**BIOGRAPHICAL SKETCH**

Senior Trainer

NAME: Pattnaik,Bikash Ranjan

eRA COMMONS USER NAME: BIKASHP

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Sambalpur University, Burla, Orissa | MS | 07/1989 | Life Sciences |
| University of Delhi South Campus, New Delhi, Delhi | MPHIL | 05/1994 | Interdisciplinary and Applied Science |
| University of Delhi, New Delhi, Delhi | PhD | 12/1999 | Biophysics |

## A. PERSONAL STATEMENT

I am a faculty in the University of Wisconsin, Department of Pediatrics, Department of Ophthalmology and Visual Sciences, UW cell and regenerative medicine program and an investigator of the UW-McPherson Eye Research Institute. Specifically, I am using my training in retinal cell biology, ion-channel biology, small animal electroretinography, and stem-cell biology to study function and dysfunction within the Retina that cause blindness. Endocrine glands secrete circulating hormones that regulate development of organs during the fetal stage and eye development in this regard is not well studied. We are interested in the role of birth hormones in the eye's transition during gestation. I have a broad background in vision physiology, cellular physiology, intensive training in patch-clamp electrophysiology, biological imaging, cellular and molecular biology. I have worked on this hypothesis for the past four years and has developed all evidence and competence to train graduate students in the laboratory towards successful completion. As PI or Co-I, I have established new collaborations, trained undergraduate and graduate students, who have gained national scholarships. My overall interest is to understand the mechanism of ROP by understanding cellular signaling components with a specific focus on oxytocin receptor mechanism that result in visual dysfunction or endocrine regulation of eye development. In summary, I have a demonstrated record of accomplished and productive research projects in an area of high relevance to pediatric blindness.


1. Meyer JS, Howden SE, Wallace KA, Verhoeven AD, Wright LS, Capowski EE, Pinilla I, Martin JM, Tian S, Stewart R, Pattnaik B, Thomson JA, Gamm DM. Optic vesicle-like structures derived from human pluripotent stem cells facilitate a customized approach to retinal disease treatment. Stem Cells. 2011 Aug;29(8):1206-18. PMID: 21678528; PMCID: PMC3412675..
2. Pattnaik BR, Hughes BA. Effects of KCNQ channel modulators on the M-type potassium current in primate retinal pigment epithelium. Am J Physiol Cell Physiol. 2012 Mar 1;302(5):C821-33. PMID: 22135213; PMCID: PMC3311298.
3. Pattnaik BR, Asuma MP, Spott R, Pillers DA. Genetic defects in the hotspot of inwardly rectifying K (+) (Kir) channels and their metabolic consequences: a review. Mol Genet Metab. 2012 Jan;105(1):64-72. PMID: 22079268; PMCID: PMC3253982.
4. Kumar M, Pattnaik BR. Focus on Kir7.1: physiology and channelopathy. Channels (Austin). 2014;8(6):488-95. PMID: 25558901.


## B. POSITIONS AND HONORS

**Positions and Employment**

| | |
|---|---|
| 1989 - 1992 | Lecturer, Government College, Rourkela |
| 1992 - 1996 | Graduate Research Assistant, University of Delhi, New Delhi |
| 1996 - 1997 | Senior Research Fellow, All India Institute of Medical Sciences, New Delhi |
| 1997 - 2000 | Research Associate, University of Louis Pasteur, Laboratory of Retina Physiopathology, Strasbourg |
| 2000 - 2003 | Research Associate, University of South Florida, Department of Pharmacology and Therapeutics, Tampa, FL |
| 2003 - 2008 | Research Investigator, University of Michigan, Kellogg Eye Center, Ann Arbor, MI |

| | |
|---|---|
| 2008 - 2013 | Associate Scientist, University of Wisconsin, Department of Pediatrics and Ophthalmology & Visual Sciences, Madison, WI |
| 2013 - 2016 | Senior Scientist, University of Wisconsin, Department of Pediatrics and Ophthalmology & Visual Sciences, Madison, WI |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 1994 - | Life Member, Indian Biophysical Society |
| 2000 - | Life Member, Association for Research in Vision and Ophthalmology |
| 2009 - | Member, American Society of Biochemistry and Molecular Biology |
| 2013 - | Member, International Society for Eye Research |
| 2014 - | Member, Perinatal Research Society |
| 2016 - | Life Member, International Society for Neurochemistry |
| 2018- | Member, ISCEV |

