BIOGRAPHICAL SKETCH

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NAME: Fanny Elahi, MD, DPhil

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

POSITION TITLE: Assistant Professor of Neurology, Neuroscience, and Pathology

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	Completion Date	FIELD OF STUDY
Columbia University	BA	2003	Comp. Lit. & Society
Oxford University	DPhil (PhD)	2007	Neurogenetics
Icahn School of Medicine at Mount Sinai	MD	2011	Medicine
University of California, Los Angeles	Residency	2015	Neurology
University of California, San Francisco	Fellowship	2018	Behavioral Neurology

A. Personal Statement

I am a physician-scientist who completed my doctorate in neurogenetics, residency in neurology, and a fellowship in neurodegenerative disorders to gain multi-disciplinary domain knowledge, clinical, scientific, and technical skills required for therapeutically oriented translational research in neurodegenerative diseases. I joined the UCSF faculty of Neurology in 2018 where I built a therapeutic discovery program for genetic vasculopathies. In 2022, I was recruited to the Icahn School of Medicine at Mount Sinai to establish a world-class fluid biomarker research program in neurodegenerative disorders and to build a bed to benchside translational research program focused on vascular neurodegenerative diseases.

Research in my lab is focused on understanding vascular contributions to brain degeneration. Our bed to bench side pipeline for discovery of therapeutics is focused on CADASIL, a monogenic form of vascular cognitive impairment and dementia. We combine molecular and cellular phenotyping using human biospecimens and iPSC-derived *in vitro* cellular models with clinical and imaging data to identify the molecular and cellular correlates of human phenotypes suitable for therapeutic interventions. Our collaborations involve investigations of fluid biomarkers across neurological disorders, especially vascular and neuropsychiatric disorders.

In my clinical practice, I evaluate and treat patients with neurodegenerative disorders and run a specialized clinic for evaluation and treatment of adult-onset leukoencephalopathies that serves out of state as well as international patients.

Ongoing and recently completed projects that I would like to highlight include:

<u>Research Support</u>

Jane Martin and Stuart Katz Research Scholar Award (Elahi, Huang, Goate) 01/01/2023 – 12/31/2023
Unbiased Discovery of Early Molecular Dysregulations in Alzheimer's Disease
Goal: Analyze Alzheimer's disease (AD) using a multi-dimensional dataset including genetics, plasma proteomics, clinical data, and demographics, uncovering proteomic signatures that predict AD pathology and symptoms; potentially leading to novel biomarkers.
Role: Principal Investigator

Chan Zuckerberg Initiative (Elahi) 12/01/2022 – 11/30/2026

CADASIL-centered modeling of immune-vascular neurodegenerative disease
Goal: Develop iPSC-derived *in vitro* multi-cellular models of CADASIL to capture clinically-relevant pathologies to serve as a platform for future therapeutic screens.
Role: Contact Principal Investigator

Rainwater Charitable Foundation 2790954 (Elahi) 11/01/2022 – 10/31/2023
Unbiased proteomics to uncover vascular contributions to tauopathy in a diverse community-based sample
Goal: Discovery of dysregulated vascular molecular pathways to target in tauopathies
Role: Principal Investigator

NIH/NINDS UF1 NS100608 (Kramer) 09/30/2021 – 07/31/2023
Novel imaging and biofluid biomarkers of small vessel cerebrovascular disease
Goal: Develop novel neuroimaging and serologic biomarkers of cerebrovascular disease with a focus on measures of endothelial dysfunction.
Role: Co-Investigator, Biofluid committee co-chair

VA/NIA IK2 CX002180 (Elahi) 01/01/2021 – 12/31/2026
A Precision Medicine Approach to Study of Targetable Pathways in Vascular Cognitive Impairment
Goal: Use of multi-modal molecular and imaging methods and advanced data analytics to investigate therapeutically relevant pathologies in VCID.
Role: Principal Investigator

NIH/NINDS U19 NS120384 (DeCarli & Fornage) 10/01/2020 – 09/30/2026
The Clinical Significance of Incidental White Matter Lesions on MRI Amongst a Diverse Population with Cognitive Complaints (Diverse VCID)
Goal: Support a large prospective clinical research study in the U.S. of patients engaged with the health care system because of incidental white matter lesions found on neuroimaging, who present with cognitive complaints, and are at risk for cognitive decline.
Role: Co-Investigator

