

**Date Prepared:** October 9, 2018

**Name:** Yihe Chen

**Education:**

2001	<i>Certificate</i>	Pre-medical Courses	Peking University, China
2006	<i>Doctor of Medicine (MD)</i>	Medicine	Peking Union Medical College, China

**Postdoctoral Training:**

2006 – 2008	Resident	Nuclear Medicine, Medical Imaging	Peking Union Medical College Hospital, China
2008 – 2014	Research Fellow	Ocular Immunology (PI: Reza Dana)	Schepens Eye Research Institute of Mass. Eye & Ear, Harvard Medical School, Boston, MA
2014 – 2017	Senior Research Associate	Ocular Immunology (PI: Reza Dana)	Schepens Eye Research Institute of Mass. Eye & Ear, Harvard Medical School, Boston, MA

**Faculty Academic Appointments:**

2017	Instructor	Department of Ophthalmology	Harvard Medical School
2017	Investigator	Immunology	Schepens Eye Research Institute of Mass. Eye & Ear

**Professional Societies:**

2009 –	Association for Research in Vision and Ophthalmology	Member
2010 – 2015	Tear Film & Ocular Surface Society	Member

**Editorial Activities:**

**Ad hoc Reviewer for Peer-reviewed Journals**

Cornea, Immunobiology, Experimental Eye Research, Investigative Ophthalmology & Visual Science, Journal of Leukocyte Biology, Molecular Immunology, Ocular Immunology and Inflammation, PLoS ONE, Scientific Report

**Reviewer for Research Grant**

2018	Peer-reviewer	Fight for Sight, UK
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**Honors and Prizes:**

2002	Excellent Student Scholarship	Peking Union Medical College, China
2003	National Excellent Student Scholarship	Ministry of Education, China
2004	Excellent Student Scholarship	Peking Union Medical College, China
2006	Intern of the Year	Peking Union Medical College Hospital, China
2010	ARVO Annual Meeting Travel Award	Tear Film & Ocular Surface Society
2012	ARVO Annual Meeting Travel Award	Tear Film & Ocular Surface Society
2013	ARVO Annual Meeting Travel Award	Tear Film & Ocular Surface Society

2015 ARVO Annual Meeting Travel Grant National Eye Institute

## **Report of Local Teaching and Training**

### **Laboratory and Other Research Supervisory and Training Responsibilities:**

2014 – Teaching and supervision of postdoctoral research fellow Two-hour lab meeting per week

### **Mentored Trainees:**

2014 Goknil Gultekin, MD student, Istanbul University Cerrahpasa Medical Faculty  
Supervision and teaching by involving her in my project “Maintenance of memory Th17 cells in dry eye disease”; and she learned the basic concept of ocular immunology and immune assay, and made a project presentation at the conclusion of her training. Current: MD student, Istanbul University Cerrahpasa Medical Faculty

2013 – 2014 Hong Qi, MD, PhD, Research fellow, Schepens Eye Research Institute / MEEI  
Supervision on her project “The role of regulatory Th17 cells in dry eye disease”; and a manuscript is under preparation. Current: Associate Professor, Dept. of Ophthalmology, Peking University Third Hospital

2014 – 2015 Xuhua Tan, MD, PhD, Research fellow, Schepens Eye Research Institute / MEEI  
Supervision on her project “The role of corneal epithelium-derived TSP-1 in dry eye disease”; and a manuscript is submitted. Current: Ophthalmologist, Sun Yat-Sen University Zhongshan Ophthalmic Center

2016 – 2017 Man Yu, MD, PhD, Research fellow, Schepens Eye Research Institute / MEEI  
Supervision on her several projects in dry eye disease; and a manuscript is under preparation. Current: Associate Professor, Dept. of Ophthalmology, Sichuan Academy of Medical Sciences & Sichuan Provincial People’s Hospital

2016 – William Foulsham, MD, PhD candidate, Research fellow, Schepens Eye Research Institute / MEEI  
Supervision on his ongoing project “Aging in dry eye disease”

