BIOGRAPHICAL SKETCH

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NAME: SWAROOP, ANAND

eRA COMMONS USER NAME (credential, e.g., agency login): swaroopa

POSITION TITLE: Senior Investigator and Chief, Neurobiology, Neurodegeneration & Repair Laboratory

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
G.B. Pant University, Pantnagar, India	M.Sc.	06/1977	Biochemistry
Indian Institute of Science, Bangalore, India	Ph.D.	06/1982	Biochemistry (laboratory of Prof. T. Ramasarma)
Dept. of Molecular Biophysics & Biochemistry, Yale University, New Haven, CT	Post-doc	06/1986	Biochemistry (laboratory of Prof. Alan Garen)
Dept. of Human Genetics, Yale University School of Medicine, New Haven, CT	Assoc. Res. Scientist	07/1987	Laboratory of Prof. Uta Francke
Dept. of Human Genetics, Yale University School of Medicine, New Haven, CT	NRSA Postdoc	08/1988	Laboratory of Prof. Sherman M. Weissman
Dept. of Human Genetics, Yale University School of Medicine, New Haven, CT	Assoc. Res. Scientist	09/1989	Laboratory of Prof. Sherman M. Weissman

A. Research Statement

The studies in my laboratory have focused primarily on (i) genetic and epigenetic regulation of retinal photoreceptor development, evolution and aging, (ii) genetic defects and mechanisms of photoreceptor dysfunction in retinal neurodegeneration, especially focusing on retinitis pigmentosa and Leber congenital amaurosis, (iii) genetics and biology of age-related macular degeneration, and (iv) design of new therapeutic paradigms using cell, gene or small molecule-based approaches.

Total Publications: 396. Scopus *h*-index, 82; Scopus Citations, 36,006; Google Scholar *h*-index, 95
A complete list of publications can be obtained at https://pubmed.ncbi.nlm.nih.gov/?term=swaroop+a

B. Positions and Employment

1990-96	Assistant Professor, Department of Ophthalmology, University of Michigan, Ann Arbor, MI.
1990-98	Assistant Professor, Department of Human Genetics, University of Michigan, Ann Arbor, MI.
1991-2007	Faculty Member, Graduate Program in Cellular & Molecular Biology.
1996-2000	Associate Professor, Department of Ophthalmology & Visual Sciences.
1996-2007	Faculty Member, Neuroscience Graduate Program.
1998-2002	Associate Professor, Department of Human Genetics
2000-2007	Professor, Department of Ophthalmology and Visual Sciences
2000-2000	Scientist (on sabbatical for 6 months), Laboratory of Genetics, Salk Institute, La Jolla, CA
2001-2007	Coordinator/Director, Center for Retinal and Macular Degeneration, University of Michigan
2002-2007	Professor, Department of Human Genetics
2003-2007	Harold F. Falls Collegiate Professor of Ophthalmology & Visual Sciences
Sept 2007–	Senior Investigator and Chief, Neurobiology-Neurodegeneration and Repair Laboratory (N-NRL), National Eye Institute, National Institutes of Health, Bethesda, MD.
2015–2016	Distinguishing Medical Scientist (visiting) for Prof. P.N. Chhuttani Chair, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

