Mohammad J. Eslamizade

Assistant professor in Neuroscience (Ph.D.)

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CAREER PROFILE

- **Assistant Professor of Neuroscience,** Novermber 2021 - current
- **Postdoctoral fellow**, Department of Biochemistry and Goodman Cancer Research Center, McGill University (April 2017 – September 2020).

Supervisors: Profs. Nahum Sonenberg (McGill University) and Jean-Claude Lacaille (University of Montreal, Department of Neuroscience)

- **Research assistant,** in Shefa Neuroscience Research Center, Khatam Al-Anbia Hospital, Tehran (2010 – 2015). Supervisor: Prof. Ali Gorji

Academic Educations

- **Ph.D. in *Neuroscience*,** Iran University of Medical Sciences, Tehran, Iran

January 2009 – September 2015
Thesis: *Intrinsic excitability of CA1 pyramidal neurons in an animal model of β-amyloid peptide toxicity: A focus on HCN channels and Ih current*
Supervisor: Prof. Mahyar Janahmadi (Department of Physiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran).

- **M.Sc. in *Medical Physiology***, Mashad University of Medical Sciences, Mashad, Iran

October 2006 - January 2009
Thesis: *Effect of inhaled corticosteroids on epithelium remodeling of experimental asthma induced in guinea pig airways and their responsiveness*
Supervisor: Prof. Mohammad H. Boskabady.

- **B.Sc. in *Nursing***, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran
  October 2002 - July 2006

POSTDOCTORAL RESEARCH FELLOW

Department of Biochemistry and Goodman Cancer Research Center, **McGill University** (Supervisor: Prof. Nahum Sonenberg) and Department of Neuroscience, **University of Montreal** (Supervisor: Prof. Jean-Claude Lacaille) April 2017 – September 2020

Key Projects (2017-2020):

***EIF4E and depressive phenotype*.** We found out changes in phosphorylation of eif4e and pharmacologic manipulation of its upstream kinases, MNK1/2, create a depressive-like behavior with underpinning changes in excitatory synaptic transmission. In this project, I recorded excitatory synaptic transmission (EPSC in voltage-clamp mode) using patch-clamp records from layer 5 pyramidal neurons in the medial prefrontal cortex of eif4e$^{ki/ki}$ and WT mice. I showed abolished phosphorylation ability of eif4e reduces EPSCs in response to serotonin (5-HT) application. In addition, I had the same results in WT mice when treated pharmacologically with cercosporamide (MNK1/2 inhibitor) (Aguilar-Valles et al., 2021. *Nature Communications*).

***EIF2α and Synaptic plasticity*.** Work on another initiation factor, eif2α that has been genetically manipulated to change its phosphorylation levels in forebrain inhibitory *vs* excitatory neurons led to the changes in inhibitory/excitatory synaptic transmission with remarkable consequences in long-term synaptic plasticity and implicit memories. Specifically, I recorded field potential records and found out that a reduction in eif2α phosphorylation in somatostatine-expressing inhibitory interneurons and CaMKIIα -expressing pyramidal neurons led to an enhancement in long-term synaptic plasticity in Schaffer-collateral pathway. Moreover, this is accompanied by changes in the EPSC and IPSC frequencies and amplitudes using patch-clamp recording (Sharma et al., 2020. *Nature*).

***BP1/2 in Inhibitory vs Excitatory neurons*.** In another study in searching for cellular mechanisms of anti-depressant mechanisms of ketamine, we found out inhibitory neurons are of essential components of ketamine anti-depressive response via mTORC1-eif4EBP2 signaling. In this project I recorded patch-clamp recordings and showed BP2 conditional deletion in GAD2-expressing interneurons led to a reduction in ketamine-induced EPSC responses, accompanied by a disturbance in inhibitory synaptic transmission through $GABA_A$ receptors. (Aguilar-Valles et al., 2021. *Nature*).

