

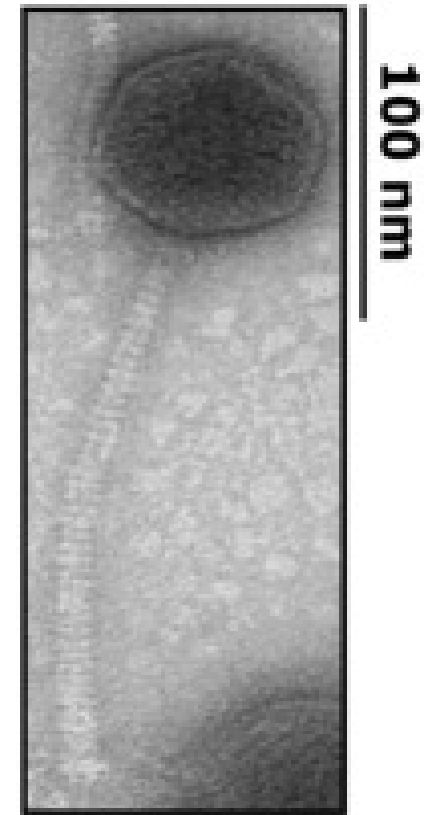
BACTERIOPHAGE THERAPY FOR RECURRENT VANCOMYCIN- RESISTANT *E. FAECIUM* BACTEREMIA

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INFECTIOUS DISEASES FELLOW
POSTDOCTORAL SCHOLAR

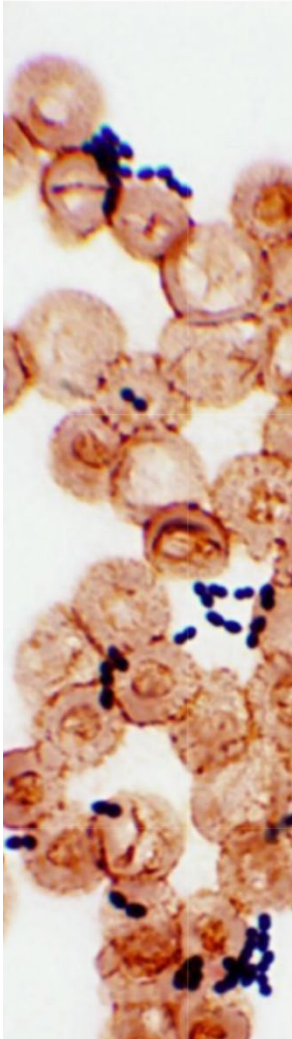
UNIVERSITY OF PITTSBURGH
MENTOR: DARIA VAN TYNE, PHD

ENTEROCOCCAL INFECTIONS & PHAGETHERAPY

- Enterococci are ubiquitous, GP GI-tract commensals, but are becoming concerning clinical pathogens (*E. faecium* and *E. faecalis*)
 - Hardy and intrinsically resistant to many classes of antibiotics
 - Growing % of healthcare-associated infections are VRE
- VRE is a significant concern in our clinical practice:
 - ~ 6 – 8 VRE blood stream infections (BSI) per month
 - ~10% are recurrent infections
 - Up to 30% of VRE infections may experience microbiologic failure



