OCULAR SURFACE CENTER
BAYLOR COLLEGE OF MEDICINE
Cintia S. de Paiva, MD, PhD
Associate Professor

Houston, January 14, 2025

2026 Helen Keller Prize for Vision Research Selection Committee

RE: Stephen C. Pflugfelder, MD nomination to the 2026 Helen Keller Prize for Vision Research

Dear Selection Committee,

I am pleased to nominate Dr. Stephen C. Pflugfelder for the 2026 Helen Keller Vision Award. He is internationally known as a pioneer in ocular surface disease. Few Ophthalmologists have received the accolades awarded to Steve – he is a gem in the international scientific community. Steve Pflugfelder joined the Department of Ophthalmology at Baylor College of Medicine in July 2000 after spending 15 years on the faculty of the Department of Ophthalmology at the University of Miami School of Medicine. He is a Professor and Director of the Ocular Surface Center in our Department and holds the James and Margaret Elkins Endowed Chair in Ophthalmology.

Steve has been studying dry eye disease for the past 30 years. Dry eye disease is a chronic, debilitating condition that affects millions of people in the US alone. Dry eye symptoms can vary from mild to severe (in some cases, the pain is compared to cardiac pain) and can lead to corneal perforation. Dry eye also affects functional vision, a type of vision that is not corrected by eyeglasses, and it is caused by ocular surface irregularity that scatters the light rays and blurs the image forming in the retina, leading to fluctuating and blurring vision. Decreased functional vision affects all daily activities, including walking, watching TV, and using a computer.

I have known Steve for over 20 years, so I am an excellent person to highlight his lifetime accomplishments. He is an ideal candidate for this Award. Being the top scientist in dry eye disease is not a small feat. Steve has published 387 articles and >50 book chapters; his work has been cited 36,839 times, and his H-index is 103 (which indicates that he has at least 103 articles cited at least 103 times). He has mentored over 50 post-doctoral research fellows and numerous medical students and residents. His works range from clinical studies and muti-centric randomized clinical trials to elegant pre-clinical studies. Steve and his team and collaborators described the desiccating stress model, which combines low-humidity, pharmacological lacrimal gland secretion blockage, and environmental stress to model aqueous-tear deficient dry eye in mice. This model has been used extensively as a pre-clinical dry eye model, worldwide.

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I was an ophthalmologic resident in Brazil the first time I encountered one of his works. My professors and I were providing clinical care for a patient with Sjögren Syndrome dry eye that was unresponsive to artificial tears with a high content of methylcellulose. There was an imminent risk of corneal perforation and loss of globe because the cornea was very thin. In perusing the literature in 1999, I found one of Steve's publications reporting the beneficial use of unpreserved methylprednisolone in treating severe cases of Sjögren Syndrome dry eye. The current dogma of treating dry eye patients in that decade was to use artificial tears or systemic anti-inflammatory therapy. The use of topical corticosteroids was completely forbidden because the thought was it would lead to corneal melting. The publication intrigued my professors, and I tried it with our patient. There was a remarkable improvement in the clinical presentation and symptoms, and we could preserve the eye without needing an emergency tectonic corneal transplant. This publication describing the use of methylprednisolone for Sjögren Syndrome dry eye patients has been cited close to 500 times. However, what is more impressive about it is not the number of citations but how it paved the way for a significant change in how dry eye was "seen" by ophthalmologists and scientists. Dry eye disease went from a disease with few therapeutic options that were mostly palliative to a treatable disease. Steve's work demonstrates the role of innate immunity, adaptive immunity, and inflammation in the dry eye has led to the approval of cyclosporine A as a topical eye drop in the early 2000s. Cyclosporine A, now available in several approved formulations, remains important for managing dry eye. Steve's work has also benefited from the other pharmacological options approved by the FDA to treat dry eye. For example, an LFA-1 antagonist approved to treat signs and symptoms of dry eye was developed after pre-clinical evidence that the immunological synapse of CD4+T cells with dendritic cells was an important feature of dry eye.

Many of the concepts and discoveries offered by Steve over the past 30 years have been translated into a clinic. He has discovered some key mediators responsible for the corneal and conjunctival epithelial disease that develops in tear dysfunction. This work has resulted in a major paradigm shift in treating tear dysfunction associated with ocular surface disease, with most clinicians now utilizing anti-inflammatory therapies to treat these conditions. His findings have been the basis for developing new and novel therapeutics targeting his discovered pathways. Steve's work has also improved ocular surface disease diagnosis, categorization, and severity grading. He pioneered impression cytology to sample conjunctival epithelial cells to assess cell morphology, protein, and gene expression. His group has recently developed a multiplex quantitative real-time PCR-based diagnostic to measure levels of disease-relevant mediators. These technologies are beginning to be used in clinical trials for dry eye therapeutics. He has discovered the pro-inflammatory effects of desiccating stress on the ocular surface and has developed environmentally controlled goggles to test the effects of desiccation on the ocular surface.