***Inhibitory vs Excitatory neurons in anesthesia-induced cognitive disturbances*.** In our latest project, we showed exposure of juvenile mice to anesthesia induces memory impairments with underpinning inhibitory, but not excitatory, synaptic deficits in hippocampal neurons. During this project, I performed patch-clamp recording in voltage clamp mode, and showed long-term exposure to general anesthesia leads to a reduction in GABAergic synaptic activity, while interestingly, excitatory synaptic transmission remains intact. (Roque et al., 2022. *Journal of Clinical Investigations*)

Research interests

- ***The mechanisms behind regulation of ion channels and synaptic receptors in neuronal processes such as synaptic plasticity and related behaviors.*** With a focus on HCN channels, due to their functional importance in (patho)physiological conditions, I am interested to find mostly two critical cellular points regulating their transcription and translation. First, we focus on pharmacologic manipulation of **transcription factors** (e.g., NF-kB) to see if this alters Ih currents and HCN1 and HCN2 expressions in the hippocampus. Second, at the level of posttranslational modifications, a focus on **microRNAs** match with 3'UTR region of HCN1 and HCN2 mRNAs. Our bioinformatic study showed there are several microRNAs from highly conserved and poorly conserved among mammals that target several regions in regulatory areas of HCN1 and HCN2 mRNAs. Although currently unavailable to me, however, I would like to find if there is a cell-type-specific, interneurons *vs* projection neurons, microRNA-HCN1/2 relationship.

- ***Hyperpolarization-activated Cyclic Nucleotide (HCN) gated ion channels in the nervous system disorders.*** During last years, I have focused on the measurement of Ih current passing through ***HCN channels in interneurons vs principal*** neurons in a variety of animal models of diseases, such as Alzheimer's disease, epilepsy, and valproate model of autism. The factors regulating this type of ion channel's expression and function and how it impacts neural circuits and disease phanotype is one of my pivotal interests.

- ***The (dys)functional significance of ionic plasticity in cortical and hippocampal interneurons.*** *Interneurons vs principal neurons* have differential and interesting roles in physiological processes like synaptic plasticity in the hippocampus and related behaviors. Moreover, interneurons have unknown contributory role in drug responses, for example ketamine, in disease models. More specifically, I am interested in **ionic plasticity** (i.e., chloride gradients across plasma membrane) and the regulatory mechanisms behind it. Recently, we are going to find the reasons underpinning **KCC2 (dys)regulation** with a focus on cell-type specific manner in epilepsy models.

- ***Regulatory mechanisms behind ion channels and synaptic receptors in the human brain.*** Ultimate goal of using animal models in neuroscience is to find new perspectives in pathophysiology of human brain disorders and drug discovery. A part of my research is to make a network to expand clinical relevance of animal research via having special investigations with **human brain sections** obtained during neurosurgery and preparation of **induced pluripotent stem cells (iPSC)** to differentiate into **lineage specific neurons** from patients with known neurodevelopmental epilepsy and autism.

Mentoring and Supervision

- **Fatemeh Saffarzadeh** (PhD. Research Assistant). Fetemeh performs RT-PCR, Western Blotting, IHC in the lab. She also manages lab members and helps in animal surgery, ECoG recordings, and behavioral tests.
- **Sanaz Khatami** (PhD student in Biotechnology, in collaboration with Dr. S. Mohammadi-Yeganeh from Department of Medical Biotechnology). To study microRNA(s) regulating HCN1 mRNA/protein expression in the mouse and human hippocampus. At the moment, we are doing bioinformatic studies to candid miRNAs potentially target HCN1 expression. For the next step, we will do PCR to detect miRNAs in human hippocampal samples from TLE surgeries. In thesis I have a ***co-supervisor*** role.
- **Zahra Soleimani** (M.Sc. student in Physiology, in collaboration with Dr. M. Janahmadi from Department of Physiology). Studying the role of NF-kB transcription factor in HCN1/2 gene regulation in an Alzheimer's disease rat model. Our pilot study showed NF-kB immunoreactivity is enhanced in hippocampal neurons in response to the injection of Amyloid beta peptides. On the other hand, incubation of hippocampal acute slices in aCSF containing JSH-23 (a NF-kB inhibitor) reduces Ih currents in CA1 pyramidal neurons. In thesis I have a ***co-supervisor*** role.
- **Vahid Ahli Khatibi** (M.Sc. student in Physiology, in collaboration with Dr. M. Janahmadi from Department of Physiology). The effects of 2-Deoxy-D-Glucose in the kainic acid model epilepsy. In thesis I have an ***advisor*** role.

