

## 2015 Research Annual Report

# Ophthalmology

### RESEARCH AND TRAINING DETAILS



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Faculty	13
Research Fellows	7
Research Students	6
Support Personnel	14
Direct Annual Grant Support	\$832,188
Peer Reviewed Publications	16

### CLINICAL ACTIVITIES AND TRAINING

Clinical Staff	26
Staff Physicians	7
Clinical Fellows	1
Clinical Students	13
Inpatient Encounters	2,059
Outpatient Encounters	28,246

# Research Highlights

## Michael Gray, MD

Dr. Gray continues to be actively involved with Pediatric Eye Disease Investigator Group (PEDIG), a multinational collaborative network dedicated to clinical research in strabismus, amblyopia and other eye diseases that affect children. This past year, Dr. Gray and colleagues have actively recruited for ATS18, a study of binocular computer activities for treatment of amblyopia, and IXT3, a pilot randomized clinical trial of overminus spectacle therapy for intermittent exotropia. Our group was selected for the PEDIG Site of the Month Award in March 2015. Dr. Gray, in collaboration with Dr. West, published a paper in JAAPOS on corneal injuries caused by liquid detergent pods, which was featured on several online news outlets, including National Public Radio (NPR).

## Fumika Hamada, PhD

Dr. Hamada's laboratory studies circadian rhythm of body temperature (body temperature rhythm). Body temperature rhythm is critical for the maintenance of homeostasis functions, such as metabolic energy generation and sleep. Her lab's progress has been remarkable as their work reveals the hitherto unknown molecular mechanisms underlying body temperature rhythm and has led to the first identification of a molecule that links circadian clock to body temperature rhythm. In the past year, Dr. Hamada has presented her work at University of Cincinnati, University of Massachusetts Medical School and Brandeis University.

## Richard A. Lang, PhD

Dr. Lang's major research interests include early eye development, vascular development, the developmental and homeostatic function of myeloid cells and more recently, the role of light response pathways in development. The Lang Lab has been investigating whether light exposure during pregnancy is a risk factor for severe retinopathy of prematurity and in collaboration with Dr. Michael Yang. In this past year, Dr. Lang has presented his work at the Massachusetts Eye and Ear Infirmary at Harvard Medical School and at the Association for Research in Vision and Ophthalmology Annual Meeting. Internationally, he presented at The Conference on Bioactive Peptides for Cell-Cell Communication in Kyoto, Japan; at The Epigenetics and Evolution in Eye Development and Disease Conference in Madrid, Spain; and at a conference entitled A Cell for All Seasons at the University of Edinburgh in Scotland.

## Michael B. Yang, MD

Working with researchers in Gothenburg, Sweden and Boston, Massachusetts, Dr. Yang along with Dr. Richard Lang and Patricia Cobb, MS, analyzed a large cohort of infants from a previous multicenter study and found evidence that length of day during early gestation was associated with increased risk for subsequent development of severe retinopathy of prematurity during the third trimester in African American premature infants.

Dr. Yang also served as site principal investigator for the Postnatal Growth and Retinopathy of Prematurity (G-ROP) multicenter study which is seeking to develop a highly accurate risk-model to predict which premature infants will develop severe ROP and therefore help determine which infants can be eliminated from screening altogether or receive less frequent screening. With Patricia Cobb's assistance, over 1200 premature infants from Cincinnati Children's Hospital Medical Center, Good Samaritan Hospital and University Hospital of Cincinnati were enrolled in the study.

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## Significant Publications

Carpenter AC, Smith AN, Wagner H, Cohen-Tayar Y, Rao S, Wallace V, Ashery-Padan R, Lang RA. Wnt Ligands from the Embryonic Surface Ectoderm Regulate 'Bimetallic Strip' Optic Cup Morphogenesis in Mouse. *Development*. 2015 Mar 1;142(5):972-82.

In this paper, we describe a mechanism for eye development that explains the epithelial bending and the formation of

curved tissue structures. This paper has implications beyond the eye because many different organs develop by generating curved epithelial structures.