2017 – Yokako Taketani, MD, PhD, Research fellow, Schepens Eye Research Institute / MEEI  
Supervision on her ongoing project “Effect of Substance P on Treg function in dry eye disease”

2017 – Joy Li, BS student, Harvard College  
Supervision and teaching by involving her in dry eye projects, and she made a presentation at the Harvard Undergraduate Program for Research in Science and Engineering (PRISE), and published an abstract “The effect of substance P blockade on dry eye disease” in Harvard College Summer Undergraduate Research Village Abstract Book 2017

### **Formal Teaching of Peers:**

#### ***No presentations below were sponsored by outside entities***

2013 Chronic Inflammation in Dry Eye Disease. Harvard Ocular Immunology and Inflammation Focus Group. Boston

### **Local Invited Presentations:**

#### ***No presentations below were sponsored by outside entities***

2009 Regulatory Effects of Early NK Cell Responses on Adaptive Immunity in Dry Eye Disease  
Fellow seminar, Schepens Eye Research Institute / MEEI, Boston

2012 Chronic Dry Eye Disease is Principally Mediated by Effector Memory Th17 Cells  
Fellow seminar, Schepens Eye Research Institute / MEEI, Boston

2016 T Cell Immunity in Dry Eye Disease  
Fellow seminar, Schepens Eye Research Institute / MEEI, Boston

## **Report of Regional, National and International Invited Teaching and Presentations**

### ***No presentations below were sponsored by outside entities***

#### **Regional**

2013 Chronic Dry Eye Disease is Principally Mediated by Effector Memory Th17 Cells  
Research talk at Harvard Cornea Center of Excellence Retreat, Cambridge

**International**

- 2010 Regulatory Effects of Early NK Cell Responses on Adaptive Immunity in Dry Eye Disease  
Research talk at Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale
- 2014 Th17-derived IFN- $\gamma$ +IL-17+ Effectors Exacerbate Dry Eye Disease  
Research talk at Annual Meeting of the Association for Research in Vision and Ophthalmology, Orlando

**Report of Technological and Other Scientific Innovations**Patents:

1. Chen Y, Chauhan SK, Dana R. A Novel Therapeutic Approach Targeting Memory Th17 Cell-Mediated Ocular Immunoinflammatory Diseases. Application# 62/275,946US; submitted: 1/7/2016.

**Report of Scholarship****Peer-Reviewed Scholarship in print or other media:****Research Investigations**

1. Chen Y, Chauhan SK, Saban DR, Sadrai Z, Okanobo A, Dana R. Interferon- $\gamma$ -Secreting NK Cells Promote Induction of Dry Eye Disease. *Journal of Leukocyte Biology*. 2011;89:965-972.
2. Sadrai Z, Stevenson W, Okanobo A, Chen Y, Dohlman TH, Hua J, Amparo F, Chauhan SK, Dana R. PDE4 Inhibition Suppresses IL-17-Associated Immunity in Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2012;53:3584-3591.
3. Dohlman TH, Chauhan SK, Kodati S, Hua J, Chen Y, Omoto M, Sadrai Z, Dana R. The CCR6/CCL20 Axis Mediates Th17 Cell Migration to the Ocular Surface in Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2013; 54:4081-4091.
4. Chen Y, Chauhan SK, Lee HS, Stevenson W, Schaumburg CS, Sadrai Z, Saban DR, Kodati S, Stern ME, Dana R. Effect of Desiccating Environmental Stress versus Systemic Muscarinic AChR Blockade on Dry Eye Immunopathogenesis. *Investigative Ophthalmology & Visual Science*. 2013; 54:2457-2464.
5. Chen Y, Chauhan SK, Lee HS, Saban DR, Dana R. Chronic Dry Eye Disease is Principally Mediated by Effector Memory Th17 Cells. *Mucosal Immunology*. 2014; 7:38-45.
6. Emami-Naeini P, Dohlman TH, Omoto M, Hattori T, Chen Y, Lee HS, Chauhan SK, Dana R. Soluble vascular endothelial growth factor receptor-3 suppresses allosensitization and promotes corneal allograft survival. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2014; 252:1755-1762.
7. Kodati S, Chauhan SK, Chen Y, Dohlman TH, Karimian P, Saban D, Dana R. CCR7 is critical for the induction and maintenance of Th17 immunity in dry eye disease. *Investigative Ophthalmology & Visual Science*. 2014; 55:5871-5877.
8. Hua J, Jin Y, Chen Y, Inomata T, Lee H, Chauhan SK, Petasis NA, Serhan CN, Dana R. The resolvin D1 analogue controls maturation of dendritic cells and suppresses alloimmunity in corneal transplantation. *Investigative Ophthalmology & Visual Science*. 2014; 55:5944-5951.
9. Stevenson W, Chen Y, Lee SM, Lee HS, Hua J, Dohlman T, Shiang T, Dana R. Extraorbital lacrimal gland excision: a reproducible model of severe aqueous tear-deficient dry eye disease. *Cornea*. 2014; 33:1336-1341.
10. Tahvildari M, Omoto M, Chen Y, Emami-Naeini P, Inomata T, Dohlman TH, Kaye AE, Chauhan SK, Dana R.

