

Curriculum Vitae

Heike Kroeger, PhD

- Assistant Research Scientist (Limited Term Faculty) • University of Georgia Athens, Department of Cellular Biology, Athens, GA • heike.kroeger@uga.edu •

1. EDUCATION

- 01/2006 – 10/2009 **Ph.D.** Structural Medicine, Cambridge Institute of Medical Research
Department of Medicine, Cambridge University, UK
Title: “The role of autophagy in the degradation of mutant serpins”
- 10/1999 – 09/2005 **Diploma in Biochemistry**, passed with 1.25, **First class degree (GPA 3.9)**, Free University Berlin, Germany
- 01/2005 – 09/2005 **Diploma Dissertation**, Cambridge Institute of Medical Research, Department of
Medicine and clinical Biochemistry; University of Cambridge, UK
Title: “Investigation of the interaction between wildtype and mutant
Neuroserpin, with the A β -peptide as an Alzheimer peptide *in vivo*”

2. PROFESSIONAL APPOINTMENTS & RESEARCH EXPERIENCES

- 11/2019 – ongoing **Assistant Research Scientist (Limited Term Faculty)**,
Department of Cellular Biology, Franklin College of the Arts and Science,
University of Georgia Athens, Athens, GA
Project 1: From Limbal Stem Cells to Corneal Epithelium Progenitor Cells,
Develop a Stem Cell Based Approach To Treat Patient With PAX6 Associated
Aniridia.
Project 2: Activation of ATF6 Signalling Events During Mesodermal
Differentiation Towards Functional Endothelial Cells.
Project 3: ATF6 Temporal Regulation During Foveal Development in the
Lizard Eye, a New Model To Study Eye Development in a Mammalian System.
- 07/2017 – 10/2019 **Assistant Project Scientist II**, Department of Pathology, UC San Diego, La Jolla,
CA, USA; Advisor: Prof. Jonathan H. Lin
ATF6 activation during stem cell differentiation results in the generation of
predominantly endothelial cells.
Project 1: What is the overall “Involvement of ATF6 activity during initiation
of vasculogenesis of stem cell derived endothelial cells.”
Project 2: Gain an understanding of the growth factor network that regulates
“ATF6 activation during hESC and iPSC differentiation”
Project 3: Patient harbouring ATF6 mutations experience vision problems,
such as colour blindness based on non-functional cone photoreceptor cells;
investigate “ATF6’s function during eye development; with a specific focus on
the differentiation towards eye specific cell types, such as rod and cone
photoreceptors”
- Small compounds are used to activate ATF6 during stem cell differentiation to generate endothelial cells that are used to characterize ATF6’s functional role during Vasculogenesis.