**Lang RA**, Herman K, Reynolds AB, Hildebrand JD, Plageman TF Jr. **P120-Catenin-Dependent Junctional Recruitment of Shroom3 Is Required for Apical Constriction During Lens Pit Morphogenesis.** *Development.* 2014 Aug;141(16):3177-87.

In this paper we show that a complex between p120 catenin, a cadherin adhesion molecule binding protein, and Shroom3, an F-actin binding protein, is important for epithelial bending during development.

**Gray ME, West CE.** **Corneal Injuries from Liquid Detergent Pods.** *J AAPOS.* 2014 Oct;18(5):494-5.

This cases series showed that significant corneal injuries can occur in children who accidentally expose their eyes to concentrated liquid detergent sold in convenient pods. These study results served as a note of caution to the public. They were widely publicized by the American Academy of Pediatrics and highlighted on National Public Radio.

Liu H, **Yang MB**, Li SK, Hao J. **Effects of Dosing Protocol on Distribution of Propranolol in Periocular Tissues after Topical Ocular Instillation.** *Curr Eye Res.* 2015 May;40(6):638-45.

This pharmacokinetic study in rabbits found that tailored dosing protocols for topical ophthalmic instillation of propranolol can result in high concentrations of propranolol in the periocular tissues while minimizing systemic exposure. High concentrations of propranolol delivered by local therapy may be effective in treating periocular capillary hemangiomas while decreasing the risk of systemic side effects.

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## Division Publications

1. Carpenter AC, Smith AN, Wagner H, Cohen-Tayar Y, Rao S, Wallace V, Ashery-Padan R, Lang RA. **Wnt ligands from the embryonic surface ectoderm regulate 'bimetallic strip' optic cup morphogenesis in mouse.** *Development.* 2015; 142:972-82.
2. Corn AL, Lusk KE. **The Expanded Core Curriculum.** In: JM Gorman, RA Jackson, eds. *Raising a Child with Albinism: A Guide to the School Years.* East Hampstead, NJ: National Organization for Albinism and Hypopigmentation (NOAH); 2014:169-184.
3. Dosunmu EO, Marcus I, Tung I, Thiamthat W, Freedman SF. **The effect of repeated measurements and the use of topical anesthetic on rebound tonometry values in children.** *J AAPOS.* 2014; 18:619-21.
4. Dosunmu EO, Marcus I, Tung I, Thiamthat W, Freedman SF. **Intraocular pressure in children: the effect of body position as assessed by Icare and Tono-Pen tonometers.** *Am J Ophthalmol.* 2014; 158:1348-1352 e1.
5. Gray ME, West CE. **Reply: To PMID 25280925.** *J AAPOS.* 2015; 19:100.
6. Gray ME, West CE. **Corneal injuries from liquid detergent pods.** *J AAPOS.* 2014; 18:494-5.
7. Head LM, Tang X, Hayley SE, Goda T, Umezaki Y, Chang EC, Leslie JR, Fujiwara M, Garrity PA, Hamada FN. **The influence of light on temperature preference in Drosophila.** *Curr Biol.* 2015; 25:1063-8.
8. Lang RA, Herman K, Reynolds AB, Hildebrand JD, Plageman TF, Jr.. **p120-catenin-dependent junctional recruitment of Shroom3 is required for apical constriction during lens pit morphogenesis.** *Development.* 2014; 141:3177-87.
9. Liu H, Yang MB, Li SK, Hao J. **Effects of dosing protocol on distribution of propranolol in periocular tissues after**

