PARKINSON'S

TEARS AS A DIAGNOSTIC TOOL FOR PARKINSON'S DISEASE

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Parkinson's disease (PD) affects 1 in 500 Canadians, a significant statistic considering the severe deterioration in quality of life induced by the disease.[1,2] PD is the result of the progressive death of dopaminergic neurons in the brain, often due to the abnormal aggregation of proteins forming Lewy bodies.[3] These Lewy bodies are formed as a result of multiple protein interactions, primarily α-synuclein, influencing the microenvironment of the cell.[4,5] Ultimately, the affliction leads to impaired control of movement with symptoms including tremors, rigidity, and disrupted balance.[1]

Although the pathophysiology underlying PD is thoroughly researched, there remains no clinically utilized method of diagnosis beyond mere observation of symptoms as the disease progresses.[1] Findings from a study conducted at the University of Southern California may represent a potential change to this, with researchers identifying tears as a reliable and non-invasive screening tool for PD.[3] To arrive at this conclusion, researchers compared the oligomeric form of α-synuclein in the tear samples of those with and without PD.[4] Their results showed significantly higher levels of α-synuclein in the tears of those with PD when measured against those without the disease.[4]

Given that symptoms of PD can be absent for years following the onset of the disease, a biomarker in tears could be useful in making an early diagnosis. However, further research is required to determine the efficacy of this biomarker, primarily in determining its sensitivity and specificity.[5] Such findings would represent a significant advancement in PD management, facilitating advanced coordination of living arrangements and services required for those experiencing symptoms. It would also allow for the employment of practices that delay the onset of symptoms.

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GENE REPAIR

β-THALASSEMIA: A NEW ROAD TO A CURE

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β-thalassemia is a recessive blood disorder characterized by a reduction in the synthesis of β-globin which can subsequently give rise to severe anemia.[1] The annual global incidence of individuals symptomatic for a form of β-thalassemia is 1 in 100,000.[1] Presently, the only available treatment focused on increasing β-globin is allogeneic bone marrow transplantation. This therapy, requiring donor stem cells, is heavily limited by the stringent criteria of human leukocyte antigen compatibility.[3]

Research by Liang and colleagues has led to the development of an alternative approach to treating β-thalassemia.[3] The specific pathogenic variant considered by these scientists is a single nucleotide polymorphism (A>G) at position 28, cited as being one of the three most prevalent mutations causing β-thalassemia in Chinese and Southeast Asian populations.[3] The researchers employed a base editor system, BE3, to repair point mutations in heterozygous embryos.[3] This base editor system allowed for high editing efficiency in correcting the point mutation. The mechanism of this edit was initiated by binding to a target nucleotide C, and catalyzing its deamination and conversion to a U.[4] The resultant U:G mismatch is detected and transformed by cellular DNA repair machinery to a T:A base pair, thereby producing a C>T or G>A substitution in the desired DNA sequence.[4] Of the 48 embryos that underwent base editing, 11 were repaired, of which 8 were restored to the wild-type state with both mutant alleles corrected.[3]

While this data illustrates the potential of such technology to repair causative mutations in β-thalassemia and other genetic diseases, future investigation is needed to optimize the precision with which BE3 can be made to repair disease mutations. For instance, the authors note that the specificity of the base editor system must be examined more comprehensively using genome-wide specificity assays to profile BE3 off-target effects.[2]

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