As a physician, Steve has made extraordinary humanitarian efforts through his dedicated work providing eye care to underprivileged populations worldwide. He has participated in several volunteer trips to Central America to provide medical and surgical eye care with the Benevolent Mission International (BMI) group. BMI is a non-profit organization dedicated to providing needy ophthalmic care to the underserved in many areas worldwide. Since its inception, BMI has made astounding contributions to eye care in seven countries in Central and South America and the Pacific. They have also screened over 2,200

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preschool children in 90 mission trips in the Houston/Montgomery County region for vision and hearing problems.

Steve was the first clinician outside Boston to start using the Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) device. The PROSE device is a treatment pioneered by the Boston Foundation for Sight, Needham, MA, that restores visual function, supports healing, reduces symptoms, and improves the quality of life for patients suffering from complex corneal disease. BostonSight PROSE treatment uses FDA-approved (1994) custom-designed and fabricated prosthetic devices to replace or support impaired ocular surface system functions. Originally, these lenses were only available to patients living in the Boston Area. Steve worked closely with the Boston Foundation for Sight to train and bring this technology to Houston. The Baylor Alkek Clinic was the first top-ranked academic center to provide PROSE to its patients. He also worked closely with the insurance companies to make this available to all patients and with charitable funds, so no patient needing this lens would be turned down if they could not afford it.

Based on his extensive work that changed not only how dry eye patients are treated but also how they are categorized and investigated, it is with great enthusiasm that I recommend Steve for the 2026 Helen Keller Prize for Vision Research. He has demonstrated excellence in research through several significant contributions to vision science and the caring of patients. I cannot think of someone else more deserving than him. Steve represents what we all aspire to – he is the consummate clinician, educator, and scientist.

Cintia S. de Paiva, MD, PhD, Gold Fellow of ARVO
Professor
Caroline Elles Endowed Professorship
Ocular Surface Center
Department of Ophthalmology
Baylor College of Medicine
Houston, TX, USA

Editor-in-Chief, *The Ocular Surface* Journal
Past President, *International Ocular Surface Society*

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January 5, 2025

2025 Helen Keller Prize for Vision Research Selection Committee

Dear Selection Committee Members,

It is a great honor to recommend my long-term friend, colleague, and collaborator, Dr. Stephen C. Pflugfelder, for the 2024 Helen Keller Award. I am an ocular immunologist and collaborated with Steve in the initial work defining dry eye as an immune-based inflammation of the ocular surface and lacrimal glands. Additionally we proposed the concept of the Lacrimal Functional Unit and the role of environment in the initiation of this disease. As Vice-President of Inflammation Research at Allergan Pharmaceuticals I led a laboratory elucidating therapeutic targets in ocular surface inflammatory diseases.
I have known and collaborated with Steve for over 30 years.

Steve is recognized as a world expert in dry eye disease. As a result of his research, both as the leader of the internationally recognized Ocular Surface Center in the Department of Ophthalmology at Baylor College of Medicine and as part of many fruitful academic and industry collaborations, we have gained important practical knowledge about the diagnosis of ocular surface/tear diseases, identified relevant therapeutic targets and changed the treatment approach for these conditions. His advice is routinely sought after by companies looking to advance candidate therapies for ocular surface inflammatory disease through a clinical program leading to FDA approval.

Dry eye affects millions of people worldwide, and it has a significant impact on patient's quality of life. Because dry eye affects an individual's functional vision/contrast sensitivity, the ability to use a computer, drive an automobile, and do daily tasks is severely impacted. Furthermore, dry eye is a chronic condition and patients suffer constant painful symptoms. The daunting aspect of dry eye is that symptoms and signs do not necessarily correlate. Until the early 90s, the only treatment for dry eye was artificial tears, which can only provide temporary palliative relief. Only after Steve's seminal works was inflammation recognized as a key player in dry eye. Work in Steve's lab resulted in the "Desiccating Stress model" of dry eye in mice. Not only could this model reproducibly produce chronic disease in mice, but it was also the first model to demonstrate environmental induction of autoimmunity. This model was validated by evaluating the tears and ocular surface cells of patients with the disease. The paper describing the model has been widely cited and it continues to be one of the most widely used experimental dry eye models. Additionally, this model has been utilized to elucidate our understanding of the role of inflammatory cells, including T-cells, B-cells, and antigen-presenting cells (dendritic cells, macrophages). The discovery that T cells are involved in pathogenesis provided the rationale for using cyclosporin A as the first FDA-approved therapy for dry eye in the early 2000s. Of the 5 FDA-approved drugs to treat dry eye, 4 have cyclosporine as the active component. While other drugs might be developed and approved in the future, cyclosporine approval for dry eye remains a landmark in the dry eye therapeutic filed. The change in the paradigm of dry eye treatment from symptomatic only (artificial tears) with drugs that can modulate the immune system (such as cyclosporin A) was only possible through the tremendous amount of scientific knowledge that Steve added to the field. It is rare that subjects can see in their lifetime a change in paradigm leading to an FDA-approved drug that can help millions.

