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Polymerase Chain Reaction Technique and Technology for Helping to Establish a Diagnosis in Patients with Uveitis

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Polymerase chain reaction (PCR) is a molecular biology method used to rapidly amplify a specific DNA segment (the target), increasing its quantity by many orders of magnitude in a short time. It was first described by Saiki and colleagues in 1985 and has revolutionized the practice of medicine.

PCR was originally developed as a research tool, but it has since become widely used across many areas of clinical care, including tissue typing, molecular genetics for genetic counseling, forensic medicine, gene identification for disease susceptibility or causation, and—particularly in uveitis—the identification of infectious causes of disease.

Our work with PCR initially began in a laboratory setting for purposes unrelated to clinical diagnosis. Specifically, we employed internally nested PCR oligonucleotide primer pairs to study the spectrum of fibronectin isoforms in normal, wounded, and healing corneas. But it soon became apparent that this laboratory technique might also be exploited in the analysis of biopsied ocular tissue, including vitreous, in an effort to identify putative microbial causes of inflammation. Accordingly, we established a “stable” of 10 oligonucleotide primer pairs, with sequences determined from the literature and GenBank data banks, for microbes which can be associated with uveitis, scleritis, and keratitis. The stringency requirements for laboratory cleanliness and for safeguards against inadvertent contamination preclude most research laboratories from offering PCR-based diagnostic assays, and this holds true for our research laboratory as well.

We first reported a case of ophthalmic Whipple’s disease in which the diagnosis was confirmed using PCR. It quickly became clear how valuable PCR can be for confirming a

diagnosis and, in certain cases, preserving vision. We have had similar experience with cases involving varicella zoster virus, tuberculosis, Lyme disease, syphilis, herpes simplex virus, and cat scratch disease, where PCR analysis of biopsied material—typically vitreous—has clarified the underlying cause of blinding inflammation. This has enabled the initiation of targeted antimicrobial therapy, with outcomes comparable to those reported in the ophthalmic Whipple's disease case.

Currently, PCR is widely used in the diagnosis and management of patients with infectious uveitis. A wide range of viral, bacterial, fungal, and parasitic infections that can cause ocular inflammation can be identified using PCR. Additionally, this powerful technique has numerous applications in diagnostic pathology, particularly in genetics and oncology. In ophthalmology, it is also useful in the evaluation of noninfectious uveitis, such as HLA-B27-associated iridocyclitis and Vogt-Koyanagi-Harada disease, as well as in masquerade syndromes, including intraocular lymphoma. However, the very high sensitivity of PCR may lead to false-positive results, while its high specificity can also contribute to false-negative findings. These limitations can be reduced by using appropriate positive and negative controls, employing real-time PCR, and conducting testing in experienced laboratories.\

In conclusion, PCR technology has opened a new era in the diagnosis and treatment of uveitis, enabling clinicians to define new infectious entities, identify pathologies in the eyes of many patients with uveitis, and facilitate prompt diagnosis and appropriate therapy.