

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

Date Prepared: October 17, 2018

Name: James D. Zieske

Education

1976	B.S.	Biology	Rockford College, Rockford, IL
1981	Ph.D.	Biological Chemistry Dr. I.A. Bernstein	University of Michigan, Ann Arbor, MI

Postdoctoral Training

09/81-06/82	Research Fellow	Cell surface glycoproteins and epidermal differentiation Mentor: I.A. Bernstein Mentor	University of Michigan, Department of Biological Chemistry
07/82-09/84	Research Fellow	Cell surface proteins in corneal epithelium Mentor: I.K. Gipson	Schepens Eye Research Institute and Harvard Medical School

Faculty Academic Appointments

09/86-09/92	Instructor	Ophthalmology	Harvard Medical School
10/92-09/02	Assistant Professor	Ophthalmology	Harvard Medical School
09/02-present	Associate Professor	Ophthalmology	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions

Past

10/84-12/84	Staff Associate	Ophthalmology	Schepens Eye Research Institute
01/85-09/90	Assistant Scientist	Ophthalmology	Schepens Eye Research Institute
10/90-09/95	Associate Scientist	Ophthalmology	Schepens Eye Research Institute

Present

10/95-present	Senior Scientist	Ophthalmology	Schepens Eye Research Institute
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Major Administrative Leadership Positions

Local

1991-2005	Radiation Safety Officer		Schepens Eye Research Institute
1997	Course co-organizer, "Cell Biology with Emphasis on the Eye"		Schepens Eye Research Institute
1997-2014	Principal Investigator, Institute Core Grant		Schepens Eye Research Institute
1997-2014	Morphology Module Head, Institute Core Grant		Schepens Eye Research Institute
1999-2007	Co-organizer, Cornea Conference		Schepens Eye Research Institute
2000-2002	Associate Director of Research		Schepens Eye Research Institute

Committee Service

Local

1987-1996	Broadhurst Visiting Lecture Committee		Schepens Eye Research Institute
	1987-1996		Chairman
1988-1990	Cornea, Pharmacology, Immunology Seminar Series		Schepens Eye Research Institute
	1988-1990		Convener
1988-1992	Small Equipment Grant Committee		Schepens Eye Research Institute
	1988-1992		Chairman
1988-2006	Radioisotope Safety Committee		Schepens Eye Research Institute
	1988-2006		Officer
1994-1995, 2004-2005	Seminar Committee		Schepens Eye Research Institute
	1994-1995		Chairman
	2004-2005		Chairman
1994-2000	Support Services Committee		Schepens Eye Research Institute
1994-2000	Research Resources Committee		Schepens Eye Research Institute
1994-2000	Committee on Responsible Conduct of Research		Schepens Eye Research Institute
1995	Molecular Biologist Search Committee		Schepens Eye Research Institute

1997-1998	Retinal Developmental Biologist Search Committee	Schepens Eye Research Institute
1997-2001, 2012-2015	Appointments and Promotions Committee	Schepens Eye Research Institute
1997-2014	Core Grant Committee 1997-2014	Schepens Eye Research Institute Chairman
1997-2008	Ocular Surface Diseases Focus Group 2000-2008	Schepens Eye Research Institute Chairman
1998-2001	Recruitment Committee, NIH Training Grant	Department of Ophthalmology, Harvard Medical School
1998-2002	Research Planning and Review	Schepens Eye Research Institute
1998-2002	Strategic Planning Committee	Schepens Eye Research Institute
2001-2002	Gene Expression/Microarray Group 2001-2002	Schepens Eye Research Institute Chairman
2001-2005	Training Committee	Schepens Eye Research Institute
2001-2014	Selection Committee, NIH Training Grant	Department of Ophthalmology, Harvard Medical School
2004-2010	Computer Committee 2008-2010	Schepens Eye Research Institute Chairman
2006-2012	Internal Communications Committee	Schepens Eye Research Institute
2007-present	Institutional Animal Care and Use Committee 2012-present	Schepens Eye Research Institute Vice-chair
2007-2008	Joint Clinical Research Center Governance Committee	Schepens Eye Research Institute
2008-2014	Lids to Lens Group 2008-2014	Schepens Eye Research Institute Chairman
2009-present	Center for Ocular Regeneration	Schepens Eye Research Institute

