Example of Research Portfolio

Although not one of my stated areas of excellence for promotion, I have a strong track record of research and scholarship. Since joining the School of Optometry in September 2006, my promotion to Associate Professor with tenure in 2011, and move to the School of Medicine as Associate Professor with tenure in 2019, I have maintained an independent, externally funded research program in the molecular mechanisms of blinding diseases, retinal development, and maintenance that has earned me national and international recognition.

More specifically, I have been studying photoreceptor proteins, their trafficking, the chromophore 11-*cis* retinal/ all-*trans* retinal entry and turnover, the role of rod cell formation and maintenance, the genetic basis of rod cell degeneration in blinding diseases, and the epigenetic and transcriptomic changes found in retinal degenerations. My lab utilizes animal models such as frogs, mice, tree shrews, and research-consented braindead human organ donors to study cellular consequences of retinal diseases such as retinitis pigmentosa, Leber's congenital amaurosis, and glaucoma.

Since being promoted to Associate Professor, I have given 8 talks at international meetings, including being the Keynote Speaker in 2022 at the annual meeting for enTRAIN, the European Network for Integrated TRAINing on innovative therapies for vision restoration, in Vanajanlinna in Håmeenlinna, Finland. I was invited to give 2 other talks at international meetings that were canceled due to COVID-19 and gave two invited international seminars at Aalto University (virtual) and the University of Helsinki in Finland (in person). Additionally, I have presented my laboratory's research as an invited symposium platform speaker at the ISER Annual Meeting in the Gold Coast, Queensland, Australia in February 2023. Since 2011 I have also given 3 invited talks at regional or local meetings, and 8 invited lectures at universities in the United States, including UAB. In 2020 I was identified as a "Leading Scientist in Vision Research" (one of five scientists nationally awarded in the Retinal Diseases group) by ScEYEnce, a national working group of 10 organizations dedicated to vision research that includes the NIH National Eye Institute.

I am currently PI of an NIH R01, and Co-Principal Director of a NIH T32 grant for Predoctoral Training in Cellular, Molecular, and Developmental Biology at UAB. I have two other pending NIH grants (R01 and R21), and numerous prior research grants from NIH and private foundations. The MPI R01 pending grant (Girkin, lead PI, AKG, PI) garnered a 9%tile at the NIH/NEI; we are awaiting notice of award from our program officer. As Associate Professor I published 18 peer reviewed papers, 13 as senior author. I currently mentor 1 postdoctoral trainee, 3 doctoral students, and 2 masters students in my lab. As an Associate Professor, I supervised an additional one postdoctoral trainee, 5 doctoral students, 5 masters students, and 7 undergraduate students in my lab, one of whom was awarded the prestigious National Goldwater Scholar Award. I currently serve on the thesis committee for 6 doctoral and 3 MSTP students. As an Associate Professor, I served on the thesis committees of an additional 12 doctoral and 2 masters students who have completed their training, serving as committee Chair for 5 of those students.

Several years ago, I experienced an extremely difficult convergence of demanding issues. These include the tumultuous period at UAB while I was Chair-Elect of the Faculty Senate through Past-Chair (2015-2017), a challenging environment in my previous School, and family issues. During this time my husband and I adopted an infant boy, and I soon thereafter gave birth to a girl with a congenital heart defect. Despite these challenges and my extensive service and teaching responsibilities at the time, I maintained my laboratory. We continued to perform research with rigor during this time, and publish high quality papers, although our productivity was somewhat delayed due to these taxing issues. Since then, I have regained momentum in my research, as evidenced by my current NIH funding, recent publications, and recent national and international invited talks.

Major research findings and publications since 2011

Complete list of published work in MyBibliography is found here.

Genetics of rod photoreceptor development and retinal health

By virtue of its laminar structure, ease of access via microscopy and genetic manipulability, the mouse retina has become a useful tool for monitoring genetic alterations and survivability. We and our colleagues have made advances in the field by making rhodopsin knock-in mice that enable one to monitor genetic fluctuations. In addition, we have discovered a novel protein in the retina necessary for maintenance of retinal health and induced domain-specific in-frame deletions of genes expressed in retina. These discoveries set a foundation for the current proposed studies to transition into the epigenetics and transcriptomic processes underlying the control of vision.

