In-Patient Antibiotic Exposure Promotes SARS-CoV-2 Persistence in the GI Tract in COVID-19 Admitted Patients

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DDW2022
Digestive Disease Week®
MAY 21-24 | SAN DIEGO, CA
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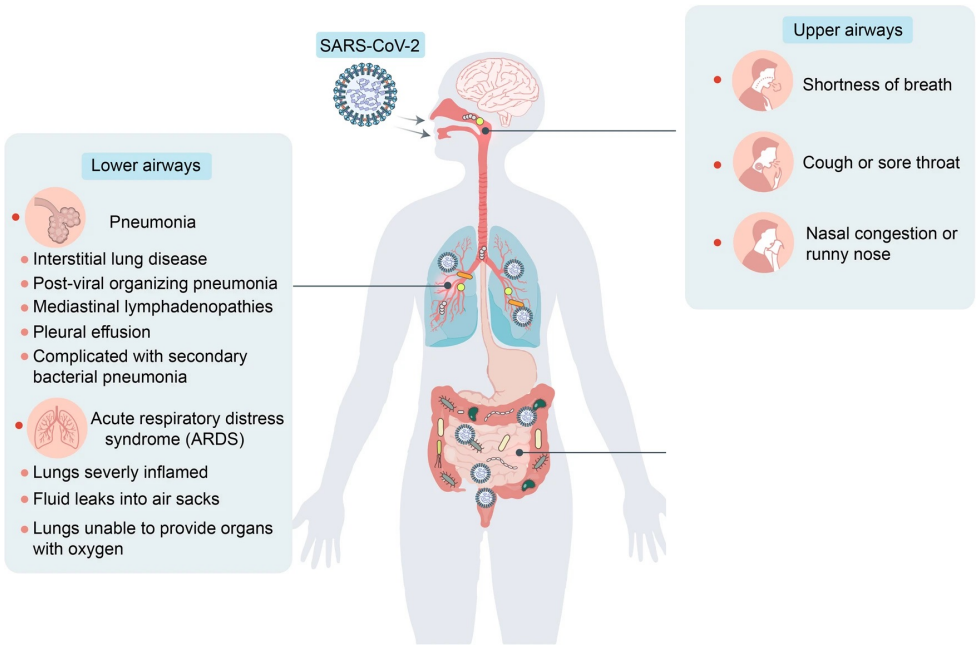
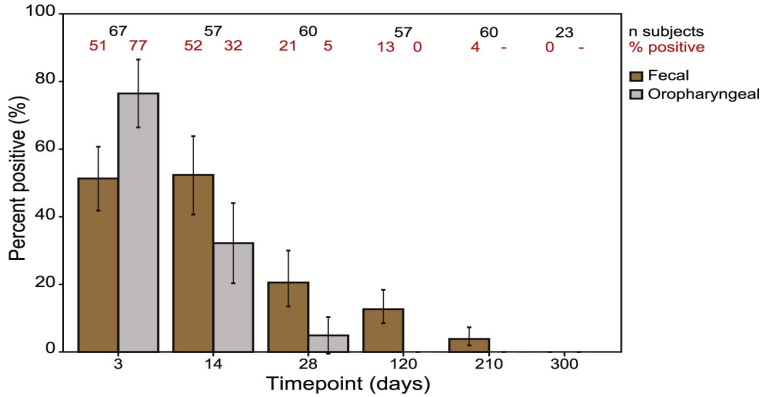
Background: COVID-19 associated respiratory and gastrointestinal symptoms and longer viral **RNA positivity rates** in fecal samples