- topical ocular instillation.** *Curr Eye Res.* 2015; 40:638-45.
10. Lusk KE, Corn AL. **Educational Assessments.** In: JM Gorman, RA Jackson, eds. *Raising a Child With Albinism: A Guide to the School Years.* East Hampstead, NJ: National Organization for Albinism and Hypopigmentation (NOAH); 2014:159-167.
  11. Mehta VJ, Utz VM, Traboulsi EI, Rychwalski PJ. **Outcomes of strabismus surgery with or without trainee participation as surgeon.** *Ophthalmology.* 2014; 121:2066-9.
  12. Pediatric Eye Disease Investigator G, Wallace DK, Lazar EL, Repka MX, Holmes JM, Kraker RT, Hoover DL, Weise KK, Waters AL, Rice ML, Peters RJ. **A randomized trial of adding a plano lens to atropine for amblyopia.** *J AAPOS.* 2015; 19:42-8.
  13. Pham C, Utz V, Marcotty A, Zeft A, Rychwalski P. **Superior oblique tendon (Brown's) syndrome as the presenting finding in childhood onset HLA-B27-related enthesitis and juvenile idiopathic oligoarticular arthritis.** *Reumatismo.* 2014; 66:240-4.
  14. Wicklow E, Blij S, Frum T, Hirate Y, Lang RA, Sasaki H, Ralston A. **HIPPO pathway members restrict SOX2 to the inner cell mass where it promotes ICM fates in the mouse blastocyst.** *PLoS Genet.* 2014; 10:e1004618.
  15. Yang J, Mowry LE, Nejak-Bowen KN, Okabe H, Diegel CR, Lang RA, Williams BO, Monga SP. **Beta-catenin signaling in murine liver zonation and regeneration: A Wnt-Wnt situation!** *Hepatology.* 2014; 60:964-76.
  16. Zhang S, Konstantinidis DG, Yang JQ, Mizukawa B, Kalim K, Lang RA, Kalfa TA, Zheng Y, Guo F. **Gene targeting RhoA reveals its essential role in coordinating mitochondrial function and thymocyte development.** *J Immunol.* 2014; 193:5973-82.
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## Faculty, Staff, and Trainees

### Faculty Members

**Michael B. Yang, MD**, Associate Professor  
Leadership Division Director

**Karl C. Golnik, MD, FACS**, Professor  
Leadership Interim Chairperson, Department of Ophthalmology

**Richard A. Lang, PhD**, Professor  
Leadership Emma and Irving Goldman Scholar; Director, Visual Systems Group

**Eniolami Dosunmu, MD**, Assistant Professor

**Fumika Hamada, PhD**, Assistant Professor

**Michael Gray, MD**, Assistant Professor

**Sarah L. Lopper, OD**, Instructor

**Kelly Lusk, PhD, CLVT**, Assistant Professor

**Virginia Miraldi-Utz, MD**, Assistant Professor

**William Walker Motley, III, MS, MD**, Associate Professor

**Andrea Prosser, MD**, Instructor

**Melissa Rice, OD, FAAO**, Instructor

**Daniele Saltarelli, OD**, Assistant Professor

**Terry Schwartz, MD**, Professor

**Constance E. West, MD**, Professor

### **Clinical Staff Members**

- **Corey Bowman, COT, LDO, ABOC**
- **Rosalyn Grant, COA**
- **JaTawna Bush, COA**
- **Shemeka Butler, CO**
- **Rebecca Bystra, COA**
- **Kaylie Davidson, COA**
- **Brandy Dearwater, COA, RN**
- **Jennifer Duncan, COA**
- **Lisa Fite, COA**
- **Amanda Johnson, COA**
- **Melody Klayer, COA**
- **Debbie Lipps, COA**
- **Patty Lucas, COA**
- **Tamara Lyons, COA**
- **Nicole McLeod, COA**
- **Debbie Meister, COA**
- **Denisha Mills, COA**
- **Erika Setser, LDO**
- **Jill Simmons, COA**
- **Miqua Stewart, CO**
- **Kelli Vieson, COT, Clinical Manager**
- **Leanne Wagner, COA**
- **Carol Weinel, COA**