Regional

1998-1999	Planning Committee	Biennial Cornea Conference, Boston, MA
	1998-2003	Co-Organizer
	2004-2005	Conference Chair
	2006-2007	Conference Co-Chair

Professional Societies

1983-present	Association for Research in Vision and Ophthalmology	
	1983-present	Member
	1995-1998	Cornea Section Program Committee
	1999-2001	Ad Hoc Member, ARVO Program Committee
1983-2005	American Society of Cell Biologists	
	1983-2005	Member
1996-present	International Society of Eye Research	
	1996-present	Member
	1996-1998	Co-Organizer: Biology of Wound Healing Symposium, Annual Congress—Paris, France, July 1998
	2003-2004	Co-Organizer: Corneal Equivalents Symposium, Annual Congress—Sydney, Australia, August, 2004
	2009-2010	Co-Organizer for Corneal Sections—2010 Montreal

Grant Review Activities

1989	VISA2 Study Section	NIH
	1989	Ad Hoc Member
1994	VISA1 Study Section	NIH
	1994	Ad Hoc Member
1997-1999	Fight-For-Sight Grants-In-Aid, Application Committee	Prevent Blindness America
	1997-1999	Reviewer
1999, 2002-2003	NEI Special Emphasis Panel	NIH
	1999, 2002-2003 (Core Center Grants)	Ad Hoc Member
	2002 (R03 Reviews)	Ad Hoc Member
	2003 (Biomedical Engineering Applications)	Ad Hoc Member
	2013	Reviewer
	2015	Reviewer
2004-2005	VISA Study Section	NIH
	2004-2005	Ad Hoc Member
2005-2008	AED Study Section	NIH
	2005-2008	Permanent Member
2009	NIBIB Study Section	NIH
	2009	Reviewer
2009	Challenge Grants	NIH
	2009	Reviewer

2011	AMS Study Section	NIH
	2011	Ad Hoc Member
2012	NEI-RFA Stem Cell Approaches to Developing New Therapies for Ocular Diseases	NIH
	2012	Reviewer
2013	K08, R24, and K99 Awards	NIH
	2013	Reviewer
2013	BVS Study Section	NIH
	2013	Reviewer
2014	Vision Research Panel	Department of Defense
	2014	Reviewer
2015	BDCN-R(02) Special Emphasis Panel	NIH/CSR
	2015	Reviewer
2018	BDCN-R (040) Special Emphasis Panel	NIH/CSR
	2018	Reviewer

Editorial Activities

Contributing Reviewer

Journal of Biological Chemistry
Current Eye Research
Experimental Eye Research
Investigative Ophthalmology and Visual Science
Journal of Investigative Dermatology
Molecular Vision
PLoS ONE
Scientific Reports
American Journal of Pathology
Tissue Research

Other Editorial Roles

1997-2002	Editorial board member	Investigative Ophthalmology and Visual Science
2001-present	Editorial board member	Cutaneous and Ocular Toxicology
2003-present	Editorial board member	Experimental Eye Research
2007-2017	Editorial board member	Investigative Ophthalmology and Visual Science
2007-present	Editorial board member	Journal of Ocular Biology

Honors and Prizes

1972-1976	Scholarship	Rockford College
1983-1984	Individual National Research Service Award	NEI
2009	Gold Fellow	ARVO
2013-present	Endowment Project	Schepens Eye Research Institute/Mass.