Wang *et al*. 2022

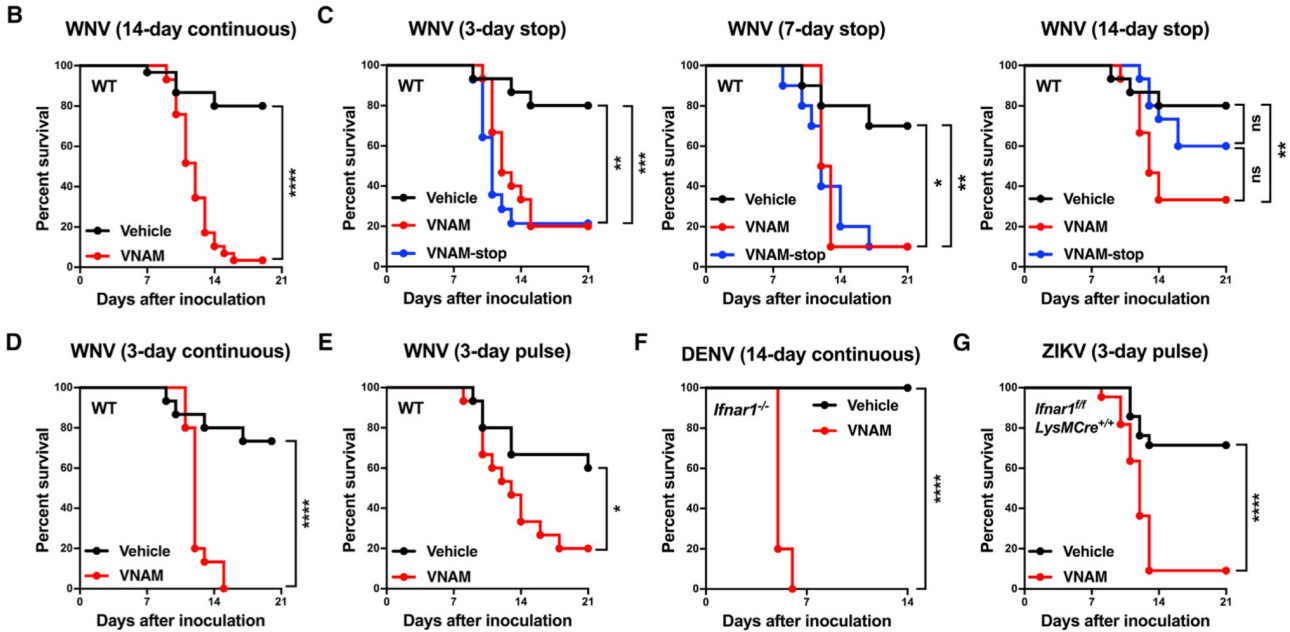


At Cedars-Sinai, ~2/3 of patients admitted for COVID-19 are placed on 2-8 antibiotics

Natarajan *et al*. 2022

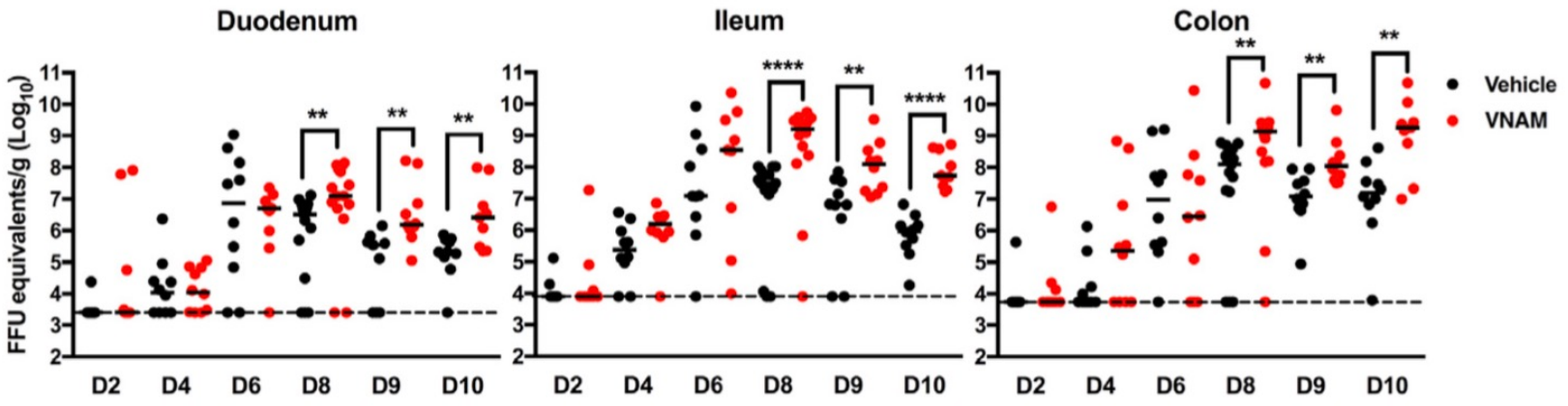
Mortality from flavivirus infection is increased in antibiotic treated mice

