2505. Integration of Next–Generation Sequencing, Viral Sequencing, and Host-Response Profiling for the Diagnosis of Acute Infections

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Background

To guide treatment of infectious diseases, clinicians need sensitive, specific, and rapid diagnostics. We aim to incorporate complementary methods of microbial sequencing and host-response profiling to improve the diagnosis of patients at risk for acute infections.

Methods

We enrolled 200 adult patients with systemic inflammatory response syndrome (SIRS) at the Stanford Emergency Department. Physicians with specialty training in infectious diseases conducted retrospective two-physician chart review to establish likely admission diagnoses. Blood samples were tested with a previously described 18-gene host-response integrated antibiotics decision model (IADM) that distinguishes noninfectious SIRS, bacterial infections and viral infections. Plasma samples were tested with shotgun metagenomic next-generation sequencing (NGS) and viral sequencing with VirCapSeq. A novel statistical algorithm was developed to identify contaminant organism sequences in NGS data.

Results

The physician chart review classified 99 patients (49%) as infected, 69 (35%) possibly infected and 32 (16%) non-infected. Compared with chart review, the IADM distinguished bacterial from viral infections with an area under curve of 0.85 (95% confi¬dence interval 0.77–0.93). NGS results to date confirmed positive blood cultures in seven of nine patients, with two of four blood culture-positive E. coli patients turning up negative on NGS due to E. coli contamination. NGS also confirmed positive cultures from other sites in two of six patients with negative blood cultures. Preliminary VirCapSeq data from 23 patients confirmed positive viral tests in five of six patients with Hepatitis C, BK Virus, Cytomegalovirus and Epstein–Barr Virus infections. VirCapSeq did not identify a causa¬tive agent in the plasma of 11 patients with confirmed respiratory viral infection and intes¬tinal Norovirus infection, and six patients with idiopathic illness. Interestingly, VirCapSeq found viral reactivation in 8 of 12 immunocompromised patients.

Conclusion

The diagnosis of suspected infections may be enhanced by integrat¬ing host-response and microbial data alongside clinical judgment. Our results and large cohort lay the foundation to demonstrate the utility of this approach and in which patients these tools may be most useful.

Disclosures

T. E. Sweeney, Inflammatix, Inc: Employee and Shareholder, Salary; T. Briese, Roche: Columbia University has licensed VirCapSeq to Roche, Licensing agreement or royalty; W. I. Lipkin, Roche: Columbia University has licensed VirCapSeq to Roche., Licensing agreement or royalty; P. Khatri, Inflammatix, Inc.: Co-founder, Scientific Advisor and Shareholder, Licensing agreement or royalty and ownership stock; D. A. Relman, Karius: Consultant, Stock options; Arc Bio LLC: Consultant, Stock options