CLINICAL CASE OF RECURRENT *E. FAECIUM* BACTEREMIA

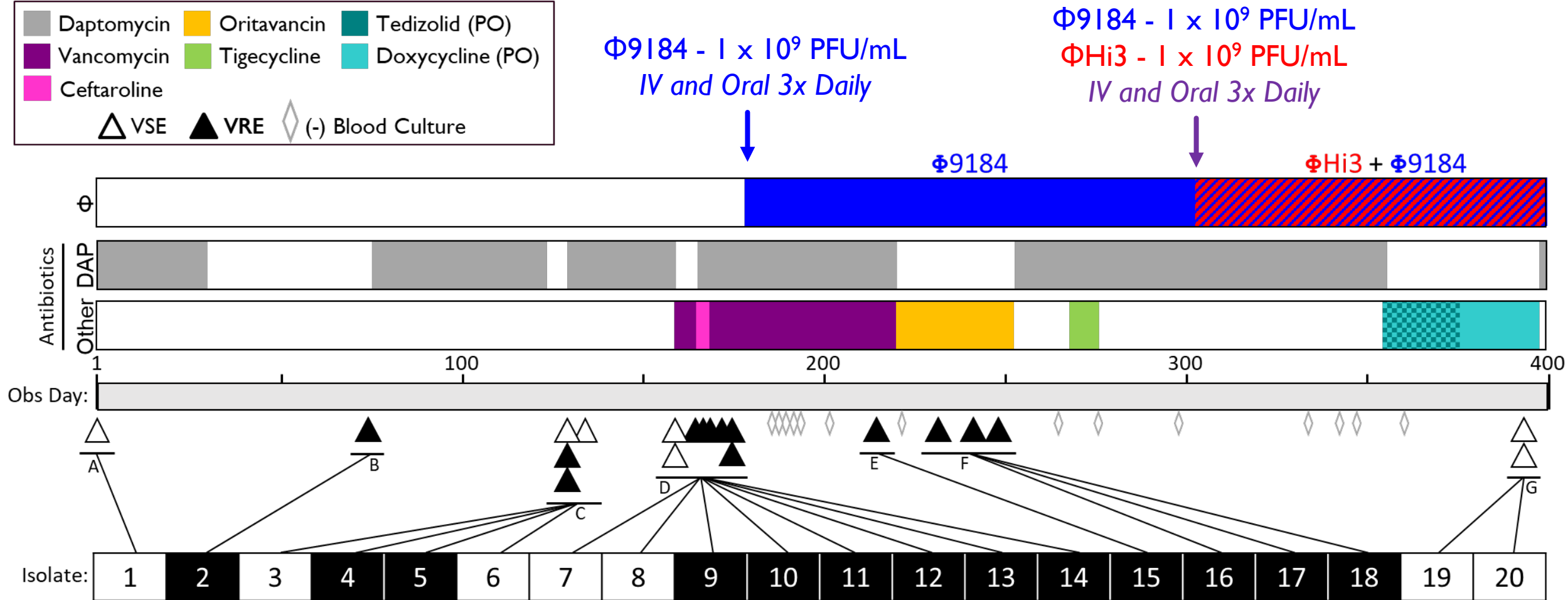
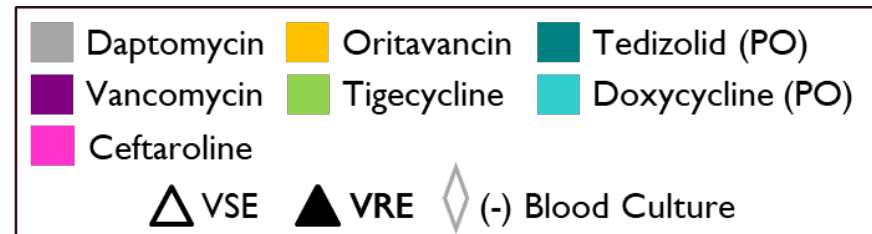


- Female patient in her 50s with mild immunosuppression and altered GI-tract anatomy due to prior Roux-en-Y bariatric surgery
- Recurrent episodes of *E. faecium* bacteremia since May 2013
 - No focal source found despite extensive search → Suspected recurrent GI translocation events
 - Increasing frequency of episodes culminating in several hospitalizations in the later half of 2020
- Failed multiple courses of IV antibiotics
- Patient was referred for adjunctive bacteriophage therapy



