BIOGRAPHICAL SKETCH

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NAME: Liu, Elaine Anna

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

POSITION TITLE: Heed Fellowship

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Berkeley (Berkeley, CA)	BA	08/2008	05/2012	Molecular and Cell Biology
Le Cordon Bleu (Paris, France)	Le Grand Diplôme	06/2012	06/2013	French Cuisine and Pastry
University of Michigan	MD, PhD	07/2014	05/2023	Medicine Cellular and Molecular Biology
University of California, San Francisco	Residency	06/2023	Present	Ophthalmology

A. Personal Statement

My long-term goal is to be a clinician-scientist and educator who leverages my MD/PhD training to bridge mechanistic understanding of disease with clinical research to improve outcomes in ocular disease. My initial research interest was sparked as an undergraduate at UC Berkeley working with Dr. Eva Nogales, where I was enthralled by how understanding structural biology of microtubules through cryo-electron microscopy could provide mechanistic insight on diseases such as cancer. The possibility of elucidating biological unknowns to advance human health inspired me to further pursue basic and translational research with Dr. David Yu at Emory University, where I contributed to work understanding mechanisms of DNA repair and cancer progression. This experience solidified my commitment to pursue an MD/PhD at the University of Michigan. In my first year of medical school, I heard a talk by Dr. Sanduk Ruit, an ophthalmologist from Nepal whose mission is to be a doctor for the poor and who coordinated limited resources to restore the sight of his patients. I realized that my previous research experiences had equipped me to transform this moment of inspiration into a purposeful career direction. I was motivated to become an ophthalmologist who bridges scientific research and clinical practice. Knowing the connection between neurobiology and ocular function, I pursued my PhD with Dr. Andrew Lieberman, where I defined mechanisms of lysosomal dysfunction and neurodegeneration in Niemann-Pick type C. It trained me to think critically about experimental design and to connect scientific data with biologically meaningful insight. I have since used my training to examine longitudinal retinal microvascular changes and neurodegeneration in patients with diabetic retinopathy. Currently, I am collaborating with laboratory investigators to translate mechanistic findings from animal models into clinically testable hypotheses, which I am evaluating using large-scale electronic health record datasets. Throughout my career, I will continue to leverage my basic science and clinical training to bridge the gap between mechanistic understanding of disease and improving ocular health and treatment.

B. Positions, Scientific Appointments and Honors

Positions and Employment

2024 – Present Ophthalmology Resident Physician, University of California, San Francisco
2023 – 2024 General Surgery Preliminary Year Intern, University of California, San Francisco
2014 – 2023 Medical Scientist Training Program Fellow – University of Michigan, Ann Arbor, MI
2015 – 2022 Children’s Ministry Lead Teacher, Harvest Mission Community Church, Ann Arbor, MI

2018 – 2021	Chemistry and Biology Tutor, Sharp Tutors, Ann Arbor, MI
2018 – 2020	Program Activity Committee Chair, Medical Scientist Training Program, University of Michigan
2018 – 2020	Career Committee Board Member, Cellular and Molecular Biology Graduate Program, University of Michigan
2018 – 2018	Graduate Student Instructor for Physiology 201, University of Michigan
2017 – 2018	Medicine in Mandarin Co-Director, University of Michigan
2015 – 2016	Christian Medical Association Co-President, University of Michigan
2015 – 2016	United Asian American Medical Student Association Health Fair Committee Board Member, University of Michigan
2015 – 2016	Health Equity Scholars Program, Retreat Committee Board Member, University of Michigan
2013 – 2014	Research Intern, David Yu Lab, Emory University, Atlanta, GA
2013 – 2014	MCAT Instructor and Tutor, Kaplan, Atlanta, GA
2013 – 2013	Pastry Intern, Dalloyau, France
2010 – 2012	Undergraduate Research Apprentice, Eva Nogales Lab, University of California, Berkeley
2009 – 2012	Food Service Member and Cashier, Golden Bear Café, University of California, Berkeley
2008 – 2012	Note Taker, Disabled Students Program, University of California, Berkeley
2010 – 2012	Peer Health Exchange Co-Coordinator, University of California, Berkeley