Report of Funded and Unfunded Projects

Funding Information

Past

- 1982-1984 Corneal Epithelial Proliferation and Repair
NIH/NEI Individual NRSA Award / PI
- 1996-1997 Human Corneal Organotypic Culture
Gillette/HSUS Alternatives Program / PI
- 1997-1998 Ocular Epithelial Organotypic Cultures
Johns Hopkins Center for Alternatives to Animal Testing / PI
- 1997-2016 Core Grant for Vision Research
NIH/NEI P30 EY03790 / PI
The major goal of this project is to provide support for four core modules available to all investigators at SERI. The four modules are Morphology, Animal Resources, Laboratory Computer Applications, and Flow Cytometry.
- 1998-2002 Ocular Gene Therapy
Schepens Eye Research Institute / PI
- 2005-2008 Development of an Anti-Infective Corneal Bandage
Department of Defense / project PI
- 2008-2009 Effect of UVB on Haze Formation Following Refractive Surgery
Department of Defense / project PI
- 2008-2010 In Vitro Model of Corneal Fibrosis
NIH/NEI R21 EY018939 / PI
- 2010-2011 Corneal Epithelial Proliferation and Repair
NIH/NEI Supplement EY05565-25S1 / PI
- 2004-2011 Engineering Biomimetic Corneal Constructs
NIH/NEI R01 EY015500 / co-PI
- 2011-2012 Prevention of Corneal Scarring by Application of 3-D Self-assembled Corneal Matrix
Department of Defense / Project PI
- 2011-2016 Transplantation of a self-assembled corneal substitute (no cost extension)
NIH/NEI R01 EY020886 / co-PI
The major goal of this project is to investigate whether our corneal stromal model can be successfully transplanted into humanized mouse corneas.
- 2013-2016 Documentation of Novel Keratoconus Markers: In Vitro and In Vivo
NIH/NEI R01-EY023568 / co-Investigator (Dimitrios Karamichos PI)
- 2015-2017 Sphingolipid signaling in corneal wound healing and fibrosis
NIH/NEI R21 EY025256/ Co-Investigator (Karamichos and Mandal Co-PIs)
The major goal of this project is to investigate a novel mechanism of corneal scar formation. We will utilize our previous experience using our human 3D culture model in order to dissect the effect of the sphingolipids in human corneal fibrosis using both in vitro and in vivo techniques.
- 2015-2018 Development of an In Vivo Model to Mimic Human Endothelial Replacement Therapy
NIH/NEI R21 EY025833
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.

Current

- 1984-2022 Corneal Epithelial-Stromal Interactions During Regeneration and Fibrosis
NIH/NEI R01 EY005665
PI (\$1,000,000 – total direct costs for current funding cycle beginning in 2018)
The major goal of this project is to demonstrate the role of extracellular vesicles in corneal wound healing, and to determine if they can be “loaded” with certain “cargo” (i.e. growth factors, cytokines, or drugs) that would be useful as therapeutics to promote healing with minimal generation of myofibroblasts.
- 2015-2019 CD147 and Corneal Wound Repair
NIH/NEI R01 EY024031
CSU (PI: Pablo Argueso)
The long-term objective of this study is to determine whether induction of CD147 clustering on the cell surface glycocalyx is a regulatory mechanism of the physiological and pathological remodeling processes associated with wound repair in the cornea.
- 2017-2022 A Cell-free Approach to the Engineering of Corneal Stroma
NIH/NEI R01-EY028234
CSU (PI: Nima Saeidi)
The major goal of this project is to develop a novel, cell-free strategy to the engineering of corneal stroma by means of regulating collagen molecules' self-assembly and organization.

Report of Local Teaching and Training

Teaching of Students in Courses

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|-----------|--|-------------------------------|
| 1987-1996 | New Pathway Project: Metabolism and Function Tutor | HMS |
| | 1st year medical students | 4.5 hours/week for 8-10 weeks |
| 1997-2002 | Project Success: Mentor | HMS |
| | 1 Undergraduate Student/year | 30 hours/week for 8-10 weeks |

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

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|--------------|---|---------------------------------|
| 1999-2007 | Grant Writing Workshop | Schepens Eye Research Institute |
| | 5 postdoctoral fellows | 2 hours contact |
| 2004-present | “Molecular Bases of Eye Diseases” Course | HMS |
| | 20-25 postdoctoral students, fellows, and graduate students | 1 hour lecture |

Laboratory and Other Research Supervisory and Training Responsibilities

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| 1990-1991,
1994-2000,
2002, 2005-
2011, 2014-
2018 | Supervision of post-doctoral research fellow/ Schepens Eye Research Institute/MEE | Two hours lab meeting per week and 1:1 supervision one hour per week |
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Formally Supervised Trainees

Graduate Students:

- 2008-2011 Jose Tomas Blanco-Mezquita
2015-2017 Wenjing Wu, B.S.; Ph.D. student in Refractive Surgery and Ophthalmology, Tianjin Medical University, China.
2018 Daisy Yao Shu, B.S.; Ph.D. student in Molecular Biology, University of Sydney, Australia.

