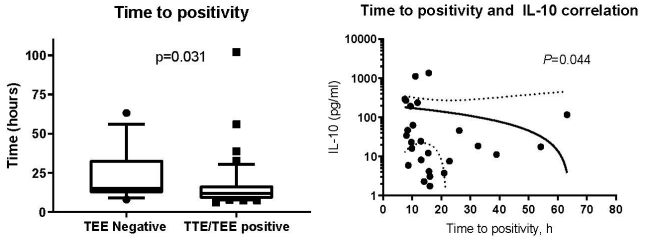
demographic and infection characteristics were collected. A 10-multiplex TH1/TH2 cytokine analysis was performed using electrochemoluminescence with the Meso-Scale Discovery platform analyzed by Mann–Whitney *U*.

***Results.*** Patients' median values were significantly elevated and above the normal range in CF for IL-1β ($P = 0.029$), IL-10 ($P = 0.018$), TNF-α ($P = 0.042$), and IL-6 ($P = 0.006$) (figure). Epidural abscess source was associated with CF, but no other host or pathogen characteristics correlated to outcome. Patients infected with isolates with VAN MIC = 2 mg/L (by Etest and broth dilution) had lower concentrations of IL-1β and IL-10 ($P = 1.5$ mg/L. In ROC analysis, IL-1β, IL-10, TNF, and IL-6 were higher sensitivity and specificity predictors of CF (AUC 0.65–0.71; $P = 0.05$).

***Conclusion.*** A suboptimal host immune response to SAB at presentation predicts adverse clinical outcomes. IL-10, TNF-α, and IL-6 serum concentrations appear to reflect immunopathology in patients with SAB. These predictive markers may be considered in therapeutic clinical decision-making, such as escalation of alternative therapies in high-risk patients and/or de-escalation treatment in low-risk patients. These data offer steps toward further refining therapeutic precision for patients with SAB beyond the standard clinical or microbiological metrics that are employed in current practice.




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

## 413. Differences in Inflammatory Mechanisms in *Pseudomonas aeruginosa* and *Staphyloccoccus auereus* Infections in Cystic Fibrosis

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**Session:** 49. Inflammation and Infectious Diseases
*Thursday, October 3, 2019: 12:15 PM*

***Background.*** Chronic bacterial lung infections are the primary cause of morbidity and mortality in cystic fibrosis (CF). The most common CF pathogens, *Pseudomonas aeruginosa* (*P. aeruginosa*) or *Staphylococcus aureus* (*S. aureus*), are common commensal or environmental organisms that adapt to the CF lung. We sought to investigate whether adaptation from early lung colonizer to chronic pathogen alters the bacterial effects on host inflammation.

***Methods.*** *P. aeruginosa* ($n = 25$) and *S. aureus* ($n = 25$) isolates from CF patients with early and chronic infections were acquired from Seattle Children's CF. Environmental ($n = 8$) and clinical, non-CF *P. aeruginosa* ($n = 8$) isolates were obtained from the University of Ottawa. *P. aeruginosa* reference strain PA14 and PA14 transposon mutants for T3SS and flagellin were used to observe the relationship between cell death and cytokine production. We infected THP-1-derived macrophages (PMA differentiated) *in vitro* for 3 hours with various MOIs. We subsequently measured cell death of THP-1-derived macrophages using neutral red assay and cytokine production using ELISAs.

***Results.*** Infections with PA14 mutants and non-CF *P. aeruginosa* isolates demonstrated that rapid cell death of THP-1-derived macrophages caused a reduction in cytokine production relative to strains that did not cause as much cell death. At 10 MOI, early *P. aeruginosa* isolates from CF patients induced more THP-1-derived macrophage cell death compared with chronic isolates ($P < 0.0001$). Chronic *P. aeruginosa* isolates induced greater production of TNF, IL-8, and IL-6 ($P < 0.01$, $P < 0.0001$, and $P < 0.0001$, respectively) compared with early strains. No difference in IL-1β production was observed. When controlling for cell death between the two groups by using heat-killed bacteria, the only difference maintained was in TNF production ($P < 0.01$). Between early and chronic *S. aureus* isolates, the one difference observed was greater IL-8 production among early isolates ($P < 0.01$).

***Conclusion.*** Chronic *P. aeruginosa* isolates from CF patients induce less cell death but more TNF, IL-8, and IL-6 production compared with early isolates. This suggests that *P. aeruginosa* producing chronic infections induce inflammatory signals that may contribute to increased morbidity among CF patients.