Honors

2023	Robert I. Goldsmith, M.D. Award – University of Michigan
2023	George R. DeMuth Medical Scientist Award for Excellence, University of Michigan
2023	Dean's Commendation for Excellence in Clinical Skills and the Art of Medicine, University of Michigan
2019	Selected for Oral Presentation at Lysosomal Diseases Gordon Research Conference, Galveston, TX
2017	Cellular & Molecular Biology Graduate Student Fellowship, University of Michigan
2012	Grace Fimognari Memorial Prize, University of California, Berkeley
2012	Phi Beta Kappa Society, University of California, Berkeley
2012	Highest Distinction in General Scholarship, University of California, Berkeley
2012	Honors in Molecular & Cell Biology, University of California, Berkeley
2011	Summer Undergraduate Research Fellow, University of California, Berkeley
2008	Edward Kraft Scholarship, University of California, Berkeley
2008 – 2012	Dean's Honor List, University of California, Berkeley
2008	Valedictorian, Lynbrook High School, San Jose, California

C. Contributions to Science

Contribution 1: Clinical, Epidemiologic, and Longitudinal Investigation of Ophthalmic Disease
My research has focused on understanding disease presentation, progression, and healthcare delivery in ophthalmology using observational and longitudinal data. During medical school, I worked with Dr. Jonathan Trobe investigating posterior cerebral artery stroke presenting with homonymous hemianopia, and characterized presenting symptoms, imaging features, and underlying etiologies. With Dr. Rajesh Rao, I examined the impact of the COVID-19 pandemic on ophthalmic care delivery for patients receiving intravitreal injections and showed that perceived exposure risk was associated with decreased care continuity, highlighting potential contributors to disease progression. With Dr. Rao I also evaluated longitudinal funding outcomes among clinician-scientists in vision research. We provided evidence of significant leaks in the clinician-scientist pipeline in sustaining funding, highlighting the importance of considering strategies stakeholders can support the ongoing work of clinician-scientists.

Building on this work, I am currently working with Dr. Jay Stewart conducting longitudinal analyses of retinal microvascular and neurodegenerative changes using optical coherence tomography angiography (OCTA) in a large urban safety-net population with diabetes. This work is has been submitted for publication and is currently under review. Furthermore, I am conducting studies examining the correlation between aqueous proteins and microvascular changes on OCTA in patients with varying stages of diabetes to identify novel treatment targets for diabetic retinopathy. In parallel, I am leveraging large-scale electronic health record

databases to examine associations between systemic exposures and the development of age-related macular degeneration, applying survival analysis approaches to better define disease risk and progression. Together, this work reflects my goals of integrating clinical insight with quantitative methods to improve prediction, monitoring, and prevention of vision-threatening disease.

a. **Liu, E.A.,** Murali, S., Rivera-de Choudens, R., Trobe, J.D. Presenting Symptoms and Imaging Features of Posterior Cerebral Artery Stroke Causing Homonymous Hemianopia. *J Neuroophthalmol* **43**, 393-398, doi:10.1097/WNO.0000000000001934 (2023).
b. **Liu, E.A.,** Murali, S., Rivera-de Choudens, R., Trobe, J.D. Demographics, Risk Factors, and Etiology of Posterior Cerebral Artery Stroke Causing Homonymous Hemianopia. *J Neuroophthalmol* **43**, 387-392, doi:10.1097/WNO.0000000000001948 (2023).
c. 5. Lindeke-Myers, A., Zhao, P.Y.C., Meyer, B.I., **Liu, E.A.,** Levine, D.A., Bennett, O.M., Ji, S., Newman-Casey, P.A., Rao, R.C., Jain, N. Patient Perceptions of SARS-CoV-2 Exposure Risk and Association with Continuity of Ophthalmic Care. **JAMA Ophthalmol** (2021)
d. 7. **Liu, E.A.,** Wang, S.Y., Rao, R.C. Sustaining Independent Careers in Vision Research: Demographics and Success in Second R01 Attainment Among Clinician-Scientists from 1985 to 2019. **Transl Vis Sci Technol** 9 (2020) 32

