Harvard Medical School/Harvard School of Dental Medicine
Format for the Curriculum Vitae

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Name: Xiaoqing Guo

Education

1989	B.S.	Biochemistry	Beijing Normal University, Beijing, China
1996	Ph.D.	Medical Science Mentors: Zhinan Zhang, Aixia Wang	Peking Union Medical College, Tsinghua University, Beijing, China

Postdoctoral Training

09/97-11/97	Research Fellow	The Monitoring of HIV in HIV/AIDS Patients with Flu Mentor: Clive Loveday	Royal Free Hospital School of Medicine, Department of Retrovirology, London, UK
12/97-02/98	Research Fellow	The Identification and Drug-sensitivity of the Bacteria from Patients Mentor: Minjun Chen	Peking Union Medical College hospital, Department of Bacteriology, Beijing, China
09/98-2000	Postdoctoral Fellowship	Gene Therapy to Inhibit Proteinase Action in Recurrent Corneal Epithelial Erosion Syndrome Mentor: James D. Zieske	Schepens Eye Research Institute and Harvard Medical School, Department of Ophthalmology, Boston, MA, USA

Academic Appointments

09/98-2017	Research Fellow	Ophthalmology	Harvard Medical School
2017-present	Instructor	Ophthalmology	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions

Past

1989-1993	Research Fellow	Internal Medicine	Peking Union Medical College Hospital, Beijing, China
1996-1998	Assistant Scientist	Infectious Diseases Department	Peking Union Medical College Hospital, Beijing, China
10/00-08/04	Research Associate	Ophthalmology	Schepens Eye Research Institute, Boston, MA

Present

09/04-2017	Senior Scientific Associate	Ophthalmology	Schepens Eye Research Institute/Mass Eye and Ear, Boston, MA
2017-present	Investigator	Ophthalmology	Schepens Eye Research Institute/Mass Eye and Ear, Boston, MA

Professional Societies

1993-1998	Chinese Medical Association, P.R. China	
	1993-1998	Member
1999-present	Association for Research in Vision and Ophthalmology (ARVO)	
	1999-present	Member
2004-present	American Association for the Advancement of Science	
	2004-present	Member

Editorial Activities

Contributing Reviewer

Cornea
Molecular Vision
Journal of Translational Medicine

Honors and Prizes

1989	Excellent Graduate Award	Beijing Normal University
1995	Excellent Graduate Student Award	Peking Union Medical College
1996	The Third-Grade Prize on G-CSF Studies	Ministry of Public Health

Report of Funded and Unfunded Projects

Funding Information

Current

2015-2017 Development of an In Vivo Model to Mimic Human Endothelial Replacement Therapy
NIH/NEI R21 EY025833
Co-PI ($275,000 – total direct costs for current funding cycle beginning in 2015)

The major goal of this project is to determine if our co-culture model, consisting of primary human corneal endothelial cells cultivated on top of a 3D self-assembled human corneal stromal matrix, can mimic the in vivo process by which the corneal endothelium responds after cell injection therapy, and to determine if the corneal endothelial cells mature and deposit a Descemet's membrane.

Report of Regional, National and International Invited Teaching and Presentations

National

2016 Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting, Seattle, WA

Report of Technological and Other Scientific Innovations

P38 MAP Kinase Inhibitors for Wound Healing

US Patent Application Number PCT/US2016/057337, Publication Number WO2017066758 A1, Published April 20, 2017

Dr. James Zieske and I have found that blocking the p38-signaling pathway in human corneal and skin fibroblast cells greatly decreases expression of α-smooth muscle actin with TGFβ1 stimulation. We postulate that the p38 pathway is an important mechanism driving the corneal and skin scaring. This finding may prevent/improve tissue fibrosis after wounding.

Report of Scholarship

Peer reviewed publications in print or other media

Research Investigations:

