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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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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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:

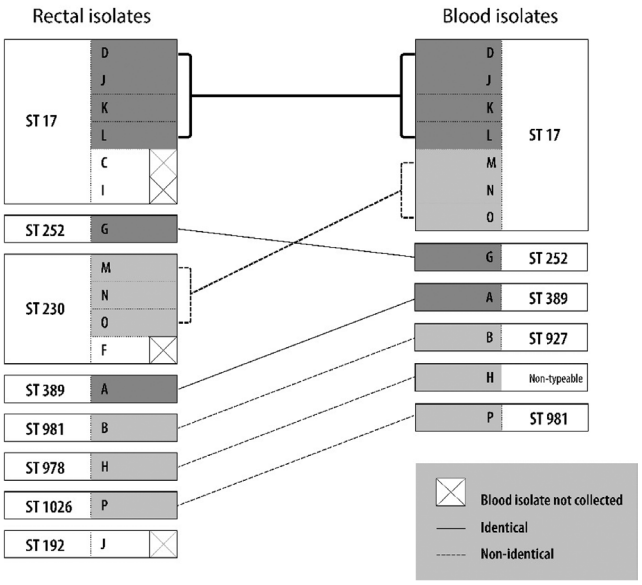
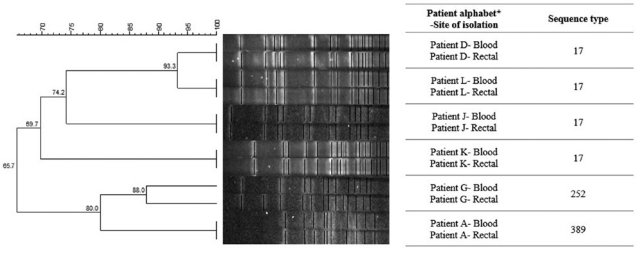


Figure 2:



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

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

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