In Vivo Expansion of Regulatory T Cells by Low-Dose Interleukin-2 Treatment Increases Allograft Survival in Corneal Transplantation. *Transplantation*. 2016; 100:525-532.

11. Chen Y, Chauhan SK, Tan X, Dana R. Interleukin-7 and -15 maintain pathogenic memory Th17 cells in autoimmunity. *Journal of Autoimmunity*. 2017; 77:96-103.
12. Chen Y, Chauhan SK, Shao C, Omoto M, Inomata T, Dana R. IFN- $\gamma$ -Expressing Th17 Cells Are Required for Development of Severe Ocular Surface Autoimmunity. *Journal of Immunology*. 2017; 199:1163-1169.
13. Hua J, Inomata T, Chen Y, Foulsham W, Stevenson W, Shiang T, Bluestone JA, Dana R. Pathological conversion of regulatory T cells is associated with loss of allotolerance. *Scientific Reports*. 2018; 8:7059.
14. Tan X, Chen Y, Foulsham W, Amouzegar A, Inomata T, Liu Y, Chauhan SK, Dana R. The immunoregulatory role of corneal epithelium-derived thrombospondin-1 in dry eye disease. *Ocul Surf*. 2018;16:470-477. (Co-first authorship with T.X.)
15. Shao C, Chen Y, Nakao T, Amouzegar A, Yin J, Tahvildari M, Lužnik Z, Chauhan SK, Dana R. Local Delivery of Regulatory T Cells Promotes Corneal Allograft Survival. *Transplantation*. 2018; doi: 10.1097/TP.0000000000002442. [Epub ahead of print] (Co-first authorship with S.C.)

#### Other peer-reviewed scholarship

1. Barabino S, Chen Y, Chauhan S, Dana R. Ocular Surface Immunity: Homeostatic Mechanisms and Their Disruption in Dry Eye Disease. *Progress in Retinal and Eye Research*. 2012;31:271-285. (Co-first authorship with B.S.)
2. Foulsham W, Marmalidou A, Amouzegar A, Coco G, Chen Y, Dana R. The function of regulatory T cells at the ocular surface. *Ocular Surface*. 2017;15:652-659.

#### Thesis:

Chen YH. Autoantibody Detection in Patients with Clinically Amyopathic Dermatomyositis (C-ADM) and Preliminary Analysis of its Clinical Significance [dissertation]. Beijing: Peking Union Medical College; 2006.

#### Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings:

1. Hua J, Stevenson W, Inomata T, Chen Y, Dohlman T, Le HS, Shiang T, Omoto M, Dana R. Elevated IL-6 and IL-23 in Dry Eye Hosts Disrupt Peripheral Induction of Tregs and Exacerbate Corneal Allograft Rejection. *Investigative Ophthalmology & Visual Science*. 2014; 55:3216.
2. Lee SM, Sadrai Z, Lee HS, Stevenson W, Chen Y, Hua J, Katikireddy KR, Dohlman TH, Chauhan SK, Dana R. Increased Substance P Expression in the Ocular Surface in Murine Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2014; 55:3664.
3. Chen Y, Chauhan S, Marmalidou A, Dana R. Interleukine-23, but Not Interleukine-2, Promotes the Generation of Memory Th17 Cells in Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2016; 57:337.
4. Marmalidou A, Mashaghi-Tabari A, Inomata T, Chen Y, Chauhan S, Dana R. Substance P suppresses Foxp3 expression in regulatory T cells in dry eye disease. *Investigative Ophthalmology & Visual Science*. 2016; 57:413.
5. Foulsham W, Tan X, Chen Y, Amouzegar A, Liu Y, Chauhan S, Dana R. Corneal Epithelium-derived Thrombospondin-1 Regulates Dendritic Cell Maturation in Dry Eye Disease. *Investigative Ophthalmology &*

*Visual Science*. 2017; 58:2065.

6. Hong Q, Chen Y, Inomata T, Liu R, Dana R. Potential Role of IL-10-producing Th17 Cells in Pathogenesis of Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2017; 58:1022.
7. Marmalidou A, Chen Y, Shao C, Nakao T, Chauhan S, Dana R. Substance P Mediates Dysfunction of NK1R+ Tregs in Dry Eye Disease. *Investigative Ophthalmology & Visual Science*. 2017; 58:466.
8. Yu M, Hong J, Amouzegar A, Fernandes M, Chen Y, Nakao T, Dana R. Topical Pigment Epithelium-Derived Factor Suppresses Corneal Epitheliopathy and Inflammation in Dry Eye disease. *Investigative Ophthalmology & Visual Science*. 2017; 58:971.

## **Narrative Report**

I am an investigator at SERI of MEE, and an instructor at Department of Ophthalmology at HMS, who specializes on ocular immunology research. After completing my training in Dr. Reza Dana's laboratory at SERI, I joined the faculty at MEE and HMS, where I supervise trainees and conduct research on ocular autoimmune and inflammatory disorders to enhance our knowledge and promote its translation to clinic.

My research interest and expertise revolves around the cellular and molecular mechanisms that drive ocular inflammation. In the past several years, I have made several novel and unexpected discoveries related to both innate and adaptive immune responses in dry eye disease. In the field of innate immunity, I have demonstrated that natural killer cells, and their secreted cytokine interferon- $\gamma$ , are critically involved in the induction of inflammation in dry eye disease. I was motivated to develop a novel mouse model of chronic dry eye disease by the observation that, although clinical dry eye disease is a chronic condition, the experimental data in the field was being derived from acute models. The resultant, highly clinically relevant, system has permitted the identification of two key attributes of the adaptive immunity at the ocular surface: (1) the induction of dry eye disease in naïve mice through the adoptive transfer of pathogenic CD4+ T helper cells, thereby demonstrating specificity; and (2) evidence of "memory" by the characterization of pathogenic memory T helper 17 (mTh17) cells in chronic dry eye disease. My further studies of immunologic memory using this model have revealed two molecules critical for the maintenance of pathogenic mTh17 cells – IL-7 and IL-15. I have also examined immunoregulatory strategies to improve the survival of corneal transplants, such as the in vivo expansion of regulatory T (Treg) cells, and subconjunctivally injection of Tregs. Currently, my investigations are focused on immunologic memory at various ocular autoimmune disorders by developing a new research program on autoimmune uveitis at SERI of MEE. Specifically, I aim to define the pathogenic role of memory T cells in autoimmune uveitis, and develop novel immunomodulatory treatments that target these key pathogenic cells.