Table 1. Pre- and Post-Intervention Test Positivity Rate of Specific Pathogens in GIP

| Pathogen | Pre-intervention % | Post-intervention % | Change | p-value |
|----------|--------------------|---------------------|--------|---------|
| Bacteria |                    |                     |        |         |
| Clostridioides difficile (total & A/B) | 0.00 | 0.00 | - | - |
| Enterococcus faecalis | 0.00 | 0.00 | - | - |
| Enterococcus faecium | 0.00 | 0.00 | - | - |
| Staphylococcus epidermidis-producing E. coli | 0.00 | 0.00 | - | - |
| Staphylococcus aureus | 0.00 | 0.00 | - | - |
| Pseudomonas stutzeri | 0.00 | 0.00 | - | - |
| Streptococcus | 0.00 | 0.00 | - | - |
| Viruses |                    |                     |        |         |
| Adenovirus/RSV | 0.00 | 0.00 | - | - |
| Astrovirus | 0.00 | 0.00 | - | - |
| Norovirus/GoCV | 0.00 | 0.00 | - | - |
| Rotavirus A | 0.00 | 0.00 | - | - |
| Rotavirus B (II, III & V) | 0.00 | 0.00 | - | - |
| Parasites |                    |                     |        |         |
| Cryptosporidium | 0.00 | 0.00 | - | - |
| Cyclospora cayetanensis | 0.00 | 0.00 | - | - |
| Entamoeba histolytica | 0.00 | 0.00 | - | - |
| Giardia lamblia | 0.00 | 0.00 | - | - |

**Conclusion.** Our study showed that restricting the ordering of GIP to the first 72 hours of hospitalization and directing providers to standalone C. difficile NAAT testing resulted in a reduction of GIPs performed. There were marginal changes in the test positivity rate of GIP. A limitation of our study is that the timing of post-intervention coincided with the COVID-19 pandemic, which had unpredictable effects on hospital practice and patient admissions. Ideally, future quality improvement projects should increase the test positivity of pathogens other than C. difficile while lowering the GIP use in diagnosing C. difficile colitis.

**Disclosures.** John C. O’Horo, Sr., MD, MPH, Bates College and Elsevier Inc (Consultant)

669. Metagenomic Plasma Microbial Cell Free DNA-Sequencing Assists in Diagnosing Infections and Critical Antimicrobial Changes in Immunocompromised Hosts

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**Session:** P-30. Diagnostics: Typing/sequencing

**Background.** Metagenomic next-generation sequencing of plasma cell-free DNA (Karius) (plasma mcf-DNA-seq) is a noninvasive approach that may have a unique role for the diagnosis of infectious complications in immunocompromised patients. The rapid turn-around time and noninvasive nature makes this a promising supplement to standard of care.

**Methods.** The aim of this study is to investigate the utility of plasma-mcf-DNA-seq in clinical practice; how it changes management, correlations between organism abundance over time from symptom onset and the value of negative tests. Retrospective review of plasma-mcf-DNA-seq performed, January 2020 -March 2021. Organism abundance was displayed as a heat map and graphed over time from initiation of antimicrobials. Management changes and concordance with standard of care were compared for positive and negative tests. This study was approved by the Virginia Commonwealth University Institutional Review Board.

**Results.** Thirty-six adult patients included: 92% immunosuppressed (11 with T cell deficits (solid organ transplant, malignancy, human immunodeficiency virus), 8 with B-cell deficits (hematologic malignancy, diabetes mellitus), and 14 with both (hematopoietic stem cell transplant, aplastic anemia)). Most tests evaluated fever (hematopoietic stem cell transplant, aplastic anemia). There was an increasing trend in the abundance of fungi detected from time of symptom onset. Seven of the 8 fungi detected were considered clinically pathogenic, 3 prompted targeted treatment; 7/8 fungi identified were clinically pathogenic and resulted in anti-fungal therapy changes to target the species identified. Antimicrobials were de-escalated treatment; 7/8 fungi identified were clinically pathogenic and resulted in anti-fungal therapy changes to target the species identified. Antimicrobials were de-escalated in 3 patients with negative tests. There was an exponential relationship between the abundance of pathogenic fungi over time from symptom onset, but no such relationship was seen with bacteria.

**Abundance of fungi and bacteria detected on plasma mcf-DNA-seq test**

There was no clear trend in bacterial abundance over time from symptom onset. Most bacteria detected were not considered clinically pathogenic.

Figure 2. Fungi abundance from date of symptom onset

There was an increasing trend in the abundance of fungi detected from time of symptom onset. Seven of the 8 fungi detected were considered clinically pathogenic.

