Background. *Streptococcus pneumoniae* is the main bacterial cause of pneumonia in the United States and globally. Although pneumococcal conjugate vaccines are highly effective against invasive pneumococcal disease, they are less effective against pneumonia, particularly in the elderly and those with immune deficiency. Given the additional challenge of antibiotic resistance, immunotherapy holds promise for treatment of pneumococcal pneumonia. The current PCV13 vaccine is less effective against serotype (ST) 3, which carries a higher risk of mortality than other vaccine-included STs. Our group has previously identified murine monoclonal antibodies (mAb) to ST3 capsular polysaccharide (PPS3) that are protective in experimental models of sepsis and pneumonia. The aim of the present study is to isolate and develop PPS3-specific human monoclonal antibodies (humAbs) as adjunctive immunotherapy for pneumonia.

Methods. We sorted individual PPS3-specific memory B cells from PBMCs isolated on days 0 and 7 post-vaccination from pneumococcal polysaccharide (PPS)-based vaccine (Pneumovax or Prevnar13) recipients using fluorescently labeled PPS3. Immunoglobulin heavy (Igh) and light (Igl) chains were sequenced, cloned into IgG1 and κ or λ vectors, and expressed in HEK-293 cells. PPS3 specificity was confirmed using ELISA.

Results. Here, we report the first 7 PPS3-specific humAbs isolated: 5 used lambda light chains and two used kappa light chains. Six of these humAbs used variable heavy 3 (V_H3) *Igh* gene elements. Kappa humAbs used V_H3-30 or V_H3-7, whilst lambda humAbs used V_H3-9, V_H3-72 or V_H3-23. Sequence analysis revealed somatic mutations in complementary determining as well as framework regions. Initial studies show that some humAbs agglutinate ST3 *in vitro*. Structure-function relationship studies are ongoing to identify specific determinants of PPS3 binding and biological efficacy against ST3 *in vitro* and *in vivo*.

Conclusion. The results of this study provide further understanding of the biology of PPS3 antibodies and may facilitate design of adjunctive immunotherapy to treat and prevent ST3 disease.

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648. Urinary Tract-Associated *Escherichia coli* Bacteraemia Strains Are Genetically More Virulent than Those Originating From Non-urinary and Neutropaenic Infective Foci

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Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. *Escherichia coli* is the leading cause of bacteremia with multi-drug-resistant strains proving increasingly problematic. Knowledge of the strain diversity associated with site-specific infections will inform the development of new preventative strategies, *e.g.* vaccines. We hypothesized that virulence factor (VF) scores of bacteremia strains from neutropenia patients with unknown infective foci (NPUIF—likely due to bowel translocation) would be lower than those from immunocompetent patients.

Methods. Immunocompetent (n = 49) and neutropaenic adults (n = 8) with *E. coli* bacteremia were prospectively enrolled and the focus of bacteremia determined. Neutropenia patients were enrolled only if there was no identifiable infective focus. Multilocus sequence typing and VF score (31 known VFs included) data were derived *in silico* following whole-genome sequencing and the results compared between patient groups.

Results. Bacteremia strains from immunocompetent patients with urinary tract infective foci (UTI-foci) harbored significantly more VFs (median VF score 16, range 8–24) than strains from both immunocompetent patients with non-UTI-foci (10, 2–22, P = 0.006) and NPUIF (8, 3–13, P < 0.0001). VF scores of strains from non-UTI-foci were not significantly different to those from NPUIF (10, 2–22 vs. 8, 3–13, respectively. P = 0.28). Logistic regression analysis demonstrated that VF score (OR 1.21, 95% CIs 1.01–1.46, P = 0.039) and recurrent urinary tract infection/urinary tract infection (OR 12.82, 95% CIs 1.24–132.65, P = 0.032) were independent predictors of bacteremia secondary to UTI-foci vs. non-UTI-foci in immunocompetent patients. Hence, for every unit increase in VF score, the odds of a bacteremia strain originating from UTI-foci increased by 1.21. *papA*, *papC*, *papE/F*, *papG*, *agn43*, *tia*, *iut*, *fyuA*, *kpsM* and *sat* were significantly more prevalent amongst strains associated with UTI-foci vs. non-UTI-foci amongst immunocompetent patients. *papC*, *papE/F*, *papG*, *agn43*, *tia*, *fyuA*, *hlyA*, *usp* and *clb* were significantly more prevalent amongst UTI-foci- vs. NPUIF-associated strains.