1. **Guo X**, Sriram S, Tran JA, Hutcheon AEK, and Zieske JD. Inhibition of Human Corneal Myofibroblast Formation. Invest Ophthalmol Vis Sci. 2018 Jul 2;59(8):3511-3520. *(Corresponding author*)
2. **Guo X**, Hutcheon AEK, Chen J, D Shu DY, and Zieske JZ. Epidermal Growth Factor Stimulates Transforming Growth Factor-Beta Receptor Type II Expression In Corneal Epithelial Cells. Scientific Report. (in process) (*Corresponding author*)
3. Sriram S, Tran JA, **Guo X**, Hutcheon AEK, Kazlauskas A**,** Zieske JD. Development of wound healing models to study TGFb3's effect on SMA. Exp Eye Res. 2017 Aug;161:52-60. Doi: 10.1016/j.exer.2017.06.005. PMID: 28599847.
4. **Guo X**, Hutcheon AE, Tran JA, Zieske JD. TGF-beta-target genes are differentially regulated in corneal epithelial cells and fibroblast. New Frontiers in Ophthalmology. 2017 January 30;3(1):1-8. doi: 10.15761/NFO1000151. NIHMSID: NIHMS857243. (*Corresponding author*)
5. Sriram S, Tran JA, **Guo X**, Hutcheon AE, Lei H, Kazlauskas A, Zieske JD. PDGFRα is a Key Regulator of T1 and T3's Differential Effect on SMA Expression in Human Corneal Fibroblasts. Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1179-1186. doi: 10.1167/iovs.16-20016. PMID: 28245298.

6. **Guo X**, Hutcheon AE, Zieske JD. Molecular insights on the effect of TGF-β1/-β3 in human corneal fibroblasts. Exp Eye Res. 2016 May;146:233-41. doi: 10.1016/j.exer.2016.03.011. Epub 2016 Mar 16. PMCID: PMC4893894. (*Corresponding author*)
7. Pal-Ghosh S, Pajoohesh-Ganji A, Tadvalkar G, Kyne BM, **Guo X**, Zieske JD, Stepp MA. Topical Mitomycin-C enhances subbasal nerve regeneration and reduces erosion frequency in the debridement wounded mouse cornea. Exp Eye Res. 2016 May; 146:361-9. doi: 10.1016/j.exer.2015.08.023. Epub 2015 Aug 30. PMCID: PMC4775450.
8. Karamichos D, Zareian R, **Guo X**, Hutcheon AE, Ruberti J, Zieske JD. Novel in Vitro Model for Keratoconus Disease. J Funct Biomater 2012;3:760-775.
9. Saeidi N, **Guo X**, Hutcheon AE, Sander EA, Bale SS, Melotti SA, Zieske JD, Trinkaus-Randall V, Ruberti JW. Disorganized collagen scaffold interferes with fibroblast mediated deposition of organized extracellular matrix in vitro. Biotechnol Bioeng 2012;109:2683-98.
10. Karamichos D, **Guo X**, Hutcheon AEK, Zieske JD. Human Corneal Fibrosis: An In Vitro Model. Invest Ophthalmol Vis Sci 2010;51:1382-8.
11. Ren R, Hutcheon AEK, **Guo XQ**, Saeidi N, Melotti SA, Ruberti JW, Zieske JD, Trinkaus-Randall V. Human primary corneal fibroblasts synthesize and deposit proteoglycans in long-term 3-D cultures. Dev Dyn 2008;237:2705-15.
12. **Guo X**, Hutcheon AEK, Melotti SA, Zieske JD, Trinkaus-Randall V, Ruberti JW. Morphological Characterization of Organized Extracellular Matrix Deposition by Ascorbic Acid-Stimulated Human Corneal Fibroblasts. Invest Ophthalmol Vis Sci 2007;48:4050-60.
13. J.D. Zieske, **X.Q. Guo**, S.A. Melotti, A.E. Hutcheon, J.W. Ruberti. Spatial organization of engineered corneal stroma: Is there a need for contact guidance OR direct mechanical stimulus? Journal of Biomechanics 2006; 39(Supp 1): S386
14. Hutcheon AEK, **Guo X**, Stepp MA, Simon KJ, Weinreb PH, Violette SM and Zieske JD. Effect of Wound Type on Smad 2 and 4 Translocation. Invest Ophthalmol Vis Sci. 2005; 46(7): 2362-2368.
15. **Guo X**, Hutcheon AEK and Zieske JD. TAT-mediated protein transduction into human corneal epithelial cells: $p15^{INK4b}$ inhibits cell proliferation and stimulates cell migration. Invest Ophthalmol Vis Sci.2004; 45(6): 1804-1811
16. **Guo X**, Hutcheon AEK and Zieske JD. Transduction of functionally active TAT fusion proteins into cornea. Exp. Eye Research 2004; 78(5): 997-1005.
17. Zieske JD, Chung E-H, **Guo X**, and Hutcheon AEK. Human Corneal Organotypic Cultures. J Toxicol Cutaneous Ocul Toxicol 2004; 23(1): 19-28.
18. Zieske JD, Hutcheon AEK, **Guo X**, Chung E-H, and Joyce NC. TGF-beta receptor types-I and -II are differentially expressed during corneal epithelial wound repair. Invest Ophthalmol Vis Sci. 2001; 42(7): 1465-71.
19. **Guo X**, Wang A, Chen S, et al. The curative effects of anti-TNF monoclonal antibody on *E. coli* infected mice. ACTA Academiae Medicinae Sinicae. 1997; 19(4): 312 (in chinese).
20. **Guo X**, Wang A, Chen S, et al. The development of monoclonal antibody against rhTNF and its curative effect on E. coli infected mice. Chin Med Sci J. 1997; 12(4): 229
21. **Guo X**, Wang A, Chen S, et al. Dynamic analysis of serum TNF from bacterially infected patients. Chin J Intern Med. 1998; 37(12): 847 (in chinese).
22. **Guo X**, Wang A. The prospects of TNF antagonists in clinical use. Chin J Inter Med. 1997; 36(1): 64 (in chinese).
23. Chen S, Zhang Z, Liu P, **Guo X**, et al. A study of the effects of chemotherapy with or without G-CSF on neurophic counts and serum G-CSF levels in leukemia patients. Chin J Inter Med. 1996; 35(4): 249 (in chinese).