The tear composition in dry eye changes from ocular surface supportive to pro-inflammatory and disease-promoting. Steve had been a driving force behind the concept of the Lacrimal Functional Unit, which defined how the composition of normal tears is strictly regulated to maintain normal nutritive homeostasis on the ocular surface. This concept provided the basis for understanding the mechanisms by which dysfunction and disease of this functional unit cause chronic ocular surface inflammatory disease. This concept was published in the first book, *Dry Eye and Ocular Surface Disorders* (Pflugfelder, Beuerman, Stern 2004). As was theorized at the time, environment plays a role in both the initiation and exacerbation of dry eye.

Steve has authored over 386 peer-reviewed publications, hundreds of abstracts, and over 50 book chapters. He was listed in the top 2% of scientists cited worldwide published in PLoS Biology based on validated citation indices. He has served on numerous editorial boards, including the American Journal of Ophthalmology (Associate Editor), Investigative Ophthalmology and Visual Science (Associate Editor), Cornea, Journal of Ocular and Cutaneous Toxicology, and Cornea. He is currently an editorial board member of The Ocular Surface. He holds the James and Margaret Elkins endowed professorship at Baylor College of Medicine. He served as the Cornea Section Trustee of ARYO (Association for Research in Vision and Ophthalmology) from 2015 to 2021 and the President in 2021. Demonstrating his scientific reach, Steve has presented two of the most prestigious invited lectures in Ophthalmology, the Edward Jackson Memorial Lecture at the American Academy of Ophthalmology in 2011 and The Binkhorst Lecture at the American Society of Cataract and Refractive Surgeons (ASCRS) in 2019.

Since this initial work, Steve and his group at Baylor have gotten deeper into the cellular mechanisms behind dry eye-induced immune cell activation and recruitment. These include the effects of dryness and products released from dead cells caused by dry eye on activating intracellular sensors and initiating the chronic inflammatory cascade on the ocular surface. Steve continues to be a research, education, and clinical training leader. He has trained hundreds of ophthalmology residents and cornea fellows and given them a deeper understanding of dry eye and ocular surface diseases which they have used to improve therapy of these conditions in their communities and disseminated globally.

Again, I am truly honored to be able to write this recommendation.

Please don't hesitate to contact me if I can provide any further information.

Thank you for your consideration,
Michael E. Stern, Ph.D., FARVO
Visiting Professor, Department of Ophthalmology
University of Cologne
Cologne, Germany

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BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Stephen C. Pflugfelder

eRA COMMONS USER NAME (credential, e.g., agency login): STEVENP

POSITION TITLE: Professor and James & Margaret Elkins Chair, Director of the Ocular Surface Center, Department of Ophthalmology, Baylor College of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colgate University, Hamilton, NY	B.A.	05/1977	Biology
SUNY Upstate Medical College, Syracuse, NY	M.D.	05/1981	Medicine
Presbyterian University of Pennsylvania Medical Center, Philadelphia, PA		07/1982	Internship
Baylor College of Medicine, Houston, TX		07/1985	Ophthalmology Residency
University of Miami School of Medicine		07/1986	Cornea Fellowship

A. Personal Statement

I am a clinician scientist with a 35-year interest in the pathogenesis of the ocular surface disease that develops in dry eye. Our Ocular Surface Center at Baylor College of Medicine has discovered that dryness and desiccating stress activate signaling pathways in ocular surface cells that trigger the production of inflammatory mediators that initiate an inflammatory cycle that senstitizes nerves and causes disease of the cornea and conjunctival epithelium. Our center has identified key mediators and pathways that contribute to the pathogenesis of dry eye (summarized in the referenced reviews). Our current work is focused on initiation of the innate inflammatory reaction to desiccation and the mechanisms by which dry eye disrupts immune tolerance. We have discovered that factors produced by the lacrimal glands and conjunctival goblet cells condition monocytes and macrophages in the conjunctiva to maintain homeostasis and a tolerogenic state. We are currently focused on determining the key cells and mediators in this process that can be leveraged to treat dry eye.