### **Trainees**

- **Maryam Ahmed, MD, PGY2**, University of Cincinnati College of Medicine

- **Zegary Allen, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
  - **Nuria Alonso**, , Research Student, Cincinnati Children's Hospital Medical Center BRIMS Program
  - **Joseph Armenia, MD**, PGY3, Reading Hospital and Medical Center, Pennsylvania
  - **Dema Atoum, MD**, PGY6, Cincinnati Children's Hospital Medical Center
  - **Jenna Bottorff, MD**, PGY2, Kettering Medical Center, Wright State University
  - **Maya Dassanyake**, , SURF Student, University of Cincinnati
  - **Tadahiro Goda, PhD**, Research Fellow, Kyushu University, Fukuoka, Japan
  - **Laura Hanson, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
  - **Tiffany Hseih, MD**, PGY2, University of Cincinnati College of Medicine
  - **Jason Lee, OD**, Pediatric Optometry Resident, Ohio State University
  - **Brian Marek, MD**, PGY2, University of Michigan Medical School
  - **Maggie McLeod**, , Research Student, UC Honors Program, University of Cincinnati
  - **Xue Mei, PhD**, Research Fellow, University of Iowa, Iowa City, IA
  - **Eileen Myers, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
  - **Ajit Muley, PhD**, Research Fellow, Anna University, Chennai, India
  - **Minh-Thanh Nguyen, PhD**, Research Associate, University of Florida, Gainesville, FL
  - **Yoshinobu Odaka, PhD**, Research Fellow, Louisiana State University Health Shreveport, Shreveport, LA
  - **Erika Osterholzer, MD**, PGY3, Boonshoft School of Medicine, Kettering Medical Center, Kettering, OH
  - **Deepam Rusia, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
  - **Ama Sadaka, MD**, PGY3, The Christ Hospital
  - **Gowri Sarangdhar, PhD**, Research Associate, University of Sussex, Brighton, United Kingdom
  - **Rachel Talbott, BA**, Research Assistant, Purdue University, West Lafayette, IN
  - **Xin Tang, PhD**, Research Associate, Vanderbilt University, Nashville, TN
  - **Uyen Tran**, , Research Student, UC Honors Program, University of Cincinnati
  - **Yujiro Umezaki, PhD**, Research Fellow, Okayama University, Okayama, JAPAN
  - **Shruti Vemaraju, PhD**, Research Fellow, Texas A&M University, College Station, TX
  - **Bhargav Vemuri**, , Research Student, UC Honors Program, University of Cincinnati
  - **Brian Zamora, MD**, PGY3, West Virginia University School of Medicine, Morgantown, WV
  - **Kevin Zhang**, , Research Student, Medical Science Training Program, University of Cincinnati
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# Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct

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## Gray, M

### Pediatric Eye Disease Investigator Group

National Institutes of Health (Jaeb Center for Health Research Foundationn, Inc)

U10 EY011751 8/22/2012-12/31/2018 \$14,042

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## Lang, R

### Retinal Microglia and Angiogenesis

National Institutes of Health

R01 EY021636 5/1/2012-4/30/2017 \$245,000

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### Light Regulated Vascular Development of the Eye

National Institutes of Health

R01 EY023179 1/1/2013-12/31/2016 \$373,028

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## Namekawa, F

### Molecular and Neural Mechanisms of Temperature Preference

National Institutes of Health

R01 GM107582 9/1/2013-8/31/2018 \$182,400

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## West, C

### Save Our Sight Ohio Amblyope Registry

Ohio Department of Health (The Research Institute at Nationwide Hospital)

7/1/2008-6/30/2015 \$5,000

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## Yang, M

### Postnatal Growth and Retinopathy of Prematurity (G-ROP) Studies

National Institutes of Health (Children's Hospital of Philadelphia)

R01 EY021137 9/1/2014-8/31/2016 \$12,718

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**Current Year Direct \$832,188**

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**Total \$832,188**





# Drosophila Research Leads to Light-Bulb Moment About Body Temperature Regulation



Fumika Hamada, PhD

PUBLISHED APRIL 20, 2015

*Current Biology*

Researchers have long known that human body temperature rises when people are exposed to light during the night. Understanding the molecular mechanisms that cause such temperature changes could advance the study of sleep disorders, seasonal affective disorders and temperature regulation.

A study published in April 2015 in *Current Biology* reports finding important clues about these mechanisms in a most-unusual place: the temperature sensitivities of the tiny, cold-blooded fruit fly, *Drosophila melanogaster*.

A research team led by Fumika Hamada, PhD, Division of Ophthalmology, found that *Drosophila* exhibit light-dependent temperature preference (LDTP) in which the flies prefer a one-degree higher temperature in light than in dark. Because the flies are cold-blooded, their body temperature is also higher in light.