Postdoctoral Fellows:

- 1990-1991 Eui-Hong Chung, M.D., Ph.D.; Chairman, Department of Ophthalmology, Ilsan Paik Hospital, Inje Medical School, Koyang City Korea
1990-1991 Stefan Trocmé, M.D.; Director of the Refractive Surgery Service and the new Center for Ocular Surface Diseases and Surgery, Lyndhurst, Ohio
1994-1996 Hiroshi Takahashi, M.D.; Associate Professor, Department of Ophthalmology, Nippon Medical School, Tokyo, Japan
1996-1997 Claudia Francesconi, M.D.; Clinical Practice, Sao Paulo, Brazil
1997-1998 Randa Garrana, M.D.; Clinical Practice, Newport Beach, CA
1997-1998 Ana Claudia Dalbone, M.D., Clinical Practice, Rio de Janeiro, Brazil
1998-1999 Sabino Rolim Guimaraes Filho, M.D.; Clinical Practice, Paraiba, Brazil
1998-2000 Xiaoqing Guo, M.D.; Research Associate, Zieske Lab., Schepens Eye Research Institute
2002 Anh Nguyen, M.D.; Clinical Practice and affiliate of the University of Montreal, Canada
2002 Kimberley Sippel, M.D.; Assistant Professor of Ophthalmology at Weill Cornell Medical Center and New York Presbyterian Hospital, New York, NY
2005-2008 Mariko Matsuba, M.D.; Clinical practice and Department of Pathology at Nippon Medical School, Tokyo, Japan
2008-2011 Dimitris Karamichos, Ph.D.; Assistant Professor, University of Oklahoma Health Sciences Center
2014-2017 Srinivas Sriram, Ph.D.
2018-present Tina McKay, Ph.D.

Visiting Scientists:

- 1994-1996 Eui-Hong Chung, M.D., Ph.D.

Formal Teaching of Peers (e.g., CME and other continuing education courses)

- 1997 “Cell Biology with Emphasis on the Eye” 2, 1 hour lectures
45 members of the Institute (postdoctoral fellows, faculty, laboratory staff) Schepens Eye Research Institute

Report of Regional, National and International Invited Teaching and Presentations

Invited Presentations and Courses

Regional

- 1991-1994 Lancaster Course in Ophthalmology / lecture
Waterville, ME
1995 Lecture

- 2002 Department of Oral Biology and Pathology, State University of New York at Stony Brook
 “Engineering Challenges in Physiology” / invited teaching presentation
 Tufts University School of Engineering, Boston MA
- 2002 Lecture
 New England Eye Center, Tufts University School of Medicine, Boston, MA
- 2007 Lecture
 Department of Biochemistry and Ophthalmology, Boston University School of Medicine,
 Boston, MA
- 2011 Lecture
 Boston University Eyes to the Brain Seminar Series, Boston University School of
 Medicine, Boston, MA

National

- 1992 Seminar
 Laboratory of Molecular and Developmental Biology, National Eye Institute, Bethesda,
 MD
- 1993 Seminar, Symposium Discussion
 ILSI Health and Environmental Sciences Institute, Washington DC
- 1993 Seminar, Visiting Professor
 Department of Ophthalmology, University of Texas Medical Branch at Galveston,
 Galveston, TX
- 1994 Seminar
 Department of Ophthalmology, Mount Sinai School of Medicine, New York, NY
- 1995 Symposium, Organizing Committee Member
 Ocular Cell and Molecular Biology, San Diego, CA
- 1995 Lecture
 Department of Oral Biology and Pathology, State University of New York at Stony Brook
- 1995 Minisymposium
 Association for Research in Vision and Ophthalmology Annual Meeting,
 Fort Myers, Florida
- 1997 Visiting Scholar
 Vision Science Research Center, The University of Alabama at Birmingham
- 1997 Symposium
 Keystone Symposia on Molecular and Cellular Biology, Tamaron, CO
- 1997 Lecture
 Department of Ophthalmology, Wake Forest University, Winston-Salem, NC
- 1997 Lecture
 Department of Anatomy and Cell Biology, George Washington University Medical Center,
 Washington DC
- 1997 Lecture
 Laboratory of Molecular and Developmental Biology, National Eye Institute of the
 National Institutes of Health, Bethesda, MD
- 1998 Symposium
 CAAT Symposium, Baltimore, MD
- 1998 Symposium
 American College of Toxicology, Orlando, FL
- 1999 Symposium
 Keystone Symposia on Ocular Molecular and Cellular Biology, Keystone, CO

