

Diagnosis of ocular infection using Nanopore Metagenomic sequencing

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While early pathogen identification and treatment are essential to the visual recovery of patients with intraocular inflammation, there remain challenges in the accurate and fast classification via clinical presentation, securing sufficient amount of ocular samples, and the single species-level verification of pathogens that requires a high cost and labor. Here, we developed a novel bioinformatics method for ocular infection using Oxford Nanopore metagenomic sequencing that addresses previous hurdles by detecting DNAs from all potential pathogens in a single test. Our algorithm distinguishes infectious uveitis patients from noninfectious, and identifies potential pathogens in a species-level with a confidence score. In a test on the 21 intraocular aqueous and vitreous samples from 20 patients (18 infectious uveitis, 3 noninfectious uveitis) and 6 samples from negative control, our algorithm marked overall 93% accuracy (sensitivity 94%, specificity 89%) in distinguishing infectious uveitis patients. Moreover, among correctly predicted patients, we could identify the potential pathogens, including cytomegalovirus, *toxoplasma gondii*, *mycobacterium tuberculosis*, *streptococcus sanguinis* and *clostridium septicum*, which were further validated by clinicians, and could be utilized in the treatment procedure. We expect that sequencing-based diagnosis of ocular infection would overcome the shortage of conventional diagnostic tests and make transition between bedside to bench faster with higher accuracy and lower cost.