- Establishing protocols to create 3D Retinal Organoid cultures that simulate the development of the human retina. Additionally, to investigate ATF6's role during cone photoreceptor development more defined protocols are developed to differentiate hESCs and patient iPSCs into cone sheets.
- 02/2014 – present** Collaborative Project between UCSD, Amydis and BioGen (confidential)
 “Development of a diagnostic tool for the early detection of Alzheimer’s Disease onset using abeta plaques labelling in unfixed human eye specimens from Alzheimer’s Disease Patients”
- Establishing protocols for the dissection of unfixed human eye specimens to extract the entire intact human retina that was used for flat-mount staining, as well as OCD embedded sectioning to detect abeta plaques
- 07/2015 – 06/2017** **Assistant Project Scientist I**, Department of Pathology, UC San Diego, La Jolla, CA, USA; Advisor: Prof. Jonathan H. Lin
Project 1: “The unfolded protein response regulator ATF6 promotes mesodermal differentiation”
Project 2: “ATF6 activation supports cell maturation events, including the growth and the maturation of the Endoplasmic Reticulum (ER).”
- generating iPSC cell lines from patient fibroblast cells harboring natural occurring mutations in *ATF6*, resulting in inhibitory effects of ATF6 activation
 - Electron microscopy imaging to establish changes of ER environment during stem cell differentiation
 - RNA-Seq data analysis to establish a gene network that was affected by ATF6 activation during spontaneous differentiation
- 05/2009 – 06/2014** **Postdoctoral Scholar**, Department of Pathology, UC San Diego, La Jolla, CA, USA; Advisor: Prof. Jonathan H. Lin
Project 1 “ER stress and unfolded protein response signaling during stem cell differentiation”
Project 2 “The unfolded protein response is shaped by the Nonsense-mediated decay (NMD) pathway”
Project 3 “Differentiation towards eye specific cell types such as the retinal pigment epithelium (RPE) cells, using human eye specimens for retinal cell marker expression controls”
Project 4 “Robust endoplasmic reticulum-associated degradation of rhodopsin precedes retinal degeneration”
- IRE1, PERK and ATF6 signaling activity were evaluated during spontaneous hESC differentiation.
 - Establishing protocols for the differentiation of hESCs towards RPE cells.
 - Performing dissections of human eye specimens for the extraction of the retina and RPE cells. Primary RPE cells were further cultured to establish a stable culture used as control for the hESC derived RPE cells.
- 01/2006 – 05/2009** **Graduate Researcher**, Cambridge Institute of Medical Research, Department of Medicine and clinical Biochemistry; University of Cambridge, UK, Advisor: Prof. David A. Lomas and Prof. Stefan Marciniak
Project “The role of autophagy in the degradation of mutant serpins”
- 01/2005 – 09/2005** **Laboratory Researcher**, Cambridge Institute of Medical Research, Department of Medicine and clinical Biochemistry; University of Cambridge, UK, Advisor: Prof. David A. Lomas and Dr. Damian Crowther

Project "Investigation of the interaction between wildtype and mutant Neuroserpin, with the A β -peptide as an Alzheimer peptide *in vivo*"

- 12/2001 - 12/2004** **Senior Research Technician**, Max-Planck-Institute of Molecular Genetics, Berlin, Germany
Project "Whole mount *in situ* hybridisation of Amphioxus and *in situ* hybridisation screen of early zebrafish embryos"
- 04/2004 - 05/2004** **Researcher Technician**, Cambridge Institute of Medical Research; Department of Medicine, University of Cambridge, UK
Project "Characterisation of nervous system specific serpin Neuroserpin mutants"
- 06/2003 - 08/2003** **Researcher Technician**, Cambridge Institute of Medical Research, Department of Medicine and clinical Biochemistry; University of Cambridge, UK,
Project "Protein translocation across the membran of the ER - purification of microsomes, and investigation of microsome-associated proteasomes"
- 09/1996 - 07/1999** **Apprentice Chemical Laboratory Assistant**, Institute for Environment and Nature Mecklenburg-Vorpommern, Germany; Examination of the water quality from lakes and rivers in the North of Germany with regard to oxygen, nitrate-, chloride, magnesium and heavy metal content.

3. AWARDS AND FELLOWSHIPS

- 09/ 2018** Travel Fellowship for the XVIIIth International Symposium on Retinal Degeneration (RD2018) in Killarney, Ireland
- 04/ 2018** Experimental Biology (EB)/ American Society for Biochemistry and Molecular Biology (ASBMB) conference in San Diego, CA
- 07/ 2018** Julia Brown Summer Scholarship, which was successfully granted at \$5000, which was successfully granted at \$5000 and prepared for an undergraduate student as part of my project
- 07/ 2017** Eureka Summer Scholarship, which was successfully granted at \$5000 and prepared for an undergraduate student as part of my project Fight for Sight Student Summer Fellowship 2014, which was prepared for an undergraduate student as part of my project
- 12/ 2013** Travel Fellowship for the American Society for Cell Biology (ASCB) Annual Meeting in New Orleans, Louisiana, USA (oral presentation)
- 12/ 2013** Additional Postdoc Travel Award for the ASCB Annual Meeting in New Orleans, Louisiana, USA (oral presentation)
- 07/ 2012** Travel Fellowship for the XVth International Symposium on Retinal Degeneration (RD2012) in Bad Gögging, Bavaria, Germany (poster presentation)