CLINICAL TIMELINE

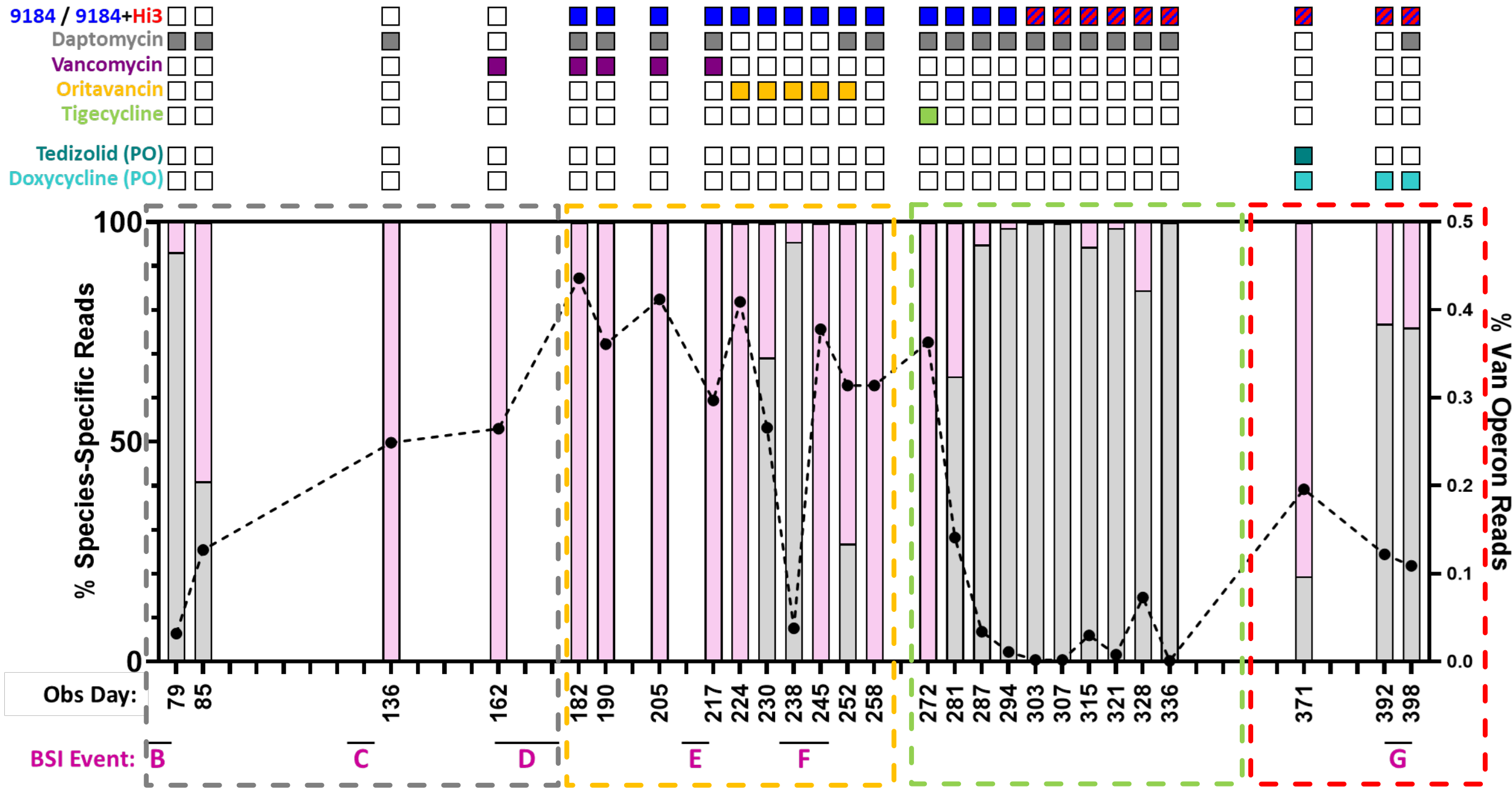






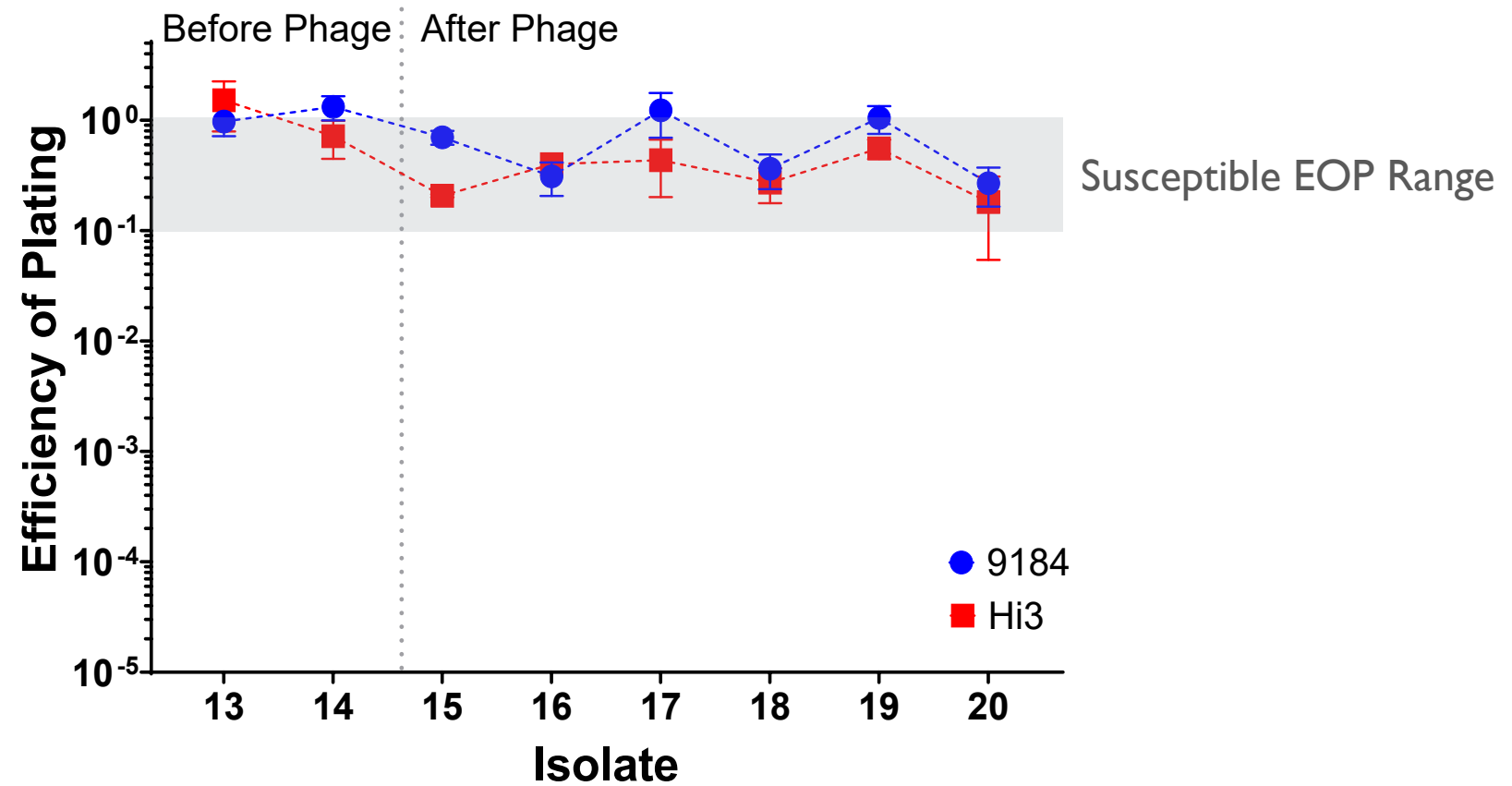
EFFECTS ON THE GASTROINTESTINAL ENTEROCOCCAL POPULATION





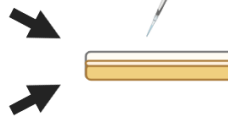
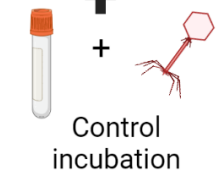
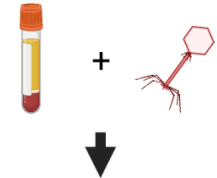
In collaboration with:
Breck Duerkop, PhD & Mike Mangalea, PhD