1999 Lecture
Laboratory of Molecular and Developmental Biology, National Eye Institute of the
National Institutes of Health, Bethesda, MD

2000 Symposium
Congress of Researchers in Eye Surgery and Technology Meeting, Ft. Lauderdale, FL

2000 Symposium
XIV International Congress of Eye Research, Santa Fe, NM

2001 Minisymposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Ft. Lauderdale, FL

2002 Lecture
Department of Cellular Biology and Anatomy, Medical College of Georgia, Augusta, GA

2003 Symposium
Congress of Researchers in Eye Surgery and Technology Meeting, Ft. Lauderdale, FL

2003 Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Ft. Lauderdale, FL

2005 Keynote Lecture
ARVO Western Eye Research Conference, Laguna Beach, CA

2005 Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Fort Lauderdale, FL

2005 Symposium
Ocular Cell & Molecular Biology Conference, Sarasota, FL

2006 Symposium
American Academy of Optometry, Denver, CO

2007 Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Ft. Lauderdale, FL

2007 Minisymposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Ft. Lauderdale, FL

2007 Symposium
Ocular Cell & Molecular Biology Conference, Sarasota, FL

2010 Keynote Lecture
World Cornea Congress VI
Boston, MA

2010 Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Ft. Lauderdale, FL

2010 Symposium
Gordon Conference 2010: Biology & Pathobiology of the Cornea
Ventura, CA

2010 Lecture
University of Pittsburgh
Pittsburgh, PA

2011 Dr. Marvin D. Henry Memorial Lecture and Workshop
University of Illinois at Chicago

- 2013 Chicago, IL
Symposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Seattle, WA
- 2014 Symposium
XXI International Congress of Eye Research, San Francisco, CA
- 2015 Minisymposium
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Denver, CO
- 2018 Symposium (SIG)
The Association for Research in Vision and Ophthalmology, Annual Meeting,
Honolulu, HI

International

- 1990 Meeting/Presentation
IX International Congress of Eye Research, Helsinki, Finland
- 1993 Meeting/Presentation
Cambridge Ophthalmologic Symposium, Cambridge, England
- 1995 Lecture
Osaka University, Osaka, Japan
- 1995 Keynote Lecture
First Annual Meeting of the Kyoto Cornea Club, Kyoto, Japan
- 1995 Lecture
Kyoto Prefectural University of Medicine, Kyoto, Japan
- 1995 Lecture
Nippon Medical University, Tokyo, Japan
- 1996 Symposium
XII International Congress for Eye Research, Yokohama, Japan
- 1996 Symposium
Santen International Symposium, Yokohama City, Japan
- 1996 Symposium
Kyoto International Symposium, Kyoto, Japan
- 1998 Symposium
XIII International Congress for Eye Research, Paris, France
- 2002 Symposium
XV International Congress of Eye Research, Geneva, Switzerland
- 2004 Symposium
XVI International Congress of Eye Research, Sydney, Australia
- 2006 Symposium
5th World Congress of Biomechanics, Munich, Germany
- 2007 Symposium
Asia ARVO, Singapore
- 2009 Symposium
The Association for Research in Vision and Ophthalmology / International Society for
Ocular Cell Biology Meeting, Portugal
- 2009 Lecture
Ottawa Health Research Institute, Ottawa, Canada
- 2010 Symposium
XIX International Congress of Eye Research, Montreal, Canada

- 2011 Corneal Rounds
Kyoto Prefectural University of Medicine, Kyoto, Japan
- 2011 Keynote Lecture
Japanese Cornea Society Meeting, Tokyo, Japan
- 2012 Symposium
XX International Congress of Eye Research, Berlin, Germany

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. Xiaoqing Guo 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 TGF β 1 stimulation. We postulate that the p38 pathway is an important mechanism driving the corneal and skin scarring. This finding may prevent/improve tissue fibrosis after wounding.