Contribution 2 : Mechanisms of Neurodegeneration and Lysosomal Dysfunction
During my PhD training with Dr. Andrew Lieberman, my research focused on understanding how defects in protein quality control impact neurodegeneration in Niemann-Pick type C (NPC), a lysosomal storage disease that causes neurodegeneration in children. I identified a role for Fbxo2 as a mediator of lysophagy (autophagy of lysosomes) in neurons and identified its functional importance in NPC in both cell culture and mouse models. I further characterized TDP-43 pathology in NPC mice. While TDP-43 mislocalisation in neuronal cells is a hallmark of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), I provided evidence that mislocalized TDP-43 in NPC mouse neurons is associated with nuclear pathology and disruption in nucleocytoplasmic transport. In related work, I contributed to our understanding of synthetic high-density lipoprotein nanoparticles as a therapeutic strategy for NPC, demonstrating dose-dependent rescue of pathologic lipid storage in NPC cells. I also reviewed the intersection of calcium signaling, lysosomal dysfunction, and autophagy, providing a conceptual framework for understanding neurodegeneration in lysosomal storage disorders. Collectively, this work advanced understanding of cellular quality control pathways and their role in neurodegenerative disease.

a. **Liu, E.A.,** Schultz, M.L., Mochida, C., Chung, C., Paulson, H.L., Lieberman, A.P. Fbxo2 mediates clearance of damaged lysosomes and modifies neurodegeneration in the Niemann-Pick C brain. **JCI Insight** 5 (2020)
b. **Liu, E.A.**, Mori, E., Hamasaki, F., Lieberman, A.P. TDP-43 proteinopathy occurs independently of autophagic substrate accumulation and underlies nuclear defects in Niemann-Pick C disease. **Neuropathol Appl Neurobiol** 47 (2021) 1019-1032.
c. **Liu, E.A**. and Lieberman, A.P. The intersection of lysosomal and endoplasmic reticulum calcium with autophagy defects in lysosomal diseases. **Neurosci Lett**, 2019;697:10-16
d. Schultz, M.L., Fawaz, M.V., Azaria, R.D., Hollon, T.C., **Liu**, **E.A.**, Kunkel, T.J., Halseth, T.A., Krus, K.L., Ming, R., Morin, E.E., McLoughlin, H.S., Bushart, D.D., Paulson, H.L., Shakkottai, V.G., Orringer, D.A., Schwendeman, A.S., Lieberman, A.P., Synthetic high-density lipoprotein nanoparticles for the treatment of Niemann-Pick diseases, BMC Med 17 (2019) 200.

Contribution 3: DNA Damage Response and Cancer Biology
My early research contributions focused on mechanisms of the DNA damage response and replication stress in cancer biology. I contributed to studies demonstrating that deacetylation of ATRIP by SIRT2 promotes ATR checkpoint activation through enhanced binding to RPA-coated single stranded DNA, providing insight into regulation of genomic stability. In parallel, I participated in work identifying NEK9 as a modulator of replication stress response and chemotherapy sensitivity, and in studies showing that CHD7 expression is associated with survival outcomes in pancreatic cancer. These studies collectively advanced understanding of molecular pathways governing DNA repair and cancer progression.

a. Zhang, H., Head, P.E., Daddacha, W., Park, S., Li, X., Pan, Y., Madden, M.Z., Duong, D.M., Xie, M., Yu, B., Warren, M.D., **Liu, E.A**., Dhere, V.R., Li, C., Pradilla, I., Torres, M.A., Wang, Y., Dynan, W.S., Doetsch, P.W., Deng, X., Seyfried, N.T., Guis, D., Yu, D.S. 2016. ATRIP deacetylation by SIRT2 drives ATR checkpoint activation by promoting binding to RPA-ssDNA. **Cell Reports**, 14(6):1435-47
b. Smith, S.C., Petrova, A.V. Madden, M.Z., Wang, H., Pan, Y., Warren, M.D., Hardy, C.W., Liang, D., **Liu, E.A.**, Robinson, M.H., Rudra, S., Wang, J., Ehdaivand, S., Torres, M.A., Wang, Y., Yu, D.S. 2014 A gemcitabine sensitivity screen identifies a role for NEK9 in the replication stress response. **Nucleic Acids Research**, 42(18): 11517-27.
c. Colbert, L.E., Petrova, A.V., Fisher, S.B., Pantazides, B.G., Madden, M.Z., Hardy, C.W., Warren, M.D., Pan, Y., Nagaraju, G.P., **Liu, E.A.**, Saka, B., Hall, W.A., Shelton, J.W., Gandhi, K. Pauly, R., Kowalski, J., Kooby, D.A., El-Rayes, B.F., Staley, C.A., Adsay, N.V., Curran, W.J., Landry, J.C., Maithel, S.K., Yu, D.S. 2014. CHD7 expression predicts survival outcomes in patients with resected pancreatic cancer. **Cancer Research**, 74, 2677-87.

