

2014 Research Annual Report

Ophthalmology



Division Summary

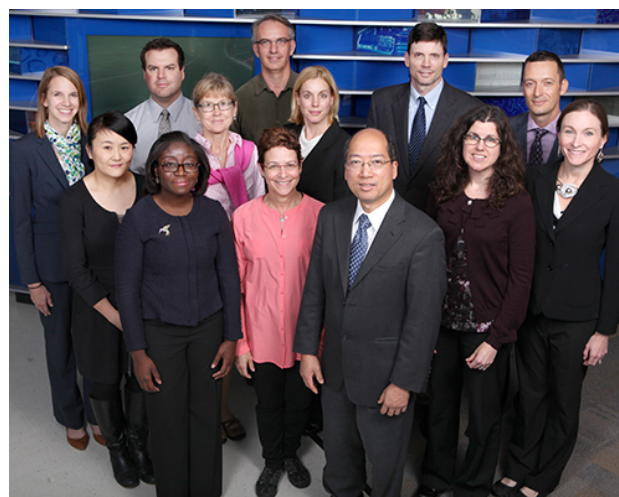
RESEARCH AND TRAINING DETAILS

Number of Faculty	16
Number of Joint Appointment Faculty	1
Number of Research Fellows	12
Number of Research Students	3
Number of Support Personnel	14
Direct Annual Grant Support	\$1,628,819
Peer Reviewed Publications	27

CLINICAL ACTIVITIES AND TRAINING

Number of Clinical Staff	21
Number of Staff Physicians	11
Number of Clinical Fellows	1
Number of Clinical Students	12
Number of Other Students	1
Inpatient Encounters	1,552
Outpatient Encounters	26,220

Division Photo



Row 1: E Dosunmu, T Schwartz, M Yang, M Rice, V Utz
Row 2: F Hamada, C West, S Lopper, W Motley, D Saltarelli
Row 3: A Prosser, M Gray, R Lang

Significant Accomplishments

Limited light exposure linked to retinopathy of prematurity

The Division of Pediatric Ophthalmology at the Abrahamson Pediatric Eye Institute has been investigating whether light exposure during pregnancy is a risk factor for severe retinopathy of prematurity (ROP), a potentially blinding vascular overgrowth in infants born prematurely. The project, led by **Richard Lang, PhD**, and **Michael Yang, MD**, is based on mouse studies of vascular development mechanisms and light response pathways. Yang has recently shown that there may be a critical threshold of light exposure during early gestation above which there is no further decrease in the risk for the subsequent development of severe ROP. This may have implications for the amount of light therapy needed to decrease the risk of severe ROP. Yang is now analyzing patient data in a multi-center database to confirm the results of the previous single center study.

Ocular genetics has an impact

The Eye Genetics Clinic completed its first full year of operations and evaluated patients with a wide array of genetic diseases linked to ocular problems. The clinic is a collaborative effort of **Howard Saal, MD**; **Robert Hufnagel, MD, PhD**, from Genetics; and **Constance West, MD**; **Virginia Utz, MD**; Zubair Ahmed, PhD; and Patricia Cobb, MS, from Ophthalmology. Some novel disease genes will be considered for future reports.

Separately, Hufnagel, Ahmed, and lead author Robert Sisk, MD, a pediatric retina specialist, reported in *Ophthalmology* the case of an infant boy diagnosed with Norrie disease, which is characterized by postnatal retinal detachment and vision loss. When the child's mother became pregnant again, genetic testing showed

that the male fetus also had the Norrie mutation. The infant was delivered preterm and treated with laser and anti-angiogenesis agents, which thus far have prevented blindness.

Reducing unnecessary screening for retinopathy of prematurity

Increased risk for retinopathy of prematurity (ROP) is associated with slow rate of weight gain after birth in premature infants, which reflects the infant's level of insulin-like growth factor 1, which is also important for retinal angiogenesis. Yang is the principal investigator in Cincinnati for the multi-center Growth in Retinopathy of Prematurity (G-ROP) study, which examines whether an infant's weight gain can help predict the severity of ROP. This could help determine which infants can be safely excluded from screening examinations. Cincinnati is one of the largest contributing centers, with more than 1,200 patients in the retrospective portion of the study.

