ANNOUNCING

Doctoral Dissertation Defense

Jonathon B. Young

Candidate for Doctor of Philosophy in Cell and Developmental Biology
Graduate School of Biomedical Sciences
Department of Cell Biology, Neurobiology, & Anatomy
Medical College of Wisconsin

Committee in charge:
Iris S. Kassem, MD, PhD (Advisor and Chair)
Janis T. Eells, PhD
Rebekah L. Gundry, PhD
Laura J. Kopplin MD, PhD
Daniel M. Lipinski, MSc, DPhil

Monday, 01 March 2021, 9:00 AM (CST)

Live public viewing:

https://mcw.hosted.panopto.com/Panopto/Pages/Viewer.aspx?id=053737ff-5cd1-4e5e-b62f-acb0012fbf26
Graduate Studies

- Biochemistry of the Cell
- Molecular and Cellular Biology
- Neuroscience Journal Club
- Fundamentals of Neuroscience
- Mechanisms of Cellular Signaling
- Special Problems in Physiology: Biostatistics
- Biomedical Technology: Standards & Regulations
- Ethics & Integrity in Science
- Advanced Systems Neuroscience
- Research Ethics Discussion Series
- Techniques in Molecular & Cellular Biology
- The Biology of Vision
- Special Topics in Biochemistry: Mass Spectrometry in Biomedical Research
- Boundaries of Science & Medical Practice
- Reading and Research (Fall 2015 – Summer 2020)
- Doctoral Dissertation
Children that need intraocular surgery, such as cataract surgery, are more challenging to manage than adults because of the high incidence of postoperative complications. In children, if a visually significant cataract is not corrected early, it could lead to permanently decreased vision. This is due to amblyopia, characterized by a loss of vision in the absence of ocular pathology caused by a disruption of the visual axis in early childhood. Cataract surgery in children is difficult because they have an exaggerated response to surgery compared to adults. Therefore, ophthalmologists must perform surgery relatively quickly to clear the vision due to risks of amblyopia, while also managing a higher risk of postoperative complications.

The underlying differences between the pediatric versus adult response to intraocular surgery and the effect of any pharmacologic interventions have not been clearly elucidated. Addressing this knowledge gap would enhance development of targeted therapeutics to treat the mechanisms of postoperative ocular inflammation and fibrin formation. In this thesis, we use a rabbit model of lens removal surgery, lensectomy with intraocular lens (IOL) insertion, to further understand the changes associated with ocular fibrin formation and inflammation, as well as investigate preventive and curative pharmacotherapies for future translational applications. Rabbit eyes are similar to human eyes in their anterior chamber size and robust immune response exhibited following intraocular surgery in juveniles, making them an ideal model for studying infantile lensectomy.

First, we examined the ocular immune response from portions of surgery using a progressive, step-wise evaluation of the major stages of the lensectomy with IOL insertion surgery in juvenile rabbits, analyzing proteomic changes of the aqueous humor before and three days after each procedure. Semi-quantitative protein discovery was performed using mass spectrometry, and we identified a number of proteins relating to the inflammatory and coagulation cascades that increased in abundance at each surgical
Second, we used an aging rabbit model of lensectomy with IOL insertion to investigate how juvenile rabbits differ from adolescent rabbits in terms of clinical and molecular (proteomic and transcriptomic) changes after lensectomy. Having identified inflammatory and coagulation proteomic changes in juvenile rabbits, we determined how the abundance of these proteins changes with aging. Furthermore, as transcripts and proteins for coagulation can be produced in ocular structures, we used RNA-sequencing to determine if inflammatory and coagulation transcript levels were altered in the cornea and iris/ciliary body following ocular surgery.

Third, we investigated the use of pharmacotherapies to prevent and treat postoperative inflammation and fibrin formation following lensectomy with IOL insertion in the juvenile rabbit. In order to prevent scarring and inflammation, we injected a combination of triamcinolone and enoxaparin immediately following lensectomy with IOL insertion surgery. For treatment of postoperative fibrin scarring, we injected tissue plasminogen activator three days following IOL insertion. We report that both measures successfully prevented and reduced fibrin volume, respectively.

