crisis of antibacterial resistance. Little is known about the genomic traits of the infant resistome, especially in areas with high endemic antibacterial resistance.

Methods. We analyzed ARGs among a subset of infants from the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) birth cohort. The subset included 75 mostly term, healthy Singaporean infants born from November 2009 to May 2011. Stool samples collected at Week 3 (W3), months 3 (M3), 6 (M6) and 12 (M12) were analyzed using shotgun metagenomics. Sequencing reads were assembled into contigs using MEGAHIT. ARGs were identified using ResFinder 2.1. Demographic, perinatal factors, pre- and postnatal antibiotic exposure were collected.

Results. One hundred and eighty-eight stool samples from 75 infants were studied. Of the 169 ARGs detected, the four commonest ARGs were blaZ, fosA, tet(M) and mef(A), conferring resistance to β-lactams, fosfomycin, tetracyclines, and macrolides respectively. The number of ARGs per infant increased over time (median: W3 = 18.0, M12 = 22.0, $P < 0.05$). At W3, 118 ARGs were detected among 28 infants. The most prevalent ARGs were fos(A) and blaZ (both 96.4%) at W3. Among the 22 infants who had samples at W3 and M12, only six of 118 ARGs detected at W3 were also present at M12. These were mef(A), msr(D), tet(W), erm(B), tet(M) and fosA, conferring macrolide and tetracycline resistance. Their prevalence among at M12 was 100%, 93.3%, 90.9%, 84.6%, 68.8% and 52.4%, respectively. ARGs were not associated with gender, race, delivery mode, peripartum or postnatal antibiotics in infancy. Of note, longitudinal analysis showed that only the cfxA gene, which confers β-lactam resistance, was more prevalent in infants whose mothers received antibiotics in pregnancy than those whose mothers did not (adjusted $P < 0.05$).

Conclusion. In regions with high endemic antimicrobial resistance such as Singapore, the infant gut harbors a diversity of ARGs as early as 3 weeks of age. Few ARGs persisted through infancy, implying the dynamic nature of the infant resistome. The lack of association of ARGs with most clinical variables evaluated here suggests that other unrecognized factors may contribute to the plasticity of ARGs in the infant gut resistome.

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624. Microbiota and Associations with Treatment Outcome in Fecal Microbiota Transplantation

Tatiana Bogdanovich, MD PhD[1]; Alison Morris, MD, MS[2]; Adam Fitch, BS[3]; Kelvin Li, MS, MBA[3]; Rachel Nettles, BS[3]; Nicolas Sluis-Cremer, PhD[3] and Barbara Methe, PhD[3]; [1]Medicine/Infectious Diseases, University of Pittsburgh, Pittsburgh, Pennsylvania, [2]Medicine (PACCM), University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, [3]Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

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Background. Fecal microbiota transplantation (FMT) can be an effective treatment of recurrent *Clostridium difficile* infection (CDI), although non-responsiveness to treatment remains poorly understood. Here we examine the bacterial composition of stool from FMT recipients using culture-independent methods to identify associations between bacterial community structure, route of FMT administration (colonoscopy or freeze-dried encapsulated FMT (capsules)), treatment outcome and donor. We hypothesized that multiple community structures could be associated with and may better define treatment outcome.

Methods. We tested this hypothesis by analyzing bacterial composition profiles and their relationship with treatment route, outcome and donor using bioinformatics and multivariate statistics on 16S rRNA gene sequences (16S) from 21 individuals (seven male, 14 female, median 68 years) with recurrent CDI prior to and after FMT. Successful endpoint was defined as no relapse of *C. difficile* associated diarrhea during 12 weeks post-FMT. There were 17 successes (four colonoscopy, 13 capsules) and four failures (all capsules). Analyses of 16S profiles included permutational analysis of variance (PERMANOVA) and linear regression models applied to bacterial abundances and diversity (as responses).

Results. Significant differences were determined between pre- and post-FMT successes and failures ($P < 1e^{-4}$, $R^2 = 0.24$). No differences were seen between route ($P = 0.15$) or donor ($P = 0.20$). Profiles of failed FMT recipients were more similar to pre-FMT profiles by multidimensional scaling. Analyses of changes in abundance of pre-FMT profiles vs. outcome, controlled for age and sex, identified significant ($P < 0.01$) differences across 19 of the 25 most abundant taxa. Of the five most abundant taxa, Enterobacteriaceae and *Esherichia-Shigella* decreased significantly in successful outcomes, while *Faecalibacterium*, *Blautia*, and *Bacteroides* increased. However, variation in individual composition was also significant suggesting that multiple profiles represent successful outcomes.

Conclusion. Increases in microbiota diversity are generally achieved in successful FMT regardless of administration route, although more than one bacterial composition profile can be identified.

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625. Metabolic Interactions Drive *Staphylococcus aureus* Adaptation to the Skin

Karen Acker, MD[1]; Tania Wong, PhD[1]; Emily S. West, MD[2]; Paul Planet, MD PhD[3] and Alice Prince, MD, FIDSA[4]; [1]Columbia University, New York, New York, [2]University of California San Francisco, San Francisco, California, [3]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, [4]Pediatrics, Columbia University, New York, New York

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Background. *Staphylococcus aureus* is the most common pathogen causing skin and soft-tissue infection and poses a particular problem to patients with atopic dermatitis who have increased colonization and infection rates. *S. aureus* is a versatile pathogen that adapts to the relatively hypoxic environment of the skin, although the underlying mechanisms of adaptation remain unclear. We hypothesized that adaptation to the skin is largely driven by metabolic interactions between *S. aureus* and keratinocytes.