Research Highlights

Michael Gray, MD

Dr. Gray is an assistant professor in Pediatric Ophthalmology and Adult Strabismus. Over the past year, Dr. Gray has been active within PEDIG, the Pediatric Eye Disease Investigator Group. This is a collaborative network dedicated to clinical research in strabismus, amblyopia, and other eye diseases that affect children. Through PEDIG, the group at Cincinnati Children's has been recruiting for the CO2 study (Pediatric Cataract Surgery Outcomes Registry) and the HTS1 study (Glasses versus Observation for Moderate Hyperopia in Young Children). We will soon be involved in ATS18, a study of Binocular Computer Activities for Treatment of Amblyopia. Dr. Gray has also evaluated several patients with ocular injuries due to exposure from newer detergent "pods", and has an upcoming paper accepted in *JAAPOS* evaluating a series of patients with these injuries.

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 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. Dr. Hamada has presented her work at The Society for Research on Biological Rhythms (SRBR) meeting.

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, published those findings in *Ophthalmology* in December 2013. In this past year, Dr. Lang has presented his work at Boston Children's Hospital, Case Western University, Columbia University and The Cole Eye Institute in Cleveland. Internationally, he presented at The Sackler Lecture Series at Tel Aviv University, Israel.

Terry Schwartz, MD

Under Dr. Schwartz's direction, the low vision rehabilitation program continues to grow. With the third year of grant support from the Ettlinger Foundation, monthly multidisciplinary clinics have been established in collaboration with the Perlman Center for the evaluation of children with cerebral palsy and cortical visual impairment. For children with permanent visual impairment, low vision rehabilitation clinics are held in multiple locations throughout Kentucky, Ohio, and West Virginia. A new collaborative effort is underway to

provide services to children in southeastern Ohio and eastern Kentucky. In collaboration with Dr. Kelly Lusk, there is ongoing clinical research in the field of pediatric low vision rehabilitation.

Michael B. Yang, MD

Dr. Yang's research focus is on retinopathy of prematurity (ROP). His major work, performed in collaboration with Dr. Lang and colleagues, on the association of average day length during early gestation with severe ROP outcome was published in *Ophthalmology* this past year. Under Dr. Yang's leadership, the division has nearly completed data collection for the retrospective portion of the G-ROP (Postnatal Growth in ROP) multicenter study which evaluates daily weight gain after birth in premature infants as a predictor of severe ROP outcome to determine if that information can help reduce the number of screening eye examinations that have to be performed on premature infants. He is also a subinvestigator for the INS-3 multicenter trial which seeks to determine if administering the complex sugar inositol to premature infants can reduce the occurrence of severe ROP. As a member of the Ophthalmic Technology Assessment Committee of the American Academy of Ophthalmology, Dr. Yang was lead author on a paper assessing the risks and benefits of using fibrin glue to close conjunctival incisions after strabismus surgery.

