**Background.** Mycobacterium tuberculosis (Mtb) is the leading infectious cause of mortality; however, there is no vaccine that confers lasting protection. To investigate the immune response to Mtb, we have developed an ultra-low dose (ULD) infection model in mice that better reflects the heterogeneous outcomes of human infection. Additionally, we have identified a blood transcriptional signature, taken at day 24, that predicts future bacterial burden after day 70.

**Methods.** Mice were infected with an ULD (1–3 CFU) of H37Rv Mtb. Control mice were infected with 50–100 CFU. Blood was drawn at day 24 for RNA signature. At day 35, the following cell populations were correlated with an RNA signature score predicting disease progression: ESAT-6 tetramer+ CD4+ T cells ($R^2=0.35$, $P<0.01$), TR10 tetramer+ CD8+ T cells ($R^2=0.34$, $P<0.01$), and B cells ($R^2=0.28$, $P<0.01$) within the lung parenchyma, as well as CD11b+ cells, negative for CD64, Ly6c, Ly6g and MHCIIR ($R^2=0.38$, $P<0.01$) within the lung vasculature. These same populations were correlated with elevated CFU at day 83, as well as dendritic cells ($R^2=0.53$, $P<0.01$). No populations were correlated with a protective RNA score. We have observed the complex spatial organization of granulomas while optimizing our histocytometry panel. This includes infected macrophages (Fig 1) interacted with B cell aggregates, associated with naïve T cells, interspersed with CD44+ T cells, with diffuse staining for Ki67, suggestive of tertiary lymphoid structures (Figure 2).

**Conclusion.** This model replicates heterogeneity of TB seen in humans, while also providing a way to correlate differences in the immune response to future outcome. We have associated distinct immune cell subsets with the failure to control TB. With a larger sample size and data from histocytometry, we will have improved resolution to discern protective elements of the immune response to TB, which we can then test mechanistically in our model.

**Results.** At day 35, the following cell populations were correlated with an RNA signature score predicting disease progression: ESAT-6 tetramer+ CD4+ T cells ($R^2=0.35$, $P<0.01$), TR10 tetramer+ CD8+ T cells ($R^2=0.34$, $P<0.01$), and B cells ($R^2=0.28$, $P<0.01$) within the lung parenchyma, as well as CD11b+ cells, negative for CD64, Ly6c, Ly6g and MHCIIR ($R^2=0.38$, $P<0.01$) within the lung vasculature. These same populations were correlated with elevated CFU at day 83, as well as dendritic cells ($R^2=0.53$, $P<0.01$). No populations were correlated with a protective RNA score. We have observed the complex spatial organization of granulomas while optimizing our histocytometry panel. This includes infected macrophages (Fig 1) interacted with B cell aggregates, associated with naïve T cells, interspersed with CD44+ T cells, with diffuse staining for Ki67, suggestive of tertiary lymphoid structures (Figure 2).

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

1765. Strain-level Determination of the Contribution of Gut Microbiota to the Development of Bacteremia in Patients Undergoing Stem Cell Transplantation

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**Session:** 214. Host–pathogen Integration

Saturday, October 7, 2017: 8:30 AM

**Results.** At day 35, the following cell populations were correlated with an RNA signature score predicting disease progression: ESAT-6 tetramer+ CD4+ T cells ($R^2=0.35$, $P<0.01$), TR10 tetramer+ CD8+ T cells ($R^2=0.34$, $P<0.01$), and B cells ($R^2=0.28$, $P<0.01$) within the lung parenchyma, as well as CD11b+ cells, negative for CD64, Ly6c, Ly6g and MHCIIR ($R^2=0.38$, $P<0.01$) within the lung vasculature. These same populations were correlated with elevated CFU at day 83, as well as dendritic cells ($R^2=0.53$, $P<0.01$). No populations were correlated with a protective RNA score. We have observed the complex spatial organization of granulomas while optimizing our histocytometry panel. This includes infected macrophages (Fig 1) interacted with B cell aggregates, associated with naïve T cells, interspersed with CD44+ T cells, with diffuse staining for Ki67, suggestive of tertiary lymphoid structures (Figure 2).

**Conclusion.** This model replicates heterogeneity of TB seen in humans, while also providing a way to correlate differences in the immune response to future outcome. We have associated distinct immune cell subsets with the failure to control TB. With a larger sample size and data from histocytometry, we will have improved resolution to discern protective elements of the immune response to TB, which we can then test mechanistically in our model.