4. RESEARCH FUNDING

- 2021** **Career Starter Grant from Knight Templar Eye Foundation (70K USD)**
"ATF6 Dependent Regulation of Mesodermal Differentiation in Retinal Vascular Network Development"
- 2007 - 2009** Two year PhD Stipendium from the German Academic Exchange Service (DAAD)
- 2009** PhD Funding from Cambridge European Trust Fund

5. PUBLICATIONS

Peer-reviewed Journal Articles

1. **Kroeger, H.**, Grandjean, J.M.D., Chiang, W.Ch., Bindels, D., Mastey, R., Okalova, J., Nguyen, A., Powers, E.T., Kelly, J.W., Grimsey, N.J., Michaelides, M., Carroll, J., Wiseman, R.L., and **Lin, J.H.**, (2021) "ATF6 is Essential for Human Cone Development", *PNAS* - **joint corresponding author**
2. Cao, K.J., Kim, J.H., Kroeger, H., Gaffney, P.M., Lin, J.H., Sigurdson, C.J., and Yang, J., (2021) "ARCAM-1 Facilitates Fluorescence Detection of Amyloid-Containing Deposits in the Retina", *Transl Vis Sci & Technol*, 0(0):3248 (accepted)
3. Lee, E.J., Chiang, W.Ch., **Kroeger, H.**, Bi, C.X., Chao, D.L., Skowronska-Krawczyk, D., Mastey, R.R., Tsang, S.H., Chea, L., Kim, K., Lampert, S.R., Grandjean, J.M.D., Moore, A.T., Wiseman, R.L., Carroll, J., and Lin, J.H., (2020) "Multiexon deletion alleles of ATF6 linked to achromatopsia", *ICI insight*, 5(7), e136041
4. **Kroeger, H.**, Grimsey, N., Paxman, R., Chiang, W.Ch., Plate, L., Ying, J., Shaw, P.X., Tsang, S.H., Powers, E., Kelly, J.W., Wiseman, R.L., and Lin, J.H. (2018) "The Unfolded Protein Response regulator, ATF6, Promotes Mesodermal Differentiation", *Science Signalling*, Vol. 11, Issue 517, DOI:10.1126/scisignal.aan5785
5. Rachid, K., Chih-Hong, L., **Kroeger, H.***, Huang, L., Lin, J.H., and Wilkinson, M. (2015) "The unfolded protein response is shaped by the NMD pathway", *EMBO Reports*, DOI: 10.15252/embr.201439696. Published online 25.03.2015. Pubmed PMID: 25807986
6. Alavi, M.V., Chaing, W.C., **Kroeger, H.**, Yasumura, D., Matthes, M.T., Iwawaki, T., LaVail, M.M., Gould, D.B., and Lin, J.H. (2015) "In Vivo Visualization of Endoplasmic Reticulum Stress in the Retina Using the ERAI Reporter Mouse", *IOVS*, 56(11): 6961-6970
7. **Chiang, W.C.**, **Kroeger, H.**, Sakami S., Messah, C., Yasumura, D., Matthes, M.T., Coppinger, J.A., Palczewski, K., LaVail, M.M. and Lin, J.H. (2014) "Robust Endoplasmic Reticulum-Associated Degradation of Rhodopsin Precedes Retinal Degeneration"; *Mol. Neurobiol*, DOI 10.1007/s12035-014-8881-8
8. **Kroeger, H.**, Messah, C., Ahern, K., Gee, J., Joseph, V., Matthes, M.M., Yasumura, D., Gorbatyuk, M.S., Chiang, W.-Ch., LaVail, M.M. and Lin, J.H.; (2012) "Induction of Endoplasmic Reticulum Stress Genes, *BiP* and *Chop*, in Genetic and Environmental Models of Retinal Degeneration"; *IOVS*, 53(11): 7159-7166
9. Chiang, W.-Ch., Hiramatsu, N., Messah, C., **Kroeger, H.** and Lin, J.H.; (2012) "Selective activation of ATF6 and PERK endoplasmic reticulum stress signaling pathways prevent mutant rhodopsin accumulation"; *IOVS*, 53(11): 7159-7166
10. **Kroeger, H.**, Miranda, E. M., MacLeod, I., Pérez, J., Crowther, D.C., Marciniak S.J and Lomas, D.A.; (2009) "ERAD and autophagy cooperate to degrade polymerogenic mutant serpins"; *JBC*, 284(34): 22793-802
11. Kalies, K.-U., Allan, S., Sergeyenkov, T., **Kroeger, H.**, & Roemisch, K. (2005) "The protein translocation channel binds to the endoplasmic reticulum membrane" *EMBO J* **24**, 2284-2293