Select Scientific Activities

- Chair, Appointments and Promotions Committee at UM Ophthalmology & Visual Sciences, 2005–2007.
- Member, UM Medical School Advisory Committee for Appointments, Promotions and Tenure, 2006–2007.
- Chair, Organizing Committee, NEI 40th Anniversary Symposia on "Genetics and Genomics in Vision", April 16-17, 2009; "Neuroscience and Vision", November 19-20, 2009; "Focus on Glaucoma", February 18-19, 2010; "Translational Research and Vision", June 24-25, 2010; Search Committee for Basic Science Tenure Track Investigator(s), NINDS. 2010; Review Committee for NiPSCC, NIH. 2010; Search Committee for NEI Clinical Tenure Track position, 2010-11. Scientific Advisory Board and Selection Committee of the Institut de la Vision, Paris, France. 2011. Genetics of Health and Disease study section, 2012. Reviewer for NIH Director's Challenge Awards, 2012. The Thiel Foundation, 2012. Federal Panel for NEI Audacious Goals Initiative, 2012-13. International Advisory Committee, Asia-ARVO in New Delhi, India, 2013. Genetics Advisory Committee, The Diabetic Retinopathy Clinical Research Network (DRCR.net). Scientific Advisory Board, GenSight Biologics, Paris, France. 2014. NEI-IRP Planning Committee 2014. Scientific Advisory Board, FFB Usher Syndrome therapy, 2014.
- Co-Editor with Dr. Emily Chew for Age-related Macular Degeneration: From Clinic to Genes and Back to Patient Management. Advances in Experimental Medicine and Biology, volume 1256. Springer. 2021
- Reviewer for several journals, including Cell journals, PLoS journals, Nature journals, Science, AJHG, IOVS, HMG, JBC, PNAS, JCI, J. Neurosci, NEJM, among others
- Editorial Boards. *IOVS*, June 2002–Dec 2007. *Molecular Vision*, 1995– . *Cilia*, 2011 – . PLoS One, 2012-. Advisory Board Member, *EBioMedicine*, 2017– **;** Guest Editor, Special Issue on Vision and Novel Therapeutics, *Clinical Genetics*, Wiley. August 2013. Guest Editor for manuscripts: *PNAS*, *PLoS Genetics.* Member, Editorial Advisory Board, *Progress in Retinal and Eye Research, March 2018 – .*
- Reviewer: The Foundation Fighting Blindness; The Wellcome Trust, U.K.; Comitato Promotore Telethon, Italy; The South Africa Retinitis Pigmentosa Foundation; The Medical Research Council of Canada; Canadian Foundation Fighting Blindness; ANR-BBSRC, UK; Juvenile Diabetes Research Foundation, National Science Foundation; Austrian Science Fund; ANR/ French National Research Agency, France. Deutsche Forschungsgemeinschaft (DFG), Germany; Action Medical Research for Children, U.K.; Medical Research Council, UK.; Swiss National Science Foundation, Switzerland; Israel Science Foundation, Israel; Netherlands Organisation for Scientific Research, Netherlands; Neuroscience and Mental Health Board, Medical Research Council, UK; Macula Society, UK; Grants Review Panel for Priority Program on "Gene and cell-based therapies to counteract neuroretinal degeneration", DFG, Germany. 2018, 2019. Austrian Science Fund, 2019. Wellcome Trust-DBT India Alliance, 2019, Medical Research Council, UK, 2019, Israel Ministry of Science & Technology, 2020. Grants Reviewer, Israel Science Foundation, July 2020. Reviewer, Retina, UK. Dec 2021. Grants Review Panel for Deutsche Forschungsgemeinschaft (DFG) (eBer-21-46107) on "Gene and cell based therapies to counteract neuroretinal degeneration", Nov 8-9, 2021. And, on "Towards immune-modulatory and anti(lymph)angiogenic therapies for age-related blinding eye diseases", April 7, 2022. Division of Biology and Medicine, Swiss National Science Foundation, Bern, Switzerland. 2022. Transformative Research Awards Panel, Fighting Blindness Canada, Toronto, Canada. 2022.
- Federal Evaluator, "Follow that Cell" Challenge. NIH Common Fund, NIH. 3D Retina Organoid Challenge, 2017, NEI/NIH. Co-Chair, 2020 Stadtman Investigator Neurodevelopment search committee. Co-Chair, 2020 Stadtman Investigator Neurodevelopment search committee. Member, NEI Quad Review Committee, 2021**.** Member, 2021 NIH Stadtman Investigator Neurodevelopment Search Committee. Member, Genes to Disease Mechanisms workgroup for 2021 NEI Strategic Plan. Member, Search Committee for Senior Scientist and Director of the Translational Bioengineering Program (TBP), Early Translation Branch, NCATS, NIH. 2022 – .
- Scientific Advisory Committee, Institut de la Vision, Paris. 2022 – .
- Member (Current and Past): AAAS, ASHG, SFN, Association for Research in Vision and Ophthalmology, American Society for Biochemistry and Molecular Biology**,** Indian Institute of Science Alumni Association of North America, Alumni Almamater Advancement Association, Pantnagar, India**,** Society for Redox Biology and Medicine
- Senior Advisory Group member, NIH India. Member, Federation of AANHPI Networks (FAN), NIH
- *Over 300 invited talks* at institutions and conferences, including several named and keynote lectures.