Division Publications

1. Ahmed ZM, Frolenkov GI, Riazuddin S. **Usher proteins in inner ear structure and function.** *Physiol Genomics*. 2013; 45:987-9.
2. Chhabra MS, Bonsall DJ, Cassedy AE, Wallace GH, Schoenberger SD, West CE. **Reliability of grading retinal hemorrhages in abusive head trauma.** *J AAPOS*. 2013; 17:343-6.
3. Choi YS, Zhang Y, Xu M, Yang Y, Ito M, Peng T, Cui Z, Nagy A, Hadjantonakis AK, Lang RA, Cotsarelis G, Andl T, Morrissey EE, Millar SE. **Distinct functions for Wnt/beta-catenin in hair follicle stem cell proliferation and survival and interfollicular epidermal homeostasis.** *Cell Stem Cell*. 2013; 13:720-33.
4. Cideciyan AV, Hufnagel RB, Carroll J, Sumaroka A, Luo X, Schwartz SB, Dubra A, Land M, Michaelides M, Gardner JC, Hardcastle AJ, Moore AT, Sisk RA, Ahmed ZM, Kohl S, Wissinger B, Jacobson SG. **Human cone visual pigment deletions spare sufficient photoreceptors to warrant gene therapy.** *Hum Gene Ther*. 2013; 24:993-1006.
5. Fan J, Ponferrada VG, Sato T, Vemaraju S, Fruttiger M, Gerhardt H, Ferrara N, Lang RA. **Crim1 maintains retinal vascular stability during development by regulating endothelial cell Vegfa autocrine signaling.** *Development*. 2014; 141:448-59.
6. Goda T, Leslie JR, Hamada FN. **Design and analysis of temperature preference behavior and its circadian rhythm in Drosophila.** *J Vis Exp*. 2014; :e51097.
7. Goodnough LH, Dinuoscio GJ, Ferguson JW, Williams T, Lang RA, Atit RP. **Distinct requirements for cranial ectoderm and mesenchyme-derived wnts in specification and differentiation of osteoblast and dermal progenitors.** *PLoS Genet*. 2014; 10:e1004152.
8. Gray ME, Shaikh AH, Correa ZM, Augsburger JJ. **Primary uveal melanoma in a 4-year-old black child.** *J AAPOS*. 2013; 17:551-3.
9. Hoffmann SA, Hos D, Kuspert M, Lang RA, Lovell-Badge R, Wegner M, Reiprich S. **Stem cell factor Sox2 and its close relative Sox3 have differentiation functions in oligodendrocytes.** *Development*. 2014; 141:39-50.
10. Katayama K, Imai F, Campbell K, Lang RA, Zheng Y, Yoshida Y. **RhoA and Cdc42 are required in pre-migratory progenitors of the medial ganglionic eminence ventricular zone for proper cortical interneuron migration.** *Development*. 2013; 140:3139-45.
11. Kausar T, Bhatti MA, Ali M, Shaikh RS, Ahmed ZM. **OCA5, a novel locus for non-syndromic**