NO DETECTABLE Φ RESISTANCE

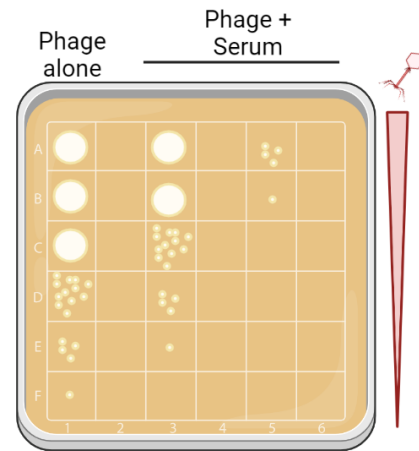


HOST SERUM NEUTRALIZATION

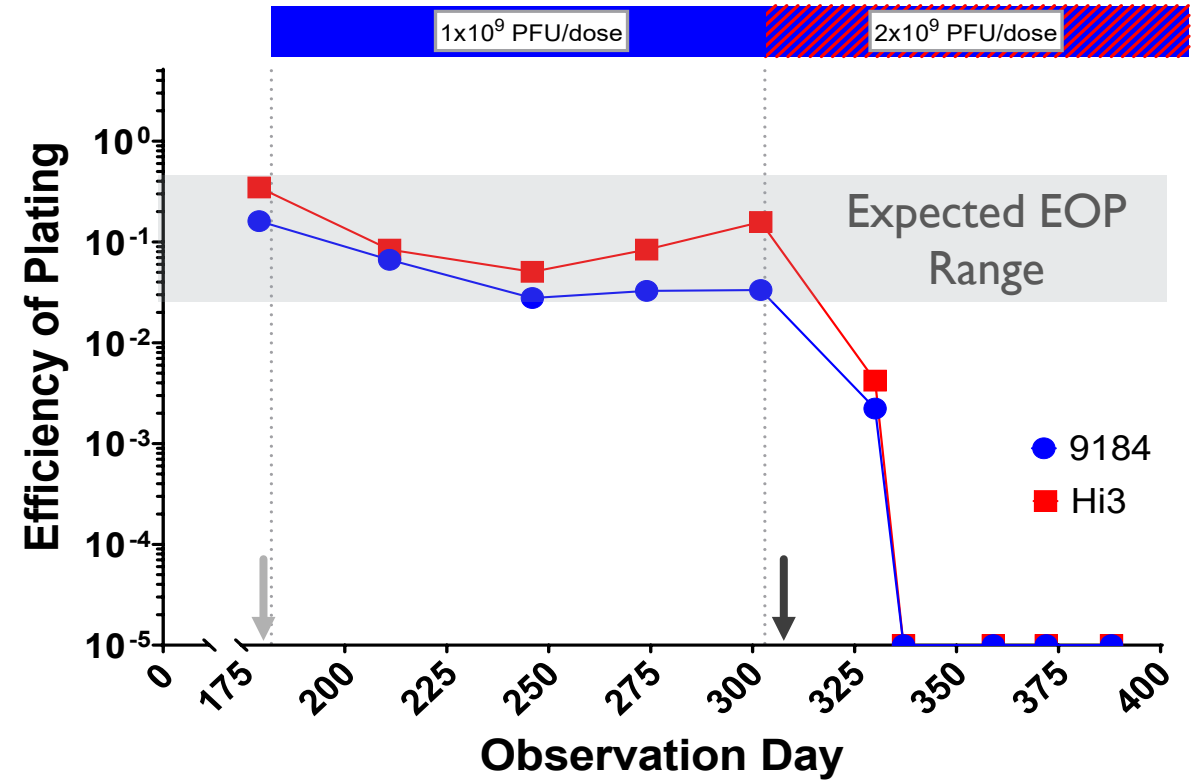
