Clinical Implementation of Metagenomic Next-Generation Sequencing for Precision Diagnosis of Acute Infectious Diseases (DAID)
Targeted Acute Infectious Diseases

Pneumonia
15 – 25%
unknown cause

Meningitis / Encephalitis
40-60%
unknown cause

Fever / Sepsis
~20% unknown cause

Up to 50% of hospitalized patients with pneumonia, sepsis, and encephalitis / meningitis are treated without a laboratory-confirmed cause of their disease, resulting in:

delayed and ineffective therapy, increased mortality, and excess healthcare costs
Nearly All Microbes can be Uniquely Identified by Nucleic Acid Sequencing

This project will impact patient outcomes by returning clinically actionable Next-Generation Sequencing (NGS) results in a timeframe (24-36 h) that allows for targeted management and treatment of critically ill patients.
Data Integration into Patient EMR (Syapse)

Patient EMR

Retrieval of clinical, laboratory, and outcomes data (including metagenomic NGS SURPI results)

Import data into Syapse interface

Visualization of data and results accessible to precision medicine consult service

Chikungunya virus (KJ405124.1, gi|815794657|, 12011 bp)
Chikungunya virus strain 99/559, complete genome

Fold coverage (bp)

Genome density

Viruses (571)
Other lineage (7)
Homo sapiens (8,035)
Unidentified (0,0665)
Caudovirales (108)
Bacteria (5)
Non-human eukaryote (38)
Biobanking

UCSF Sample Biobanking (10/2008 – present) (n=500)

- ~1000 CSF samples available, 15-20 per month collected at UCSF (including 500 from the California Encephalitis Project 6/1998 – present)
- ~1000 Bronchoalveolar lavage (BAL) samples available
- ~2000 plasma samples available
- Samples linked to EMR with clinical, laboratory testing, and outcomes data

Quest Diagnostics (n=200)

- Will provide 200 samples as in-kind support

Collaborating Hospitals (samples for clinical laboratory validation)

- Children’s National Medical Center (Dr. Brittany Goldberg)
- St. Jude’s Medical Center (Dr. Randall Hayden)

Clinical samples currently being stored in -80° freezers at the UCSF Clinical Microbiology Laboratory. Data is in Excel on Clin Labs server.
Prospective Clinical Study Comparing Metagenomic NGS to Conventional Testing (n=300)

- Patient enrollment (n=300) and sample / metadata collection
- Running CLIA-validated NGS assay
- Cloud or server-based SURPI NGS bioinformatics analysis
- Results reporting in EMR and visualization in Syapse interface

Initial deployment at UC hospitals will set the stage for future deployment in clinical labs.
Participant Recruitment

- Patient selection and enrollment done by Precision Medicine consult service

- Metagenomic NGS case series (pending publication) reveals “high-yield” instances:
  1. Confirmation of ambiguous or suggestive laboratory results
  2. Evidence of microorganisms or clear pathology on histological analysis
  3. Epidemiologic or clinical links pointing to infection
  4. Broad differential diagnosis
  5. As a “rule-out” assay in patients remaining undiagnosed despite extensive testing

Planned enrollment for prospective study at UCSF, UCLA, and UCD from January – December 2016.
How UC-BRAID Can Help

Participant recruitment

- Communication about patients that meet study criteria at UC Health campuses.
- Facilitation of participation of patients not located in SF (UCLA and UCD)

Biobanking

- Ability to efficiently access interesting specimens and associated data at other UC’s

Product Development

- Adoption of SURPI as a standard bioinformatics pipeline by labs running metagenomic NGS
- Deployment of SURPI to other clinical and public health laboratories
Key Personnel and Collaborators

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