Technical expertise

- **Electrophysiology:** Patch clamp recordings using different voltage-clamp and current-clamp modes in different neurons (interneurons and principal neurons), in acute brain slices, organotypic cultures, and dissociated cultured neurons
- **Electrophysiology:** Field Potential Recordings from acute brain slices
- **Electrophysiology:** Electro-cortico-graphy (ECoG) recording from mice/rats

- Electrophysiology: Human electroencephalography (EEG) analysis
- Acute brain slicing and organotypic hippocampal culture
- Optogenetics
- Animal cognitive and behavioral tests (Morris Water Maze, Barnes Maze, Passive/Active Avoidance, Elevated Plus Maze, Social Novelty and Avoidance tests)
- Mice/rat Stereotaxic Surgery
- Primer design, PCR, Western blot, Histological stainings, Morphometric analyses, Immunohistochemistry, and Immunofluorescence
- Bioinformatics to find candid microRNAs: TargetScan, MiRDB, mirVestigator, MIRANDA, DIANA Tools
- Softwares: pClamp (patch-clamp analysis), MATLAB (curve fitting to measure (in)activation voltages), Prism, SPSS, CorelDraw, and Microsoft Office

Teaching experience (2021-current)

- ***Neurobiology*** (Audiences: PhD students in Physiology, Biotechnology, and Molecular medicine). Neurobiology of synapse, protein translation in synaptic plasticity, neurobiology of epilepsy and autism
- ***Cellular and Molecular Neurophysiology*** (Audiences: PhD students in Physiology, Biotechnology, Molecular medicine): voltage-gated and ligand-gated ion channels, GABA receptors, Glutamate receptors, synaptic transmission, dendritic excitability.
- ***Electrophysiology*** (Audiences: PhD students in Physiology and Neuroscience): principles of bioelectricity, intracellular and extracellular recordings, patch-clamp and field potential recordings.
- ***Laboratory Animals*** (Audiences: PhD students in Physiology, Tissue Engineering, Biotechnology, Molecular medicine, Medical students): animal anesthesia and surgery, animal house, animal breading, injections, brain and blood sampling.

Society and Journal Memberships (2014-current)

- Iranian Neuroscience Society
- International Brain Research Organization
- Japan Neuroscience Society
- Editorial board member in the journal of **Basic and Clinical Neuroscience**
- Editorial board member in the journal of **Frontiers in Cellular Neuroscience**

Awards

- Travel award for the "38th Japan Neuroscience Society Congress", July 2015.

- Training scholarship award "Pathophysiology of basal ganglia disorders", 12-24 September 2011. Neuroscience School of Advanced Studies (NSAS), San Quirico dOrcia, Siena, Italy.

Publications (recent and relevant)

- Patricia Soriano Roque, Carolina Thörn Perez, Mehdi Hooshmandi, Calvin Wong, **Mohammad Javad Eslamizade**, Nicole Brown, Vanessa Magalie Goyon, Laura Neagu-Lund, Cathy Shen, Nicolas Daccache, Hiroaki Sato, Tamaki Sato, Jeffrey S. Mogil, Christos G. Gkogkas, Mihaela D. Iordanova, Masha Prager-Khoutorsky, Heidi M. McBride, Jean-Claude Lacaille, Linda Wykes, Thomas Schricker,

Arkady Khoutorsky. Parvalbumin interneuron loss mediates repeated anesthesia-induced memory deficits. *Journal of Clinical Investigation* 2023 Jan 17;133(2):e159344. doi: 10.1172/JCI159344.

