Ribaxamase was evaluated in a phase 2b clinical study that met its primary endpoint of to degrade certain β-lactam antibiotics in the GI tract to preserve the gut microbiome. SYN-006 (ribaxamase) is a clinical-stage β-lactamase formulated for oral delivery intended to degrade β-lactam antibiotics systemically and orally. Antibiotic inactivation represents a new paradigm for preservation of the gut microbiome and reduction of antibiotic resistance.

**Methods.** For use with oral β-lactams, a ribaxamase formulation, SYN-007, was engineered for release in the lower small intestine, distal to the site of antibiotic absorption. For use with IV carbapenems, SYN-006, a novel metallo-β-lactamase, was formulated for oral delivery. SYN-007 (10 mg, PO, TID) was evaluated in dogs treated with oral amoxicillin (30 mg/kg, PO, TID) for 5 days. SYN-006 (50 mg, PO, QID) was evaluated in pigs treated with ertapenem (30 mg/kg, IV, SID) for 4 days. Serum antibiotic levels were measured and fecal DNA whole-genome shotgun sequence analyses were performed.

**Results.** In dogs and pigs, systemic antibiotic levels were not significantly different between INTERACT and SYN-006. Fecal DNA-based metagenomics analyses demonstrated that oral amoxicillin and IV ertapenem resulted in significant changes to the gut microbiome. SYN-007 and SYN-006 attenuated microbiome damage and reduced emergence of antibiotic resistance.

**Conclusion.** Ribaxamase, SYN-007, and SYN-006 have the potential to protect the nonnal gut microbiota from antibiotic-mediated collateral damage and to mitigate emergence and spread of antibiotic resistance, thereby broadening the utility of this prophylactic approach to include all classes of β-lactam antibiotics, delivered both systemically and orally. Antibiotic inactivation represents a new paradigm for preservation of the gut microbiome and reduction of antibiotic resistance.

**Disclosures.** All authors: No reported disclosures.

619. Intestinal Microbiome Changes Associated with Immune Status and *Clostridium difficile* Colonization in Hospitalized Children

Sindhu Mohandas, MD1; VGA Soma, MD2; Tresa Ambrookan, MD3; David Goldman, MD4; Dong-Ninh Tran, PhD5; George Weinstock, PhD6; Erica Sodergren, PhD7 and Betty C. Herold, MD, FIDSA, FPID8; 1Children’s Hospital of Wisconsin, Milwaukee, Wisconsin; 2Division of Pediatric Infectious Diseases, Children’s Hospital at Montefiore, Bronx, New York; 3Pediatrics, Bronx Lebanon hospital, Bronx, New York; 4Children’s Hospital at Montefiore, Bronx, New York; 5Jackson Laboratory for Genomic Medicine, Farmington, Connecticut; 6Department of Pediatrics and Microbiology-Immunology, Albert Einstein College of Medicine, Bronx, New York.

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**Background.** The intestinal microbiome modulates local and systemic immune responses and may impact clinical outcomes. However, there are few studies in pediatric patients. We conducted a cross-sectional study of fecal microbiomes in hospitalized children on a single inpatient unit at Children’s Hospital at Montefiore, Bronx, New York in 2016–2017 to test the hypothesis that “high-risk” children with chronic illnesses (cancer, transplant and sicle cell disease [SCD]) have decreased microbial diversity and higher rates of asymptomatic colonization with *C. difficile* compared with children hospitalized on the same ward but without similar risk factors.

**Methods.** Stool was collected within 72 hours of admission from patients who provided consent and assayed for *C. difficile* colonization by glutamate dehydrogenase (GDH); microbiome analysis was performed by 16S RNA sequencing. Clinical and demographic data were obtained from the EMR.

**Results.** One hundred and six unique patients provided a sample for analysis. Sixty-nine were categorized as high-risk, including 32 SCD patients. *C. difficile* colonization rates were 22% and 19% in the high-risk and low-risk groups, respectively, but highest in the subset of SCD patients on penicillin prophylaxis (33%). The high-risk group had a trend toward lower microbial diversity than controls, and SCD patients exhibited a diversity index greater than other high-risk patients. Antibiotic use in the last 3 months and PPI use were associated with decreased microbial diversity across the entire study population (*P* = 0.004, *P* = 0.007, respectively). Among children with SCD, those on penicillin prophylaxis had a trend toward decreased alpha diversity while folic acid was associated with increased diversity (*P* = 0.02). SCD patients had greater quantities of *Bacteroides* and *Parabacteroides* and fewer *Escherichia* and *Shigella* than the other cohorts.

**Conclusion.** *SCD* and penicillin prophylaxis might be risk factors for *C. difficile* colonization and intestinal dysbiosis. The implications of these findings require further longitudinal study.