In summary, this work shows that 1) the juvenile rabbit is an ideal animal model for investigating complications related to pediatric lensectomy with IOL insertion, 2) proteins related to the inflammatory and coagulation cascades are significantly different in abundance in the aqueous humor before and after surgical intervention, and can be accurately quantified by mass spectrometry, 3) aging studies demonstrate differences in inflammatory and coagulation protein abundance changes, and 4) enoxaparin with triamcinolone and tissue plasminogen activator present promising options for future clinical trials to prevent or reduce fibrin scarring in the anterior chamber. These findings provide an excellent foundation for future research to help explain why children experience an exaggerated immune response to intraocular surgery, ultimately leading to options to improve sight for children affected by cataracts across the globe.
CURRICULUM VITAE
Jonathon B. Young

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2) PLACE OF BIRTH: Milwaukee, Wisconsin

3) CITIZENSHIP: United States of America

4) EDUCATION:
09/2010 – 05/2012: University of St. Thomas, St. Paul, MN
08/2012 – 05/2014 – B.S., Biomedical Science, Marquette University, Milwaukee WI
07/2015 – (present) PhD Candidate, Neuroscience Doctoral Program, Cell Biology,
Neurobiology and Anatomy Department, Medical College of Wisconsin,
Milwaukee, WI (*Thesis defense date: March 1, 2021)

4) POSITIONS & EMPLOYMENT:
05/2009 – 01/2012: Certified Ophthalmic Assistant, Verre-Young Eye Clinic, WI
01/2012 – 05/2012: General Chemistry Teaching Assistant, University of St. Thomas, MN
05/2012 – 06/2015: Research Technologist, Advanced Ocular Imaging Program, Medical
College of Wisconsin

5) AWARDS AND HONORS:
09/2010 – 05/2012: St. Thomas Academic Scholarship
09/2010 – 05/2012: Dean’s List, University of St. Thomas (4 semesters)
08/2012 – 05/2014: Marquette University Ignatius/Magis Scholarship
08/2012 – 05/2014: Dean’s List, Marquette University (4 semesters)
05/2014 – Recipient, Summer Student Fellowship, Fight for Sight
05/2016 – National Eye Institute Travel Award, ARVO Annual Meeting
05/2016 – Members in Training Poster Award Finalist, ARVO Annual Meeting
03/2019 – Center for Imaging Research Pilot Award, Medical College of Wisconsin
01/2021 – Winter: Paper of the Season Award, Medical College of Wisconsin

6) MEMBERSHIPS IN HONORARY AND PROFESSIONAL SOCIETIES:
05/2015 – present: Association for Research in Vision and Ophthalmology (ARVO)
08/2016 – present: Clinical & Translational Science Institute, PhD in Basic and
Translational Science
7) **JOURNAL REVIEWS**
   **Ad hoc Journal Reviewer (past 1 year)**
   Metabolic Brain Disease

8) **COMMITTEE SERVICE:**
   **Medical College Committees**
   07/2019 – present – Member, MCW Institutional Review Board Committee (#1)

9) **TEACHING ACTIVITIES:**
   **Graduate Student Education**
   01/2019 – moderator, Neuroscience Journal Club

   **Community/Lay Public**
   Young, J.B., Kassem, I.S. “Improving outcomes for children after cataract surgery,” presented at Harmony 4 Hope poster session, Medical College of Wisconsin, Milwaukee Wisconsin (September, 2018).

10) **INVITED LECTURES/WORKSHOPS/PRESENTATIONS:**
    **Regional**

    2) Young, J.B., Kassem, I.S. “Juvenile rabbit as a model for pediatric intraocular surgery with translational applications: Research in progress,” presented at the Clinical & Translational Science Institute (CTSI) Research Seminar, Medical College of Wisconsin, Milwaukee, Wisconsin (April, 2019)

11) **PEER REVIEWED WORKSHOPS/PRESENTATIONS:**
    **International**

12) **BIBLIOGRAPHY:**
    **REFEREED JOURNAL PUBLICATIONS/ORIGINAL PAPERS:**


7) Young, J.B., Buchberger, A.R., Bogaard, J.D., Runquist, M., Skumatz, C.M.B., Kassem, I.S. “Tissue plasminogen activator effects on fibrin volume and the ocular proteome in a juvenile rabbit model of lensectomy.” (submitted)

**ABSTRACTS:**


7) **Young J.,** Bogaard J.D., Arpinar, V.E., Skumatz, C., Runquist, M., Nencka, A., Kassem, I.S. “Magnetic Resonance Imaging (MRI) of anterior chamber fibrosis to evaluate therapeutic interventions after lensectomy with intraocular lens (IOL) insertion in a rabbit animal model.” ARVO Imaging in the Eye; Honolulu, HI (04/2018).


10) **Young, J.B.,** Collery R.F., Skumatz, C.M.B., Kassem, I.S. “RNA sequencing of transcriptome analyses of juvenile rabbit cornea and iris/ciliary body following lensectomy with intraocular lens insertion.” Accepted for presentation at ARVO Annual Meeting; Baltimore, MD (2020). *Meeting cancelled due to the COVID-19 pandemic.*