**Honors**

| | |
|---|---|
| 1987 | National Scholarship, Government of India |
| 1988 | Post-Graduate Merit, Government of India |
| 1989 | University Rank Holder in Merit with Distinction, Sambalpur University, India |
| 1997 | CSIR Research Scholarship, CSIR-India |
| 1997 | CSIR and DBT travel grant, Government of India |
| 1999 | Research Fellowship, Fondation de France |
| 2009 | Rebecca Meyer Brown Professorship, Retina Research Foundation |
| 2010 | 2nd Biswambar Rajguru Oration, Orissa State Ophthalmology Association |
| 2015 | National Eye Institute “Audacious Goals Initiative” grant |
| 2017 | National Eye Institute “Retinal Organoids Challenge” Honorable Mention |

## C. CONTRIBUTIONS TO SCIENCE

RPE shares apical processes with photoreceptor outer segments and defines the narrow subretinal space. Kir7.1 lines the apical processes and control subretinal space ionic homeostasis. Only recently it was discovered that mutations in Kir7.1 gene (KCNJ13) causes blindness such as Snowflake Vitreoretinal Degeneration and Leber Congenital Amaurosis. We showed the regulation of Kir7.1 channel in bovine RPE cells by intrinsic phosphoinositides to propose a model for cell-cell communication between retina and RPE. In a translational approach, we have used cell culture model and a mouse model to significantly contribute to the understanding of the pathophysiology of Kir7.1 channelopathy leading to blindness.

a. **Pattnaik BR**, Hughes BA. Regulation of Kir channels in bovine retinal pigment epithelial cells by phosphatidylinositol 4,5-bisphosphate. Am J Physiol Cell Physiol. 2009 Oct;297(4):C1001-11. PMID: 19641096; PMCID: PMC2770741.
b. **Pattnaik BR**, Tokarz S, Asuma MP, Schroeder T, Sharma A, Mitchell JC, Edwards AO, Pillers DA. Snowflake vitreoretinal degeneration (SVD) mutation R162W provides new insights into Kir7.1 ion channel structure and function. PLoS One. 2013;8(8): e71744. PMID: 23977131; PMCID: PMC3747230.
c. **Pattnaik BR**, Shahi PK, Marino MJ, Liu X, York N, Brar S, Chiang J, Pillers AM, Traboulsi EI. A Novel KCNJ13 Nonsense Mutation and Loss of Kir7.1 Channel Function Causes Leber Congenital Amaurosis (LCA16). Hum Mutat. 2015 Apr 29; PMID: 25921210, PMCID Policy Exempt – Not Resulting from NIH Funding.
d. Shahi PK, Liu X, Aul B, Moyer A, Patnaik A, Denton J, Pillers DM, **Pattnaik BR**. Abnormal Electroretinogram after Kir7.1 Channel Suppression Suggests Role in Retinal Electrophysiology. Sci Rep. 2017 Sep 6;7(1):10651. PMID: 28878288, PMCID: PMC5587531

Induced pluripotent stem cells have seen enormous advancement and evolution to the extent that 3-D retinoid organs are becoming a reality. By performing patch-clamp electrophysiology recordings on human iPS-photoreceptors, we were first to demonstrate the physiologic light response at a single cell level. This set the stage for photoreceptor transplantation as a viable option for photoreceptor degenerative diseases. We have thus far also used cellular physiology assays to recapitulate complexities of Bests disease in a dish approach using patient-derived iPS-RPE cells. Understanding of human disease using cell culture and patient-in-a-dish models is key to improve human health through translational science.