Book Chapters

1. Chiang W.C., **Kroeger H.**, Chea L., and Lin J.H. (2018) "Pathomechanisms of ATF6-Associated Cone Photoreceptor Diseases", *Adv. Exp. Med. Biol.* (In Press)
2. **Kroeger, H.**, Chiang, W.C., Felden, J., Nguyen, A., and Lin, J.H. (2018) "ER Stress and Unfolded Protein Response in Ocular Health and Disease", *FEBS*, DOI: 10.1111/febs.14522 - **corresponding author**

3. Wert, K.J., **Kroeger H.**, Tsang, S.H., and Lin, J.H. (2017) "Pathology and Mechanism of Eye Diseases", book chapter at *Ophthalmic Disease and Drug Discovery*; DOI: 10.1142/9789814663076_0002
4. **Kroeger, H.**, LaVail, M.M. And Lin, J. (2014) "Endoplasmic Reticulum Stress in Vertebrate Mutant Rhodopsin Models of Retinal Degeneration"; *Adv Exp Med Biol*, Springer, Volume 801, 585-592
5. **Kroeger, H.**, Chiang, W.-Ch. And Lin, J. (2012) "Endoplasmic Reticulum-Associated Degradation (ERAD) of Misfolded Glycoproteins and Mutant P23H Rhodopsin in Photoreceptor Cells"; (2012) Retinal Degenerative Diseases; *Advances in Experimental Medicine and Biology*, Springer Science + Business Media, Volume 723, Part 8, 559-565
6. Ekeowa U.I., Gooptu B., Belorgey D., Hägglöf P., Karlsson-Li S., Miranda E., Pérez J., MacLeod I., **Kroeger H.**, Marciniak S.J., Crowther D.C. and Lomas D.A.; (2009) "alpha1-Antitrypsin deficiency, chronic obstructive pulmonary disease and the serpinopathies"; *Clin Sci (Lond)*; 116(12):837-50

4. D. Press Releases

UCSD PRESS RELEASE REGARDING SCIENCE SIGNALING PUBLICATION NO.1
[HTTPS://HEALTH.UCSD.EDU/NEWS/RELEASES/PAGES/2018-02-13-IN-EFFORT-TO-TREAT-RARE-BLINDING-DISEASE-RESEARCHERS-TURN-STEM-CELLS-INTO-BLOOD-VESSELS.ASPX](https://health.ucsd.edu/news/releases/pages/2018-02-13-in-effort-to-treat-rare-blinding-disease-researchers-turn-stem-cells-into-blood-vessels.aspx)

6. PATENTS

- 04/ 2017 Listed Inventor on Patent, UCSD Ref. No. SD2017-221 "Use of ATF6 Activators to enhance mesodermal differentiation" (U.S. Provisional Application Serial No._62/492,016)

7. PRESENTATIONS

INVITED TALKS

- 10/2019 University of California Stanford, Vision Seminar, Department of Ophthalmology, Stanford, CA
Title: "ATF6-Associated Achromats Develop Rod Dominant Retinas"
- 05/ 2019 Association for Research in Vision and Ophthalmology (ARVO) Conference in Vancouver, Canada
Title: "Cone Photoreceptors Fail to Form in ATF6- Related Achromatopsia Retinal Organoids"
- 04/ 2018 American Society for Investigative Pathology (ASIP) conference in San Diego, CA
Title: "The Unfolded Protein Response Regulator, ATF6, Promotes Mesodermal Differentiation"
- 12/ 2013 Annual American Society for Cell Biology (ASCB) Conference in New Orleans, LA
Title: "bFGF Activates ATF6 to Trigger Differentiation in Human Embryonic Stem Cells"
- 11/ 2013 Shiley Eye Center Seminar Series in San Diego, CA
Title: "Growth Factor Signaling and ATF6 Promote Differentiation of RPE Cells from Human Embryonic Stem Cells"
- 08/ 2013 Oral Presentation for Research Group from Genetech, San Diego, CA
Title: "The Dissection of Human Eye Specimens Towards the Generation of Human Retinal Pigment Epithelium Cells"