Report of Scholarship

Peer reviewed publications in print or other media

Research Investigations:

1. Weiss TL, **Zieske JD**, Bernstein IA. Reversible microsomal binding to hepatic aldolase. *Biochem Biophys Acta* 1981 Oct 13;611(2):221-9. PMID: 6794627.
2. **Zieske JD**. Addition of fucosyl residues to cell surface glycoprotein during epidermal differentiation. Ph.D. Thesis, University of Michigan, 1981.
3. **Zieske JD**, Bernstein IA. Modification of cell surface glycoprotein: Addition of fucosyl residues during epidermal differentiation. *J Cell Biol* 1982 Nov;95(2 Pt 1):626-31. PMID: 6292241.
4. **Zieske JD**, Bernstein IA. Molecular changes in the cell surface of differentiating epidermal keratinocytes. *Curr Prob Dermatol* 1983;11;243-51. PMID: 6197244.
5. **Zieske JD**, Bernstein IA. Epidermal fucosylation of cell surface glycoprotein. *Biochem Biophys Res Commun* 1984 Mar 30;119(3):1028-33. PMID: 6712661.
6. **Zieske JD**, Gipson IK. Protein synthesis during epithelial wound healing. *Invest Ophthalmol Vis Sci* 1986 Jan;27(1):1-7. PMID: 3941030.
7. **Zieske JD**, Higashijima SC, Gipson IK. Con A- and WGA-binding glycoproteins of stationary and migratory corneal epithelium. *Invest Ophthalmol Vis Sci* 1986 Aug;27(8):1205-10. PMID: 3755423.
8. **Zieske JD**, Higashijima SC, Spurr-Michaud SJ, Gipson IK. Biosynthetic responses of the rabbit cornea to a keratectomy wound. *Invest Ophthalmol Vis Sci* 1987 Oct;28(10):1668-77. PMID 3308758.
9. **Zieske JD**, Bukusoglu G, and Gipson IK. Enhancement of vinculin synthesis by migrating stratified squamous epithelium. *J Cell Biol* 1989 Aug;109(2): 571-6. PMID: 2503524.
10. **Zieske JD**, Bukusoglu G. Effect of protease inhibitors on corneal epithelial migration. *Invest Ophthalmol Vis Sci* 1991 Jun;32(7):2073-8. PMID: 2055700.

11. Matsubara M, **Zieske JD**, Fini ME. Mechanism of basement membrane dissolution preceding corneal ulceration. *Invest Ophthalmol Vis Sci* 1991 Dec;32(13):3221-37. PMID: 1660857.
12. **Zieske JD**, Bukusoglu G, Yankauckas MA. Characterization of a potential marker of corneal epithelial stem cells. *Invest Ophthalmol Vis Sci* 1992 Jan;33(1):143-52. PMID: 1730535.
13. **Zieske JD**, Bukusoglu G, Yankauckas MA, Wasson ME, and Keutmann HT. Alpha-enolase is restricted to basal cells of stratified squamous epithelium. *Dev Biol* 1992 May;151(1):18-26. PMID: 1577187.
14. Chung E-H, Bukusoglu G, **Zieske JD**. Localization of corneal epithelial stem cells in the developing rat. *Invest Ophthalmol Vis Sci* 1992 Jun;33(7):2199-2206. PMID: 1607230.
15. **Zieske JD**, Wasson M. Regional variation in distribution of EGF receptor in developing and adult corneal epithelium. *J Cell Sci* 1993 Sep;106(Pt 1):145-52. PMID: 8270620.
16. Trocmé SD, Gleich GJ, Kephart GM, **Zieske JD**. Eosinophil granule major basic protein inhibition of corneal epithelial wound healing. *Invest Ophthalmol Vis Sci* 1994 Jun;35(7):3051-6. PMID: 8206722.
17. **Zieske JD**, Mason VS, Wasson ME, Meunier SF, Nolte CJM, Fukai N, Olsen BR, Parenteau NL. Basement membrane assembly and differentiation of cultured corneal cells: Importance of culture environment and endothelial cell interaction. *Exp Cell Res* 1994 Oct;214(2):621-33. PMID: 7523155.
18. Wilson SE, He Y-G, Weng J, **Zieske JD**, Jester JV, Schultz GS. Effect of epidermal growth factor, hepatocyte growth factor, and keratinocyte growth factor, on proliferation, motility, and differentiation of human corneal epithelial cells. *Exp Eye Res* 1994 Dec;59(6):665-78. PMID: 7698260.
19. Chung E-H, DeGregorio PG, Wasson M, **Zieske JD**. Epithelial regeneration after limbus-to-limbus debridement: Expression of a-enolase in stem and transient amplifying cells. *Invest Ophthalmol Vis Sci* 1995 Jun;36(7):1336-43. PMID: 7775111.
20. Dartt DA, McCarthy DM, Mercer HJ, Kessler TL, Chung E-H, **Zieske JD**. Localization of nerves adjacent to goblet cells in rat conjunctiva. *Curr Eye Res* 1995 Nov;14(11):993-1000. PMID: 8585938.
21. Kessler TL, Mercer HJ, McCarthy DM, **Zieske JD**, Dartt DA. Stimulation of goblet cell mucous secretion by activation of nerves in rat conjunctiva. *Curr Eye Res* 1995 Nov;14(11):985-92. PMID: 8585937.
22. Dartt DA, Kessler TL, Chung E-H, **Zieske JD**. Vasoactive intestinal peptide-stimulated glycoconjugate secretion from conjunctival goblet cells. *Exp Eye Res* 1996 Jul;63(1):27-34. PMID: 8983961.
23. Joyce NC, Meklir B, Joyce SJ, **Zieske JD**. Cell cycle protein expression and proliferative status in human corneal cells. *Invest Ophthalmol Vis Sci* 1996 Mar;37(4):645-55. PMID: 8595965.
24. Takahashi H, Kaminski AE, **Zieske JD**. Glucose transporter 1 expression is enhanced during corneal epithelial wound repair. *Exp. Eye Res* 1996 Dec;63(6):649-59. PMID: 9068372.
25. Joyce NC, Navon SE, Roy S, **Zieske JD**. Expression of cell cycle-associated proteins in human and rabbit corneal endothelium in situ. *Invest Ophthalmol Vis Sci* 1996 Jul;37(8):1566-75. PMID: 8675399.
26. Fini ME, Parks WC, Rinehart WB, Girard MT, Matsubara M, Cook JR, West-Mays JA, Sadow PM, Burgeson RE, Jeffrey JJ, Raizman MB, Kreuger RR, **Zieske JD**. Role of matrix metalloproteinases in failure to reepithelialize following corneal injury. *Am J Path* 1996 Oct;149(4):1287-1302. PMID: 8863676.