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

1766. The Gut Microbiota of Healthy Infants in the Community is a Reservoir for ESBL and Carbapenemase Producing Bacteria

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**Session:** 214. Host–pathogen Integration

Saturday, October 7, 2017: 8:30 AM

**Background.** The recent rapid rise of Extended-spectrum β Lactamase producing Gram-negative bacteria (ESBL-GNB) has seriously threatened the treatment of common infectious diseases. Neonates have an immature immune system and a delay in appropriate treatment due to ESBL-GNB sepsis can be fatal. This problem of delayed therapy is magnified in the developing world, where 99% of the population is unvaccinated. The widespread colonization of infants in a developing country with gut microbiota acquired neonatal sepsis occur. Additionally ESBL E. coli such as the strain ST131 are known to be persistent gut and vaginal colonizers. In animal models, these strains out-compete colonization with drug-sensitive, commensal E. coli. Gut colonization with ESBL isolates in infants may therefore have a profound impact on the infant microbiome and increase their risk of sepsis. Pakistan is a lower middle income country with high antibiotic use per capita and a sharp increase in ESBL-GNB infections. Recent data show that >50% of E. coli isolates from reproductive-aged women of Pakistan are resistant to more than one class of antibiotics. We aimed to determine the rates of gut colonization with ESBL-GNB among healthy infants in a community setting.

**Methods.** Stool samples were collected from 100 healthy infants living in a Pakistani suburban community between the ages of 5 and 7 months. Samples were plated on MacConkey agar to select for Gram-negative bacteria. Isolates were screened for resistance against several antimicrobial classes. Molecular testing of the stool samples was done using primers targeting conserved regions of ESBL and carbapenemase genes.

**Results.** Forty-eight percent of the infants were positive for ESBL producing Gram-negative bacteria, the majority of which were E. coli, and 7.5% were positive for carbapenemase producers, all of which belonged to Klebsiella spp. Molecular testing showed that 87% of the infant stools were positive for TEM β-lactamase gene, 68% for the CTX-M β-lactamase gene and 33% for the KPC carbaperemase gene.

**Conclusion.** The widespread colonization of infants in a developing country with ESBL-GNB is highly concerning. Further, our studies have revealed that the resistome of otherwise healthy infants may be a major reservoir of antibiotic resistant genes in the community. Gut microbiome analysis of the potential impact of colonization with antibiotic resistant bacteria is on-going.

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

1767. Longitudinal Comparison of the Microbiota During Klebsiella pneumoniae Carbapenemase: Producing Klebsiella pneumoniae (KPC-Kp) Acquisition in Long-Term Acute Care Hospital (LTACH) patients

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**Session:** 214. Host–pathogen Integration

Saturday, October 7, 2017: 8:30 AM

**Background.** Infection is a major preventable cause of transplant-related morbidity and mortality in patients undergoing hematopoietic stem cell transplantation (HCT). Bacteremia is the most common infectious complication in HCT, often occurring during periods of mucositis when the risk for microbial translocation from the intestine is increased. Prior research in HCT patients using 16S rRNA sequencing has identified that gut microbiota dominance by either Enterococcus spp. or Proteobacteria was associated with the development of bacteremia with Enterococcus spp. and Gram-negative organisms, respectively. No studies to date, however, have compared bacteremia isolates and gut microbiota samples at a strain-specific level using next-generation shotgun metagenomic sequencing (NGS).

**Methods.** In order to assess the degree of genetic similarity between bacteremia isolates and the gut microbiota, we identified patients who had undergone HCT at Stanford and developed a bacteremia between October 2015 and September 2016 for whom we had both saved blood culture isolates and stool samples within 30 days preceding bacteremia. We identified 15 patients from whom we had 17 bacteremia isolates, and performed NGS (Illumina HiSeq 4000) on stool and isolate DNA. We generated draft assemblies of isolate genomes using the SPAdes assembler, and aligned stool metagenomic reads to the draft isolate genomes using Bowtie2, filtering reads for perfect end-to-end alignment.

**Results.** Enteric gram-negative bacteremia isolates were identical to those in the gut microbiota, as has been demonstrated in prior studies using older strain-typing methods. Surprisingly, we also identified gram-negative organisms that were isolated in both the blood and stool prior to bacteremia, which challenges existing dogma regarding sources of gram-positive bacteremia-causing organisms.