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

## 414. Developing Digital Phenotypes of Primary Immune Deficiencies Using Machine Learning on a Large Electronic Health Record Database

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***Background.*** More than 350 genetic disorders cause immune deficiencies; given the rarity of these conditions, in-depth study of infections associated with primary immune deficiencies (PID) requires extremely large sample sizes from broad populations. Using a large electronic health record (EHR) dataset, we linked clinical and microbiologic data to develop digital phenotypes for PID.

***Methods.*** Using the Cerner *HealthFacts* EHR dataset from 2009 to 2017 we extracted clinical and microbiologic data for hospitalizations from patients <18 years old with ICD9/10 PID diagnoses and ≥1 positive culture for infection. Machine learning models were used to identify key features to predict PID diagnosis. Features included patient and hospitalization characteristics; infectious agent and infection site; and selected comorbidities. Model validation was done using the area under the receiver operating characteristic (AUC) curve.

***Results.*** Overall 1316 patients with a PID were identified (Table 1). The 10 most common pathogens identified by PID are listed in Table 2. The models classified DiGeorge syndrome (positive predictive value 49%), functional disorders of polymorphonuclear neutrophils (PMN) (PPV 43%), and common variable immunodeficiency (CVID) (PPV 47%) better than combined immunodeficiency (CID) (PPV 20%); the overall true positive rate was 47% with an AUC of 0.73. Predictive features for each PID were as follows: CVID—having enteritis, hypertension, and pneumonia (Figure 1a); PMN—having hypoxia and hypertension (Figure 1b); DiGeorge syndrome—having congenital deformities and not having hypertension (Figure 1c); CID—finding *Staphylococcus aureus* in a wound or *Escherichia coli* in the blood were predictive of CID (Figure 1d).

***Conclusion.*** Early models demonstrate some discrimination, specifically for more common PIDs (CVID) and those with highly identifying factors (DiGeorge syndrome). These models can be improved by including a wider array of clinical data, and they provide a first look at a new methodology to digitally phenotype PIDs for future diagnostic use.

**Table 1. Patient counts by PID diagnoses**

| PID Diagnoses | Number of Patients | Percentage of Patients |
|---|---|---|
| Common Variable Immunodeficiency | 485 | 36.9% |
| DiGeorge Syndrome | 442 | 33.6% |
| Functional Disorders of Polymorphonuclear Neutrophils | 207 | 15.7% |
| Combined Immunodeficiency - Unspecified | 182 | 13.8% |
| Total | 1316 | 100% |