Conclusion. UTI-associated *E. coli* bacteremia strains have distinct VF profiles from those originating from non-UTI-foci and NPUIF. Future vaccines must consider this diversity to ensure adequate coverage of strains associated with site-specific disease.

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

649. The Clinical Significance of Sequence Type 17 of Vancomycin-Resistant *Enterococcus faecium*

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Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. Sequence type (ST) 17 of *vancomycin-resistant Enterococcus faecium* (VREF) is known to be associated with nosocomial isolates. However, there is no evidence of the effect of ST17 VREF on the patient`s clinical outcome. We conducted a retrospective cohort study to identify ST17 VREF would contribute to developing subsequent bacteremia among VREF-colonized patients.

Methods. VREF-colonized patients and its non-repetitive rectal VREF isolates were collected between March 2014 and February 2015. Subsequent bacteremia event within 1 year after colonization was reviewed from electronic medical records. STs were identified by multi-locus sequence typing. Cohort was defined as VREF with ST17 or non-ST17. Multivariable cox regression model was used to adjust effect of ST17 for developing subsequent bacteremia. If available, pulsed field gel electrophoresis (PFGE) was conducted to compare similarity between rectal and blood VREF isolates.

Results. Fifty-two patients with ST17 and 169 patients with non-ST17 VREF carriage were included in each cohort. There were six cases and 10 cases of subsequent bacteremia in cohorts ST17 and non-ST17, and 1-year VREF bacteremia free rates were 85.9% and 90.2%, respectively. There was no significant difference of subsequent bacteremia (P = 0.257) in log-rank test. However, after adjusted in multivariable models, VREF ST 17 was associated with subsequent bacteremia (adjusted relative risk, 4.02; 95% CI, 1.32–12.29, P = 0.015). Of 16 patients who had developed to subsequent VREF bacteremia, 12 VREF blood isolates could be analyzed. Only six cases (50%) of rectal and blood isolates had identical ST, whereas all available ST17 VREF cases (four cases) had identical ST and PFGE pattern (Figures 1 and 2). Patients who had identical ST isolates had shorter time difference than those who had non-identical ST isolates (P = 0.041).

Conclusion. In our study, ST17 VREF was risk factors of subsequent bacteremia and the strain that showed strong concordance between rectal and blood isolates. Further study is needed to improve clinical outcome of patients carrying VREF using genotype data of rectal VREF isolates.

Figure 1:

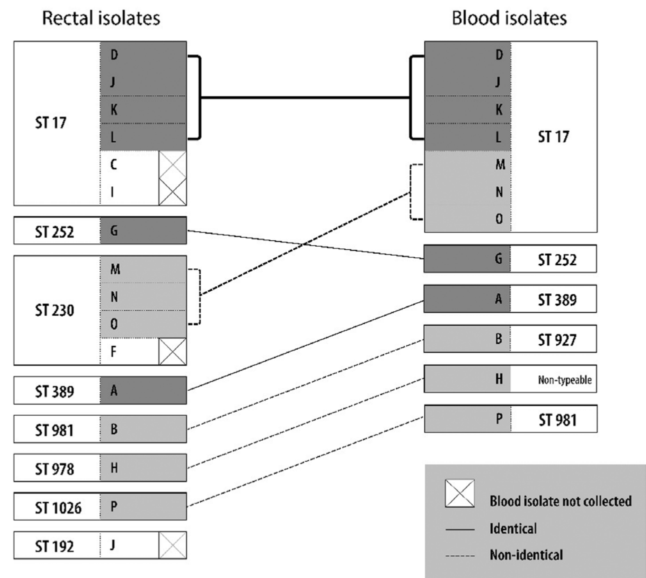
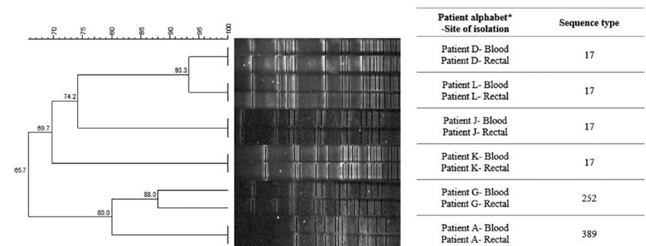


