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Age related cataract: Pathogenesis and possible therapy

Age-related cataract is the most common cause of blindness in the world, causing more blindness by many magnitudes greater than the other causes of blindness. The only effective treatment is surgery, which requires expert surgeons and special equipment. Because of this, there is a backlog of millions of cataract cases around the world, as there are more new cases each year than can be treated by surgery. There is therefore a need for development of alternative medical treatment. It has been shown in laboratory studies that alpha-crystallin lens proteins act as anti-cataract molecular chaperone proteins, preventing the aggregation of other lens proteins that cause the lens to become cloudy and cataractous. In the clinic, we have developed a NASA-NEI Dynamic Light Scattering (DLS) device that detects and measures alpha-crystallins in the lenses of patients safely and non-invasively. In a series of clinical studies done at the National Eye Institute of NIH, the Wilmer Eye Clinic of Johns Hopkins University, and at the University of Tokyo, we found that as the alpha-crystallins proteins decreased in patients, there was development and progression of nuclear cataracts, in both cross sectional and longitudinal studies. In addition, there was also a consistent decrease of alpha-crystallin associated with normal aging. These clinical studies support the hypothesis that alpha-crystallins serve as the built-in, endogenous anti-cataract protein in the lens. Hence as long as one has sufficient supplies in the lens, one can avoid cataract; but when one's supplies dwindle, then one develops cataracts. Recently, we looked at the distribution of alpha crystallins in the different compartments of the lens. We studied 112 patients from 20 to 90 years of age (Mean±SD: 54.63±13.32 years) of whom 51 were female. This study was approved by NEI-IRB and all tenets of the Declaration of Helsinki were followed. Each participant gave their written informed consent. The NEI-NASA DLS device was used to measure alpha-crystallin index (ACI) in vivo at nuclear, anterior and posterior cortical areas in participants' lenses. Participants were examined by slit-lamp and lenses were graded using the AREDS system.

Results: DLS assessment in normal clear lenses revealed that ACI was significantly abundant at lens nucleus (16.17±6.20%) and anterior cortex (15.67±9.03%), compared to posterior cortex (12.44±7.35%, both $p<0.05$). There was a significant inverse correlation between age and DLS -ACI at all three regions in non-cataractous lens: specifically, ACI significantly decreased 0.40±0.05%, 0.30±0.03% and 0.18 ± 0.07% per year at nucleus, anterior cortex, and posterior cortex respectively (all, $p<0.05$). We also found great variability in the ACI distribution among young normal.

Conclusion: ACI is highest in the lens nucleus, followed by the anterior cortex and is lowest in the posterior cortex. There was a decrease in alpha crystallin proteins in all compartments associated with aging, as well as with cataract progression, consistent with previous findings. There was also a great variability in ACI distribution in young normal which may suggest genetic variability. Preservation of one's lens alpha-crystallin proteins may help minimize one's risk for age-related cataract.

Biography

Manuel B Datiles currently diagnoses eye patients as part of clinical trials and research studies at NIH, including an ongoing study of ocular graft-versus-host disease in recipient of adult stem cell transplants. His long-term research focuses on cataract development and clinical trials involving anti-cataract drugs. He also collaborates with NEI lens researchers to study the genetic causes of cataracts, and with Johns Hopkins University researchers to study the aggregation of lens proteins, which may lead to cataract development. He is the author of more than one hundred scientific manuscripts and textbook chapters. He has also served as an Editorial Board Member and Reviewer for major ophthalmology journals, including *Archives of Ophthalmology, Ophthalmology and Investigative Ophthalmology & Visual Science*.

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