Select Honors and Awards

- The Foundation Fighting Blindness Board of Directors Award in recognition of outstanding research achievements, January 26, 2007.
- Distinguished Faculty Lectureship Award, 2007. The highest honor bestowed by the Univ of Michigan Medical School on a scientist/faculty member.
- Bireswar Chakrabarti Memorial Oration, awarded by Indian Eye Research Group at their 17th annual meeting in Madurai, India. July 26-27, 2008.
- Inducted in the inaugural class of ARVO Fellows, ARVO Silver Fellow, 2009. ARVO Gold Fellow, 2012.
- Director's Award, National Eye Institute, 2010.
- Alcon Research Institute Award, 2011.
- NIH Director's Ruth L. Kirschstein Award "For exemplary performance while demonstrating significant leadership, skill and ability in serving as a mentor," June 2013.
- Distinguished Medical Scientist (visiting), Prof. P.N. Chhuttani Chair, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. July 2015, Feb-Mar 2016.
- 2019 Outstanding Alumnus of College of Basic Sciences & Humanities, G.B. Pant University of Agriculture & Technology, Pantnagar, India. November 2019.
- 2020 National Eye Institute Director's Diversity Champion Award "in recognition of a long-standing commitment to diversity, equity and inclusion."
- 2022 National Eye Institute Director's Award "in recognition of trans-institute collaboration and exemplary teamwork to distill, prioritize, and translate the NEI Strategic Plan into concrete implementable actions."

C. Contributions to Science

1. Genetic and Epigenetic Regulation of Retinal Development, Aging and Evolution

Our goals are to elucidate gene regulatory networks that guide differentiation of photoreceptor subtypes in the mouse and human retina and in retinal organoids derived from embryonic or induced pluripotent stem cells (iPSCs). We are investigating transcriptional, epigenetic as well as post-transcriptional regulationof retinal development, aging and evolution. NRL, discovered in my laboratory, is a critical determinant of photoreceptor cell fate; its loss results in complete lack of rods with concomitant gain of S-cones, and ectopic expression of NRL generates rods from photoreceptor precursors. Disruption of gene networks mediated by NRL and it's interactor CRX leads to vision impairment and blindness.

1. Mears AJ, Kondo M, Swain PK, Takada Y, Bush RA, Saunders TL, Sieving PA, **Swaroop A**: Nrl is required for rod photoreceptor development. *Nat Genet* 29:447-452, 2001.
2. Akimoto M, Cheng H, Zhu D, Brzezinski JA, …… Glaser T, **Swaroop A**: Targeting of GFP to newborn rods by Nrl promoter and temporal expression profiling of flow-sorted photoreceptors. *Proc Natl Acad Sci. USA* 103:3890-3895, 2006. PMID: 16505381
3. Oh ECT, Khan N, Novelli E, Khanna H, Strettoi E, **Swaroop A**: Transformation of cone precursors to functional rod photoreceptors by bZIP transcription factor NRL. *Proc Natl Acad Sci USA* 104:1679-1684, 2007. PMID: 17242361
4. **Swaroop A**, Kim D, Forrest D: Transcriptional regulation of photoreceptor development and homeostasis in the mammalian retina. *Nat Rev Neurosci*. 11:563-576, 2010. PMID: 20648062
5. Kim J-W, Yang H-J, Oel AP, Brooks MJ, Jia L, Li W, Allison WT, **Swaroop A**: Recruitment of rod photoreceptors from short-wavelength-sensitive cones during the evolution of nocturnal vision in mammals. *Dev Cell* 37, 520-532, 2016. PMID: 27326930
6. Corso-Diaz X, Gentry J, Rebernick R, Jaeger C, Brooks M, van Asten F, Kooragayala K, Gieser L, Nellissery J, Covian R, Cogliati T, Mondal AK, Jiang K, **Swaroop A**: Genomewide profiling identifies DNA methylation signatures of aging in rod photoreceptors associated with alterations in energy metabolism. *Cell Rep.* 31:107525, 2020. PMID: 32320661
7. Campello L, Singh N, Advani J, Mondal AK, Corso-Diaz, X, **Swaroop A**: Aging of the retina: Molecular and metabolic turbulences and potential interventions. *Annu Rev Vis Sci*, 2021. doi: 10.1146/annurev-vision-100419-114940. PMID: 34061570
8. Liang X, Brooks MJ, **Swaroop A**: Developmental genome-wide occupancy analysis of bZIP transcription factor NRL uncovers the role of c-Jun in early differentiation of rod photoreceptors in the mammalian retina. *Hum Mol Genet.* 2022 July 01:ddac143. Doi: https://doi.org/10.1093/hmg/ddac143. PMID: 35776116
9. Marchal C, Singh N, Batz Z, Advani J, Jaeger C, Corso Diaz X, **Swaroop A**: High-resolution genome topology of human retina uncovers super enhancer-promoter interactions at tissue-specific and multifactorial disease loci. *Nat Commun.* 13:5827, 2022. doi: 10.1038/s41467-022-33427-1. PMID: 36207300