Figure 2:



Patient alphabet* -Site of isolation	Sequence type
Patient D- Blood Patient D- Rectal	17
Patient L- Blood Patient L- Rectal	17
Patient J- Blood Patient J- Rectal	17
Patient K- Blood Patient K- Rectal	17
Patient G- Blood Patient G- Rectal	252
Patient A- Blood Patient A- Rectal	389

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650. Genomic Analysis of Shiga Toxin-producing *Escherichia coli* From Symptomatic Patients and Asymptomatic Carriers

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Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. Shiga toxin-producing *Escherichia coli* (STEC) causes serious gastrointestinal illness. Although O157 is predominant, non-O157 infections have been increasingly reported worldwide. We used whole-genome sequencing (WGS) to investigate molecular characteristics and phylogeny of STEC isolates.

Methods. A total of 22 STEC isolates from symptomatic patients (n = 13) and asymptomatic carriers (n = 9) in a Japanese region during 2016–2017 were used. Serogroups were O157, O26 and O103 (n = 5, 12, and 5, respectively). WGS was performed using an Illumina Miseq. Genomic analysis was performed using web-based tools by the Center for Genomic Epidemiology. Single nucleotide polymorphism detection and construction of phylogenetic tree were performed using Mauve software.

Results. Of 76 virulence genes, 32 (42%) were detected (Figure 1). Eighteen (82%) and 7 (32%) isolates contained *stx1* and *stx2*, respectively. Twelve (91%) contained *eae*. *stx2* was more frequent in isolates from patients (P < 0.05), whereas *cba* was more frequent in isolates from carriers (P < 0.05). *stx2*, *etpD* were more frequent in O157 isolates (P < 0.05, respectively), whereas *stx1*, *efa1*, *cif*, *tccP*, *cba*, *lpfA* were more frequent in non-O157 isolates (P < 0.05, respectively). Nine acquired resistance gene (*aph(3´)-Ia*, bla_{TEM-1b}, *dfrA5*, *dfrA8*, *strA*, *strB*, *sul2*, *tetA*, *tetB*) were detected, while at least one was found in 6 (27%) isolates. Isolates from patients (5/13, 38%) were likely to have more resistance genes than isolates from carriers (1/9, 11%) (P = 0.33). Genotyping and multilocus sequence typing revealed all O26 isolates belonged to O26:H11 ST21, O103 belonged to O103:H2 ST17 and novel O103:H8 ST2836, while O157 belonged to O157:H7 ST11 and ST2966 (Figure 2). Phylogenetic tree showed O103:H8 ST2836 isolates clustered with O26, separated from O103:H2 ST17 (Figure 3). In a cluster of O26:H11 ST21 isolates, isolates from carriers formed a subcluster. O157 isolates clustered in a separate lineage. O157:H7 ST2966 isolates evolved from ST11.

Conclusion. Of the non-O157 isolates, O26:H11 ST21, which contained as many virulence genes as O157, was prevalent among both patients and carriers in our region, highlighting the importance of monitoring genomic characteristics of non-O157 STEC.

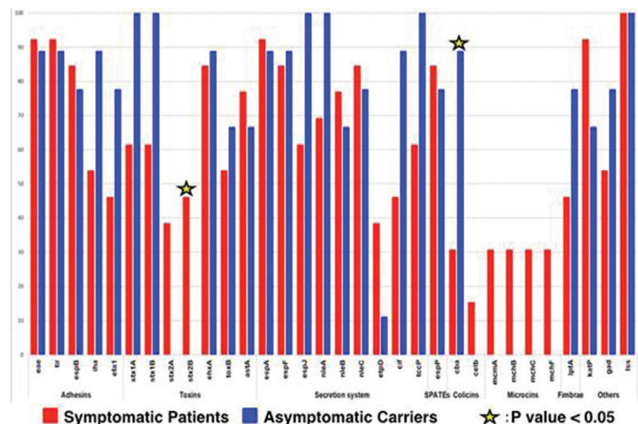

Fig. 1. Comparison of virulence genes in STEC isolates from symptomatic patients and asymptomatic carriers.

