Wei Liu, Ph.D.., Ph.D.

Positions:

Associate Professor, Depts. of Ophthalmology and Genetics

Research interests:

Millions of people are suffering from retinal degenerations due to disease mutations. Since the mammalian retina does not regenerate, loss of retinal neurons is permanent, causing incurable blindness. Regenerative medicine of the retina provides hope for saving and restoring vision.
Research in my laboratory is focused on the molecular mechanisms underlying retinal differentiation and inherited retinal degenerations, aiming to make contributions to regenerative medicine of the retina. To achieve our research goals, we utilize interdisciplinary approaches, including engineered mice, pluripotent stem cell-derived organoids, and genomic and proteomic assays. One main project is to study the functions of homeodomain transcription factors Six3 and Six6 in retinal differentiation. Using genetic and genomic approaches, our studies have demonstrated that Six3, by itself at early stages and together with Six6 at later stages, is required for retinal differentiation. We are now studying how Six3 and Six6 execute their functions in retinal development. Another main project is to model human retinal differentiation and the functions of disease gene CRB1 using human pluripotent stem cell-derived organoids. Human retinal tissues have become increasingly important for studying retinal differentiation and degenerations because the human retina differ from that of mice in numerous aspects, including the anatomy, cell types, and gene expression. We recently established a retinal differentiation system that faithfully recapitulates retinal development in vivo. Our system is well recognized by the field, as indicated by publications and prizes in the NEI 3-D Retina Organoid Challenge. Using our organoid system, we are studying the functions of CRB1 using engineered stem cell lines that mimic disease mutations. Human organoid models of CRB1 disease mutations are attractive since CRB1 mutations in mice does not faithfully recapitulate disease phenotypes. We expect to elucidate CRB1 functions in human retinal tissues, facilitating therapeutic development for CRB1-associated retinal disease.

Current grant funding:

R01EY022645, Wei Liu (PI) National Eye Institute, NIH	5/1/2013 – 08/31/2023 Title: Gene regulation of retinal cell differentiation
R21EY029806, National Eye Institute, NIH	08/01/2019 – 07/30/2022 (NCT) Title: Modeling CRB1-related retinal disease using 3-D human retinal organoids

Recent publications (selected):

1. Guo X, Zhou J, Starr C, Mohns EJ, Li Y, Chen E, Yoon Y, Kellner CP, Tanaka K, Wang H, **Liu W**, LR, Demb JB, Crair MC, and Chen B. "Preservation of vision after CaMKII-mediated protection of retinal ganglion cells." Published online July 22, 2021 in **Cell**. DOI: 10.1016/j.cell.2021.06.031

2. Li, B., Zhang, T., **Liu, W**., Wang, Y., Xu, R., Zeng, S., Zhang, R., Zhu, S., Gillies, M.C., Zhu, L., et al. (2020). Metabolic Features of Mouse and Human Retinas: Rods versus Cones, Macula versus Periphery, Retina versus RPE. **iScience** 23, 101672.

3. Kim S, Lowe A, Dharmat R…Zhou Z, Chen R, **Liu W** (2019). **PNAS**, doi.org/10.1073/pnas.1901572116.

4. Diacou R, Zhao Y, Zheng D, Cvekl A, **Liu W** (2018) Six3 and Six6 are jointly required for the maintenance of multipotent retinal progenitors through both positive and negative regulation. **Cell Reports** (2018) 25: 2510-2523. https://doi.org/10.1016/j.celrep.2018.10.106

5. **Liu W**¶, Cvekl A (2017) Six3 in a small population of progenitors at E8.5 is required for neuroretinal specification via regulating cell signaling and survival in mice. **Developmental Biology**. http://dx.doi.org/10.1016/j.ydbio.2017.05.026. ¶ Corresponding author.

6. Lowe A, Harris R, Bhansali P, Cvekl A, **Liu W**. Intercellular adhesion-dependent cell survival and ROCKregulated actomyosin-driven forces mediate self-formation of a retinal organoid. **Stem Cell Reports** (2016), http://dx.doi.org/0.1016/j.stemcr.2016.03.011.