a. Singh R, Shen W, Kuai D, Martin JM, Guo X, Smith MA, Perez ET, Phillips MJ, Simonett JM, Wallace KA, Verhoeven AD, Capowski EE, Zhang X, Yin Y, Halbach PJ, Fishman GA, Wright LS, **Pattnaik BR**, Gamm DM. iPS cell modeling of Best disease: insights into the pathophysiology of an inherited macular degeneration. Hum Mol Genet. 2013 Feb 1;22(3):593-607. PMID: 23139242; PMCID: PMC3542866.
b. Meyer JS, Howden SE, Wallace KA, Verhoeven AD, Wright LS, Capowski EE, Pinilla I, Martin JM, Tian S, Stewart R, **Pattnaik B**, Thomson JA, Gamm DM. Optic vesicle-like structures derived from human pluripotent stem cells facilitate a customized approach to retinal disease treatment. Stem Cells. 2011 Aug;29(8):1206-18. PMID: 21678528; PMCID: PMC3412675.
c. Phillips MJ, Jiang P, Howden S, Barney P, Min J, York NW, Chu LF, Capowski EE, Cash A, Jain S, Barlow K, Tabassum T, Stewart R, **Pattnaik BR**, Thomson JA, Gamm DM. A Novel Approach to Single Cell RNA-Sequence Analysis Facilitates In Silico Gene Reporting of Human Pluripotent Stem Cell-Derived Retinal Cell Types. Stem Cells. 2018 Mar;36(3):313-324. doi: 10.1002/stem.2755. Epub 2017 Dec 25. PMID: 29230913; PMCID: PMC5823737.
d. Shahi PK, Hermans D, Sinha D, Brar S, Moulton H, Stulo S, Borys KD, Capowski E, Pillers DM, Gamm DM, **Pattnaik BR**. Gene augmentation and readthrough rescue channelopathy in an iPSC-RPE model of congenital blindness. Am J Hum Genet. 2019 Feb; 104:1-9. Doi: 10.1016/j.ajhg.2018.12.019.

In the field of developmental biology, endocrine regulation of organ development is well studied, but we know very little about its role in eye development. Only a few anecdotal mentions were for oxytocin in the posterior retina. We reasoned that since oxytocin levels are well controlled during pregnancy and it plays an important role in child birth, oxytocin-oxytocin receptor system might have a role in eye development. We were first to discovered that OXT is present in the cone photoreceptors and OXTR is localized to RPE cells and controls cellular signaling. This is an important discovery, besides what it might do during eye development, which points to a cone photoreceptor and RPE cell-cell communication mediated by OXT-OXTR signaling.

a. Halbach P, Pillers DA, York N, Asuma MP, Chiu MA, Luo W, Tokarz S, Bird IM, **Pattnaik BR**. Oxytocin expression and function in the posterior retina: a novel signaling pathway. Invest Ophthalmol Vis Sci. 2015 Jan 15;56(2):751-60. PMID: 25593022, PMCID: PMC4554231
b. York N, Halbach P, Chiu MA, Bird IM, Pillers DM, **Pattnaik BR**. Oxytocin (OXT)-stimulated inhibition of Kir7.1 activity is through $PIP_2$-dependent $Ca^{2+}$ response of the oxytocin receptor in the retinal pigment epithelium in vitro. Cell Signal. 2017 Sep; 37:93-102. doi: 10.1016/j.cellsig.2017.06.005. Epub 2017 Jun 8. PMID: 28603013, PMCID: PMC5554455

Study of ion channel structure and function is my primary interest. We have used extensive electrophysiology, both at a single cell, retina tissue and *in vivo* rodent models, to study ion-channel function and regulation. Our use of electroretinogram has revealed pathophysiology of retinal disease and degeneration. Several of these discoveries are already impacting the field as one investigator notes, “the data makes a lot of sense and debunks a lot of preconceived notions’, on our study of the independent action of sigma receptor ligands. Although it is well known about the function of RPE apical membrane K+-channel, the identity and physiology of RPE basal membrane K+ conductance pathway are elusive. We showed that M-type potassium channel, that too KCNQ5 subtype underlies K+ conductance of the RPE basal membrane.