27. Sugrue SP, **Zieske JD**. ZO-1 in corneal epithelium: Association to the zonula occludens and adherens junctions. *Exp Eye Res* 1997 Jan;64(1):11-20. PMID: 9093016.
28. Hodges RR, Zoukhri D, Sergheraert C, **Zieske JD**, Dartt DA. Identification of VIP receptor subtypes in the lacrimal gland and their signal transducing components. *Invest Ophthalmol Vis Sci* 1997 Mar;38(3):610-9. PMID: 9071214.
29. Joyce NC, **Zieske JD**. Transforming growth factor- β receptor expression in human cornea. *Invest Ophthalmol Vis Sci* 1997 Sep;38(10):1922-8. PMID: 9331255.
30. Joyce NC, Harris DL, **Zieske JD**. Mitotic inhibition of corneal endothelium in neonatal rats. *Invest Ophthalmol Vis Sci* 1998 Dec;39(13):2572-83. PMID: 9856767.
31. Garrana RMR, **Zieske JD**, Assouline M, Gipson IK. Matrix metalloproteinases (MMPs) in epithelia from human recurrent corneal erosion. *Invest Ophthalmol Vis Sci* 1999 May;40(6):1266-1270. PMID: 10235563.
32. Chung E-H, Hutcheon AEK, Joyce NC, **Zieske JD**. Synchronization of the G1/S transition in response to corneal debridement. *Invest Ophthalmol Vis Sci* 1999 Aug;40(9):1952-8. PMID: 10440248.
33. Rios JD, Zoukhri D, Rawe IM, Hodges RR, **Zieske JD**, Dartt DA. Immunolocalization of muscarinic and VIP receptors and their role in stimulating goblet cell secretion. *Invest Ophthalmol Vis Sci* 1999;40(6):1102-1111. PMID: 10235543.
34. **Zieske JD**, Takahashi H, Hutcheon AEK, Dalbone AC. Activation of epidermal growth factor receptor during corneal epithelial migration. *Invest Ophthalmol Vis Sci* 2000 May;41(6):1346-55. PMID: 10798649.
35. Francesconi CM, Hutcheon AEK, Chung E-H, Dalbone AC, Joyce NC, **Zieske JD**. Expression patterns of retinoblastoma and E2F family proteins during corneal development. *Invest Ophthalmol Vis Sci* 2000 Apr;41(5):1054-62. PMID: 10752941.
36. Takahashi H, Akiba K, Noguchi T, Ohmura T, Takahashi R, Ezure Y, Ohara K, **Zieske JD**. Matrix metalloproteinase activity is enhanced during corneal wound repair in high glucose condition. *Curr. Eye Res* 2000 Aug;21(2):608-15. PMID: 11148597.
37. Dartt DA, Rios JR, Kanno H, Rawe IM, **Zieske JD**, Ralda N, Hodges RR, Zoukhri D. Regulation of conjunctival goblet cell secretion by Ca^{2+} and protein kinase C. *Exp Eye Res* 2000 Dec;71(6):619-28. Erratum in: *Exp Eye Res* 2001 Mar;72(3):357. Rios JR [corrected to Rios JD]. PMID: 11095914.
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Narrative Report