10. Liang X, Yadav SP, Batz ZA, Nellissery J, **Swaroop A**: Protein kinase CK2 modulates the activity of Maf-family bZIP transcription factor NRL in rod photoreceptors of mammalian retina. *Hum Mol Genet.* 2022 Oct 13:ddac256. doi: 10.1093/hmg/ddac256. PMID: 36226585
11. Weinberg J, Gaur M, **Swaroop A**, Taylor A: Proteostasis in aging-associated ocular disease. *Mol Aspects Med*. 88:101157, 2022. doi: 10.1016/j.mam.2022.101157. PMID: 36459837

2. Inherited retinal degeneration, development of pre-clinical models and therapies

My scientific career in the retina began with X-linked forms of retinitis pigmentosa (RP) and later expanded to other inherited diseases such as Leber congenital amaurosis (LCA) and ciliopathies with photoreceptor death as a highly penetrant phenotype. Over the years, my laboratory (in collaboration with clinicians worldwide) has identified mutations in two genes - *RPGR* and *RP2* - in hundreds of RP patients and discovered that mutated *RPGR* constitute the most common cause of RP, accounting for 15-20% of all patients. We developed several mouse models for *RPGR* and *RP2* disease and demonstrated successful AAV-based gene replacement therapy for both forms in preclinical models. My group has also been involved in discovering several RP and LCA genes. In collaborative studies, we have identified mutations in genes including *NRL*, *NR2E3*, *CRX*, *CEP290*, *NPHP5*, *RD3*, *RD11, CERKL, GUCY2D*, *EYS*, *ALMS1*, *IDH3A*, *CEP78*, among others.

Primary cilium acts as the sensory organelle in most cells and altered biogenesis or function of cilium can lead to pleiotropic phenotypes (termed ciliopathies). My lab identified a cilia-centrosomal gene *CEP290* by studying the retinal degeneration (rd) 16 mouse model and as a cause of Joubert syndrome. CEP290 has turned out to be a very important protein that is likely involved in ciliary gating during photoreceptor outer segment biogenesis. Mutations in *CEP290* account for 20-25% of LCA and a number of other syndromic ciliopathies. We have also been involved in elucidating how mutations in several ciliopathy genes (specifically *CEP290*, *NPHP5* and *CC2D2A*) cause defects in cilia biogenesis using animal models and stem cell derived organoids and suggested novel insights for developing therapy.

Our focus has also been on developing gene-independent therapy paradigms by identifying common cellular pathways that are induced in early stages of retinal degeneration and targeting specific nodal proteins for drug discovery. Given that rod photoreceptors are more vulnerable to genetic insult and many RP genes are highly expressed in rods, our lab used AAV-delivered CRISPR-CAS9 to knockdown the master regulator NRL in rods and demonstrated rescue of cone function in different mouse models. We have identifying novel targets for drug discovery to rescue photoreceptor cell death in inherited retinal degeneration by network analysis and machine learning.

