

Stanford



Yang Hu, MD, PhD

Associate Professor of Ophthalmology

Bio

ACADEMIC APPOINTMENTS

- Associate Professor, Ophthalmology
- Member, Bio-X
- Member, SPARK at Stanford
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Douglas Johnson Award for Glaucoma Research, BrightFocus Foundation (2013)
- The Knights Templar Eye Foundation Travel Fellowship Award, The Knights Templar Eye Foundation/ISER (2016)
- William & Mary Greve Special Scholar Award, Research to Prevent Blindness (2018)
- Catalyst for a Cure Research Consortium-3, Glaucoma Research Foundation (2019)

PROFESSIONAL EDUCATION

- Postdoc, Harvard Medical School , Neuroscience (2009)
- Ph.D, Weill Medical College of Cornell University , Neuroscience (2006)
- Residency, Beijing Friendship Hospital , Ophthalmology (1998)
- MD, Beijing Medical University , Medicine (1996)

LINKS

- Hu Lab Site: <http://med.stanford.edu/hulab.html>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Regenerative and neuroprotective therapies have long been sought for CNS neurodegenerative diseases but none have been found. That there is no curative neuroprotective or restorative therapy for neurodegeneration is a central challenge for human health. My lab focuses on the mechanisms responsible for neuronal degeneration and axon regeneration after injury or diseases with the goal of building on this understanding to develop effective combined strategies to promote neuroprotection and functional recovery: 1) Through established collaborations with experts in immunology, physiology and cancer, we were the first to demonstrate that axon-injury induced neuronal ER stress is a common mechanism for both RGC soma and axon neurodegeneration. We are currently developing ER stress modulators and AAV-mediated gene therapy strategies for neuroprotection. 2) We are pioneering in the application of AAV-mediated therapies for safer and more effective treatment of glaucoma and related optic neuropathies. We have identified an RGC-specific promoter for CRISPR/Cas9-based gene therapy in RGCs. We

are screening mutated AAV capsid libraries to identify AAVs that can specifically infect RGCs but not other retinal cells and make RGC targeting more precise, including in human tissues. 3) We have recently developed novel inducible mouse and NHP glaucoma models that faithfully replicates a secondary post-operative glaucoma following vitreoretinal surgeries; and a genetic mouse glaucoma model to mimic normal tension glaucoma. 4) Through collaboration with experts in adaptive optics, machine deep learning and genetics, we are developing reliable morphological and functional in vivo readouts of RGCs and illustrating genetic causes of RGC degeneration. 5) Previously, we performed molecular dissection of the PTEN/mTOR pathway in mouse RGCs in vivo and illuminated the mechanisms by which AKT interacts with mTORC1 and mTORC2 and their downstream effectors S6K1, 4E-BP and GSK3 β to regulate optic nerve regeneration. We currently use a newly developed tracing method to purify regenerating RGCs and survival but non-regeneration RGCs, by which we identified true axon regeneration-associated genes. In summary, our work emphasizes understanding fundamental molecular mechanisms while maintaining a consistent focus on clinically relevant scenarios and therapies that will allow us to translate lab discoveries into effective vision restoration treatments.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Kathy Heng

Postdoctoral Faculty Sponsor

Fuyun Bian, Xue Feng, Dong Liu, Liping Liu, Ming Yang

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **Silicone Oil-Induced Glaucomatous Neurodegeneration in Rhesus Macaques.** *International journal of molecular sciences*
Moshiri, A., Fang, F., Zhuang, P., Huang, H., Feng, X., Li, L., Dalal, R., Hu, Y.
2022; 23 (24)
- **Longitudinal in vivo Ca²⁺ imaging reveals dynamic activity changes of diseased retinal ganglion cells at the single-cell level.** *Proceedings of the National Academy of Sciences of the United States of America*
Li, L., Feng, X., Fang, F., Miller, D. A., Zhang, S., Zhuang, P., Huang, H., Liu, P., Liu, J., Sredar, N., Liu, L., Sun, Y., Duan, et al
2022; 119 (48): e2206829119
- **Maprotiline restores ER homeostasis and rescues neurodegeneration via Histamine Receptor H1 inhibition in retinal ganglion cells.** *Nature communications*
Chen, W., Liu, P., Liu, D., Huang, H., Feng, X., Fang, F., Li, L., Wu, J., Liu, L., Solow-Cordero, D. E., Hu, Y.
2022; 13 (1): 6796
- **Clinically relevant small-molecule promotes nerve repair and visual function recovery.** *NPJ Regenerative medicine*
Au, N. P., Kumar, G., Asthana, P., Gao, F., Kawaguchi, R., Chang, R. C., So, K. F., Hu, Y., Geschwind, D. H., Coppola, G., Ma, C. H.
2022; 7 (1): 50
- **Single-cell transcriptome analysis of regenerating RGCs reveals potent glaucoma neural repair genes.** *Neuron*
Li, L., Fang, F., Feng, X., Zhuang, P., Huang, H., Liu, P., Liu, L., Xu, A. Z., Qi, L. S., Cong, L., Hu, Y.
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- **Multiplexed genome regulation in vivo with hyper-efficient Cas12a.** *Nature cell biology*
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2022
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Zhang, Y., Li, M., Yu, B., Lu, S., Zhang, L., Zhu, S., Yu, Z., Xia, T., Huang, H., Jiang, W., Zhang, S., Sun, L., Ye, et al