My long time research interest has been to understand the mechanisms involved in corneal wound repair. This interest has helped support a grant from NEI since 1984. During the course of this grant, my laboratory has published over 90 peer-reviewed articles in this area. We are currently investigating how the stroma and epithelium interact during corneal fibrosis and regeneration. Fibrosis, or scarring, is an evolutionarily developed method to rapidly close and repair a wound. Excessive deposition of extracellular matrix and the generation of contractile fibroblasts (myofibroblasts) characterize fibrosis. In the cornea, severe wounds that damage the basement membrane heal using fibrosis. However, in contrast to other tissues where function is maintained, fibrosis in the cornea leaves an opaque cornea that can impair vision.

Over the past two years, we made the exciting observation that the epithelium releases exosomes that stimulate fibrosis in human corneal fibroblasts (HCF). Exosomes are nanovesicles (30-100nm) that are released from most cells, and are part of a larger group of vesicles released from cells, termed extracellular vesicles (EVs). EVs have been the subject of intense research efforts in the past five years after the discovery that they carry “cargo” consisting of proteins, mRNA, and miRNA, which can affect the behavior of adjacent cells. Indeed, this appears to be a major mechanism in the initiation of cancer, where EVs from cancer cells invade host cells and stimulate them to secrete matrix that supports the cancer cells. While examining EVs from the cornea, we made several interesting observations: 1) All three major cell types of the cornea release EVs; 2) EVs isolated from human corneal epithelial cells stimulate the expression of α -smooth muscle actin (a marker of fibrosis) in HCF; 3) Epithelial EVs do not appear to penetrate the epithelial basement membrane; and 4) EVs from unwounded corneal epithelial cells do not appear to stimulate fibrosis, but EVs from wounded epithelium do stimulate fibrosis in HCF. These observations suggest that the cargo in EVs released by wounded epithelium is altered compared to those from unwounded.

These observations lead us to our current hypothesis that EV cargo from epithelial cells is altered during wound repair to contain proteins that stimulate fibrosis in HCF. Over the course of the next few years, we will examine several aspects of EV biology in the cornea: 1) We will compare proteins, and possibly mRNA and/or miRNA, in the cargo of EVs isolated from wounded and unwounded corneal epithelial cells, as well as examine the effect of matrix using our 3-dimensional HCF constructs; 2) We will examine if EV cargo is altered in keratocytes compared to myofibroblasts, and if the EVs from myofibroblasts contain cargo that enhance the fibrotic response; and 3) We will use time-lapse microscopy to examine migration characteristics of the EVs in the cornea. During this time, several questions will be examined, including the following: 1) Do epithelial EVs penetrate the epithelial basement membrane; 2) What are the dynamics of EV penetration into the cornea; and 3) Do endothelial EVs penetrate the Descemet’s membrane? Our preliminary findings indicate that epithelial EVs interact with stromal cells and endothelial EVs do penetrate the Descemet’s membrane. Overall, our goal is to understand the interactions of EVs in the cornea. In the process, if we find that topically applied EVs can alter corneal activities, this would have great clinical potential, as EVs could be loaded with cargo that could blunt fibrosis or other corneal diseases.