WNV= West Nile
DENV= Dengue
ZIKV=Zika



Thackrey et al, *Cell Reports* 2018

Antibiotics promoted flavivirus persistence in GI tract

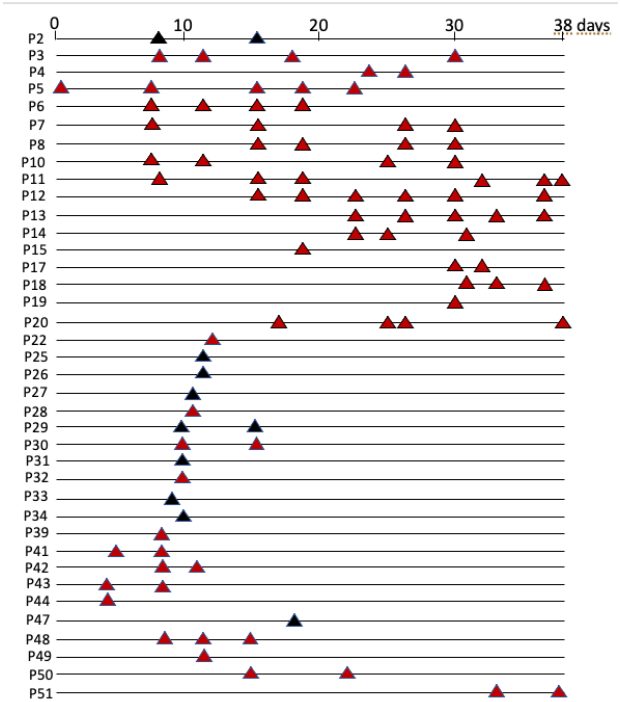


Thackrey et al, *Cell Reports* 2018

Hypothesis

Antibiotic exposure significantly depletes the bacterial gut microbiota thus disturbing stable communities and impairing colonization resistance, therefore facilitating SARS-COV-2 persistence in the GI tract.