1. Breuer DK, Yashar BM, …..Jacobson SG, Sieving PA, **Swaroop A**: A comprehensive mutation analysis of *RP2* and *RPGR* in a North American cohort of families with X-linked Retinitis Pigmentosa. *Am J Hum Genet* 70:1545-1554, 2002. Errata: *Am J Hum Genet* 71:1258, 2002.
2. Chang B, Khanna H, ……. Williams DS, Heckenlively JR, **Swaroop A**: In-frame deletion in a novel centrosomal/ciliary protein CEP290/NPHP6 perturbs its interaction with RPGR and results in early-onset retinal degeneration in the *rd16* mouse. *Hum Mol Genet*. 15:1847-1857, 2006.
3. Roger JE, Hiriyanna A, Gotoh N, Hao H, Cheng DF, Ratnapriya R, Kautzmann MA, Chang B, **Swaroop A**: OTX2 loss causes rod differentiation defect in CRX-associated congenital blindness. *J Clin Invest*. 124:631-643, 2014. PMID: 24382353
4. Veleri S, Manjunath SH, Fariss RN, May-Simera H, ……. Rachel RA, Li T, Dong L, **Swaroop A**: Ciliopathy-associated gene *Cc2d2a* promotes assembly of subdistal appendages on the mother centriole during cilia biogenesis. *Nat Commun*. 5:4207, 2014. PMID: 24947469
5. Wu Z, Hiriyanna S, Qian H, Mookherjee S, Campos M, Gao C, Fariss R, Sieving PA, Li T, Colosi P, **Swaroop A**: A long-term efficacy study of gene replacement therapy for *RPGR*-associated retinal degeneration. *Hum Mol Genet.* 24:3956-3970, 2015. PMID: 25877300
6. Chen HY, Kelley RA, Li T, **Swaroop A**: Primary cilia biogenesis and associated retinal ciliopathies. *Semin Cell Dev Biol.* S1084-9521:30167-3, 2020. PMID: 32747192
7. Hargrove-Grimes P, Mondal AK, Gumerson J, Nellissery J, Aponte A, Gieser L, Qian H, Fariss RN, Bonifacino JS, Li T, **Swaroop A**: Loss of endocytosis-associated RABGEF1 causes aberrant morphogenesis and altered autophagy in photoreceptors leading to retinal degeneration. *PLoS Genet.* 16:e1009259, 2020. PMID: 33362196. PMCID: PMC7790415
8. Chen HY, Lehmann OJ, **Swaroop A**: Genetics and therapy for pediatric eye diseases. *EBioMedicine* 67:103360, 2021. PMID: 33975254
9. Jiang K, Mondal AK, Adlakha Y, Gumerson J, Aponte AM, Gieser L, Kim JW, Boleda A, Brooks MJ, Nellissery J, Fox D, Balaban RS, Covian R, **Swaroop A***: Multiomics analyses reveal early metabolic imbalance and

mitochondrial stress in neonatal photoreceptors leading to cell death in *Pde6b*$^{rd1/rd1}$ mouse model of retinal degeneration. *Hum Mol Genet.* 31:2137-2154, 2022. doi: 10.1093/hmg/ddac013. PMID: 35075486. [*Co-corresponding authors]
10. Smith AJ, Advani J, Brock DC, Nellissery J, Gumerson J, Dong L, Aravind L, Kennedy B, **Swaroop A**: GATD3A, a mitochondrial deglycase with evolutionary origins from gammaproteobacteria, restricts the formation of advanced glycation endproducts. *BMC Biol*. 20:68, 2022. Doi: 10.1186/s12915-022-01267-6. PMID: 35307029
11. Nagel-Wolfrum K, Fadl BR, Becker MM, Wunderlich KA, Schafer J, Sturm D, Gur B, Kaplan L, Goldmann T, Brooks M, Starostik MR, Lokhande A, Apel M, Fath KR, Stingl K, Kohl S, Andrade M, Vetter JM, Pfeiffer N, Grosche A, **Swaroop A**, Wolfrum U: Expression and subcellular localization of *USH1C*/harmonin in human retina provides insights into pathomechanisms and therapy. *Hum Mol Genet.* 2022. Doi:10.1093/hmg/ddac211. PMID: 35997788