- oculocutaneous albinism, maps to chromosome 4q24.** *Clin Genet.* 2013; 84:91-3.
12. Marcus I, Tung IT, Dosunmu EO, Thiamthat W, Freedman SF. **Anterior segment photography in pediatric eyes using the Lytro light field handheld noncontact camera.** *J AAPOS.* 2013; 17:572-7.
 13. Miraldi Utz V, Coussa RG, Marino MJ, Chappelow AV, Pauer GJ, Hagstrom SA, Traboulsi EI. **Predictors of visual acuity and genotype-phenotype correlates in a cohort of patients with Stargardt disease.** *Br J Ophthalmol.* 2014; 98:513-8.
 14. Miraldi Utz V, Coussa RG, Traboulsi EI. **Surgical management of lens subluxation in Marfan syndrome.** *J AAPOS.* 2014; 18:140-6.
 15. Miraldi Utz V, Kaufman AR. **Allergic eye disease.** *Pediatr Clin North Am.* 2014; 61:607-20.
 16. Montoliu L, Gronskov K, Wei AH, Martinez-Garcia M, Fernandez A, Arveiler B, Morice-Picard F, Riazuddin S, Suzuki T, Ahmed ZM, Rosenberg T, Li W. **Increasing the complexity: new genes and new types of albinism.** *Pigment Cell Melanoma Res.* 2014; 27:11-8.
 17. Nathan ST, Jain V, Lykissas MG, Crawford AH, West CE. **Transient cortical blindness as a complication of posterior spinal surgery in a pediatric patient.** *J Pediatr Orthop B.* 2013; 22:416-9.
 18. Saltarelli DP, Motley WW. **Optical penalization with contact lenses for children with unilateral aphakia: an alternative to patching.** *Eye Contact Lens.* 2013; 39:405-9.
 19. Santos-Cortez RL, Lee K, Giese AP, Ansar M, Amin-Ud-Din M, Rehn K, Wang X, Aziz A, Chiu I, Hussain Ali R, Smith JD, University of Washington Center for Mendelian G, Shendure J, Bamshad M, Nickerson DA, Ahmed ZM, Ahmad W, Riazuddin S, Leal SM. **Adenylate cyclase 1 (ADCY1) mutations cause recessive hearing impairment in humans and defects in hair cell function and hearing in zebrafish.** *Hum Mol Genet.* 2014; 23:3289-98.
 20. Shahzad M, Sivakumaran TA, Qaiser TA, Schultz JM, Hussain Z, Flanagan M, Bhinder MA, Kissell D, Greinwald JH, Jr., Khan SN, Friedman TB, Zhang K, Riazuddin S, Riazuddin S, Ahmed ZM. **Genetic analysis through OtoSeq of Pakistani families segregating prelingual hearing loss.** *Otolaryngol Head Neck Surg.* 2013; 149:478-87.
 21. Sisk RA, Hufnagel RB, Bandi S, Polzin WJ, Ahmed ZM. **Planned preterm delivery and treatment of retinal neovascularization in norrie disease.** *Ophthalmology.* 2014; 121:1312-3.
 22. Utz VM, Beight CD, Marino MJ, Hagstrom SA, Traboulsi EI. **Autosomal dominant retinitis pigmentosa secondary to pre-mRNA splicing-factor gene PRPF31 (RP11): review of disease mechanism and report of a family with a novel 3-base pair insertion.** *Ophthalmic Genet.* 2013; 34:183-8.
 23. Utz VM, Chappelow AV, Marino MJ, Beight CD, Sturgill-Short GM, Pauer GJ, Crowe S, Hagstrom SA, Traboulsi EI. **Identification of three ABCA4 sequence variations exclusive to African American patients in a cohort of patients with Stargardt disease.** *Am J Ophthalmol.* 2013; 156:1220-1227 e2.
 24. West CE, Hunter DG. **Displacement of optical centers in over-the-counter readers: a potential cause of diplopia.** *J AAPOS.* 2014; 18:293-4.
 25. Yang MB, Melia M, Lambert SR, Chiang MF, Simpson JL, Buffenn AN. **Fibrin glue for closure of conjunctival incision in strabismus surgery: a report by the american academy of ophthalmology.** *Ophthalmology.* 2013; 120:1935-41.
 26. Yang MB, Rao S, Copenhagen DR, Lang RA. **Length of day during early gestation as a predictor of risk for severe retinopathy of prematurity.** *Ophthalmology.* 2013; 120:2706-13.
 27. Yeo EJ, Cassetta L, Qian BZ, Lewkowich I, Li JF, Stefater JA, 3rd, Smith AN, Wiechmann LS, Wang Y, Pollard JW, Lang RA. **Myeloid WNT7b mediates the angiogenic switch and metastasis in breast cancer.** *Cancer Res.* 2014; 74:2962-73.

Faculty Members

Constance E. West, MD, Associate Professor

Leadership Division Director

James J. Augsburger, MD, FACS, Professor

Leadership Chairperson, Department of Ophthalmology

Richard A. Lang, PhD, Professor

Leadership Emma and Irving Goldman Scholar; Director, Visual Systems Group

Zubair Ahmed, PhD, Associate Professor

Tiffany Cook, PhD, Associate Professor

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, Instructor

Terry Schwartz, MD, Professor

Michael B. Yang, MD, Associate Professor

Joint Appointment Faculty Members

Saima Riazuddin, PhD, Associate Professor (Department of Otolaryngology)

Clinical Staff Members

- **Corey Bowman, COT, LDO, ABOC**
- **Rosalyn Grant, COA**
- **JaTawna Bush,**
- **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**
- **Erika Setser, LDO**
- **Jill Simmons, COA**
- **Miqua Stewart, CO**
- **Kelli Vieson, COT,**
Clinical Manager
- **Leanne Wagner, COA**

