CCMID Advancing Diagnostic Sequencing for Infectious Diseases

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The Consortium for Clinical Metagenomics in Infections Diseases (CCMID) is a collaborative group of microbiologists, scientists, physicians, and industry partners working to facilitate implementation of next-generation sequencing (NGS) approaches for infectious disease diagnostics. The CCMID engages stakeholders at multiple levels of care via patient-centered, value-focused projects, education, and research. Proposed in a Journal of Clinical Microbiology editorial and established in October 2022, the CCMID meets monthly on a virtual platform to discuss needs in this field and opportunities for advancement that leverages the combined expertise of consortium participants. Current participants include national and international leaders from academia, industry, and public health, with new participants joining monthly. The governance structure is de-centralized to allow collaborations through open engagement between participants and to maintain scientific independence.

The efforts of the CCMID address current barriers to use of metagenomics and NGS approaches for infectious disease diagnostics with the primary goal of advancing the field as a whole. Examples of currently active and pending activities are summarized as follows:

- <u>Field need assessments and gap analyses</u>: 1) CCMID participants recently published manuscript² describing a trail design to investigate use of plasma metagenomic sequencing for immunocompromised patients with neutropenic fever. Importantly, this manuscript contained a table of power calculations indicating estimates of patients needed to enroll for differing clinically significant outcomes. 2) Participants are currently developing a national survey to assess use of currently available sequencing assays at reference laboratories, as well as overall perceived needs to widely implement NGS-technologies for infectious disease diagnostics. Finding from this survey will be submitted for publication to help drive study development.
- <u>Education</u>: CCMID participants are submitting conference proposals to multiple national and international conferences. One proposal was accepted to the 2024 American Society of Microbiology Microbe meeting, the largest annual microbiology conference in the United States.
- <u>Guideline development</u>: Few guidelines for use of NGS-based assays for infectious disease diagnostics are available. CCMID participants will draft evidence-based expert-opinion guidelines regarding standardized definitions for the field and best-use practices with diagnostic stewardship. Additionally, content generated by the CCMID will address and propose standardized outcome measurements for clinical trials that are value-focused and allow comparison of differing analytic approaches.
- Methodology advancement: Monthly CCMID meetings will involve focused research presentations from
 participants to share methodologic approaches. Meetings also allow coordination of studies drawing on
 the expertise of clinical trialists and methodology experts to inform design and implementation.
- <u>Clinical trials</u>: The CCMID strives to become a coordinating center for multi-site and multi-national clinical trials, following models such as the ECOG-ACRIN Cancer Research Group. As described in the manuscript proposing the consortium¹, "affiliated laboratories developing metagenomic approaches for clinical diagnostics could enroll in ongoing consortium-lead studies to collaboratively contribute sequencing data and de-identified patient metadata into a central repository available to members. This approach could generate adequately powered studies spanning multiple institutions to address questions less amenable to publicly funded research, as well as provide avenues for replication and confirmation of impactful findings."

Founding committee: David Gaston MD PhD (Vanderbilt University Medical Center), Steve Miller MD PhD (Delve Bio), Catherine Hogan MD CM (British Columbia CDC), Anne Piantadosi MD PhD (Emory University), Esther Babady PhD (Memorial Sloan Kettering Cancer Center), and Trish Simner PhD (Johns Hopkins)

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- 1. Gaston DC. Clinical Metagenomics for Infectious Diseases: Progress toward Operational Value. J Clin Microbiol. 2023 Feb 22;61(2):e0126722. doi: 10.1128/jcm.01267-22. Epub 2023 Feb 2. PMID: 36728425; PMCID: PMC9945490.
- 2. Hogan CA, Miller S, Piantadosi A, Gaston DC, Simner PJ, Nash S, Babady NE. Which trial do we need? Plasma metagenomic next-generation sequencing to diagnose infections in patients with haematological malignancies and febrile neutropenia: proposal for a randomized-controlled trial. Clin Microbiol Infect. 2023 May 25:S1198-743X(23)00248-3. doi: 10.1016/j.cmi.2023.05.024. Epub ahead of print. PMID: 37244468.