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April 4th, 2025

Re: AI Pilots 2025 Grant

Dear Ann,

I am delighted to write a strong letter of support for your AI Pilot 2025 proposal entitled “**Predictive Factors for Positive Yield and Clinical Impact from a Metagenomic Sequencing Assay for Diagnosis of Infections**” and to express my enthusiasm in contributing to this project. Your proposal addresses a high-priority area of diagnostic stewardship in optimizing the use of novel genetic (sequencing-based) tests in clinical practice. Here you propose to integrate a prediction algorithm for determining which patients would benefit the most from clinical metagenomic next-generation sequencing (mNGS) testing of cerebrospinal fluid (CSF) for diagnosis of central nervous system infections into the patient HER. This algorithm will thus be available for use by clinicians ordering this expensive but high-impact clinical test. I believe that you have the biostatistical background and operational experience to lead this project and am happy to offer my clinical expertise to leverage this AI tool to maximally benefit patients, both at and outside of UCSF.

We have been working closely together for more than a year on a number of projects and have co-submitted a paper on predictive factors of COVID-19 severity (Brazer, et al., 2025) currently under review at *Communications Medicine*. As you know, I have extensive research and clinical translational experience on the development and implementation of metagenomic testing for diagnosis of infections. Over 7 years, we have been performing cerebrospinal fluid and plasma mNGS testing for patients at and outside of UCSF that have greatly improved and impacted the lives of patients with undiagnosed infections (Brazer, et al., 2024, *Nature Medicine*). Combined with your biostatistics and data science expertise, I am confident that this project will be successful. Furthermore, close collaboration with the UCSF EPIC/APeX Electronic Medical Records (EHR) team will be instrumental in this project. Previously, I have worked with them on implementing an APeX survey to clinicians when ordering the test to pre-screen patients for CSF mNGS testing. Finally, I have previously provided you with metadata obtained from chart review by infectious disease physicians and microbiologists from ~2,000 patients that you are doing to develop and refine the algorithm. I have also received much interest in a clinical study to prospectively investigate the utility and performance of this algorithm in collaboration with neurologists and infectious disease physicians at UCSF.

I look forward to continue working with you on this exciting and impactful project and wish you much success with your application.

Sincerely yours,

A handwritten signature in black ink that reads 'Charles Chiu'.

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