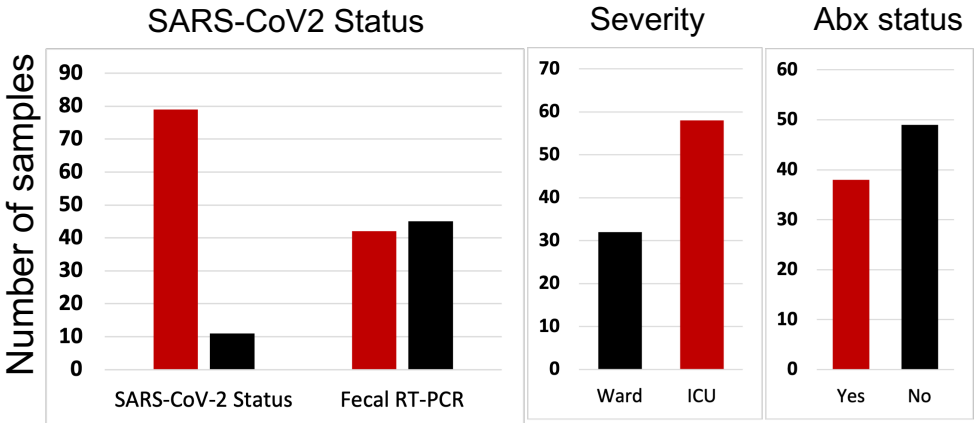
Patient population



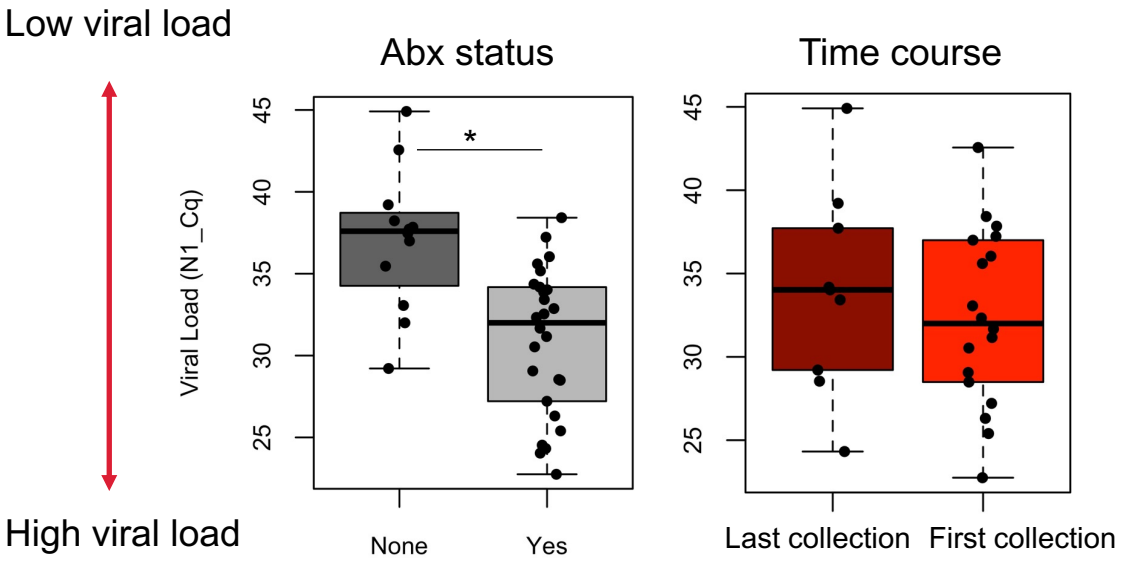
Positive

Negative

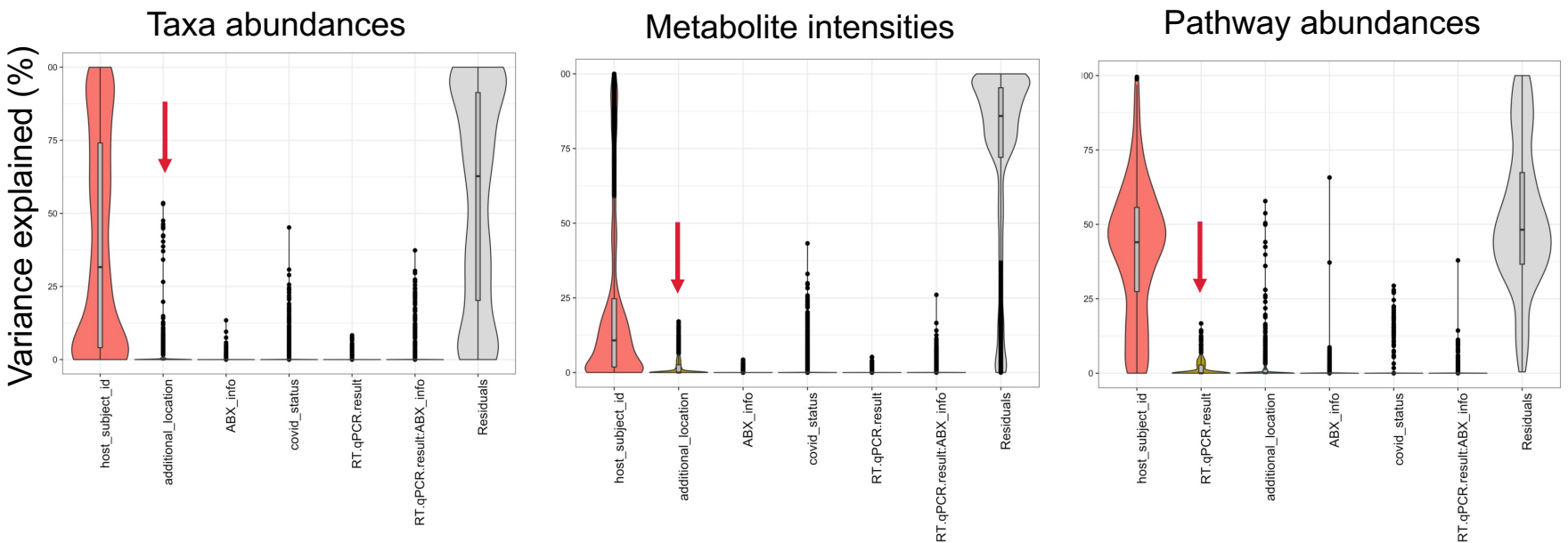
Sample distribution from total **38 patients (29 Positive and 9 Negative)** based on different variables