**Disclosures.** All authors: No reported disclosures.

620. Oral β-Lactamase Therapies Prevent Microbiome Damage and Attenuate Antibiotic Resistance From IV and Oral Antibiotics in Large Animal Models of Antibiotic-Mediated Gut Dysbiosis

Shela Connolly, PhD1; Christian Furlan-Freguia, PhD2; Brian Fanelli, BS3; Nur X. Hasan, PhD4; Rita R. Colwell, PhD5 and Michael Kaleko, MD, Ph.D6; 7Synthetic Biologics, Inc., Rockville, Maryland; 8CosmosID, Inc., Rockville, Maryland

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**Background.** Antibiotics can damage the gut microbiome leading to overgrowth of pathogens and provide selective pressure for emergence of antibiotic resistance. SYN-004 (ribaxamase) is a clinical-stage β-lactamase formulated for oral delivery intended to degrade certain β-lactam antibiotics in the GI tract to preserve the gut microbiome. Ribaxamase was evaluated in a phase 2b clinical study that met its primary endpoint of significantly reducing *C. difficile* infection in patients treated with IV ceftazidime and demonstrated protection of the gut microbiome with reduced emergence of antibiotic resistance. Ribaxamase is intended for use with IV penicillins and cephalosporins, but does not degrade carbapenems. β-lactamase-mediated microbiome protection was expanded to include oral and carbapenem antibiotics.

**Methods.** For use with oral β-lactams, a ribaxamase formulation, SYN-007, was engineered for release in the lower small intestine, distal to the site of antibiotic absorption. For use with IV carbapenems, SYN-006, a novel metallo-β-lactamase, was formulated for oral delivery. SYN-007 (10 mg, PO, TID) was evaluated in dogs treated with oral amoxicillin (30 mg/kg, PO, TID) for 5 days. SYN-006 (50 mg, PO, QID) was evaluated in pigs treated with ertapenem (30 mg/kg, IV, SID) for 4 days. Serum antibiotic levels were measured and fecal DNA whole-genome shotgun sequence analyses were performed.

**Results.** In dogs and pigs, systemic antibiotic levels were not significantly different between INTERACT and SYN-006. Fecal DNA-based metagenomics analyses demonstrated that oral amoxicillin and IV ertapenem resulted in significant changes to the gut microbiome. SYN-007 and SYN-006 attenuated microbiome damage and reduced emergence of antibiotic resistance.

**Conclusion.** Ribaxamase, SYN-007, and SYN-006 have the potential to protect the nonnal gut microbiota from antibiotic-mediated collateral damage and to mitigate emergence and spread of antibiotic resistance, thereby broadening the utility of this prophylactic approach to include all classes of β-lactam antibiotics, delivered both systemically and orally. Antibiotic inactivation represents a new paradigm for preservation of the gut microbiome and reduction of antibiotic resistance.

**Disclosures.** All authors: No reported disclosures.

621. Treatment of Recurrent *Clostridium difficile* Infection with SER-109 Increases the Concentration of Secondary Bile Acids in a Dose-Dependent Manner

Matthew Hess, PhD1; Christopher Ford, PhD2; Edward OBrien, PhD3; Jennifer Wortman, PhD1; Liyang Diao, PhD1; Christopher Desjardins, PhD1; Amelia Tomlinsion, PhD1; Kevin Litofsky, PhD2; Mark Wilcox, MD2; Anthony Buckley, PhD2; Patricia Bernardo, ScD1; Barbara McGovern, MD3; John G. Aurnos, PhD4; David N. Cook, PhD5 and Michele Trucksis, PhD, MD6; Seres Therapeutics, Inc., Cambridge, Massachusetts; 7Leeds Teaching Hospitals & University of Leeds, Leeds, UK; 8University of Leeds, Leeds, UK

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**Background.** *C. difficile* recurs when dormant spores germinate in the dysbiotic gut, facilitated by an increase of 1° vs. 2° bile acids. SER-109, an ecology of bacterial spore-forming species richness, (ii) concentrations of secondary bile acids, and (iii) reduced rCDI in our Phase 2 trial (Ph2). We explored whether higher doses of SER-109 were associated with an increase in 2° bile acids.

**Methods.** Whole metagenomic shotgun (WMS) data were generated from stool, and species were identified using a proprietary build of MetaPhAn. Evaluation of spore-forming species richness and bile acid concentrations identified effects of SER-109 treatment. A triple stage bioreactor model of the human gut and rCDI was used to evaluate the impact of microbial therapeutics.

**Results.** Phlb subjects who received a higher dose (>1.5 x 10^9 SporQ) had significantly higher spore-forming species richness than subjects who received a low dose (<1.5 x 10^9 SporQ) at Week 1 (post treatment *P* = 0.017, Figure 1). Spore-forming species richness in patients receiving a low dose in Phlb was comparable to that observed in non-recurrent patients in Ph2, who received the same mean dose (Figure 1). Phlb subjects in the high dose group had a significantly higher concentration of 2° bile acids as compared with Phlb low dose subjects (non-recurrent and recurrent) (Phlb subjects *P* = 0.036, *P* = 0.001, respectively, Figure 2). A higher dose (3 x 10^9 SporQ x 3 days) suppressed recurrence in a gut model of rCDI, a single dose did not.