NIH/NINDS R01 NS116990 (Wilcock) 02/01/2020 – 01/31/2023
Elucidating the role of placental growth factor in diffuse white matter disease
Goal: Use cell-type specific exosomal methods to dissect the biological underpinnings of vascular dementia.
Role: Co-Investigator

NIH/NIA RF1 AG074608 (Paulsen) 02/01/2020 – 01/31/2023
Unraveling the earliest phases of vascular cognitive impairment and dementia using CADASIL - a monogenic small vessel cerebrovascular disease
Goal: Create a national observational cohort of individuals affected with CADASIL for future clinical trials.
Role: Co-Investigator

AHA/Paul Allen Frontiers Group (Wyss-Coray) 01/01/2019 – 01/31/2024
Immunomodulation to Promote Cerebrovascular and Cognitive Health
Goal: Identify and target immune pathways in order to maintain healthy brain function during aging and post-stroke.
Role: Co-Investigator

B. Positions, Scientific Appointments, and Honors
Positions and Employment

2022 – present	Assistant Professor, Neurology, Neuroscience, and Pathology, ISMMS
2021 – present	Neurologist and Investigator, Veterans Affairs Health Care System
2018 – 2022	Assistant Professor, Neurology, UCSF
2018 – 2021	Instructor for Brain Movement and Behavior, UCSF Medical School
2016 – 2018	AAN Clinical Research Fellow in Neurodegenerative Disorders, UCSF
2015 – 2016	Clinical Fellow in Neurodegenerative Disorders, Memory and Aging Center, UCSF
2012 – 2015	Resident Physician, Neurology, UCLA

2011 – 2012 Intern in Medicine, Banner-University Medical Center Phoenix

Clinical License

2015 – present Board Certification, Neurology, American Board of Psychiatry and Neurology
2012 – present Medical License, California and New York

Academic and Professional Honors

2021 – 2022 Organizing Committee, Albert White Matter Research Institute meeting
2021 Scientific Advisory Board, Albert White Matter Research Institute
2021 – 2023 Chair, Vascular Cognitive Disorders Professional Interest Area (PIA) Executive Committee, ISTAART
2019 – 2021 Vice Chair, Vascular Cognitive Disorders PIA Exec. Comm., ISTAART
2019 New Vision Award, Charleston Conference on Alzheimer's Disease
2017 UCSF Advanced Training in Clinical Research Scholar
2017 Travel Fund Friday Harbor Genetics of Cognitive Aging Workshop
2016 – 2018 AAN / Allergan Clinical Research Training Fellowship Recipient
2015 Best Research Poster at UCLA Neuroscience Trainee Annual meeting
2014 Best Clinical Poster at UCLA Neuroscience Trainee Annual meeting
2013 Record Stroke Response Time: "Door to Needle Time" UCLA Stroke Neurology
2008 Alpha Omega Alpha, Carolyn L. Kuckein Research Scholarship
2004 – 2008 Medical Research Council DPhil Scholarship
2004 – 2007 Northwick Park Institute for Medical Research Scholarship (NPIMR)
2003 Royal Society Student Scholarship
2002 Columbia University Departmental Honors Nomination

Other Experience

2022 External Grant Reviewer, European Research Council
2022 Biofluid Biomarker Lead, Diverse VCID Consortium
2022 Review Committee Member, Target ALS
2022 Guest Editor, Journal of Cerebral Circulation
2022 Chair, MarkVCID Biospecimen Committee
2022 Associate Editor, Frontiers in Neurology, Dementia and Neurodegenerative Diseases
2022 Associate Editor, Alzheimer's and Dementia
2021 Scientific Advisory Board, Albert Research Institute for White Matter and Cognition
2019 Guest Editor, Frontiers in Neurology: Lipids in the Brain
2018 Organizer, UCSF MAC - Pitié-Salpêtrière Collaborative Meeting
2019 – 2021 Abstract reviewer, AAIC
2019 – 2021 Grant Reviewer for Medical Research Council (UK,) Alzheimer's Research (UK), American Heart Association, and cureCADASIL Foundation
2017 UCSF Advanced Training in Clinical Research Scholar
2015 – present Ad hoc Reviewer (1-2 manuscripts per year) for over 20 scientific journals including Brain, JAMA Neurology, Nature Medicine, Cell Reports, Alzheimer's and Dementia, Annals of Neurology, Neurology, Journal of Alzheimer's Disease, Journal of Neuroscience, Neuroimage Clinical, Human Brain Mapping, Stroke, Journal of Stroke and Cerebrovascular Disease, Neurobiology of Aging, Neurobiology of Disease, Frontiers journals, PLOS journals, FASEB