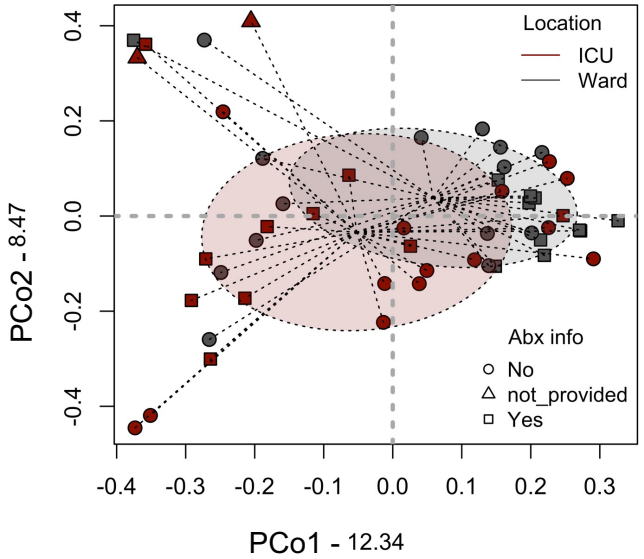
Viral load time course

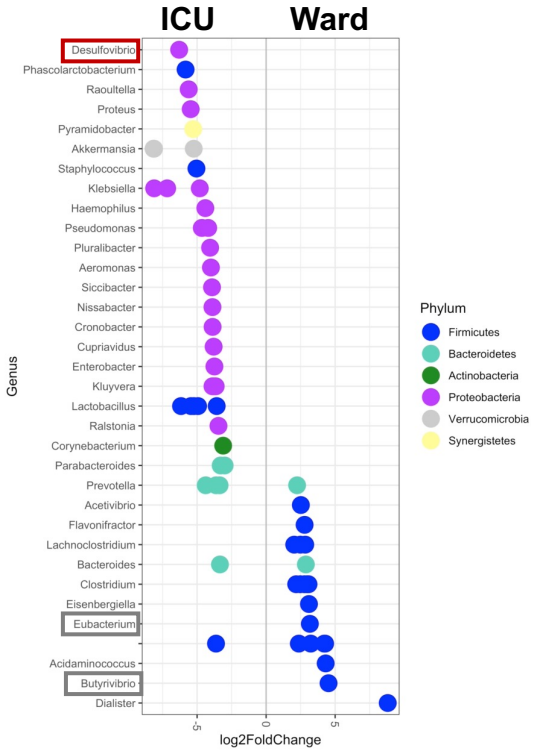


SARS-CoV-2 status, severity, and antibiotic status contribute to the explained variance based on microbial and metabolic features