**Table 2. Ten most frequent infections per PID diagnosis**

| Diagnosis Description | Isolate Name | Infection Site | Infection Count | Infection % |
|---|---|---|---|---|
| Common variable immunodeficiency | *Pseudomonas aeruginosa* | Respiratory | 315 | 10.0% |
| Common variable immunodeficiency | *Candida albicans* | Respiratory | 248 | 7.9% |
| Common variable immunodeficiency | *Staphylococcus aureus* | Respiratory | 155 | 4.9% |
| Common variable immunodeficiency | *Staphylococcus aureus* | Wound | 105 | 3.3% |
| Common variable immunodeficiency | *Staphylococcus aureus* Methicillin Resistant | Respiratory | 103 | 3.3% |
| Common variable immunodeficiency | *Streptococcus pneumoniae* | Respiratory | 85 | 2.7% |
| Common variable immunodeficiency | *Haemophilus influenzae* | Respiratory | 79 | 2.5% |
| Common variable immunodeficiency | *Stenotrophomonas maltophilia* | Respiratory | 77 | 2.4% |
| Common variable immunodeficiency | *Candida glabrata* | Respiratory | 56 | 1.8% |
| Common variable immunodeficiency | *Serratia marcescens* | Respiratory | 54 | 1.7% |
| **Total** | | | **1277** | **40.60%** |
| DiGeorge Syndrome | *Pseudomonas aeruginosa* | Respiratory | 148 | 12.2% |
| DiGeorge Syndrome | *Staphylococcus aureus* | Respiratory | 54 | 4.5% |
| DiGeorge Syndrome | *Stenotrophomonas maltophilia* | Respiratory | 48 | 4.0% |
| DiGeorge Syndrome | *Moraxella catarrhalis* | Respiratory | 43 | 3.6% |
| DiGeorge Syndrome | *Serratia marcescens* | Respiratory | 31 | 2.6% |
| DiGeorge Syndrome | *Staphylococcus epidermidis* | Blood | 29 | 2.4% |
| DiGeorge Syndrome | *Coliforms* | Respiratory | 28 | 2.3% |
| DiGeorge Syndrome | *Klebsiella pneumoniae* | Respiratory | 28 | 2.3% |
| DiGeorge Syndrome | *Staphylococcus aureus* Methicillin Resistant | Respiratory | 28 | 2.3% |
| DiGeorge Syndrome | *Enterobacter cloacae* | Respiratory | 26 | 2.1% |
| **Total** | | | **463** | **38.3%** |
| Functional disorders of polymorphonuclear neutrophils | *Pseudomonas aeruginosa* | Respiratory | 52 | 5.5% |
| Functional disorders of polymorphonuclear neutrophils | *Candida albicans* | Respiratory | 49 | 5.2% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* | Wound | 30 | 3.2% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* | Respiratory | 28 | 3.0% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* | Miscellaneous | 28 | 3.0% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* Methicillin Resistant | Respiratory | 23 | 2.4% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* | Miscellaneous | 22 | 2.3% |
| Functional disorders of polymorphonuclear neutrophils | *Stenotrophomonas maltophilia* | Respiratory | 18 | 1.9% |
| Functional disorders of polymorphonuclear neutrophils | *Mycobacterium avium-intracellulare* complex | Respiratory | 17 | 1.8% |
| Functional disorders of polymorphonuclear neutrophils | *Staphylococcus aureus* Methicillin Resistant | Wound | 16 | 1.7% |
| **Total** | | | **283** | **30.1%** |
| Combined immunodeficiency, unspecified | *Staphylococcus aureus* | Wound | 41 | 5.0% |
| Combined immunodeficiency, unspecified | *Pseudomonas aeruginosa* | Respiratory | 33 | 4.0% |
| Combined immunodeficiency, unspecified | *Staphylococcus aureus* | Respiratory | 30 | 3.6% |
| Combined immunodeficiency, unspecified | *Staphylococcus aureus* | Blood | 25 | 3.0% |
| Combined immunodeficiency, unspecified | *Candida albicans* | Respiratory | 21 | 2.6% |
| Combined immunodeficiency, unspecified | *Escherichia coli* | Blood | 21 | 2.6% |
| Combined immunodeficiency, unspecified | *Staphylococcus aureus* Methicillin Resistant | Wound | 17 | 2.1% |
| Combined immunodeficiency, unspecified | *Escherichia coli* | Gastrointestinal | 15 | 1.8% |
| Combined immunodeficiency, unspecified | *Staphylococcus aureus* Methicillin Resistant | Respiratory | 15 | 1.8% |
| Combined immunodeficiency, unspecified | *Stenotrophomonas maltophilia* | Respiratory | 15 | 1.8% |
| **Total** | | | **233** | **28.3%** |

The most common infection/site pairs for each of the PIDs in the model. The percentage of infections is out of the total per PID.

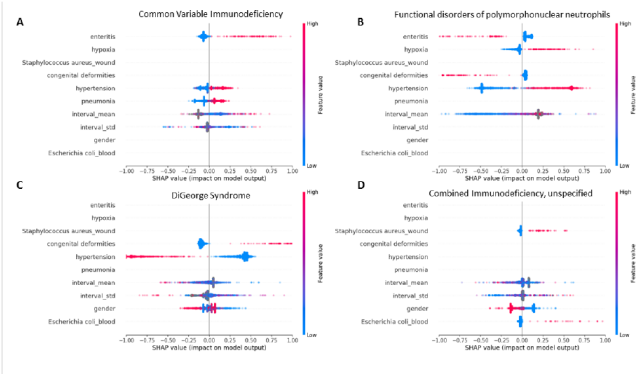


**Figure 1.** Five most important features per PID for the model's classification. Gradient Boosted Machine was used to classify primary immune deficiencies using a variety of clinical features. Each dot represents one patient. Red dots indicate presence of feature (binary variables= "ever had" or "female", continuous variables= "high"), blue dots indicate absence of feature (binary variables= "never had" or "male", continuous variables= "low"). The "interval" features refer to the time between microbiology tests. Positive SHAP (SHapley Additive exPlanations) values indicate the feature was predictive of being in the cluster (i.e. having that PID). Negative SHAP values indicate the feature was predictive of not being in the cluster.

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