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- **NMNAT2 Is Downregulated in Glaucomatous RGCs and RGC-Specific Gene Therapy Rescues Neurodegeneration and Visual Function.** *Molecular therapy : the journal of the American Society of Gene Therapy*
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- **Optic chiasmatic potential by endoscopically implanted skull base microinvasive biosensor: a brain-machine interface approach for anterior visual pathway assessment** *THERANOSTICS*
Zhang, Y., Lu, S., Huang, S., Yu, Z., Xia, T., Li, M., Yang, C., Mao, Y., Xu, B., Wang, L., Xu, L., Shi, J., Zhu, et al
2022; 12 (7): 3273-3287
- **Chronic mild and acute severe glaucomatous neurodegeneration derived from silicone oil-induced ocular hypertension.** *Scientific reports*
Fang, F., Zhang, J., Zhuang, P., Liu, P., Li, L., Huang, H., Webber, H. C., Xu, Y., Liu, L., Dalal, R., Sun, Y., Hu, Y.
2021; 11 (1): 9052
- **Optogenetic stimulation of phosphoinositides reveals a critical role of primary cilia in eye pressure regulation.** *Science advances*
Prosseda, P. P., Alvarado, J. A., Wang, B., Kowal, T. J., Ning, K., Stamer, W. D., Hu, Y., Sun, Y.
2020; 6 (18): eaay8699
- **Mouse gamma-Synuclein Promoter-Mediated Gene Expression and Editing in Mammalian Retinal Ganglion Cells.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
Wang, Q. n., Zhuang, P. S., Huang, H. n., Li, L. n., Liu, L. n., Webber, H. C., Dalal, R. n., Siew, L. n., Fligor, C. M., Chang, K. C., Nahmou, M. n., Kreymerman, A. n., Sun, et al
2020
- **Silicone oil-induced ocular hypertension and glaucomatous neurodegeneration in mouse** *ELIFE*
Zhang, J., Li, L., Huang, H., Fang, F., Webber, H. C., Zhuang, P., Liu, L., Dalal, R., Tang, P. H., Mahajan, V. B., Sun, Y., Li, S., Zhang, et al
2019; 8
- **AKT-dependent and -independent pathways mediate PTEN deletion-induced CNS axon regeneration.** *Cell death & disease*
Huang, H., Miao, L., Yang, L., Liang, F., Wang, Q., Zhuang, P., Sun, Y., Hu, Y.
2019; 10 (3): 203
- **Neuroprotection by eIF2 alpha-CHOP inhibition and XBP-1 activation in EAE/optic neuritis** *CELL DEATH & DISEASE*
Huang, H., Miao, L., Liang, F., Liu, X., Xu, L., Teng, X., Wang, Q., Ridder, W. H., Shindler, K. S., Sun, Y., Hu, Y.
2017; 8: e2936
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Yang, L., Li, S., Miao, L., Huang, H., Liang, F., Teng, X., Xu, L., Wang, Q., Xiao, W., Ridder, W. H., Ferguson, T. A., Chen, D. F., Kaufman, et al
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- **mTORC1 is necessary but mTORC2 and GSK3B are inhibitory for AKT3-induced axon regeneration in the central nervous system.** *eLife*
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Yang, L., Miao, L., Liang, F., Huang, H., Teng, X., Li, S., Nuriddinov, J., Selzer, M. E., Hu, Y.
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Li, S., Yang, L., Selzer, M. E., Hu, Y.
2013; 74 (6): 768-777
- **Differential Effects of Unfolded Protein Response Pathways on Axon Injury-Induced Death of Retinal Ganglion Cells** *NEURON*
Hu, Y., Park, K. K., Yang, L., Wei, X., Yang, Q., Cho, K., Thielen, P., Lee, A., Cartoni, R., Glimcher, L. H., Chen, D. F., He, Z.
2012; 73 (3): 445-452
- **Promoting Axon Regeneration in the Adult CNS by Modulation of the PTEN/mTOR Pathway** *SCIENCE*
Park, K. K., Liu, K., Hu, Y., Smith, P. D., Wang, C., Cai, B., Xu, B., Connolly, L., Kramvis, I., Sahin, M., He, Z.

