Swetha Mohan, Ph.D.

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Neurodegeneration, Aging, Mechanisms of disease, Target Prioritization, Due Diligence, Project Management

References upon request

PROFESSIONAL SUMMARY

- Over 17 years of technical expertise spanning cell biology, molecular biology, biochemistry, and microscopy
- Cellular and molecular expertise in neurodegeneration with a focus on Frontotemporal lobar degeneration (FTLD) and Tauopathies
- Developed projects independently and established collaborations across multiple organizations
- Skills and expertise to collect, analyze, and interpret data and communicate effectively between cross-functional teams and management
- Ability to work efficiently, organize and develop strategies to address complex problems

SERVICES

- Due diligence on specific targets, in-licensing opportunities, and scientific data
- New target identification in disease from large datasets working alongside data scientists
- Deep dive into target biology for prioritization and platform validation
- Perform literature reports on topics of interest
- Assay development to validate targets in collaboration with biologists and chemists
- Design, outsource, and/or manage early PoC studies
- Licence technologies and source appropriate cell lines to use as disease models in collaboration with the legal team
- Program planning and project management in-house and with CROs
- Disease landscaping in different countries for new clinical trial sites
- Write manuscripts, research proposals, and progress reports for journals and grant agencies
- Design disease-specific summaries for investor and partnering slide deck

SELECTED CONSULTING EXPERIENCES

Project Management

I have worked with companies focusing on oncology, neurodegeneration, and aging. I have established successful relationships with both academic labs and CROs to perform experiments from conceptualization, data analysis, and data presentation. As a Project Manager, I have coordinated

across all functions (CROs, finance, program lead, and management) to move projects forward. My role also involved presenting the data to the clients in their standardized style and in their slide decks which are used for partnering and upper management presentations. I have used multiple software to do these services, MS Office software (word, excel, PowerPoint), GraphPad Prism, CDD, etc., as per the client's request.

Subject Matter Expert

I was hired as an expert in the pathologies of brain and aging. My clients have large datasets, that require an expert to provide essential disease context to prioritize targets related to aging and neurodegeneration.

This included:

1. Working with data scientists for platform development
2. Provide biological relevance for the specific indication
3. Deep dive into the biology of the target
4. Work with chemists to identify tool compounds
5. Design feasible experiments to perform for validation of the target in different model systems
6. Execute these experiments through collaborations with CROs and academic labs or using in-house expertise

Bringing Technologies in-house

An essential part of starting new programs is to make sure all the technologies needed to efficiently perform the experiments can be performed. As a consultant, I have previously worked with my client's in-house counsel to bring in cell lines and licenses to use specific technologies in-house to have a seamless start to your program. For example, A client was starting a neurodegeneration program and wanted to perform CRISPR-based screening in iPSC-derived neurons using patient cells. I collated all the licenses necessary for these technologies and helped with negotiations with the universities and institutes to bring the technology in-house.

Reporting on Disease Landscapes

A non-profit organization requested a report on the disease landscape of a specific indication in India to help bring new clinical trials to the country. I worked with clinicians from four different centers across India to understand their cohort demographics, center limitations, current knowledge and capabilities to perform primary outcome measures, etc. This report was very successfully received and will become the basis for further studies and potential funding for the centers.

TECHNICAL SKILLS

- Generated cell-based models for neurodegeneration using gene editing technology, CRISPR/Cas9
- Designed and performed experiments using CRISPR/Cas9, shRNA, and siRNA to test varying phenotypes in neuronal and non-neuronal cells in culture
- Designed and performed experiments to test the target engagement of tool compounds
- Designed and performed GO/NO GO experiments to evaluate in-licensing efforts in neurodegeneration
- iNeuron differentiation from iPSCs and characterization to study the effects of disease-associated mutations

- Experience in using invertebrate models (*Caenorhabditis elegans*) to understand molecular aspects of disease

- Experience designing age-associated stress experiments on differentiated neurons and patient-derived fibroblasts to understand proteostasis and disease biology in neurodegeneration

- Extremely competent at diverse methodologies such as confocal imaging, image analysis, protein analysis, subcellular fractionation, and statistical analysis (Prism)

E D U C A T I O N and T R A I N I N G

University of California, San Francisco; Mission Bay, California
Postdoctoral Scholar, Memory and Aging Center, 2015 – 2019

Stanford University; **Palo Alto**, California
Postdoctoral Scholar, 2014-2015

Simon Fraser University, Burnaby; British Columbia
Postdoctoral Scholar, Molecular Biology and Biochemistry, 2013 - 2014

Simon Fraser University, Burnaby; British Columbia
Ph.D., Department of Molecular Biology and Biochemistry, 2007 - 2013