Trainees

- **Zegary Allen, MD**, PGY3, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Joseph Armenia, MD**, PGY2, Reading Hospital and Medical Center, Pennsylvania
- **Mark Charlton-Perkins, BS**, Graduate Student, University of Otago, Dunedin, New Zealand
- **Jieqing Fan, BS**, Graduate Student, Tsinghua University, Beijing, China
- **Arnaud Giese, PhD**, Research Fellow, Université Victor Segalen Bordeaux II, Bordeaux, France
- **Tadahiro Goda, PhD**, Research Fellow, Kyushu University, Fukuoka, Japan
- **Laura Hanson, MD**, PGY3, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Jason Lee, OD**, Pediatric Optometry Resident, Ohio State University
- **Luke Lindsell, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Greg Mecoli, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Eileen Myers, MD**, PGY3, 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**, PGY2, Boonshoft School of Medicine, Kettering Medical Center, Kettering, OH
- **Jon Pargament, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Sujata Rao, PhD**, Research Associate, Cornell University, Ithaca, New York
- **Elodie Richard, PhD**, Research Fellow, Université Victor Segalen Bordeaux II, Bordeaux, France
- **Deepam Rusia, MD**, PGY3, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Ama Sadaka, MD**, PGY2, The Christ Hospital
- **Gowri Sarangdhar, PhD**, Research Fellow, University of Sussex, Brighton, United Kingdom
- **Mohsin Shazad, PhD**, Research Fellow, Center for Excellence in Molecular Biology, University of The Punjab, Lahore, Pakistan
- **Rachel Talbott, BA**, Research Assistant, Purdue University, West Lafayette, IN
- **Xin Tang, PhD**, Research Fellow, Vanderbilt University, Nashville, TN
- **Yujiro Umezaki, PhD**, Research Fellow, Okayama University, Okayama, JAPAN
- **Shruti Vemaraju, PhD**, Research Fellow, Texas A&M University, College Station, TX
- **Aaron Weber, MD**, PGY4, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- **Rizwan Yousaf, MS**, Graduate Student, Center for Excellence in Molecular Biology, University of The Punjab, Lahore, Pakistan
- **Brian Zamora, MD**, PGY2, West Virginia University School of Medicine, Morgantown, WV
- **Fareeha Zulfiqar, PhD**, Research Associate, University of The Punjab, Lahore, Pakistan

Analysis of DFNB26 mutation using Zebrafish as a model system (Zubair Ahmed, PhD)

Developmental Biology » Saulius Sumanas, PhD

Molecular modeling of USH1 protein to identify the effect on the structure (Zubair Ahmed, PhD)

Developmental Biology » Rashmi Hegde, PhD

Eyes absent proteins in vascular development, cancer and the retinal vasculopathies (Richard Lang, PhD)

Developmental Biology » Rashmi Hegde, PhD

Role of RhoA and Cdc42 in pre-migratory progenitors of the medial ganglionic eminence (Richard Lang, PhD)

Experimental Hematology & Cancer Biology - Cell Signaling » Yi Zheng, PhD

Role of new deafness protein in the mitochondrial function (Zubair Ahmed, PhD)

Human Genetics » Taosheng Huang, PhD

Functional analysis of newly retinal disorder genes (Zubair Ahmed, PhD)

Human Genetics » Robert Hufnagel, MD, PhD

Grants, Contracts, and Industry Agreements

Grant and Contract Awards	Annual Direct
AHMED, Z	
Research to Prevent Blindness Career Development Award	
Research to Prevent Blindness(University of Cincinnati)	
07/01/10-06/30/14	\$50,000
Usher Proteins in the Inner Ear Structure and Function	
National Institutes of Health	
R01 DC 012564	12/01/12-11/30/17
	\$286,507
COOK, T	
Defining Glial Programs that Support Adult Photoreceptor Form and Function	
National Institutes of Health	
R21 EY 024405	04/01/14-03/31/16
	\$150,000
LANG, R	
Light Regulated Vascular Development of the Eye	
National Institutes of Health	
R01 EY 023179	01/01/13-12/31/16
	\$433,622
Retinal Microglia and Angiogenesis	
National Institutes of Health	
R01 EY 021636	05/01/12-04/30/17
	\$245,000
Wnt Pathway Regulation of Lens Polarity	
National Institutes of Health	
R01 EY 016241	03/01/11-02/28/15
	\$245,000

NAMEKAWA, F

Molecular and Neural Mechanisms of Temperature Preference

National Institutes of Health

R01 GM 107582 09/01/13-08/31/18 \$190,000

YANG, M

Postnatal Growth and Retinopathy of Prematurity (G-ROP)

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

R01 EY 021137 09/20/12-08/31/17 \$23,690

WEST, C

Save Our Sight Ohio Amblyope Registry

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

07/01/08-06/30/15 \$5,000

Current Year Direct \$1,628,819

Total \$1,628,819