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Kowal, T. J., Dhande, O. S., Wang, B., Wang, Q., Ning, K., Liu, W., Berbari, N. F., Hu, Y., Sun, Y.
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Wang, B., He, W., Prosseda, P. P., Li, L., Kowal, T. J., Alvarado, J. A., Wang, Q., Hu, Y., Sun, Y.
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- **Optogenetic Modulation of Intraocular Pressure in a Glucocorticoid-Induced Ocular Hypertension Mouse Model.** *Translational vision science & technology*
Kowal, T. J., Prosseda, P. P., Ning, K., Wang, B., Alvarado, J., Sendayen, B. E., Jabbehdari, S., Stamer, W. D., Hu, Y., Sun, Y.
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- **In vivo interactome profiling by enzyme-catalyzed proximity labeling.** *Cell & bioscience*
Xu, Y., Fan, X., Hu, Y.
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- **Post-translational modification of Sox11 regulates RGC survival and axon regeneration.** *eNeuro*
Chang, K., Bian, M., Xia, X., Madaan, A., Sun, C., Wang, Q., Li, L., Nahmou, M., Noro, T., Yokota, S., Galvao, J., Kreymerman, A., Tanasa, et al
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Liu, P., Huang, H., Fang, F., Liu, L., Li, L., Feng, X., Chen, W., Dalal, R., Sun, Y., Hu, Y.
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- **Inhibition of GCK-IV kinases dissociates cell death and axon regeneration in CNS neurons.** *Proceedings of the National Academy of Sciences of the United States of America*
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- **Comparing silicone oil-induced ocular hypertension with other inducible glaucoma models in mice** *NEURAL REGENERATION RESEARCH*
Zhang, J., Hu, Y.
2020; 15 (9): 1652–53
- **Gene therapy for neurodegenerative disorders: advances, insights and prospects** *ACTA PHARMACEUTICA SINICA B*
Chen, W., Hu, Y., Ju, D.
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Zhang, Y., Zhang, S., Xia, Y., Ji, Y., Jiang, W., Li, M., Huang, H., Xu, M., Sun, J., Ye, Q., Hu, Y., Wu, W.
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- **Defective INPP5E distribution in NPHP1-related Senior-Loken syndrome.** *Molecular genetics & genomic medicine*
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- **Longitudinal Morphological and Functional Assessment of RGC Neurodegeneration After Optic Nerve Crush in Mouse.** *Frontiers in cellular neuroscience*
Li, L. n., Huang, H. n., Fang, F. n., Liu, L. n., Sun, Y. n., Hu, Y. n.
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- **Developmental Distribution of Primary Cilia in the Retinofugal Visual Pathway.** *The Journal of comparative neurology*
Alvarado, J. A., Dhande, O. S., Prosseda, P. P., Kowal, T. J., Ning, K. n., Jabbehdari, S. n., Hu, Y. n., Sun, Y. n.
2020
- **A Reversible Silicon Oil-Induced Ocular Hypertension Model in Mice.** *Journal of visualized experiments : JoVE*
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- **Increased ER Stress After Experimental Ischemic Optic Neuropathy and Improved RGC and Oligodendrocyte Survival After Treatment With Chemical Chaperon.** *Investigative ophthalmology & visual science*
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- **Role of Translational Attenuation in Inherited Retinal Degeneration.** *Investigative ophthalmology & visual science*
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- **Lab review: Molecular dissection of the signal transduction pathways associated with PTEN deletion-induced optic nerve regeneration.** *Restorative neurology and neuroscience*
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- **Loss of OCRL increases ciliary PI(4,5)P2 in Lowe oculocerebrorenal syndrome.** *Journal of cell science*
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- **The necessary role of mTORC1 in central nervous system axon regeneration** *NEURAL REGENERATION RESEARCH*
Hu, Y.
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- **PTEN/mTOR and axon regeneration** *EXPERIMENTAL NEUROLOGY*
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