**Conclusion.** Using a highly sensitive and accurate NGS-based strain typing method, we provide evidence of translocation of organisms from the gut microbiota and subsequent bacteremia. The gut was confirmed as a source for both classic enteric gram-negative and classically non-enteric Gram-positive bacteremia in HCT patients. These findings may have implications for the origins of bacteremia in HCT patients previously classified as CLABSIs.

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Background. Colonization with KPC-Kp precedes infection and represents a potential target for intervention. To identify microbial signatures associated with KPC-Kp acquisition, we conducted a prospective, longitudinal study of the fecal microbiota in LTACH patients at risk of acquiring KPC-Kp.

Methods. We collected admission and weekly rectal swab samples from patients admitted to one LTACH from May 2015 to May 2016. Patients were screened for KPC-Kp by PCR at each sampling time. KPC acquisition was confirmed by culture of KPC-Kp. To assess changes in the microbiota related to acquisition, we sequenced the 16S rRNA gene (V4 region) from collected rectal swabs. Diversity, intra-individual changes, and the relative abundance of the operational taxonomic unit (OTU) that contains KPC-Kp were compared in patients who were KPC-negative upon admission and who had at least one additional swab sample collected.

Results. 318 patients (247 samples) were eligible for analyses; 3.7 samples (mean) were collected per patient. Sixty-two patients (19.5%) acquired KPC-Kp (cases) and 256 patients remained negative for all carbapenem-resistant Enterobacteriaceae throughout their stay (controls). Median length of stay before KPC-Kp detection was 16 days. At time of KPC-Kp acquisition, levels of an OTU increased significantly compared with pre-acquisition samples and to samples from control patients (Wilcoxon test, \(P < 0.0001\)). Similarly, we observed a decrease in total diversity of the fecal microbiota at time of acquisition in cases (\(P < 0.01\)). Compared with controls, cases exhibited decreased intra-individual fecal microbiota similarity immediately prior to acquisition of KPC-Kp (\(P < 0.01\)). Comparison of microbial features at time of admission using random forest revealed a higher abundance of Enterococcus and Escherichia OTUs in controls vs cases.

Conclusion. We observed intra-individual-level shifts in the fecal microbiota of case patients prior to acquisition of KPC-Kp. Compared with patients who did not acquire KPC-Kp, cases exhibited significant changes in microbiota diversity and increased abundance of potential KPC-Kp at acquisition. Our results suggest that shifts in the microbiota may precede colonization by KPC-Kp.

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1769. Assessing The Impact of The National Healthcare Safety Network’s (NHSN) New Baseline on Acute Care Hospital Standardized Infection Ratios (SIRs)

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Background. More accurately measure the progress of healthcare-associated infection (HAI) prevention efforts, the CDC’s National Healthcare Safety Network (NHSN) surveillance system updated risk-adjustment models for computation of updated Standardized Infection Ratios (SIRs), the primary HAI summary measure by NHSN. This study sought to examine how the updated SIRs varied from the previous SIRs calculated using older baselines for acute care hospital HAIs.

Methods. We analyzed NHSN data for healthcare facility-onset laboratory-identified Clostridium difficile [CDI] and methicillin-resistant Staphylococcus aureus [MRSA] bacteremia reported in accordance with the CMS’ inpatient quality reporting program Data. The unit of analysis was CMS-defined community-onset CDI or MRSA facility reporting in 2015. We compared overall distributions of CDNN-level SIRs (CCN-SIRs) between new risk-adjustment models using a 2015 baseline (SIR_NEW) and old models using a 2011 baseline (SIR_OLD) and tested location shift (median from row to row) of pairwise differences. We also examined the magnitude of shift in SIR from old to new baseline.

Results. For each HAI, the national pooled mean SIR of the new baseline was \(< 1.0\). For CDI, the overall distribution of CCN_SIR_NEW and CCN_SIR_OLD were from 0.33 to 1.86, and the median SIRs were from 0.69 to 1.26. For MRSA, the SIR differences were not significant. Most CCN_SIRs (83% for CDI, 93% for MRSA) remained in the same significance category across the old and new baselines (“worse,” “better,” “not different from national benchmark”), and few CCN_SIRs were reallocated to a less favorable category. For 75% of