a. Pflugfelder SC, Stern ME. Mucosal environmental sensors in the pathogenesis of dry eye. Expert Rev Clin Immunol. 2014; 30:1-4. PMID: 25075545

b. Pflugfelder SC De Paiva C. The pathophysiology of dry eye disease: What we know and future directions for research. *Ophthalmology.* 2017; 124(11S):S4-S13. PMID:29055361

c. Alam J, de Paiva CS, Pflugfelder SC. Immune - Goblet Cell Interaction in the Conjunctiva. *The ocular surface.* 2020; 18:326-334. PMID: 31953222

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1984-1985 Chief Resident and Ophthalmology Instructor - Cullen Eye Institute, Baylor College of Medicine, Houston, Texas

1985-1986 Cornea and External Disease Fellowship and Ophthalmology Instructor - Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida

1986-1992 Assistant Professor of Ophthalmology - Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida

1992-1998 Associate Professor of Ophthalmology- Bascom Palmer Eye Institute, University of Miami

School of Medicine, Miami, Florida
1998-2000 Professor of Ophthalmology- Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida
2000-present Professor of Ophthalmology, James and Margaret Elkins Chair, Ophthalmology Department - Baylor College of Medicine, Houston, TX
2018-2020 Clinical Professor, Ophthalmology Division of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center

Other Experience and Professional Memberships

1998-2013 Editorial Board of *Cornea*
2002-2017 Editorial Board and Associate Editor of *American Journal of Ophthalmology*
2002-2102 Editorial Board of *Eye and Contact Lens*
2002-present Editorial Board of *Ocular Surface*
2000-2005 Secretary, Tear Film & Ocular Surface Society (TFOS)
2007-2018 Associate Editor of *Investigative Ophthalmology and Visual Science*
2014-2017 Editorial Board of *Scientific Reports*
2009-2018 President, International Ocular Surface Society
2017-2021 ARVO Board of Directors, Cornea trustee
2021-2022 ARVO President

Awards and Honors

1991 American Academy of Ophthalmology Honor Award
1990 Outstanding Professor Award for resident education, Bascom Palmer Eye Institute
2000 American Academy of Ophthalmology Senior Honor Award
2000 Named in America's Top Physicians. Consumers' Research Council of America
2001 James and Margaret Elkins Chair, Department of Ophthalmology, Baylor College of Medicine
2002 Research to Prevent Blindness Senior Investigator Award
2003 Best Doctors in Southeastern America, Woodward/White, Inc
2005 Best Doctors in America, Woodward/White, Inc,
2005-2019 Texas Super Doctors, Texas Monthly
2006-2019 Americas Top Doctors, Castle Connolly
2011 LXVII Edward Jackson Memorial Lecture, American Academy of Ophthalmology
2012 Best of the Best Cless Award, University of Illinois Eye and Ear Infirmary
2016 Master Clinician Award, Baylor College of Medicine
2018 American Academy of Ophthalmology Lifetime Achievement Award
2019 Binkhorst Medal Lecture, American Society of Cataract and Refractive Surgeons

C. Contributions to Science

1. My early research was directed toward improving diagnosis and characterization of dry eye. My published studies identified shared and unique features of different tear dysfunction conditions. These studies found that ocular surface inflammation is a common feature of dry eye. In particular, we showed that activity of the inflammatory protease MMP-9 increases in the tears in aqueous sufficient and deficient tear disorders. MMP-9 is now used as a biomarker for dry eye/tear dysfunction. We have found that conjunctival goblet cell loss occurs in aqueous tear deficiency and is associated with greater ocular surface inflammation and epithelial disease. These findings have led to a major change in perception of dry eye from simply a tear deficiency to a disease of altered tear composition that can no longer adequately support and protect the ocular surface. We also developed a desiccation stress model of dry eye in mice that has been used extensively in pathogenesis studies performed in our lab and that has become the standard model used by many dry eye researchers worldwide.
    a. Jones DT, Yen M, Monroy D, Ji X, Atherton SS, Pflugfelder SC. Sjogren's syndrome: cytokine and Epstein Barr viral gene expression within the conjunctival epithelium. Invest Ophthalmol Vis Sci 1994; 35:3493-3504. **PMID: 8056525**
    b. Pflugfelder SC, Tseng SCG, Yoshino K, Monroy D, Felix C, Reis B. Correlation of goblet cell density and mucosal epithelial mucin expression with rose bengal staining in patients with ocular irritation. Ophthalmology 1997; 104:223-235. **PMID: 90526262**

c. Pflugfelder SC, Farley W, Luo L, Zhuo Chen L, de Paiva CS, Olmos LC, Li D-Q, Fini ME. Matrix Metalloproteinase-9 (MMP-9) Knockout Confers Resistance to Corneal Epithelial Barrier Disruption in Experimental Dry Eye. Am J Pathol 2005;166:61-71. **PMID:15632000**

d. Dursun D, Wang M, Monroy D, Li DQ, Lokeshwar BL, Stern ME, Pflugfelder SC. A mouse model of keratoconjunctivitis sicca. Invest Ophthalmol Vis Sci. 2002;43:632-8. **PMID: 11867577**