Incubate phage O/N
with patient serum



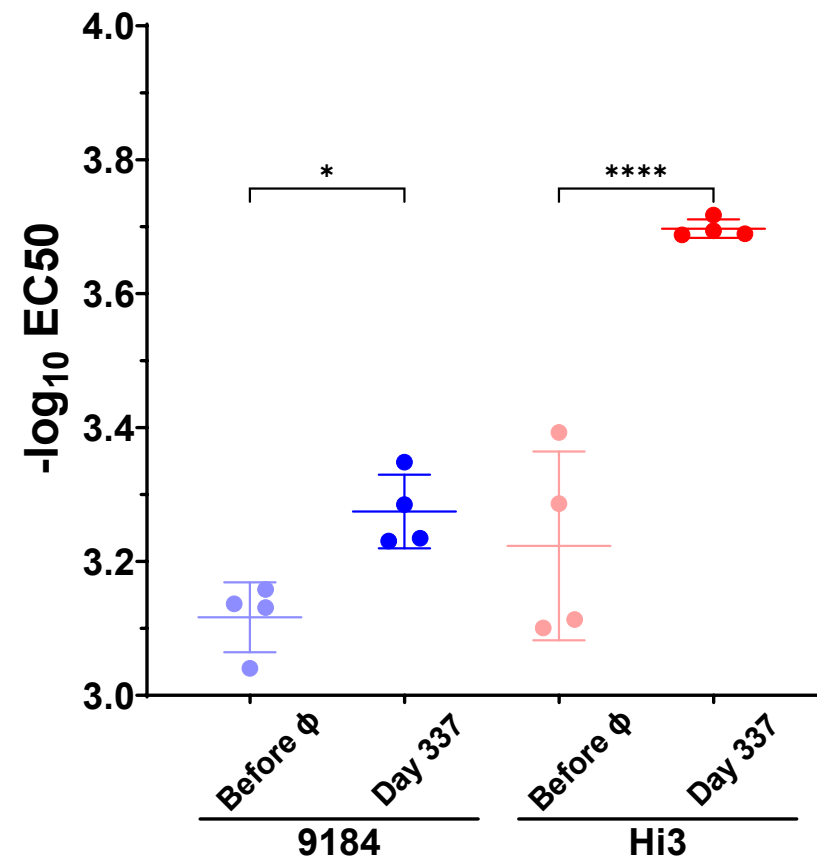
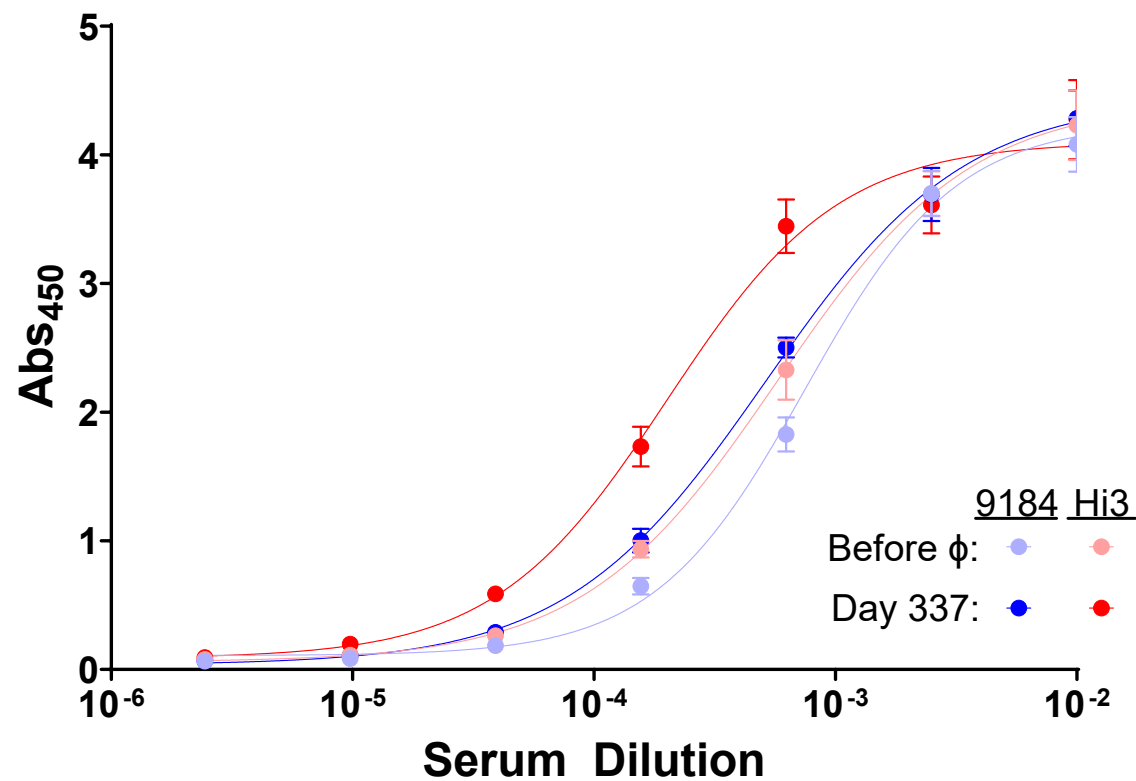
Incubate O/N
37°C