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	UNIVERSITY OF CALIFORNIA, BERKELEY	
2008	General Chemistry 1A	A+
2008	Calculus 1A	A
2008	Introduction to Human Nutrition	A+
2008	Craft of Writing	A
2009	Organic Chemistry (CHEM 3A)	A+
2009	Organic Chemistry Lab (CHEM 3AL)	A
2009	Reading and Composition	A-
2009	Calculus 1B	A+
2009	Intro Physics (PHYSICS 8A)	A+
2009	General Biology (BIOLOGY 1B)	A
2009	Organic Chemistry (CHEM 3B)	A+
2009	Organic Chemistry Lab (CHEM 3BL)	A+
2009	U.S. History	A
2009	Introduction to Western Music	A+
2010	General Biology (BIOLOGY 1A)	A
2010	General Biology Lab (BIOLOGY 1AL)	A
2010	Elementary French	A
2010	World Regions	A
2010	Intro Philosophy of Religion	A
2010	Biophysical Chemistry	A
2010	Intro Physics (PHYSICS 8B)	A
2010	Elementary French II	A
2011	Biochemistry: Metabolic Pathways	A+
2011	Molecular Neurobiology	A
2011	Intro to Statistics	A+
2011	Intermediate French	A
2011	Developmental Psychology	A+
2011	Social Psychology	A+
2011	General Biochemistry	A+
2011	General Genetics	A
2011	Advanced Intermediate French	A
2012	Molecular Immunology	A
2012	Global Health	A

YEAR	COURSE TITLE	GRADE
2012	Personality Psychology	A+
2012	Advanced French Conversation	A
	UNIVERSITY OF MICHIGAN MEDICAL SCHOOL[1]	
2014	Patients and Populations	S
2014	Cells & Tissues	S
2014	Cardiovascular/Respiratory	S
2014	Renal	S
2014	Musculoskeletal	S
2015	GI/Liver	S
2015	Endocrine/Reproduction	S
2015	Immunology	S
2015	CNS/Head & Neck	S
2015	ID/Microbiology	S
2015	Histopathology	S
2015	Human Growth & Development	S
2015	Cardiovascular	S
2015	Respiratory	S
2015	Renal	S
2015	Psychiatry	S
2015	Neurosciences	S
2015	Musculoskeletal/Rheumatology	S
2015	Dermatology	S
2016	Hematology/Oncology	S
2016	Gastrointestinal	S
2016	Endocrine	S
2016	Reproduction	S
2016	Developmental Genetics	A
2016-2021	Seminar and Dissertation Research Courses	S
2021	Obstetrics & Gynecology Clerkship	High Pass
2021	Surgery Clerkship	High Pass
2021	Family Medicine Clerkship	Honors
2021	Psychiatry Clerkship	Honors
2021	Neurology Clerkship	High Pass
2022	Internal Medicine Clerkship	Honors
2022	Pediatrics Clerkship	Honors
2022	Ophthalmology Clinical Elective	Honors
2022	Advanced Ophthalmology Clinical/Research	Honors
2022	General Medicine SubI	Honors
2022	Intensive Care SubI/ICU	Honors
2023	Neuropathology	High Pass
2023	Emergency Medicine	Honors

[1] The first two pre-clinical years at University of Michigan, and Seminar and Dissertation Research Courses are graded S (Satisfactory) or F (Fail). The clinical courses are graded Honors, High Pass, Pass, or Fail