**Conclusion.** Higher doses of SER-109 are significantly associated with (i) higher spore-forming species richness, (ii) concentrations of secondary bile acids, and (iii) prevention of recurrence in an gut model of CDI. These results suggest that SER-109 in the Phase 2 trial was biologically active and catalyzed a functional change in the microbiome of a subset of subjects; a dose increase may optimize efficacy across a broad population. Sears has initiated a Phase 3 study of SER-109 to reduce rCDI, which includes all disease titer and frequency.
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622. Increased IgA Coating of Gut Microbes After Administration of Killed, Whole-Cell Oral Cholera Vaccine

Ana Wei, MD, MPH; Tausiq Bhuyan, PhD; Meti Debela, BSc; Fahima Chowdhury, MBBS; Ashraful Khan, MBBS; Regina LaRocque, MD, MPH, FIDSA; Edward Ryan, MD; Stephen B. Calderwood, MD, FIDSA; Firdausa Qadri, PhD; Harris, MD, MPH, FIDSA; Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts. Infectious Diseases Division, International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B), Dhaka, Bangladesh

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Background. Cholera vaccines are recommended for use in outbreaks to prevent infections and reduce severity of disease. Variable immune responses are observed after administration of killed, whole-cell cholera vaccines, and limited data suggest that the gut microbiome may be one factor influencing immune responses to vaccination.

Methods. We used microbial DNA sequencing of stool and serum vibriocidal titers to examine the gut microbiome and immune responses to vaccination at day 0, 7, 17 and 44 in adult vaccine recipients in Dhaka, Bangladesh. Using gating by try-based bacterial cell sorting, we identified IgA-coated gut microbes in stool before and after vaccination in a subset of patients.

Results. Vibriocidal titer magnitude and kinetics were used to classify participants. Within 17 days of vaccination, 86/89 (96%) adults developed a four-fold rise in vibriocidal titer. Gut microbial diversity was not significantly changed after vaccination. Rate of seroconversion (four-fold increase in vibriocidal titer by Day 3 after vaccination) was faster in participants with increased bacteria from the genus Prevotella (multivariate analysis using linear models, p value 0.04). The gut microbes of participants with higher peak vibriocidal titers was characterized by increased Prevotella copri (nonparametric signed rank test, linear discriminant analysis score >3.5), particularly the species Prevotella copri (P < 0.001 unpaired t-test, linear discriminant analysis score >3.5), particularly the species Prevotella copri (P < 0.001, unpaired t-test, linear discriminant analysis score >3.5). Lipopolysaccharide from Prevotella species is known to increase vaccination-associated antigen-specific antibody titers in animal models. Additionally, IgA coating of gut microbes in stool increased after vaccination, from 8.9% IgA coated at baseline to a peak level of 19% during follow-up (Wilcoxon signed rank test, P < 0.01).

Conclusion. Certain microbiome profiles are correlated with greater immune responses to cholera vaccination, and IgA coating of gut microbes indicates which components of the gut microbiome may be participating in the mucosal immune response. The potential for modulation of mucosal immune responses based on gut microbial species warrants further study.

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623. Dynamic Nature of the Gut Resistome Among Infants in Singapore

Amanda Zain, MMEd; Gaik Chin Yap, MSc; Ricky W. Purbojati, MSc; Daniela Isabel Moses, PhD; Lynette P.C. Shek, FRCPCH; Anne Goh, MMEd; Hugo P.S. Van Bever, PhD; Oon Hooi Tooh, MMEd; Jian Yi Soh, MMed; Biju Thomas, MD; Mahesh Babu Ramanurthy, MD; Daniel Y. T. Goh, MMed; Christophe Lay, PhD; Evelyn Loo Xiu Ling, PhD; Shu-E Soh, PhD; Fabian Yap, MMEd; Kok Hian Tan, MRCPG; Yap-Seng Chong, PhD; Keith M. Godfrey, PhD; Peter D. Gluckman, MD; Stephan Schuster, PhD; Ritu Banerjee, MD, PhD and Bee Wah Lee, MBBS

1Department of Paediatrics, Khoo Teck Puat-National University Children’s Medical Institute, National University Health System, Singapore, Singapore. 2Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. 3Singapore Center On Environmental Life Sciences Engineering (SCELSE), Nanyang Technological University, Singapore, Singapore. 4Department of Paediatrics Allergy and Respiratory, KK Children’s Hospital and Women’s Hospital, Singapore, Singapore. 5Department of Paediatrics, Yong Loo Lin School of Medicine, Singapore, Singapore. 6Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research Singapore, Singapore, Singapore. 7Department of Obstetrics & Gynaecology, National University of Singapore, Singapore, Singapore. 8MRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom. 9Division of Pediatric Infectious Diseases, Vanderbilt University, Nashville, Tennessee

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Background. The gut microbiome harbors antibiotic resistance genes (ARGs), known as the resistome, that has the potential to spread and contribute to the global