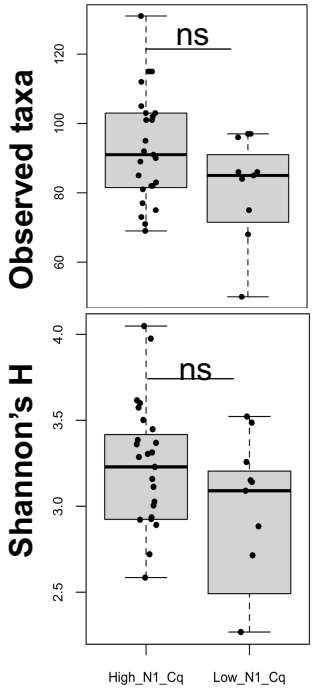
Microbiome composition differs based on COVID-19 severity

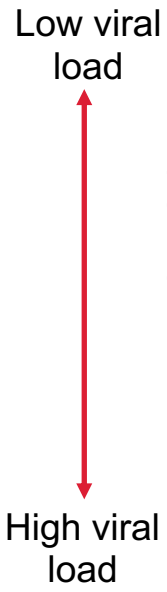




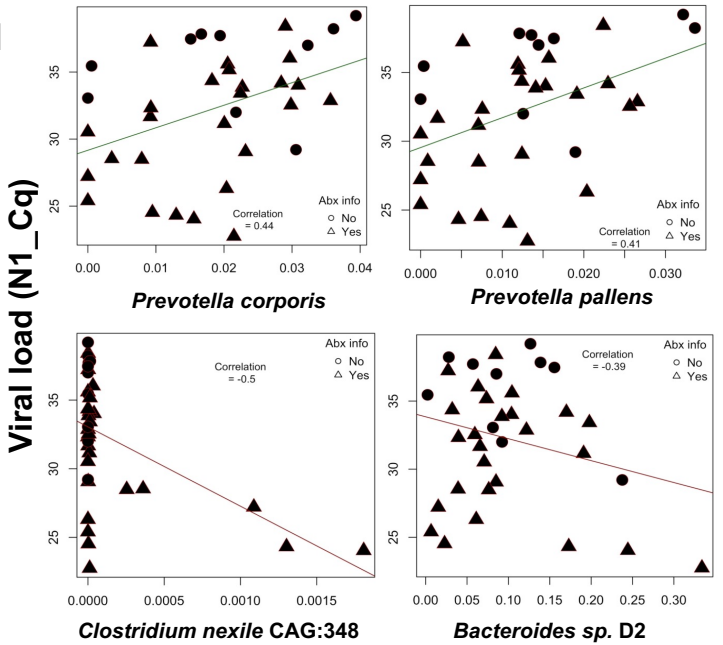
- Bloom of Proteobacteria in ICU patients
- Enrichment of opportunistic *Desulfovibrio* in patients admitted to ICU
- Butyrate producers (SCFAs in general) were mostly enriched in less severe patients or at the start of the treatment

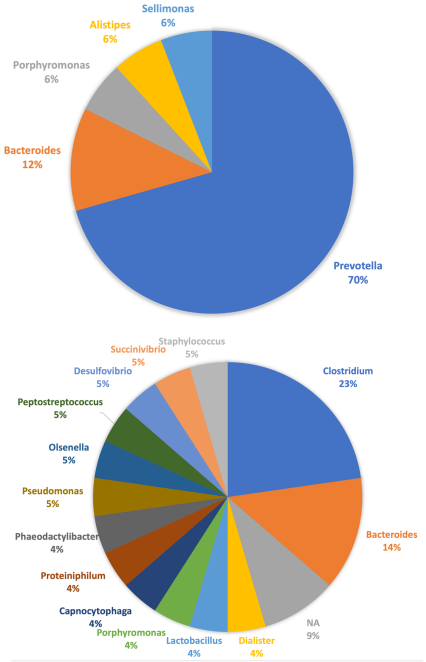
Higher microbial diversity and *Prevotella* enrichment associated with gut viral clearance