24. Niu Z, Ge Z, Fang J, **Guo X**, et al. Proportion and application of ELISA kit for detection of G-CSF the diagnosis of fever patients. ACTA Academiae Medicinae Sinicae. 1994; 16(5): 370 (in chinese).
25. Li T, Wang A, **Guo X**. The clinical use of G-CSF ELISA kit. Natl Med J China. 1993; 93(4): 226 (in chinese).
26. **Guo X**, Wang A, Guo Z. Purification of G-CSF by affinity chromatography. Chin J Microbiol Immunol. 1993; 13(1): 59 (in chinese).
27. Li T, Wang A, **Guo X**. Using McAb to produce G-CSF ELISA kit. Natl Med J China. 1992; 72(4): 224 (in chinese).
28. **Guo X**, Wang A. The development of monoclonal antibody against G-CSF and its clinical application. Foreign Med Inform. 1992; 13(14): 1 (in chinese).
29. **Guo X**, Wang A, Li X, et al. Studies on monoclonal antibody against recombinant human G-CSF. Chin Med Sci J. 1991; 6(4): 212.

Reviews and Chapters:

1. Zieske JD, Francesconi CM, **Guo X**. Cell cycle regulators at the ocular surface. Exp Eye Res 2004; 78:447-456.

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings:

1. **Guo XQ**, Hutcheon AE, and Zieske JD. Expression of TSP1 in Human Corneal Cells. Poster Presentation, ARVO 2018.
2. **Guo XQ**, Hutcheon AE, and Zieske JD. Descemet's Membrane Formation in a 3D Culture Model. Poster Presentation, 30th Biennial Cornea Conference 2017.
3. **Guo XQ**, Sriniwas S, Tran JA, Hutcheon AE, and Zieske JD. Potential approach to reverse corneal myofibroblast formation. Poster Presentation, ARVO 2017.
4. **Guo XQ**, Sriniwas S, Tran JA, Hutcheon AE, and Zieske JD. Potential Approach to Prevent Corneal Fibrosis. Paper Presentation, ARVO 2016.
5. **Guo XQ**, Tran JA, Hutcheon AE, and Zieske JD. Blockage of Smad-Signaling Pathway in Human Corneal Fibroblasts. Poster Presentation, ARVO 2015.

Narrative Report

Over the past decade, my research interest has focused on understanding the mechanisms of corneal wound healing, and developing methods to alter wound-healing mechanisms in a way that allows healing without scarring. All corneal blindness is ultimately due to corneal scarring, regardless of initial disease or trauma, and currently, there are no commercial products available to prevent or reverse this scarring without causing significant side effects. Scarring in the cornea involves the differentiation of the host's stromal keratocytes into myofibroblasts, which generate stress fibers that consist of alpha-smooth muscle actin (SMA). In culture, when human corneal fibroblasts (HCFs) are stimulated with transforming growth factor-beta 1 (TGF-β1), the HCFs differentiate into myofibroblasts similar to scarring in vivo. Our previous studies have shown that Trx-SARA, a specific Smad-signaling inhibitor, can efficiently block the Smad pathway when stably expressed in human corneal cells by competing with endogenous SARA protein. We've used Trx-SARA and p38 inhibitor (SB202190) to dissect the roles of different TGF-β-signaling pathways in corneal fibrosis (scar) formation. When HCF ± Trx-SARA were treated with 2ng/ml of TGF-β1 for 24 hours, we found that the presence of Trx-SARA had little, if any, effect on SMA expression, indicating that blocking the Smad pathway did not inhibit SMA-gene expression in HCF. This suggests that TGF-β1 stimulation of corneal fibrosis is not mainly through the Smad pathway in this cell type. To understand which TGF-β-signaling pathway controls SMA expression in HCF, a p38 inhibitor, SB202190, was used in HCF culture. We found that the addition of the p38 inhibitor greatly decreased