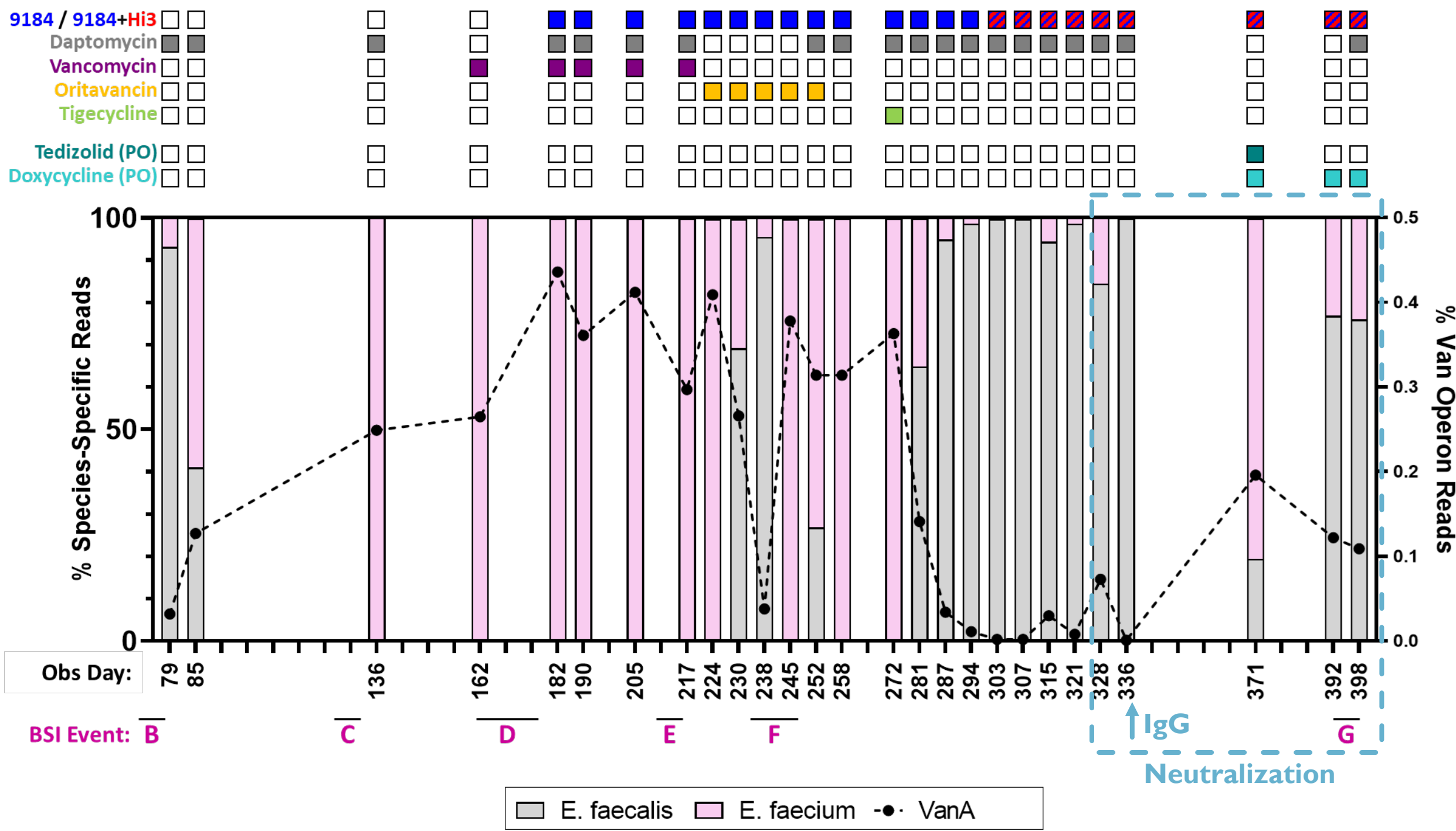


Count plaques to titer
PFU/mL



ASSESSING ANTI-PHAGE HOST IMMUNE RESPONSE



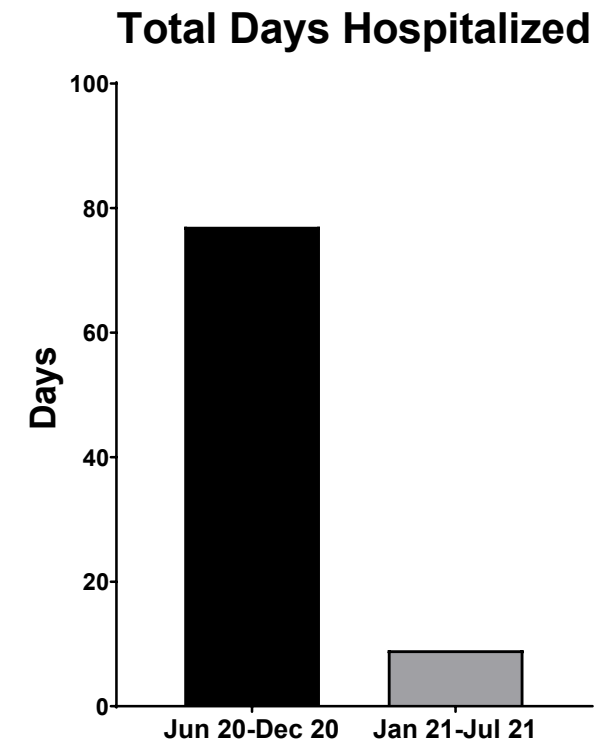


CASE SUMMARY

- Transient reduction VRE intestinal burden with combination therapy
 - Phage cocktail + tigecycline + daptomycin
- Suppressed bacteremia for 147 days (longest since observation began)
- Reduced days hospitalized and improved patient quality of life

However

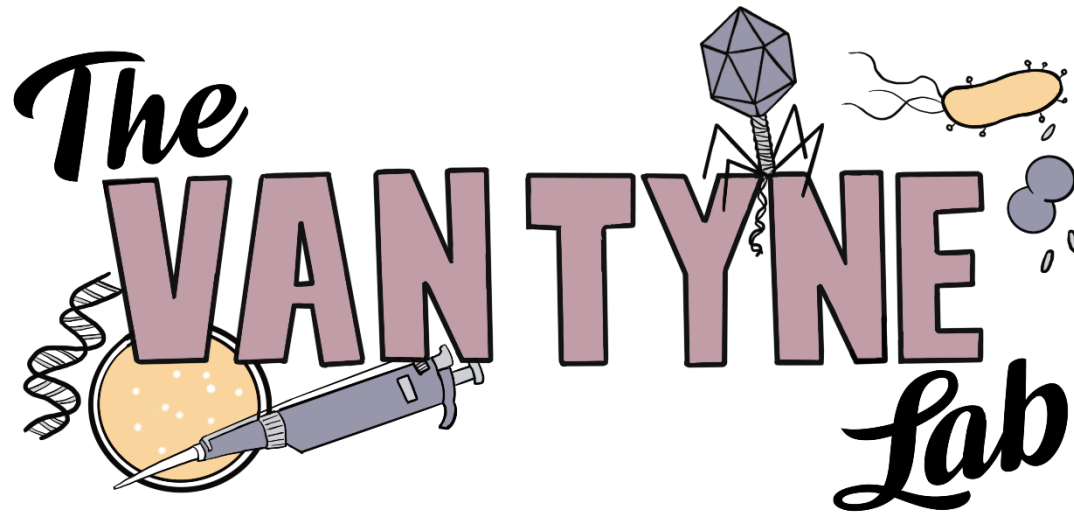
- Not curative therapy
- Possible anti-phage immune response that may have undermined therapy
 - Increased phage dose?
 - Hi3 more immunogenetic than 9184?



REMAINING QUESTIONS & NEXT STEPS

- How applicable would similar phage-antibiotic regimens be in our hospital system and beyond?
 - Biorepository of VRE BSI samples ($\sim 1/4^{\text{th}}$ of which are recurrent infections)
 - Phage host range screening and fishing for additional VRE-targeting phages
 - Antibiotic + phage combination synergy/antagonism assessments
- Further study of a possible treatment-limiting anti-phage host immune response
- Explore the changes in the gut microbiome during phage therapy

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 - Shu-Ting Cho, M.S.
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- **Mike Mangalea, PhD**
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