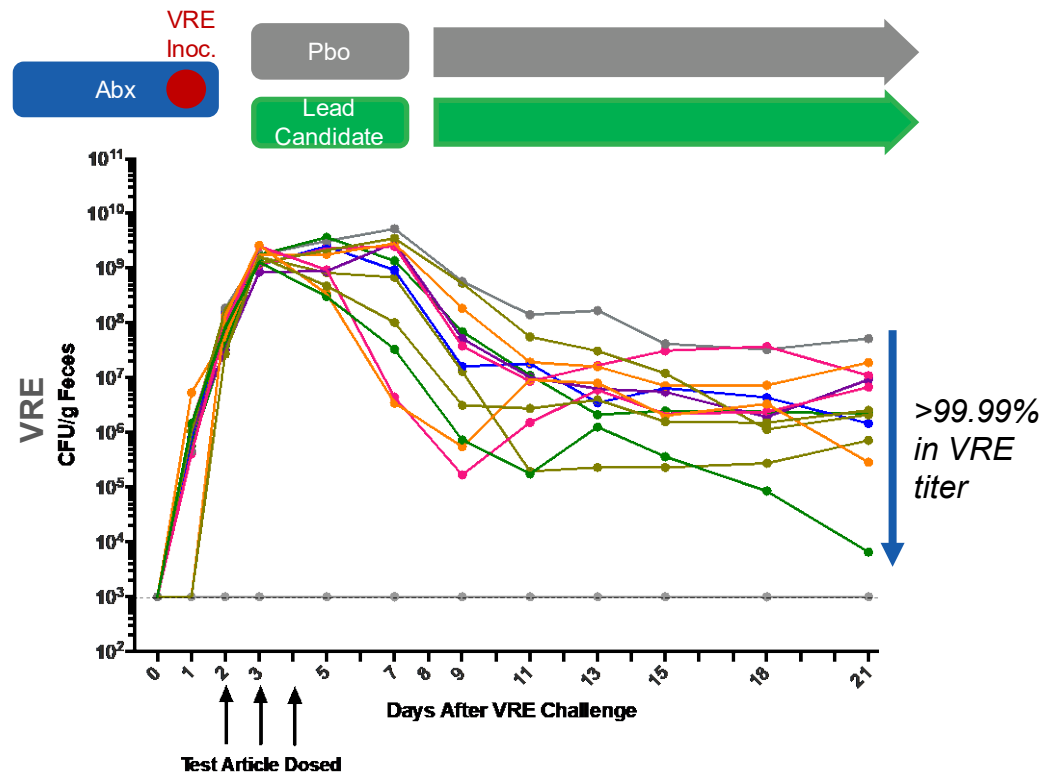
Vancomycin Resistant Enterococcus (VRE)

Lead candidate can decolonize VRE (data shown) & CRE *in vivo*

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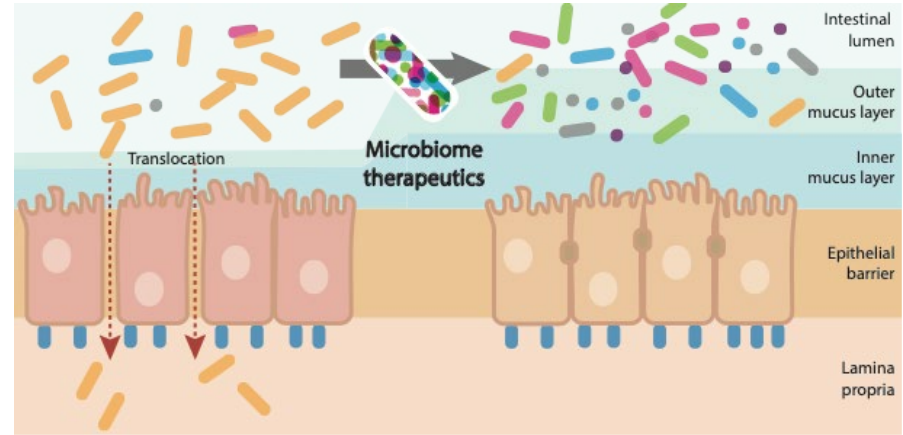
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Vancomycin Resistant Enterococcus (VRE)

Conclusions

- (1) Clinical studies support potential to use microbiome live biotherapeutics to modulate host inflammation/immunity and to target infection.
- (2) Antibiotic resistant infections can derive from reservoirs of antibiotic resistant organisms living in the GI microbiome. Inflammation and barrier compromise facilitate translocation of MDRO bacteria into bloodstream with clinical consequences.
- (3) Proof of concept studies suggest microbiome therapeutics can reduce the abundance of antibiotic resistant organisms and genes in the GI microbiome.
- (4) Seres is leveraging clinical & preclinical data to develop microbiome therapeutics to take-on the challenge of antibiotic resistant infection.





Thank You

Patients & Participating Clinical Sites
Seres Clinical Trials

Seres R&D, Manufacturing, Clinical,
& Regulatory Teams

Support from CARB-X

Collaborations with NHSc & MSKCC

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