SMA-protein expression in HCF with TGF-β1 stimulation. Thereby indicating that TGF-β1 regulates SMA-gene expression in HCF through the p38 pathway. Similar results were obtained by western blot, indirect-immunofluorescence (IF), and qRT-PCR. Our newest data has shown that the p38 inhibitor accelerates the conversion of these myofibroblasts back to their normal fibroblast phenotype, even in the presence of TGF-β1. These results indicate that by inhibiting p38, we may not only be able to prevent scarring, but also reverse existing corneal scar tissue back to normal. The next logical step is to examine the effects of p38 inhibitor on the prevention/repairing processes involved in corneal scarring in an in vivo animal model. If successful, the use of the p38 inhibitor may be a potential approach to prevent/reverse corneal scarring. Since scarring plays a role in almost all corneal diseases, the blockage of scarring would be highly beneficial. Due to the exciting data that we have gathered concerning p38 inhibitor and scarring, Dr. Zieske and myself have filed and received a patent entitled, "p38 MAP Kinase Inhibitors for Wound Healing".

In addition to the research described above, which was performed in Dr. James Zieske's laboratory under his R01 grant, I began focusing on becoming an independent researcher. In 2015, I co-authored and received a R21 from NIH/NEI entitled, "Development of an In Vivo Model to Mimic Human Endothelial Replacement Therapy". Dr. Zieske allowed me to take the lead on this grant, which gave me the opportunity to gain experience in independently managing a big project. The basis of this project is to develop a 3D co-culture model that will allow for the examination of human corneal endothelial maturation and Descemet's Membrane (DM) reformation in a controlled environment that mimics the human cornea. This project utilizes a 3D stroma model that I helped develop, which mimics the *in situ* stroma. While I find the research with the corneal endothelial co-culture fascinating, I am intrigued by the data concerning the p38 inhibitor. Therefore, I've written an R01 grant where I will pursue the role of p38 inhibitor on the prevention/repair of a corneal scar after wounding, which I have resubmitted for review in the Summer 2018. This grant will be the continuation of Dr. Zieske's previous research in the field of cell signaling in a corneal wound. Dr. Zieske has graciously allowed me to pursue this topic for he is now focusing on the role of extracellular vesicle involvement in cell-cell communication after a corneal wound.

As well as working on Dr. Zieske's projects and my own, I train fellows/technicians in Dr. Zieske's laboratory and other laboratories both at Schepens Eye Research Institute/Mass. Eye and Ear and externally in the following techniques: mouse wound models (debridement and keratectomy), primary corneal epithelial cell and keratocyte isolation and cultivation, and 3D stroma model. Currently, I've supervised Daisy Yao Shu, who is a Ph.D. student from Australia. She is working on a project involving the crosstalk of EGF and TGFβ in human corneal cells, which will assist her in her Ph.D. thesis. In addition, I helped Dr. Zieske with the lab running during his sickness leave. I have assisted Dr. Zieske with the training and supervision of Dr. Sriniwas Sriram, who moved on last year from our laboratory to work in industry. Some of the other fellows/technicians that I have trained are as follows: Drs. Chi Zhang, Yang Liu, and Tomo Suzuki from Dr. Sullivan's laboratory; Tomas Blanco from Dr. Zieske's laboratory; Dr. Ping Lui from Dr. Pedram Hamrah's laboratory; Dr. Nima Saeidi and Suzi Melotti from Dr. Jeffery Ruberti's lab (Northeastern University); and Dr. Junko Hori from Dr. Streilein's laboratory. In addition, I have trained fellows from the laboratories of Dr. Reza Dana, Dr. Bruce Ksandar, Dr. MaryAnn Stepp (George Washington University), and Dr. James Funderburgh (University of Pittsburgh).