1. Boitet ER, Reish NJ, Hubbard, MG, **Gross AK**. (2019) NudC regulates photoreceptor disk morphogenesis and rhodopsin localization. *FASEB J* 33(8):8799-8808. Doi: 10.1096/fj.201801740RR. PMC6662962.
2. Challa AK, Boitet ER, Turner AN, Johnson LW, Kennedy D, Downs ER, Hymel KM, **Gross AK** and Kesterson RA. (2016) Novel hypomorphic alleles of the mouse tyrosinase gene induced by CRISPR-Cas9 nucleases cause non-albino pigmentation phenotypes. PLoS One 11 (5):e0155812. PMC4880214.
3. Sandoval IM, Price BA, **Gross AK**, Chan F, Sammons JD, Wilson JH, Wensel TG. (2014) Abrupt onset of mutations in a developmentally regulated gene during terminal differentiation of post-mitotic photoreceptor neurons in mice. *PLOS ONE* 9 (9): e108135. PMCID PMC4180260.
4. Rana T, Shinde VM, Starr CR, Kruglov AA, Boitet ER, Kotla P, Zolotukhin S, **Gross AK**, Goratyuk MS (2014). An activated unfolded protein response promotes retinal degeneration and triggers an inflammatory response in the mouse retina. *Cell Death and Disease* 18 (5): e1578. PMCID: PMC4454166.

<u>The role of rhodopsin in the blinding diseases congenital stationary night blindness and retinitis pigmentosa</u>

To better understand the biochemical role of rhodopsin in healthy and diseased states to aid in future therapeutics, we are interested in the most severe, earliest onset cases of rhodopsin mediated ADRP and the relatively benign rhodopsin mutants that cause CSNB. This gives both human and translational relevance to all our work.

1. Hollingsworth TJ, Hubbard MG, Levi HJ, White W, Wang X, Simpson R, Jablonski MM, and **Gross AK**. (2021) Proinflammatory pathways are activated in the human Q344X rhodopsin knock-in mouse model of retinitis pigmentosa. *Biomolecules*. 11(8):1163. doi: 0.3390/biom11081163. PMCID: PMC8393353.
2. Hollingsworth TJ and **Gross AK**. (2020) Innate and autoimmunity in the pathogenesis of inherited retinal dystrophy. *Cells*. 9(3). Pii: E360. PMCID PMC7140441.
3. Bales KL, Ianov L, Kennedy AJ, Sweatt JD, and **Gross AK**. (2018) Autosomal dominant retinitis pigmentosa rhodopsin mutant Q344X drives specific alterations in chromatin complex gene transcription. *Mol Vis.* 24:153-164. PMCID: PMC5815338.
4. Hollingsworth TJ and **Gross AK**. (2013) The Severe Autosomal Dominant Retinitis Pigmentosa Rhodopsin Mutant Ter349Glu Mislocalizes and Induces Rapid Rod Cell Death. *J. Biol. Chem.* 288 (40): 29047-29055. PMCID PMC3790004.

<u>The molecular consequences of high intraocular pressure in the living human eye</u>

Glaucoma is the leading cause of irreversible blindness and is characterized by damage to retinal ganglion cells and the optic nerve. Our team uses a completely novel *in vivo* human model that we have developed at the UAB. We follow *in vivo* studies with molecular and cellular studies immediately post-mortem *ex vivo*, providing a paradigm shift in the field of glaucoma research. We are the only team in the world manipulating human eyes *in vivo* to study the pathological consequences of acute and prolonged IOP. Using this model, we are determining the relationship between IOP-induced changes in vascular perfusion density in the retina with cellular transcript and protein changes in living human eyes for the first time.

1. Strickland RG, Garner MA, **Gross AK**, Girkin CA. (2022) Remodeling of the Lamina Cribosa: Mechanisms and Potential Therapeutic Approaches for Glaucoma. Int J Mol Sci. Jul 22;23(15). doi: 10.3390/ijms23158068. PubMed PMID: 35897642; PMCID: PMC9329908.
2. Garner MA, Strickland RG, Girkin CG, **Gross AK**. Mechanisms of retinal ganglion cell injury following acute increases in intraocular pressure. *Front. Ophthalmol*., 2022, 2:2007109. Doi:10.3389/fopht.2022.1007103. https://www.frontiersin.org/articles/10.3389/fopht.2022.1007103/full
3. Girkin CA, Garner MA, Fazio MA, Clark M, Karuppanan U, Hubbard M, Bianco G, Hubbard S, Fortune B, **Gross AK**. Retinal electrophysiologic response to IOP elevation in brain-dead organ donors. *Experimental Eye Research*, 2023, doi: https://doi.org/10.1016/j.exer.2023.109420

<u>Current extramural funding</u>

"Photoreceptor disk formation and retinal degenerations"
National Institutes of Health (NEI R01EY030096-01A1, PI: Alecia K. Gross),
Project period: 07/01/2020-06/30/2024

The objective of this proposal is to understand the molecular mechanisms controlling cytoskeletal regulation in rod and cone photoreceptor cells. We will uncover the process of disk formation and mitochondrial transport and how it relates to photoreceptor degenerations.