The team uncovered the molecular mechanisms that control LDTP in flies, and theorize that acute light on temperature regulation may be conserved evolutionarily between flies and humans. “Light affects many physiological responses, but the underlying mechanisms of it are unclear,” Hamada says.

The team also found a well-known circadian clock molecule — pigment dispersing factor receptor — in subsets of the circadian clock cells that control the flies’ LDTP. The result suggests a connection between light and circadian clock neurons. Given that LDTP occurs irrespective of the state of the circadian rhythms, the research provides new insights into how circadian clock mechanisms impact light and temperature regulation.

Heat generation is different between humans and flies, but the light/temperature connection has similarities. Eventually, this line of research could benefit people who work night shifts and are exposed to light in nighttime.

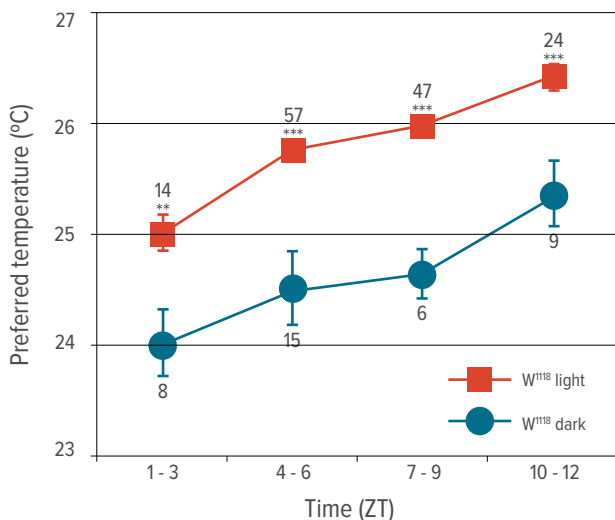
“Long-term sleep deprivation may increase the risk of obesity, diabetes and cardiovascular disease,” Hamada says. “This evening light exposure increases body temperature, which causes abnormal circadian rhythmicity.”

## RESEARCH AND TRAINING DETAILS

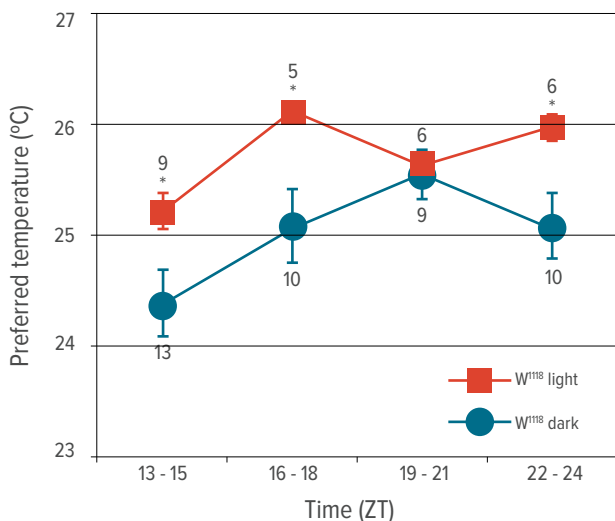
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Head LM, Tang X, Hayley SE, Goda T, Umezaki Y, Chang EC, Leslie JR, Fujiwara M, Garrity PA, Hamada FN. The influence of light on temperature preference in *Drosophila*. *Curr Biol*. 2015;25(8):1063-1068.

A LD DAYTIME



B LD NIGHTTIME



The two figures here show how acute light positively influences temperature preference in cold-blooded *Drosophila*, commonly known as fruit flies. Understanding these elusive molecular mechanisms could one day advance how light affects sleeping humans, leading to improved treatment of sleep disorders.

Chart A (top) compares preferred temperature between light and dark conditions for w1118 flies during the daytime.

Chart B (bottom) does the same for nighttime. The w1118 flies were raised in alternating 12-hour cycles of light and dark. Ambient light was either on or off when the behavioral experiments were performed for 30 minutes.