INTERDISCIPLINARY GRADUATE PROGRAM IN

# MOLECULAR AND CELLULAR BIOLOGY

DISSERTATION SEMINAR

**Generating patient-specific iPSC-derived choroidal endothelium to study and treat macular degeneration**

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October 25, 2016
9:00 a.m.
2117 Medical Education Research Facility (MERF)

# Generating patient-specific iPSC-derived choroidal endothelium to study and treat macular degeneration

Age-related macular degeneration (AMD) is the leading cause of incurable blindness in western countries. In the United States alone, there are two million people with advanced AMD and an additional seven million with early AMD. Individuals with advanced AMD have severely impaired central vision, making everyday activities very difficult. Although AMD is a common blinding disease, it is not well understood how the disease progresses. There is strong evidence showing that the choroidal vasculature bed behind the retina is the first tissue to degenerate in AMD. Therefore, it is crucial to study these special blood vessels involved in AMD at a cellular level to identify its cause and develop cures to help patients regain their lost vision.

The work described in this dissertation used mouse and human induced pluripotent stem cells (iPSCs) to generate the choroidal vascular tissue behind the retina. Co-culture systems, RNA-seq analysis, and statistical screens were used to identify connective tissue growth factor as the key component required for driving choroidal vascular development. To our knowledge, this work is the first in the field to regenerate the choroidal tissue from control and AMD patient stem cells. The choroidal endothelium generated from patient AMD stem cells also showed disease-like signs, such as increased membrane attack complex formation and cytolysis, indicating that the AMD choroidal endothelium modeled the disease *in vitro*. Therefore, this work provides an invaluable tool for researchers to perform in depth studies on the choroidal tissue to better understand AMD pathophysiology and develop cell-based therapies.

Overall, the work presented in this dissertation will push the AMD research field forward by providing a way to directly study AMD patient-specific iPSC-derived choroidal endothelium. In combination with retinal pigment epithelium and photoreceptors, patient-specific choroidal endothelium will make it possible to better understand AMD pathogenesis and to develop autologous cell replacement therapies to rebuild patients' damaged choroids.

# Allison Songstad
# Biographical Sketch

Originally from Saskatoon, Saskatchewan, Canada, Allison grew up in St. Louis, MO. In 2012 she graduated *cum laude* from Abilene Christian University in Abilene, TX with a major in biochemistry and a minor in Spanish. After graduation she came to the University of Iowa and entered the Molecular and Cellular Biology PhD program. After her rotations, Allison joined Dr. Budd Tucker's lab at the Wynn Institute for Vision Research, in which she used induced pluripotent stem cells to study age-related macular degeneration (AMD). While studying in the Tucker lab, she developed a novel system to generate the choroidal vasculature behind the retina from mouse and human induced pluripotent stem cells. Allison used this system to generate patient-specific choroidal endothelium to model AMD *in vitro*. Her PhD work now makes it possible for researchers in field to directly study the choroidal vasculature from individual patients to better understand AMD pathophysiology and develop cell replacement therapies.

After she graduates in December, Allison will be joining Dr. Larry Goldstein's lab as a postdoctoral scholar in the Sanford Consortium for Regenerative Medicine at the University of California-San Diego. She will continue using patient-specific induced pluripotent stem cells to study the underlying causes of Autism spectrum disorder.

Allison would like to thank the amazing people she met during her time at the University of Iowa, in particular Dr. Budd Tucker and the members of the Tucker lab, WIVR, and MCB. She is honored to have worked alongside these extraordinary individuals and very grateful for the incredible opportunities they brought into her life.

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