3. Genetic architecture of age-related macular degeneration

In late 1990s when genetic underpinnings of AMD were less than clear, our group was among the first to identify genetic loci for advanced AMD by high-resolution genome scan (2004), the association of Complement Factor H (Y402H), and even larger contribution of numerous non-coding variants to disease (2005-2006). In 2010, we reported a large genome-wide association study (GWAS) identifying several additional AMD susceptibility loci. I was one of the co-leaders in the international consortium that described 52 independent variants at 34 genetic loci associated with AMD in a large case-control study of almost 34,000 individuals using data from over 12 million variants. In addition to defining novel AMD-associated common variants, this study pointed to genetic causality based on several rare coding variants. We hypothesized that most associated variants impact AMD progression and pathology through their effect on context- or tissue-specific gene regulation. Our group generated transcriptomes of over 400 human donor retinas from healthy and disease individuals and performed eQTL analysis to uncover the role of non-coding variants in regulating the expression of retinal genes (2019). Integrating this data with GWAS of AMD has helped in identifying the target genes at six loci. This study provides the largest resource of retinal transcriptome and eQTLs and identified the genes and pathways associated with AMD. We have now identified retinal mQTLs and sQTLs and deciphered their relationship to AMD candidate target genes. A detailed genome-wide transcriptional regulatory map is being constructed for the human retina with a goal to identify how genetic variants modify or cause healthy and disease retinal phenotypes.

1. Li M, Atmaca-Sonmez P, Othman M, …. Li Y, Liang L, Zareparsi S, **Swaroop A**, Abecasis GR: CFH haplotypes without the Y402H coding variant show strong association with susceptibility to age-related macular degeneration. *Nature Genet.* 38:1049-1054, 2006. PMID: 16936733
2. Chen W, Stambolian D, …… Gorin MB, Abecasis GR, **Swaroop A**: Genetic variants near TIMP3 and high-density lipoprotein-associated loci influence susceptibility to age-related macular degeneration. *Proc Natl Acad Sci USA.* 107:7401-7406, 2010. PMID: 20385819
3. Fritsche LG, Farris RN, Stambolian D, Abecasis GR, Curcio CA, **Swaroop A**: Age-related macular degeneration: genetics and biology coming together. *Annu Rev Genomics Hum Genet.* 15:151-171, 2014. PMID: 24773320
4. Fritsche L, Igl W, ……Stambolian D, Haines JL, Iyengar SK, Weber BHF, Abecasis GR, Heid IM: A large genome-wide association study of age-related macular degeneration highlights contributions of rare and common variants. *Nat Genet*. 48:134-143, 2016. [AS is one of the 18 group leaders for AMDGene Consortium] PMID: 26691988.
5. Ratnapriya R, Sosina OA, Starostik MR, …., Gieser L, Pietraszkiewicz A, Montezuma SR, Chew EY, Battle A, Abecasis GR, Ferrington DA, Chatterjee N, **Swaroop A**: Retinal transcriptome and eQTL analyses identify genes associated with age-related macular degeneration. *Nat Genet*. 51:606-610, 2019. PMID:30742112. Correction, PMID:31068672, PMCID : PMC6441365
6. Marchal C, Singh N, Batz Z, Advani J, Jaeger C, Corso Diaz X, **Swaroop A**: High-resolution genome topology of human retina uncovers super enhancer-promoter interactions at tissue-specific and multifactorial disease loci. Under review. Preprint at https://doi.org/10.21203/rs.3.rs-1650982/v1

4. Stem Cell based modeling and therapies of retinal diseases

My laboratory has been developing therapies for LCA caused by *CEP290*, *NPHP5* and *CRX* using stem cell-based approaches combined with gene therapy and small molecule screening. We have modified and simplified a widely used protocols for efficient differentiation of retinal organoids from mouse and human pluripotent stem cells. We also took a novel approach to culture retinal organoids in a microgravity bioreactor to enhance delivery of oxygen and nutrients. Bioreactor organoids better

recapitulated temporal development of *in vivo* retina and displayed improved survival of multiple cell types including light-sensing photoreceptors compared to those cultured in static environment. We used retinal organoids from induced pluripotent stem cells derived from patients with *CEP290*, *NPHP5* and *CRX* mutations for disease modeling. For dominant *CRX*-LCA, we have established an AAV gene therapy approach for which a patent application has been filed by NEI.