ADDITIONAL ORAL PRESENTATIONS

- 06/2018 Mesa-wide ER Stress Association in San Diego, CA
Title: "Loss of ATF6 Causes Conversion of Cone to Rod Photoreceptors"
- 06/ 2017 Pathology Research Lecture Series (PRLS) in San Diego, CA

- 12/ 2016 Title: "Small Molecule ATF6 Activators Promote Mesodermal Differentiation"
Mesa-wide ER Stress Association in San Diego, CA
- 05/ 2016 Title: "Small Molecule ATF6 Activators Promote Early Stem Cell Differentiation"
Neurodegeneration Seminar Series in San Diego, CA
- 05/ 2015 Title: "Small Molecule ATF6 Activators Promote Early Stem Cell Differentiation"
Mesa-wide ER Stress Association in San Diego, CA
- 04/ 2014 Title: "ATF6 Promotes Early Stem Cell Development"
Oral Presentation at the Chemistry Department at UC in San Diego, CA
- 01/ 2014 Title: "Induction of ATF6 through bFGF Signaling Expands the ER and Enhances hESC
Differentiation"
Neurodegeneration Seminar Series in San Diego, CA
- 06/ 2013 Title: "ATF6 Activation by Growth Factor Signaling Promotes Human Embryonic Stem
Cell Differentiation of Retinal Pigment Epithelium Cells"
Pathology Research Lecture Series (PRLS) in San Diego, CA
- 01/ 2013 Title: "Growth Factor Signaling Links ATF6 to Human Embryonic Stem Cell
Development"
Mesa-wide ER stress Association in San Diego, CA
- 03/ 2012 Title: "Growth Factor Signaling Links ATF6 to Human Embryonic Stem Cell
Development"
CMM Symposium at the Sandford Consortium for Regenerative Medicine, San Diego,
CA
- 08/ 2006 Title: "bFGF links ATF6 to Human Embryonic Stem Cell Development"
Respiratory seminar, Cambridge Institute for Medical Research
Title: "The Role of ERAD and Autophagy in the Degradation of Mutant Serpins"

POSTER PRESENTATIONS

- 10/ 2019 University of California Stanford, Stanford Pathology Research Retreat, Stanford, CA
- 05/ 2018 Association for Research in Vision and Ophthalmology (ARVO) Conference in
Honolulu, Hawaii
- 04/2018 Experimental Biology (EB)/ American Society for Biochemistry and Molecular Biology
(ASBMB) conference in San Diego, CA
- 06/ 2017 XVth International Society of Stem Cell Research (ISSCR) conference in Boston, MA
- 06/ 2013 Mesa Wide Stem Cell Meeting in San Diego, CA
- 09/ 2013 UCSD Postdoctoral Association Research Symposium in San Diego, CA
- 07/ 2012 XVth International Symposium on Retinal Degeneration (RD2012) in Bad Gögging,
Bavaria, Germany
- 11/ 2011 Mesa Wide Stem Cell Meeting, San Diego, CA
- 07/ 2008 Serpin Conference, Leuven, Belgium
- 06/ 2007 Graduate Research Symposium, CIMR, University of Cambridge

8. TEACHING EXPERIENCES

- 11/2016 - present **Amanda Nguyen** - Teaching and Supervising undergraduate students at the
University of California San Diego, teaching general lab techniques, stem cell
culture and differentiation approaches
- 07/ 2017 - 08/ 2017 **Julia Felden** - German graduate exchange student from the University of
Tübingen, teaching general stem cell culture techniques with a focus on the
generation of organoids, e.g., eye-cup differentiation and their procedures of
characterization
- 05/ 2015 - 08/ 2015 **Moana Santiago** - supervising a visiting undergraduate student from Sao Paolo
University, Brazil during her summer internship at UCSD
- 11/ 2013 - 05/ 2014 **Allen Chen** - Teaching and Supervising an undergraduate students at the
University of California San Diego as part of the UCSD graduate program,