National Center for Biological Sciences; Bangalore, India
Junior Research Fellow, Neurobiology, 2005 - 2007

University of Madras, Chennai, India
M.Sc., Biotechnology, 2003
B.Sc., Biochemistry, 2001

I N D U S T R Y E X P E R I E N C E

Consultant – Remote
Neurodegeneration, Aging, Project Management, Due Diligence, Target prioritization
Multiple Biotech Clients, USA, **2021- present**

- Collaborate with the data science team to analyze, refine, and adapt an existing ML-based platform to identify novel targets in neurodegeneration
- Deep dive into the target biology and prioritize for further validation and scope toward the clinic
- Design validation studies
- Coordinate licensing efforts for technology and cell lines with legal team
- Identify qualified CROs to perform complex assays
- Establish successful collaborations with academic labs to help perform validation studies
- Act as a liaison for the company while interacting with academic SAB members
- Identify resources and budget needed to build in house team for a new program
- Worked on multiple projects involving FTD, ALS, AD, and Tauopathies
- Acted as an interim program lead managing all aspects of the ongoing studies
- Contribute towards slide deck for partnering calls
- Project management for *in vivo* studies

Neuroscience Consultant and Technical Writer (Remote)
Stellate Communications LLC, New York, **2022 – 2023**

- Technical writing for manuscripts, grants, and reports submissions for academic PIs
- Draft rebuttals for reviewer responses from scientific journals and streamline workflow for resubmission
- Work as a team to improve scientific communication with academic clients

Scientist II
Engine Biosciences, San Carlos, California **2019 - 2021**

- Design and develop an *in vitro* platform to perform CRISPRi screens in iPSC-derived neurons (cortical and motor)
- Design and perform GO/NO GO experiments for in-licensing efforts in neurodegeneration
- Collect, analyze, and present data to cross-functional teams and determine the path forward

R E S E A R C H E X P E R I E N C E

Post-doctoral Researcher
Advisor: Dr. Aimee Kao
University of California, San Francisco, Memory and Aging Center (MAC)
Mission Bay, California **2015 – 2019**

Project I – Allen Foundation grant in collaboration with 3 other labs at UCSF

To understand the regulated cleavage of progranulin into granulins by lysosomal proteases and its impact on frontotemporal dementia (FTD) – (2015 - 2019)

- Developed enzyme assays to cleave human progranulin *in vitro* by lysosomal proteases across a wide pH range of 3.4-7.4
- Determined the cleavage sites by western blot analysis and mass spectrometry analysis
- Developed assays to study the cleavage of endogenous progranulin in mammalian cells
- Determined the effects of different drugs and stressors on progranulin cleavage in different mammalian cells and primary patient fibroblasts.
- Used CRISPR/Cas9-based genome editing to make progranulin KO and haploinsufficient mutant cell lines in human neuroblastoma cells (SH-SY5Y) to use as a cell-based model for FTD and NCL
- Effects of stress on differentiated PGRN haploinsufficient lines
- Differentiate the iPSCs derived from the patient fibroblasts into iNeurons to evaluate the effect of the mutation on proteostasis and lysosome biology

Project II – QB3/Calico Fellowship

Comparative assessment of proteostasis in control and Alzheimer's disease patient fibroblasts **2017- 2019**

- Team-based project working closely with one other post-doc
- Assess stress signaling pathways, unfolded protein response (UPR), and autophagy, in control and disease mutation carriers
- Design assays to induce chronic and acute UPR and autophagic stress on primary human cells and assess the effect of mutations on stress response
- Will assess the effect of ISR inhibitor on stress response in mutation carriers

- Will perform direct differentiation of fibroblasts into neurons to study the effect of the mutation

Project III - Design a genetically encoded lysosomal protease cleavage reporter **2016 - 2018**

- Re-engineered a fluorogenic reporter to assay lysosomal protease activity in cell culture.
- Generated stable lines and FACS sorted for low expressing cells that target a cathepsin D activity reporter to the lysosomes
- Confirmed the lysosomal localization of the reporter with immunofluorescence
- Performing control experiments on the specificity of the cleavage

Post-doctoral Researcher
Advisor: Dr. Rajat Rohatgi
Stanford University; Palo Alto, California **2014 — 2015**

Understanding molecular aspects of Hedgehog signaling and primary cilia in Medulloblastoma.