- Argel Aguilar-Valles, Danilo De Gregorio, Edna Matta-Camacho, **Mohammad J. Eslamizade**, Abdessattar Khlaifia, Agnieszka Skaleka, Martha Lopez-Canul, Angelica Torres-Berrio, Sara Bermudez, Gareth M. Rurak, Stephanie Simard, Natalina Salmaso, Gabriella Gobbi, Jean-Claude Lacaille, Nahum Sonenberg. Antidepressant actions of ketamine engage cell-specific translation via eIF4E. *Nature* 2021 Feb;590(7845):315-319. doi: 10.1038/s41586-020-03047-0.

- Vijendra Sharma, Rapita Sood, Abdessattar Khlaifia, **Mohammad Javad Eslamizade**, Noah Cohen,, Tzu-Yu Hung, Danning Lou, Adonis Yiannakas, Shunit Gal-Ben Ari, Shravan Murthy, Fatemeh Saffarzadeh, Vinh T Truong, Peng Wang, A. Claudio Cuello, Karim Nader, Randal J. Kaufman, Arkady Khoutorsky, Jean-Claude Lacaille, Kobi Rosenblum, Nahum Sonenberg. Somatostatin-positive GABAergic INs regulate memory consolidation via eIF2α. *Nature*. 2020 Oct;586(7829):412-416. doi.org/10.1038/s41586-020-2805-8

- Argel Aguilar-Valles, Nabila Haji, Danilo De Gregorio, Edna Matta-Camacho, Jelena Popic, **Mohammad J. Eslamizade**, Vijendra Sharma, Ruifeng Cao, Christoph Rummel, Arnaud Tanti, Laura Fiori, Shane Wiebe, Nicolas Nunez, Stefano Comai, Robert Nadon, Giamal Luheshi, Naguib Mechawar, Gustavo Turecki, Jean-Claude Lacaille, Gabriella Gobbi and Nahum Sonenberg. Translational control of depression via phosphorylation of eukaryotic translation initiation factor 4E. *Nature Communications*. 2018. 9(1):2459

- **Mohammad J. Eslamizade**, Fatemeh Saffarzadeh, Sayed Mostafa Modarres Mousavi, Gholamhossein Meftahi, Narges Hosseinmardi, Mehdi Mehdizadeh, Mahyar Janahmadi. Alterations in CA1 pyramidal neuronal intrinsic excitability mediated by Ih channel currents in a rat model of amyloid beta pathology. *Neuroscience* 2015;305:279-292.

- Fatemeh Saffarzadeh, **Mohammad Javad Eslamizade**, Sayed Mostafa Modarres Mousavi, Mahmoudreza Hadjighassem, Ali Gorji. TRPV1 receptors augment basal synaptic transmission in CA1 and CA3 pyramidal neurons in epilepsy. *Neuroscience*. 2016;314:170-8.

- Fatemeh Saffarzadeh, **Mohammad Javad Eslamizade**, Tahereh Ghadiri, Mahmoudreza Hadjighassem, Ali Gorji. Effects of TRPV1 on the hippocampal synaptic plasticity in the epileptic rat brain. *Synapse* 2015;69(7):375-83.

Referees

1. Nahum Sonenberg (professor in McGill University)

My supervisor during postdoctoral fellowship.

Department of Biochemistry and Goodman Cancer Research Center, McGill University

Nahum.sonenberg@mcgill.ca

2. Jean-Claude Lacaille (professor, retired recently)

My supervisor during postdoctoral fellowship.

Department of Physiology and Neuroscience, Université de Montréal

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3. Mahyar Janahmadi (professor in neurophysiology and Head of Department of Physiology)

My supervisor in PhD thesis. She is currently one of my colleagues and collaborators in Shahid Beheshti University of Medical Sciences.

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4. Samira Mohammadi-Yeganeh (Associate professor in Medical Biotechnology)

One of my current colleagues and collaborators as an Associate professor of Department of Medical Biotechnology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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5. Hossein Ghanbarian (Associate professor and Head of Department of Medical Biotechnology)

One of my current colleagues and collaborators as an Associate professor and Head of Department of Medical Biotechnology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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