- teaching general lab techniques, stem cell culture work, human eye dissection and culturing of primary RPE cells
- 01/ 2013 - 03/ 2013 **Chelsea Stewart and Anna Wakeland** - Supervising graduate students during rotation at the University of California San Diego as part of the UCSD graduate program
- 12/2010 - 11/2011 **Oleg Sten** - Training and supervising a new undergraduate student at the University of California San Diego, teaching general lab techniques and cell culture work
- 10/2007 - 12/2007 **Stephen Lu, Marie-Louise Daly and Elke Malzer** - Supervising Wellcome Trust / MRC PhD students during their 10-week rotation at the CIMR, University of Cambridge, UK
- 12/2001 - 12/2004 Training and supervising new students and Technicians during my time as Student Research Assistant at the Max-Planck-Institute of Molecular Genetics, Berlin

9. KEY EXPERIMENTAL TECHNIQUES

CELL BIOLOGY AND STEM CELL BIOLOGY

- Stem Cell Cultures: HUES9 hESC, H9 hESC, generation and maintenance of human fibroblast derived iPSC's
 - Differentiation Techniques: spontaneous and directed differentiation towards ectodermal lineage to generate neuronal cell types, with specific focus on eye specific cell types (rod and cone photoreceptors, retinal pigment epithelium (RPE) cells)
 - Differentiation of stem cells to organoids to simulate eye development as 3D eye cups
- Other Cell lines: COS7, HeLa, MEF, HEK293T, PC12 lines, primary hRPE cells, hESC derived RPE cells, primary human fibroblast cells
- Mammalian cell plasmid transfection
- Sendai-, Adeno- and Retroviral infection of mammalian cells
- siRNA in mammalian cells
- Radioactive labelling of proteins in living cells using ³⁵S and other radioisotopes
- Light and confocal fluorescence laser microscopy

PATHOLOGY

Preparation, dissection and preserving of human eye specimens

BIOCHEMISTRY AND MOLECULAR BIOLOGY

- Standard molecular biology techniques, e.g. RT-PCR, qPCR, RNA and DNA isolation and purification
- Immunoblotting,
- Immunoprecipitation
- Sandwich ELISA
- Proteasome enzyme assay
- ChiP-qPCR analysis

10. PROFESSIONAL SOCIETY MEMBERSHIPS AND COMMITMENTS

MEMBERSHIPS

- 2017 member of the American Society of Investigative Pathology (ASIP)
- 2017 member of the Association for Research in Vision and Ophthalmology (ARVO)
- 2013 member of the American Society for Cell Biology (ASCB)
- 2009 member of the International Society for Stem Cell Research (ISSCR)

SCIENTIFIC COMMITMENTS

2009 peer-reviewing papers as part of their submission process for various Journals, such as Investigative Ophthalmology & Visual Science (IOVS), Molecular Biology of the Cell (MBoC), Journal of Biological Chemistry (JBC), Proceedings of the National Academy of Sciences (PNAS), PLoS One and Aging Cell

NON-SCIENTIFIC COMMITMENTS

2015 UCSD Postdoc Ambassador (in support and guidance of newly accepted postdocs at the UCSD postdoc program)

11. CERTIFIED COURSE

06/ 2015 - 08/ 2015 **Micro-MBA** Program at UCSD Rady School of Management, San Diego, CA (8-week course)

08/ 2017 **MB-205** "Introduction to CRISPR-Cas9 Genome Editing" by Life Technologies, Carlsbad, CA (1-week course)

12. LANGUAGES

English - fluent spoken and written

German - fluent spoken and written

13. AFFILIATION

The University of Georgia
Department of Cellular Biology
Franklin College of the Arts and Sciences
Paul D Coverdell Center for Biomedical and Health Sciences
500 DW Brooks Drive
Athens, GA 30602-7394