- Generate transgenic strains that express the protein of interest in different mutant backgrounds.
- CRISPR/Cas9-based genetically modified line generation for disease modeling

Post-doctoral Researcher
Advisor: Dr. Michel Leroux
Simon Fraser University; Burnaby, British Columbia **2013 — 2014**

Worked on multiple projects alongside two other postdocs in a highly collaborative and productive setting. Whole genome RNAseq analysis in *C. elegans* to identify new ciliary genes. Assisted in identifying the ciliary zone of exclusion (CIZE) needed for compartmentalizing signaling proteins. Assisted in validating hits from a SKAT-based analysis

- Team-based projects working closely with two other postdocs
- Generate transgenic strains that express the protein of interest in different mutant backgrounds.
- Designed and developed microscopy assays for time-lapse confocal imaging.
- Determined and statistically analyzed the velocity of ciliary protein transport in live worms
- Proposed a new model for the anterograde transport of cytoplasmic dynein to the ciliary tip

Graduate Student researcher
Advisor: Dr. Michel Leroux
Simon Fraser University; Burnaby, British Columbia **2007 — 2013**

Functional aspects of ciliary maintenance in *Caenorhabditis elegans*. The scope of my Ph.D. dissertation was to expose the functional aspects of two previously uncharacterized proteins concerning their role as regulators of ciliary maintenance. Both proteins, CHE-10/Rootletin and DYF-18/CDK1/CCRK maintain ciliary function at least in part by modulating Intraflagellar transport (IFT) and insights into these mechanisms may help us understand the degeneration of sensory perception with age.

- Mapped the genetic mutations and characterized the mutant's sensory defects
- Designed constructs and generated stable transgenic lines expressing all the sub-classes of IFT proteins
- Time-lapse imaging of protein transport within neuronal cilia in live animals and determining the velocity, flux, and defects in IFT
- A comprehensive study of the process of ciliary degeneration in these mutants

P U B L I C A T I O N S

Mohan S., Sampognaro P.J., Argouarch A.R., Maynard J.C., Welch M., Patwardhan A., Courtner E.C., Zhang

J., Mason A., Li K.H., Huang E.J., Seeley W.W., Miller B.L., Burlingame A., Jacobson M.P., Kao A.W. (**2021**) *Processing of progranulin into granulins involves multiple lysosomal proteases and is affected in frontotemporal lobar degeneration* Molecular Neurodegeneration Aug 3;16(1):51

Jensen V.L., Lambacher N.J., Li C., **Mohan S.**, Williams C.L., Inglis P.N., Yoder B.K., Blacque O.E., Leroux M.R., (**2018**) *Role for intraflagellar transport in building a functional transition zone* EMBO Reports Dec; 19(12):e45862

Sure G.R., Chatterjee A. Mishra N., Sabharwal V., Devireddy S., Awathi A., **Mohan S.**, and Koushika S.P. (**2018**) *UNC-16/JIP3 and UNC-76/FEZ1 limit the density of mitochondria in C. elegans neurons by maintaining the balance of anterograde and retrograde mitochondrial transport.* Scientific Reports June 12;8 (1):8938

Timbers, T.A., Garland, S., **Mohan, S**., Flibotte, S., Edgley, M., Muncaster Q., Au V., Li-Leger E., Rosell FI., Cai J., Rademakers S., Jansen G., Moerman, D., and Leroux, M. R. (**2016**) *Accelerating gene discovery by phenotyping whole-genome sequenced multi-mutation strains and using the sequence kernel association test (SKAT)* Plos Genetics Aug 10;12 (*8*).

Jensen V.L., Li C., Bowie R.V., Clarke L., **Mohan S.**, Blacque O.E., and Leroux M.R. (**2015**) *Formation of ciliary transition zone by Mks5/Rpgrip1L establishes a PIP2-enriched ciliary zone of exclusion (CIZE) needed for compartmentalizing signaling proteins*. EMBO Journal Oct 14;34 (*20)*, 2537-56.

Mohan S., Timbers T.A., Kennedy J., Blacque O.E., and Leroux M.R. (**2013**). *Striated rootlet and non-filamentous forms of rootletin maintain ciliary function*. Current Biology, Oct 21; 23 (*20*): 2016-22.

Phirke P., Efimenko E.*****, **Mohan S.***, Burghoorn J., Crona F., Bakhoum M.W., Trieb M., Schuske K., Jorgensen E.M., Piasecki B.P., Leroux M.R., Swoboda P. (**2011**) *Transcriptional profiling of C. elegans DAF-19 uncovers a ciliary base-associated protein and a CDK/CCRK/LF2p-related kinase required for intraflagellar transport*. Developmental Biology, *357*, 235-47. *** equal contribution**

Williams C.L., Li C., Kida K., Inglis P.N., **Mohan S.**, Semenec L., Bialas N.J., Stupay R.M., Chen N., Blacque O.E., Yoder B.K., Leroux M.R. (**2011**) *MKS and NPHP modules cooperate to establish basal body/transition zone membrane associations and ciliary gate function during ciliogenesis*. Journal of Cell Biology, *192*,1023-41.