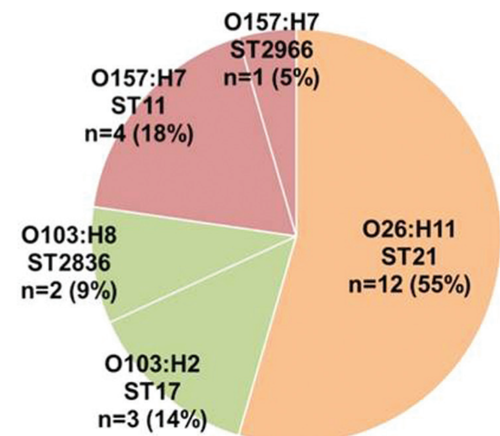

Fig. 2. Distribution of genotypes and sequence types (STs) among STEC isolates.

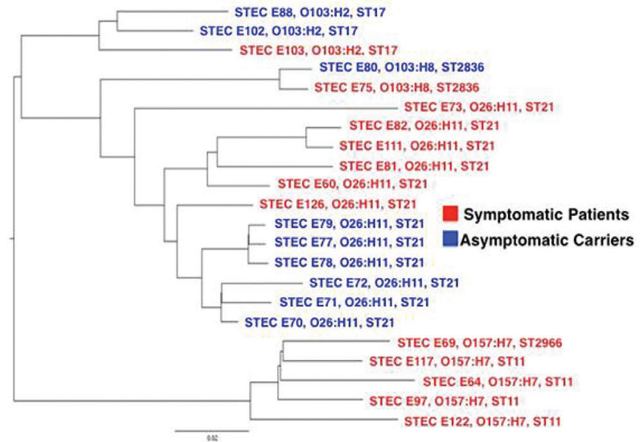

Fig. 3. Neighbor-joining phylogenic tree of STEC isolates.

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651. Non-encapsulation of Pneumococci as a Potential Evasion Mechanism From Vaccines

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Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. Our group has been continuously performing epidemiological analyses on capsular types of pneumococci since 2007. Pneumococcal conjugate vaccine decreased the proportion of nonvaccine capsular types. Furthermore, null-capsule isolates that produced PspK were also identified in our analysis. In this study, we analyzed the genetic background of null-capsule pneumococci and the mechanism of nonencapsulation.

Methods. Twenty-seven null-capsule isolates from 430 pneumococci that were isolated between 2010 and 2014 were used for this study. The capsular type was identified by DNA sequence-based methods, and genetic backgrounds were compared by multilocus sequence typing. Among the null-capsule isolates, the SP2852 strain was employed for non-encapsulation analysis. The *pspK* gene of this strain was replaced with *ermB* by homologous recombination (SP2852 Δ*pspK*::*ermB*). Then, genomic DNA from SP2852 Δ*pspK*::*ermB* was transformed into encapsulated isolates via natural transformation. Clindamycin-resistant isolates were further analyzed by sequence.

Results. The proportion of null-capsule isolates tended to increase from 5% in 2010–2011 to 12.3% in 2014. These null-capsule isolates were classified into 14 STs that included STs previously identified as capsule-positive isolates. To assess non-encapsulation via natural transformation, two encapsulated strains (serotype 19F and 14) were cultured with genomic DNA from SP2852 Δ*pspK*::*ermB*. Subsequently, clindamycin-resistant null-capsule isolates were detected with high frequency (2.5×10^{-4}–8.7×10^{-5}). Sequence analysis showed capsular coding regions of these null-capsule isolates were replaced with that of Δ*pspK*::*ermB*. Furthermore, these isolates grew significant faster than their parent strains.

Conclusion. Null-capsule isolates with various genetic backgrounds were revealed gradually after introduction of vaccine. Moreover, encapsulated strains could take up genomic DNA of null-capsule isolates more easily and become a null-capsule strain by homologous recombination, suggesting that non-encapsulation and acquiring PspK resulted in the emergence of null-capsule strains by natural transformation. Furthermore, non-encapsulation could be beneficial for pneumococci as an evasion mechanism from vaccines.

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

652. What Is Blood Got to Do with It? Genetic Susceptibility to Norovirus and Rotavirus Infection: Results From the SUPERNOVA Network

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