**Conclusion.** Plasma-mcf-DNA-seq assisted in making critical management changes including initiation of treatment for identified organisms and de-escalation of antimicrobials. Plasma-mcf-DNA-seq is a promising approach for a non-invasive rapid diagnosis.

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

670. Precision Metagenomic (PM) Sequencing Outperforms Conventional Urine Culture in Detecting Clinically Relevant Microorganisms

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**Session:** P-30. Diagnostics: Typing/sequencing

**Background.** Morbidity from urinary tract infection (UTI) is high. Urine culture is the reference method for UTI diagnosis. Its diagnostic yield is limited as prior antibiotic use prevents growth of established uropathogens, many emerging uropathogens do not grow under routine culture conditions, and results interpretation can be subjective. Faster, more comprehensive diagnostics could help manage recurrent and/or drug-resistant infections. We evaluated the diagnostic yield of a precision metagenomic (PM) workflow for pathogen detection & antimicrobial resistance (AMR) characterization directly from urine.

**Methods.** Residual urine samples from symptomatic adults evaluated by culture in Detecting Clinically Relevant Microorganisms included initiation of treatment for identified organisms and de-escalation of antimicrobials. Plasma-mcf-DNA-seq is a promising approach for a non-invasive rapid diagnosis.

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

Abundance of bacteria and fungi detected on plasma mcf-DNA-seq test. Data classified by organism and level of immunosuppression. Abundance is expressed in microbial cell free DNA per microliter. Warmer colors toward red represent higher abundance.

Figure 1. Bacteria abundance from date of symptom onset.
with Enrichment for clinically relevant targets (191 pathogens, 1976 AMR markers) with the Explify Urinary ID/AMR Panel (IDbyDNA). Enriched libraries were sequenced on the NextSeq500 (Illumina) and data analyzed with the Explify UPiP Data Analysis Solution (IDbyDNA).

Results. For bacterial uropathogens, 94% positive agreement was observed between this PM workflow and culture. PM detected fastidious and/or anaerobic potential uropathogens in 30% and 7% of samples reported as culture-negative or positive for other bacteria, respectively. Total agreement between AMR marker detection and phenotypic resistance was 78%. Notably, PM predicted phenotypes of ESBL E. coli and K. pneumoniae (10/10), MRSA (9/9), and vancomycin-resistant E. faecium (4/4). PM also detected pathogens associated with sexually-transmitted infection (C. trachomatis, HSV) and bacterial vaginosis (G. vaginalis). PM produced complete results within 24-36 hours of sample receipt (vs culture & susceptibility 42-72 hrs).

Conclusion. The sensitivity of PM for uropathogen detection was noninferior to culture (A = 0.05; Nam RMLE; p < 0.0005). PM predicted antimicrobial resistance phenotypes for common uropathogens and identified potential pathogens not detected by conventional culture. Future studies should assess the impact of PM-guided management on clinical outcomes.

Disclosures. Rita C. Stinnett, PhD, MHS, IDbyDNA (Employee) Marta Mangifesta, PhD, IDbyDNA (Employee) Anagha Kadam, PhD, IDbyDNA (Employee) Heng Xie, PhD, IDbyDNA (Employee) Stacie Staufter, BS, IDbyDNA (Employee) Jamie Lemon, PhD, D(ABMM), IDbyDNA (Employee) Benjamin Briggs, MD, PhD, IDbyDNA (Employee) Lauje Farnaes, MD, PhD, Cardesa Bio (Advisor or Review Panel member)IDbyDNA (Employee) Robert Schlaberg, MD, MPH, IDbyDNA (Consultant, Shareholder, Co-founder)

Table 1. Explify Respiratory Testing

| Next Generation Sequence Testing | Turn around time: 5 days (including shipping time) |
|----------------------------------|--------------------------------------------------|
| Capable of identifying > 900 pathogens (bacteria, fungi, virus, parasites) | Cost: $470 (compared to $1284.18 for Universal PCR Testing) |

Table 2. Patient Characteristics

| Ages 40 - 77 | 5 immunocompromised patients |
|-------------|-------------------------------|
| 1 solid organ transplant recipient (heart) | 1 hematopoietic stem cell transplant recipient |

Results. The test resulted in: lack of identified organism (5 patients), identification of non-pathogenic organisms (6 patients), and identification of organisms that were either identified by other traditional testing or did not impact provider’s therapeutic plan (5 patients). The results of Explify testing in all 16 patients did not have a clinical impact on patient care or treatment plan.