We are developing gene therapy protocols using adeno-associated virus (AAV) for *CEP290*-LCA. As *CEP290* is a large gene (coding for a 290 kDa protein), we are examining AAV vectors carrying shorter overlapping CEP290 domains to rescue phenotypes in patient-derived retinal organoids. In addition, organoid-derived photoreceptors have been employed for high throughput screening to rescue *CEP290*-LCA phenotypes in retinal organoids. A multiplex screening platform was designed for selecting drug candidates that maintain photoreceptor survival (in collaboration with NCATS). Five positive hits that survived multiple screening assays are good candidates for potential therapeutic intervention and are part of another patent application submitted by NEI.

1. Kaewkhaw R, Kaya KD, Brooks M, Homma K, Zou J, Chaitankar V, Rao M, **Swaroop A**: Transcriptome dynamics of developing photoreceptors in 3-D retina cultures recapitulates temporal sequence of human cone and rod differentiation revealing cell surface markers and gene networks. *Stem Cells* 33:3504-3518, 2015. PMID: 26235913.
2. Shimada H, Lu Q, Insinna-Kettenhofen C, ….., Cogliati T, Westlake CJ*, **Swaroop A***: Distinct ciliogenesis defects revealed by in vitro modeling of CEP290-associated Leber congenital amaurosis and Joubert syndrome. *Cell Rep* 20:384-396, 2017. PMID:28700940
3. DiStefano T, Chen HY, Panebianco C, Kaya KD, Brooks MJ, Gieser L, Morgan NY, Pohida T, **Swaroop A**: Accelerated and improved differentiation of retinal organoids from mouse pluripotent stem cells in rotating wall bioreactors. *Stem Cell Rep.* 10:300-313, 2018. PMID: 29233554
4. Kaya KD, Chen HY, ……, Welby E, **Swaroop A**: Transcriptome-based molecular staging of human stem cell-derived organoids uncovers accelerated photoreceptor differentiation by 9-cis retinal. *Mol Vis*. 25:663-678, 2019. PMID: 31814692
5. Mahato B, Kaya KD, Fan Y, Sumien N, Shetty RA, Wei Z, Davis D, Mock T, Batabyal S, Ni A, Mohanty S, Han Z, Farjo R, Forster MJ, **Swaroop A**, Chavala SH: Pharmacologic fibroblast reprogramming into photoreceptors restores vision. *Nature* 581:83-88, 2020. PMID: 32376950
6. Kruczek K, **Swaroop A**: Pluripotent stem cell-derived retinal organoids for disease modeling and development of therapies. *Stem Cells*, 2020. doi: 10.1002/stem.3239. PMID: 32506758
7. Kruczek K, Qu Z, …….. Campello L, Brooks BP, Wu Z, **Swaroop A**: Gene therapy of dominant CRX-Leber congenital amaurosis using patient stem cell-derived retinal organoids. *Stem Cell Reports* 16:252-263, 2021. PMID: 33513359. PMCID: PMC7878833
8. Kruczek K, Qu Z, Welby E, Shimada H, Hiriyanna S, English MA, Zein WM, Brooks BP, **Swaroop A**: *In vitro* modeling and rescue of ciliopathy associated with *IQCB1/NPHP5* mutations using patient-derived cells. *Stem Cell Rep*. 17:2172-2186, 2022. doi: 10.1016/j.stemcr.2022.08.006. PMID: 36084637.
9. Chen HY, Swaroop M, Papal S, Mondal AK, Tawa GJ, Regent F, Shimada H, Nagashima K, de Val N, Jacobson SG, Zheng W, **Swaroop A**: Reserpine maintains photoreceptor survival in retinal ciliopathy by resolving proteostasis imbalance and ciliogenesis defects. *eLife*, under review. Preprint 10.1101/2022.09.14.22279917 posted on medRxiv: https://medrxiv.org/cgi/content/short/2022.09.14.22279917v1