Prevotella enrichment and viral clearance

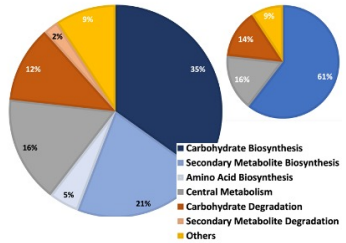




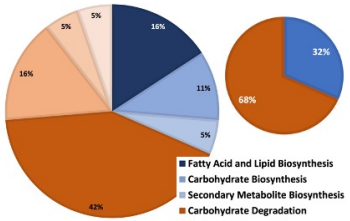
Clostridium and *Bacterioides* enrichment and viral persistence

Microbial biosynthetic pathways are enriched in patients with low viral load

Pathway summary associated with **Low** viral load

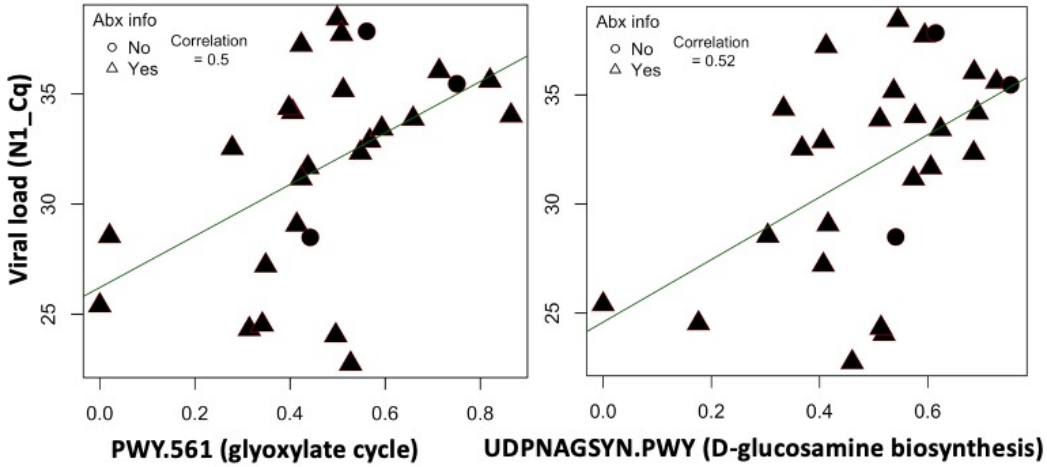


Pathway summary associated with **High** viral load

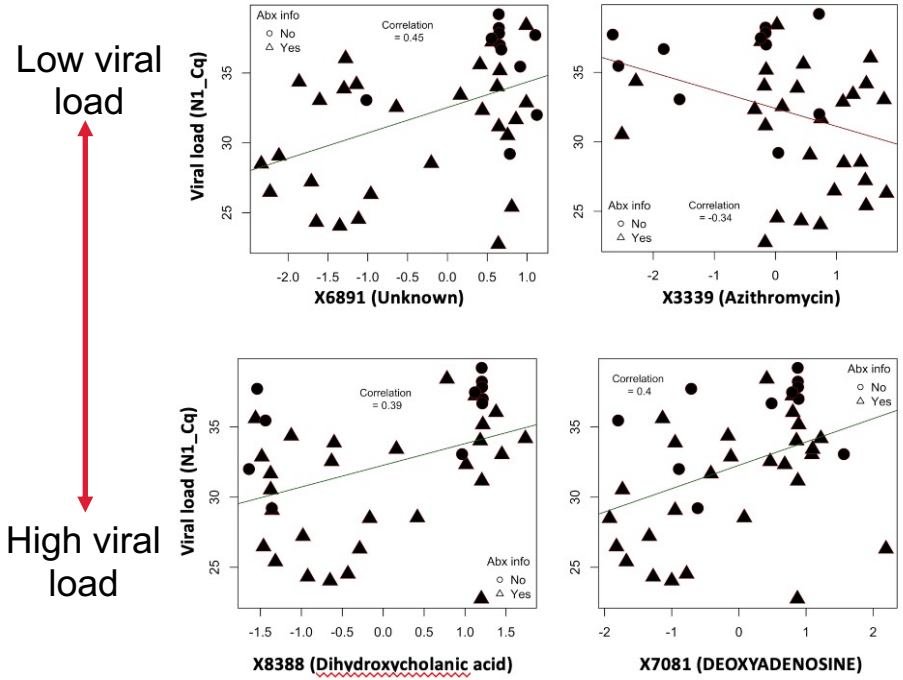


Low viral load

High viral load

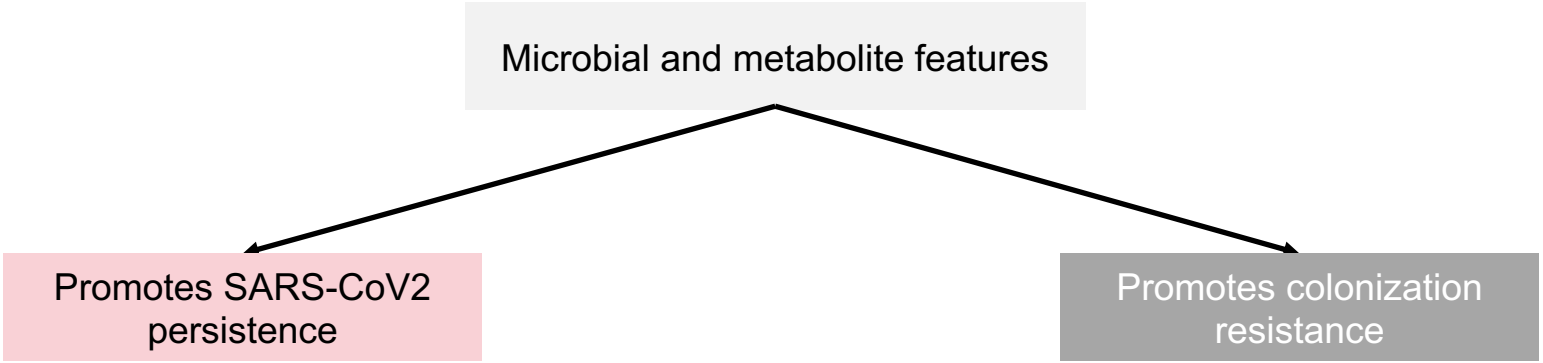


Enrichment of bile acid and purine metabolites is associated with gut viral clearance over time



- Higher concentration of antibiotics such as Azithromycin and their derivatives associated with higher gut viral persistence
- Higher concentration of other metabolites specifically metabolites involved in normal human metabolism associated with viral clearance

Summary



- Higher antibiotics usage
- *Clostridium* and *Bacteroides* enrichment
- Degradation pathways specifically degradation of simple polysaccharides
- Higher intensity of antibiotics or their derivates

- Low/No antibiotics
- *Prevotella* enrichment
- Biosynthetic pathways specifically synthesis of SCFAs and Glucosamine
- Higher intensities of metabolites involved in bile acid and purine metabolism

Acknowledgments

Cedars-Sinai

Suzanne Devkota, PhD
Anthony Martin, PhD
Jacob Moskowitz, DVM/PhD
Stephanie Bora, Ph.D

David Underhill, PhD
Kate Legree, PhD
Peter Chen, MD

Univ of California-San Diego

Rob Knight, PhD
Pieter Dorrestein, PhD