OMICS Group Conferences
Accelerating Scientific Discovery
3rd International Conference on
Clinical & Experimental Ophthalmology
April 15-17, 2013 Hilton Chicago/Northbrook, USA

A novel approach to pathogenesis and treatment of fuchs endothelial corneal dystrophy

Alireza Ziaei
Harvard Medical School, USA

Background: Fuchs' endothelial corneal dystrophy (FECD) is a significant cause of corneal blindness and a leading cause of corneal transplantation. The mechanism of corneal endothelial cell loss in FECD is currently not known and the only available treatment for FECD is corneal transplantation. It has been shown by our laboratory that there is an oxidant-antioxidant imbalance in FECD as compared to normal corneal endothelium (CE). Our previous studies have shown accumulation of oxidized DNA lesions in FECD, co-localization of oxidative DNA damage and apoptosis, and down regulation of Nrf2 (NF-E2-related factor 2), which is a major transcription factor responsible for activation of antioxidant genes. We detected an increased level of p53 and phospho-p53 in FECD compared to normal endothelium. Increased activation of p53 and down regulation of Nrf2 in FECD suggests that p53 and Nrf2 plays a critical role in complex mechanisms regulating oxidative-stress-induced apoptosis in FECD.

Aim: Sulforaphane (SFN) is a naturally occurring glucosinolate, which confer cytoprotection by activating Nrf2. The purpose of this study was to investigate the effect of SFN on Nrf2 activation and apoptosis in FECD.

Materials & Methods: Specimens of corneal endothelial cells (CECs) with Descemet's membrane were cut in 2 halves and one half was treated with 50 μM SFN for 4 hours at 37°C. In separate specimens, SFN treatment was followed by induction of oxidative stress by incubation with tert-Butyl hydroperoxide (tBHP) (500 μM for 4 hours). CECs apoptosis was detected by a TUNEL assay using confocal microscopy. Cellular localization of Nrf2 and p53 was assessed by immunohistochemistry. Cell counting was performed by Image-J (NIH) software. Western blot and Real-time PCR were used to analyze Protein levels and mRNA relative expression in (FECDi) and (HCECi) cell lines.

Results: CECs apoptosis in FECD was 31%, decreasing to 14% ($n=5$, $p<0.01$) with SFN treatment. SFN decreased CECs apoptosis by 43% ($n=6$, $p<0.05$) in specimens exposed to pro-oxidants. Nrf2 protein level was significantly increased in SFN-treated as compared to non-treated CECs ($n=4$, $p=0.03$). Exposure of normal CECs to tBHP increased nuclear localization of Nrf2, which was further enhanced by SFN. Oxidative stress did not increase nuclear localization of Nrf2 in FECD, but pre-treatment with SFN significantly enhanced nuclear translocation of Nrf2. FECD CECs treated with SFN demonstrated lower level of p53 in basal and oxidative stressed condition. SFN increases protein level of Nrf2 in normal endothelium, but its effect is enhanced in pro-oxidant condition in FECD. SFN, interestingly, increases protein level of DJ-1 in FECD at baseline and in pro-oxidant condition. SFN significantly increases mRNA level of Nrf2, NQO1, and DJ-1 in normal CE and Hmox-1 in pre-oxidant co condition.

Conclusions: SFN is a potent antioxidant agent, which significantly diminishes CECs apoptosis and potentially provides novel pharmacotherapeutic agent.

Biography

Alireza Ziaei, MD is a recipient of numerous awards and grants including National Excellent Researchers Award and the Science Excellence Prize in Iran. Postdoctoral Fellow at Harvard Medical School, as a Research Scientist, he performs basic science research at Schepens Eye Research Institute, Massachusetts Eye and Ear in Boston. Dr. Ziaei's interest and current research focus is on corneal and ocular surface diseases and his seminal work has been recognized several times. He published and presented numerous articles in highly ranked peer-reviewed journals and conferences. Dr. Ziaei has participated as a scientific and organizing committee of several International meetings and presented at numerous International meetings, including a number of invited presentations. Dr. Ziaei is member of Association for Research in Vision and Ophthalmology (ARVO), International Society for Eye Research (ISER), Tear Film & Ocular Surface Society (TFOS). He is serving as an Executive Editor and Editorial Board member of reputed journals and scientific societies. Dr. Ziaei serves as a Reviewer of various scientific journals including the American Journal of Ophthalmology (AJO), British Journal of Ophthalmology (BJO), the Journal of Clinical and Experimental Ophthalmology, International Journal of Ophthalmic Pathology (IJOP) and the Journal of Cell Biology: Research & Therapy (CBRT).

Alireza_Ziaei@MEEI.HARVARD.EDU