a. Liu X, Fu Y, Yang H, Mavlyutov T, Li J, McCurdy CR, Guo LW, **Pattnaik BR**. Potential independent action of sigma receptor ligands through inhibition of the Kv2.1 channel. Oncotarget. 2017 Jul 26;8(35):59345-59358. doi: 10.18632/oncotarget.19581. eCollection 2017 Aug 29. PMID: 28938641, PMCID: PMC5601737
b. Lee WH, Higuchi H, Ikeda S, Macke EL, Takimoto T, **Pattnaik BR**, Liu C, Chu LF, Siepka SM, Krentz KJ, Rubinstein CD, Kalejta RF, Thomson JA, Mullins RF, Takahashi JS, Pinto LH, Ikeda A. Mouse *Tmem135* mutation reveals a mechanism involving mitochondrial dynamics that leads to age-dependent retinal pathologies. Elife. 2016 Nov 15;5. pii: e19264. doi: 10.7554/eLife.19264. PMID: 27863209, PMCID: PMC5117855
c. **Pattnaik BR**, Hughes BA. Effects of KCNQ channel modulators on the M-type potassium current in primate retinal pigment epithelium. Am J Physiol Cell Physiol. 2012 Mar 1;302(5):C821-33. doi: 10.1152/ajpcell.00269.2011. Epub 2011 Nov 30. PMID: 22135213, PMCID: PMC3311298
d. Yang H, Fu Y, Liu X, Shahi PK, Mavlyutov TA, Li J, Yao A, Guo SZ, **Pattnaik BR**, Guo LW. Role of the sigma-1 receptor chaperone in rod and cone photoreceptor degenerations in a mouse model of retinitis pigmentosa. Mol Neurodegener. 2017 Sep 19;12(1):68. doi: 10.1186/s13024-017-0202-z. PMID: 28927431, PMCID: PMC5606113

Feedback regulation of photoreceptors is known to mediate center-surround response to decoding key visual information such as contrast enhancement and edge detection. Of the secondary retina neurons, horizontal cells synapse with the photoreceptor terminals. Several theories exist about the involvement of horizontal cells and photoreceptor synapse feed-back mechanisms. We were first to demonstrate that GABAc receptors are present in the mammalian cone photoreceptor and are suited to a mediated feed-back circuit for signal processing in the outer retina. We used both photoreceptors in culture and photoreceptor recording from mouse flat mount preparations to demonstrate functional GABAc receptors in the mammalian cone photoreceptor terminals.

a. Picaud S, **Pattnaik B**, Hicks D, Forster V, Fontaine V, Sahel J, Dreyfus H. GABAA and GABAC receptors in adult porcine cones: evidence from a photoreceptor-glia co-culture model. J Physiol. 1998 Nov 15;513 (Pt 1):33-42. PMID: 9782157; PMCID: PMC2231280.
b. **Pattnaik B**, Jellali A, Sahel J, Dreyfus H, Picaud S. GABAC receptors are localized with microtubule-associated protein 1B in mammalian cone photoreceptors. J Neurosci. 2000 Sep 15;20(18):6789-96. PMID: 10995822.

**Complete List of Published Work in My Bibliography:**
http://www.ncbi.nlm.nih.gov/myncbi/bikash.pattnaik.1/bibliography/43928320/public/?sort=date&direction=ascending

**D. RESEARCH SUPPORT**

Ongoing Research Support

R01 EY024995 (Pattnaik, PI) 09/30/15 – 08/31/19
NIH/NEI
Molecular Therapies for Leber Congenital Amaurosis Caused by KCNJ13 Mutations
The goal is to create an iPS-RPE model of KCNJ13 nonsense mutations, use to functional analyze Kir7.1 channel, test readthrough drugs to overcome truncation due to a premature stop codon and also test gene therapy to overcome disease phenotype.
Role: PI