2. In the last fifteen years, we have used our mouse dry eye model in numerous studies investigating the pathogenesis of the ocular surface disease in dry eye and we developed a model to adoptively transfer T cells from dry eye donor mice to naïve recipients. These studies have found that IL-17 produced by Th17 cells stimulates production of MMPs that disrupt corneal barrier function and IFN-γ from monocyte/macrophage, Th1 and NK cells that causes apoptosis of the ocular surface epithelium and inhibits conjunctival goblet cell differentiation and mucin production. We have also found that the Th2 cytokine IL-13 stimulates goblet cell proliferation and production of mucus and immunomodulatory factors. Loss of conjunctival goblet cells is associated with a higher number of mature antigen presenting cells and this is due in part to loss of goblet cell produced retinoic acid. These findings form the basis for our current investigations of the functional immunomodulatory properties of conjunctival goblet cells and the conditioning activity of retinoid nuclear receptors. These studies have provided important new insight into the mechanisms responsible for inflammatory mediated ocular surface disease. The following publications report significant findings during this 15-year period (selected from 185 peer-reviewed publications).

   a. Niederkorn JY, Stern ME, Pflugfelder SC, de Paiva CS, Corrales RM, Gao J, Siemasko K. Desiccating stress induces T cell-mediated Sjogren's Syndrome-like lacrimal keratoconjunctivitis. J Immunol. 2006;176:3950-7. **PMID: 6547229**
   b. Tuckler Henricksson JC, T.G.; Corry, D.B.; DePaiva, C.S.; Pflugfelder, S.C. IL-13 stimulates proliferation and expression of mucins and immunomodulatory gene in cultured conjunctival goblet cells. *Investigative ophthalmology & visual science.* 2015;56: 4186-97. **PMID: 26132778**
   c. Ko BY, Xiao Y, Barbosa FL, de Paiva CS, Pflugfelder SC. Goblet cell loss abrogates ocular surface immune tolerance. JCI Insight. 2018 Feb 8;3(3). pii: 98222. doi: 10.1172/jci.insight.98222. [Epub ahead of print] **PMID: 29415888**
   d. Xiao Y, De Paiva CS, Yu Z, Guimaraes de Souza R, Li DQ, Pflugfelder SC. Goblet cell produced retinoic acid suppresses CD86 expression and IL-12 production in bone marrow derived cells. Int Immunol. 2018 Jul 12. doi: 10.1093/intimm/dxy045. [Epub ahead of print] **PMID: 30010888**

3. Our group has also characterized the ocular surface inflammation that develops in human dry eye disease using a number of techniques that have been developed or refined by our group. We have also investigated the acute ocular surface response to experimental desiccation.

   a. Lam H, Bleiden L, de Paiva CS, Farley W, Stern ME, Pflugfelder SC. Tear cytokine profiles in dysfunctional tear syndrome. Am J Ophthalmol. 2009;147:198-205. **PMID: 18992869**
   b. Moore QL, DePaiva CS, Pflugfelder SC. Effects of dry eye therapies on environmentally induced ocular surface disease. Am J Ophthalmol 2015;160(1):135-42 **PMID: 25868759**
   c. Pflugfelder SC, Moore QL, Volpe EA, Li DQ, Gumus K, Zaheer ML, Corrales RM. Aqueous tear deficiency increases conjunctival interferon-gamma (IFN-γ) expression and goblet cell loss. Investigative ophthalmology & visual science. 2015;56(12):7545-50. **PMID: 26618646**
   d. Coursey TG, Tukler Henriksson J, Barbosa FL, de Paiva CS, Pflugfelder SC. Interferon-gamma-Induced Unfolded Protein Response in Conjunctival Goblet Cells as a Cause of Mucin Deficiency in Sjogren Syndrome. The American journal of pathology. 2016;186(6):1547-58. **PMID: 27085137**

Complete List of Published Work in MyBibliography:
https://pubmed.ncbi.nlm.nih.gov/?term=SC+Pflugfelder&sort=date