Professional Memberships

2022 – present Member, Diverse VCID Consortium
2020 – present Member, International Frontotemporal Dementia Society
2018 – present Member, Bio-fluid Biomarker Research Group
2014 – present Member, New York Academy of Sciences
2012 – present Member, American Academy of Neurology
2012 – present Junior Member, American Neurological Association

C. Contributions to Science

1. Novel diagnostic and prognostic biomarkers for neurovascular disease: The following manuscripts demonstrate the utility of non-invasive fluid biomarker analyses in the study of brain-specific processes such as neurovascular dysfunction and white matter degeneration using biofluids, such as plasma. This body of work especially highlights the syndrome-agnostic biological dysregulations uncovered with use of molecular biomarkers in plasma. We identified complement activation as a therapeutically targetable pathology in non-demented older adults with elevated blood pressure and brain white matter disease and demonstrated that levels of complement factor are associated with slowed cognitive processing speed and lower executive function. Additionally, our study on chronic microglia activation post-stroke has led to the identification and validation of activation-state specific microglia extracellular vesicles (MEVs) in vitro and in an experimental stroke model, reporting a significant increase in specific indicators in plasma 28-days post-stroke. This research marks the first description of an extracellular vesicle biomarker for activated microglia following stroke, representing a future tool for the measurement of microglia activity *in vivo*. Measurement of molecules from cell-specific extracellular vesicles could serve as a "liquid biopsy" approach for inaccessible organs—we are developing novel technology to increase technical reliability and generalizability of these tools.

    a. Roseborough AD, Myers SJ, Khazee R, Zhu Y, Zhao L, Iorio E, **Elahi FM,** Pasternak SH, Whitehead SN. Plasma derived extracellular vesicle biomarkers of microglia activation in an experimental stroke model. *Journal of Neuroinflammation,* 2023; 20. PMID: 36721258
    b. **Elahi FM**, Harvey D, Altendahl M, Casaletto KB, Staffaroni AM, Maillard P, Hinman JD, Miller BL, DeCarli C, Kramer JH, Goetzl EJ. Endothelial-derived exosomes demonstrate a link between endothelial innate inflammation and brain dysfunction and injury in aging. *Sci Reports*, 2021. PMID: 34376699.
    c. **Elahi FM**, Farwell GD, Nolta JA, Anderson JD. Preclinical translation of exosomes derived from mesenchymal stem/stromal cells. *Stem Cells* 2020; 38(1): 15–21. PMID: 31381842
    d. **Elahi FM**, Casaletto KB, Altendahl M, Staffaroni AM, Fletcher E, Filshtein TJ, Glymour MM, Miller BL, Hinman JH, DeCarli C, Goetzl EJ, JH Kramer. "Liquid Biopsy" of white matter hyperintensity in functionally normal elders. *Frontiers in Aging Neuroscience*. 2018; 10: 343. PMID: 30483114

2. Phenotypic diversity and the utility of biomarkers in neurodegenerative disease: deep clinical phenotyping in addition to biomarkers such as fluid proteomics, genetic markers, and neuroimaging, can uncover neurodegenerative disease trajectories and improve our diagnostic classifications as well as mechanistic understanding of disease. The manuscripts below contribute to the understanding of neurodegenerative disease phenotypes and classifications and how multi-modal, non-invasive biomarkers can connect phenotypes to underlying pathological processes.