Ateresa Avigail (Pattnaik, PI) 08/01/18 – 07/31/20
Restoration of potassium channel function using mouse models of LCA16 as a means to treat retinal channelopathies
GOAL: The goal of this project is to achieve preclinical restoration of sight in mouse models of LCA16 using gene therapy for KCNJ13.
Role: PI

R01 EY024588 (Stone et al.) 09/01/15 – 06/30/19
NIH/NEI & University of Iowa
Disease mechanisms in Best Disease
Currently, there is no treatment or cure for the Best disease. In this multicenter, multi-PI proposal, we will evaluate the pathophysiology of Best disease using RPE cells derived from induced pluripotent stem cells (iPSCs) from patients with known BEST1 mutations.
Role: Senior Scientist

U01 HL145792 (Gamm/Roy/Saha/Skala, MPIs) 09/05/18 – 06/30/23
NIH/NHLBI
Single Cell Profiling to Define Biomarkers of Photoreceptor Dysfunction After Gene Editing Within PSC-Derived Organoids. My role in the project is to help with the functional evaluation of light response detection by retinal organoids.
Role: Co-Investigator

MSN215499, (Saha, PI; Gong/Gamm/Pattnaik, Co-PI) 06/01/2018 - 05/31/2021
Gund-Harrington: Foundation For Fighting Blindness
Title: "*Gene Editing Nanomedicines to Correct Pathogenic Mutations in the Retina"*
Major Goal: This project utilizes novel methods to deliver gene editing tools into retinal cell types, specifically the RPE, in vivo and in vitro.
Role: Co-PI

657 (Pattnaik, PI) 01/01/18 – 12/31/18
Meriter Foundation
Retinopathy of Prematurity due to Oxytocin Deprivation
GOAL: In this study, we test the role that oxytocin signaling plays in the retina and determine circulating oxytocin in premature, full-term ad C-section babies to determine any correlation with ROP.
Role: PI

R01 EY022086 (Ikeda, PI) 07/01/18 – 06/30/23
NIH/NEI
Molecular Genetics of Age-Dependent Retinal Degeneration
My effort in this grant is to provide expert advice and to determine the electrophysiological phenotypes in mouse models with early onset of age-dependent retinal degeneration and synaptic defects, to determine the molecular mechanisms underlying these conditions.
Role: Co-Investigator

Completed Research Support
W81XWH-16-0775 (Washington, PI) 09/30/16 – 05/31/18
USAMRAA & University of Pittsburgh
A Comprehensive Approach to Whole Eye Transplantation: Building a Scientific Foundation for New Therapies in Vision Restoration
Role: Co-Investigator

R24 EY022883 (Sheibani, PI) 03/01/13 – 02/28/18
NIH/NEI
Novel Anti-angiogenic Peptides for Treatment of Exudative AMD
The specific goals of this project are to (1) determine whether the peptide mechanisms of action in the eye are through their mimicry of these natural inhibitors; (2) Produce and identify optimal new derivatives of benchmark peptides best suited to intravitreal treatment of AMD, where these are ranked by efficacy in CNV models, individually and in combination; (3) Select and test the most active peptide(s) and their most slowly cleared formulations for efficacy in AMD models.
Role: Co-Investigator

R01 EY022678 (Guo, PI) 09/01/12 – 07/31/17
NIH/NEI
Sigma-1 Chaperone-Mediated in vivo Neuroprotection in the Retina
The ultimate goal of this project is to develop new methods for the rescue of retinal neurodegeneration by exploiting a unique endogenous neuroprotective agent, the σ1R chaperone, whose anti-apoptotic properties are being uncovered
Role: Co-Investigator

233-PRJ73JH (Pattnaik, PI) 06/01/13 – 05/31/16
Anonymous Donation
LCA16 Research
The goal of this project is to study the cause of LCA16 so that new treatment for ion channel function rescue can be achieved.
Role: PI