Methods. We characterized 10 clinical *S. aureus* isolates obtained from individual patients with atopic dermatitis using whole genome sequencing and qRT-PCR to evaluate their genotypic and phenotypic properties. The metabolic and inflammatory responses of keratinocytes to *S. aureus* infection were assessed *in vitro* in primary human keratinocytes and *in vivo* in a murine cutaneous abscess model.

Results. Host-adapted *S. aureus* isolates from atopic dermatitis patients are phylogenetically diverse and are associated with varying severity of disease. They stimulate glycolysis and stabilize HIF1α in keratinocytes, and produce a similar infectious phenotype to WT USA300 LAC in a murine cutaneous abscess model. Numerous metabolic nonsynonymous mutations in genes encoding glycolytic and TCA cycle enzymes were identified in these strains. Increased expression of *fumC*, that encodes fumarase which hydrates fumarate to malate in the TCA cycle, was observed in the clinical isolates compared with WT LAC. Based on this finding and recent literature demonstrating that fumarate accumulation in immune cells is vital for trained immunity and that it inhibits glycolysis via GAPDH inactivation, we hypothesized that host-adapted *S. aureus* strains upregulate fumarase in response to increased fumarate levels in the skin. Keratinocytes infected with our clinical strains secrete increased fumarate compared with uninfected keratinocytes.

Conclusion. *S. aureus* strains from atopic dermatitis skin represent a diverse population that are unified in their ability to adapt via metabolic interactions with keratinocytes. They adapt to increased fumarate levels in the skin by upregulating fumarase which likely represents a feedback inhibitory response to increased glycolysis in keratinocytes.

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626. An Inexpensive Quantitative Method for Testing Anti-Fungal Drug Activity Using the Invertebrate *Caenorhabditis elegans*

Ielyzaveta Pomytkina, BS; Jon Olson, MS and Jill Adler-Moore, PhD; Biological Sciences, California State Polytechnic University, Pomona, California

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Background. Due to ethical and budgetary concerns associated with the use of vertebrate animals in research, interest in alternative models has increased over the past several decades. In the present study, we developed a *Candida albicans* quantitative infection model in *Caenorhabditis elegans*, a nonparasitic invertebrate nematode, to test the antifungal effects of liposomal amphotericin B (L-AmB).

Methods. To establish a lethal *C. albicans* infection, larval Stage 4 worms [$n = 30$/group (gp)] were fed various doses of yeast (2.5×10^2–2.5×10^5 cells/gp) for 4 hours at 20°C or 30°C. The infection was evaluated by monitoring worms for mortality and determining fungal burden in worm homogenates by plating for colony forming units every 24 hours for 4 days post-challenge. To examine the worm's ability to ingest L-AmB and to determine drug toxicity, uninfected worms were fed L-AmB (6.3–25 μg/gp) for 4 hours at 30°C, and drug toxicity evaluated by survival with drug concentrations determined by bioassay of worm homogenates. The lack of toxicity allowed us to evaluate L-AmB activity in worms challenged for 4 hours at 30°C with 2.5×10^5 yeast cells/gp and then treated with L-AmB (0.5–25 ug/gp) for 4 hours at 30°C, with survival rate and fungal burden to assess L-AmB treatment.

Results. *Calbicans* infection was established in worms challenged with all yeast doses, with optimum infection observed with 2.5×10^5 yeast cells/gp at 30°C (13% survival in-infected worms vs. 87% in uninfected worms). We observed that uninfected worms could take up L-AmB at doses of 6.3–25 μg/gp and yet was not toxic for the worms (93–95% survival). In worms exposed to yeast and treated with L-AmB, complete clearance of infection was achieved with the higher doses (6.3–25 μg/gp), while lower doses (1.6–3.1 μg/gp) significantly reduced the fungal burden ($P \leq 0.05$). Infected worms, not treated with L-AmB had only 10% survival, while L-AmB improved survival in a dose-dependent manner giving 40% survival for 0.5 μg L-AmBi/gp and 100% survival for doses of 6.3 μg/gp and higher.

Conclusion. By using fungal burden as a readout of efficacy, along with survival, we have established a quantitative, reproducible, flexible method for examining the activity of L-AmB in *C. elegans* which could be expanded for use in evaluating other antifungal drugs and different pathogenic fungi.

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627. Differences in *C. difficile* Toxin A Binding in Humans: Adults vs. Infants

David Goldman, MD[1]; Ahmed Elshazly, MBBCh[2]; Ekaterina Dadachova, PhD[3] and Michelle Ewart, MD[4]; [1]Division of Pediatric Infectious Disease, Children's Hospital at Montefiore, Bronx, New York, [2]Internal Medicine, Atlantic Care Regional Hospital/Geisenger, Atlantic City, New Jersey, [3]Radiopharmacy, University of Saskatchewan, Saskatoon, SK1, Canada, [4]Pathology, Montefiore Medical Center, Bronx, New York

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Background. Children less than 1 year of age are commonly colonized with toxin-producing *C. difficile*, but appear to be immune to the associated colitis. Animal studies suggest that young infants lack receptors for *C. difficile* toxin, though this has never been documented in humans.