    a. Snyder A, Grant H, Chou A, Lindbergh CA, Kramer JH, Miller BL, **Elahi FM**. Immune cell counts in cerebrospinal fluid predict cognitive function in aging and neurodegenerative disease. *Alzheimer's & Dementia*, 2023; 1-11. PMID: 36791265
    b. **Elahi FM**, Casaletto KB, La Joie R, Walters SM, Danielle Harvey, Wolf A, Edwards L, Rivera-Contreras W, Karydas A, Cobigo Y, Rosen HJ, DeCarli C, Miller BL, Rabinovici GD, Kramer, JH. Plasma biomarkers of astrocytic and neuronal dysfunction in early and late onset Alzheimer's disease. *Alzheimer's and Dementia*, 2020 Apr;16(4):681-695. PMID: 31879236
    c. Staffaroni A.M., Brown J.A., **Elahi F.M.**, Casaletto K.B., Deng J., Neuhaus J., Mumford P., Saloner R., Karydas A., Coppola G., Rosen H.J., Miller B.L., Seeley W.W., Kramer J.H. The longitudinal trajectory of default mode network connectivity in healthy older adults varies as a function of age and is associated with changes in episodic memory. *J Neuro*, 2018 Mar 14;38(11):2809-2817. PMID: 29440553
    d. **Elahi FM**, Miller BL. A clinicopathological approach to the diagnosis of dementia. *Nat. Rev. Neurol.* 2017; 13: 457–476. PMID: 28708131

3. White matter degeneration in neurodegenerative disease: both vascular disease and non-vascular neurodegenerative pathologies strongly affect white matter health and integrity. Studies of these intermediate phenotypes or endophenotypes may provide therapeutically relevant advances in neurodegenerative disease research. We investigated the rate of white matter degeneration across clinical disease categories, including amnestic Alzheimer's disease, and three canonical frontotemporal dementia

syndromes (behavioral variant, semantic variant primary progressive aphasia, and non-fluent variant primary progressive aphasia). Higher rates of white matter degeneration were noted in areas that would correspond to the clinical phenotype, e.g., posterior brain regions for AD and anterior in FTD subtypes. However, we observed that white matter degeneration was rather extensive in all, and not entirely limited to peak areas of grey matter degeneration; suggesting the possibility of contributions from systemic processes, including inflammation and subclinical vascular pathologies. Additionally, our evaluation of plasma neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) in older adults, across various cognitive statuses, revealed that higher plasma GFAP levels were associated with lower white matter volume and executive function scores. This finding highlights plasma GFAP as a sensitive marker for white matter and cognitive changes, emphasizing the complex dynamics of aging and neurodegenerative disease and strengthening our understanding of white matter degeneration. We are now employing proteomics methods to further dissect the biological contributions to vascular white matter disorders, such as genetic vasculopathies and cerebral amyloid angiopathy.

a. Torres-Espin A, Rabadaugh H, Fitzsimons S, Harvey D, Chou A, Lindberg C, Casaletto KB, Goldberger L, Staffaroni AM, Maillard P, Miller BL, DeCarli C, Hinman JD, Ferguson AR, Kramer JH, **Elahi FM*.** Sexually dimorphic differences in angiogenesis markers predict brain aging trajectories. *BioRxiv,* 2023; 07.16.549192. PMID: 37503183
b. Abdelhak A, Solomon I, Saias A, Condor Montes A, Cordano C, Asken B, Fonseca C, Cosima Oertel F, Arfanakis K, Staffaroni AM, Kramer JH, Geschwind M, Miller BL, *Green AJ, **Elahi FM***. Changes in wall thickness of retinal arterioles as a surrogate marker of intracranial vascular pathology. *Alzheimer's & Dementia,* 2021; 14:e12338. PMID: 35814617
c. Altendahl M, Maillard P , Harvey D, Cottera D, Walters S, Wolf A, Singh B, Kakarla V, Azizkhanian I, Sheth SA, Xiao G, Fox E, You M, Leng M, Elashoff D, Kramer JHH, Decarli C, **Elahi FM***, Hinman JD*. An IL-18-centered inflammatory network as a biomarker for cerebral white matter injury. 2020. *Plos One* 2020; 15(1):e0227835. PMID: PMC6980497
d. **Elahi FM**, Marx G, Cobigo Y, Staffaroni AM, Kornak J, Tosun D, Boxer AL, Kramer JH, Miller BL, Rosen HJ. Longitudinal white matter change in frontotemporal dementia subtypes and sporadic late onset Alzheimer's disease. *NeuroImage Clin.* 2017; 16:595-603. PMID: 28975068

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/fanny.elahi.1/bibliography/public/
I attest that I have not published under any other name.