NAME: Simon Chen

POSITION TITLE: Associate Professor in Cellular and Molecular Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of British Columbia	BSc.	05/2007	Cell Biology
University of British Columbia	Ph.D.	07/2012	Neuroscience
University of California, San Diego	Postdoctoral	05/2016	Neuroscience

A. Personal Statement

One of the most important unresolved questions in neuroscience is how memories are encoded and stored in the brain. Motor learning differs from other forms of learning, whereby repetitive training and practice is required in order to achieve highly skilled and reproducible movement. The primary motor cortex in the brain is known to initiate voluntary movement, but it has also been shown to be involved in motor memory formation and storage. Loss of function in the motor cortex can lead to motor dysfunction, as seen in stroke and Parkinson's Disease. Hence, a determination of the mechanisms involved in motor learning will enhance our understanding of post-traumatic recovery in motor-related brain injury and diseases. The **overarching goal** of my lab's research is to decipher the intricate interrelationships between molecular, structural, and functional dynamics of neural networks within the motor cortex while mice acquire and execute new motor movements in both normal and diseased brains.

Throughout my graduate and postdoctoral training, I produced original and innovative work that was published in top-tier scientific journals. During my Ph.D. (Kurt Haas Lab, UBC), I utilized *in vivo* two-photon imaging to examine molecular mechanisms that direct the functional and structural plasticity in the developing brain of *Xenopus* tadpoles (***Chen et al. Neuron. 2010; Chen et al. Cell. 2012***). For my postdoctoral training (Takaki Komiyama Lab, UCSD), I continued using *in vivo* two-photon imaging but moving to awake and behaving mice and examined cell-type specific circuit interactions underlying motor learning (***Peters, Chen, Komiyama. Nature. 2014; Chen et al. Nature Neuroscience. 2015***). My diverse background has offered me a broad foundation in molecular, cellular, and circuit techniques at both *in vitro* and *in vivo* levels, which endowed my lab to have emergent, distinctive, and sophisticated approaches to establish a vibrant research program.

My lab is specialized in combining chronic *in vivo* two-photon imaging with genetic and molecular approaches to dissect how cell type- and projection- specific neurons among different neuronal ensembles orchestrate plastic changes in the motor cortex while acquiring new motor movements in healthy and diseased brainswe. Over the past 6 years, we have pioneered an array of newly-developed tools that allowed us to directly visualize cellular and molecular events within distinct cell type-, projection-, or activity dependent-neuronal populations and track their changes in the intact brain of awake and behaving mice during motor learning. We have uncovered major neuronal subtypes in the motor cortex show differential responses to reward and reward-associated stimuli during reinforcement motor skill learning (***Lee et al., eLife, 2022***). We have also identified an activity-dependent transcription factor, NPAS4, that is uniquely expressed only in a subset of the somatostatin inhibitory neurons during motor learning, and it regulates SOM-mediated inhibition during the circuit reorganization process (***Yang et., Neuron 2022***). Lastly, we established a new research direction in the lab on deciphering abnormal neural circuits in mouse models of autism, in which we unveiled an unanticipated role of noradrenaline modulation in rescuing the circuit deficits and improving delayed motor learning in 16p11.2 deletion mice (***Yin et al. Nature Neuroscience 2021***). Our work not only provides unique and novel insights into the network dynamics in the motor cortex during motor skill acquisition, but it also identifies underlying molecular and cellular mechanisms relevant for designing novel clinical approaches to ameliorate dysfunctional circuitry in the diseased brain.

B. Positions and Honors

POSITION	FIELD	Completion Date MM/YYYY	INSTITUTION/ SUPERVISOR
Research Assistant	Neuroscience	08/2007	University of British Columbia / Dr. Kurt Haas
Postdoctoral Fellow	Neuroscience	04/2016	University of California, San Diego / Dr. Takaki Komiyama
Assistant Professor	Neuroscience	06/2016 – 05/2022	University of Ottawa
Associate Professor	Neuroscience	06/2066 – present	University of Ottawa

Academic and Professional Honors
Awards:

1. Canada Research Chair Tier II (2021-2016)
2. Brain Canada Future Leader (2021 – 2023)
3. NARSAD Young Investigator (2019 – 2021)
4. Canada Research Chair Tier II (2016-2021)
5. Human Frontier Science Program Postdoctoral Fellowship (2013-2016)
6. Canadian Institute of Health Research Postdoctoral Fellowship (declined)
7. Life Science Research Foundation Postdoctoral Fellowship (declined)
8. Canadian Institute of Health Research Michael Smith Foreign Study Supplements (2012)
9. Canadian Institute of Health Research Senior Graduate Scholarship (2009 – 2012)
10. Program of Neuroscience Entrance Scholarship (2007)
11. Epilepsy Canada Summer Research Scholarship (2006)

Honors:

1. uOttawa Faculty of Medicine - Biomedical Publication of the Year (2021)
2. 2012 Canadian Institute of Neurosciences Mental Health and Addiction Marlene Reimer Brain Star of the Year Award (2012)
3. Canadian Institute of Neurosciences Mental Health and Addiction Brain Star Award (2012)
4. UBC Department of Cellular and Physiological Sciences Graduate Student Research of the Year Award (2012)
5. Canadian Institute of Neurosciences Mental Health and Addiction (CIHR-INMHA**)** Brain Star Award (2010)
6. UBC Department of Cellular and Physiological Sciences Graduate Student Research of the Year Award (2010)
7. Society for Neuroscience Pacific Northwest Chapter Meeting Best Speaker Award (2010)
8. Eli Lilly/Canadian Neuroscience Association Young Neuroscientist Award (2008)

C. Contribution to Science

1. Lee, C.*, Côté, S.L.*, Raman, N., Chaudhary, H., Mercado, B.C., **Chen, S.X.** (2023) Whole-brain mapping of long-range inputs to the VIP-expressing inhibitory neurons in the primary motor cortex. ***Frontiers in Neural Circuits*** *co-first authors

2. Yang, J.*, Serrano, P.*, Yin, X.*, Sun, X., Lin, Y., **Chen, S.X.** Functionally distinct NPAS4-expressing somatostatin interneuron ensembles critical for motor learning. ***Neuron*** *110, 3339-3355*
*co-first authors

- Preview in Neuron – Park, E., Barth A.L. (2022) IEG expression defines SST neuron ensembles critical for motor learning. Neuron *110, 3222-3224*

3. Lee, C., Harkin, E., Yin, X., Naud, R., **Chen, S.X**. Cell-type specific responses to associative learning in the primary motor cortex ***eLife*** 11:e72549

4. Yin, X., Jones, N., Yang, J.W., Asraoui, N., Mathieu, M.E., Cai, L., **Chen, S.X.** (2021). Delayed motor learning in 16p11.2 deletion mouse model of autism is rescued by locus coeruleus activation. ***Nature Neuroscience*** *24, 646–657*

5. Lee, C., Lavoie, A., Liu, J.X., **Chen, S.X.*,** Liu, B.H.* (2020) Light Up the Brain: the application of optogenetics in cell-type specific dissection of brain circuits. ***Frontiers in Neural Circuits*** *14:18*
*co-corresponding last authors

6. **Chen, S.X.,** Kim, A.N., Peters, A.J., Komiyama, T. Subtype-specificity of inhibitory circuits in motor cortex during motor learning. ***Nature Neuroscience*** *18(8):1109-15*

- News and Views in Nature Neuroscience - Grillo, F.W., West, L., De Paola, V. (2015) Removing synaptic brakes on learning. Nature Neuroscience *18(8):1162-64*

7. Peters, A.J., **Chen, S.X**., Komiyama, T. (2014) Emergence of reproducible spatiotemporal activity during motor learning. ***Nature*** *510(7504)*:263-7

8. **Chen, S.X.,** Cherry, A., Tari, P.K., Podorgski, K., Kwong, KH, Haas, K. (2012). The transcription factor MEF2 directs developmental visually-driven functional and structural metaplasticity. ***Cell*** *151*, 41-55.

- Preview in Cell – Della Santina, L., Wong, R.O. (2012) A molecular link tethering neuronal responses with the past. Cell *151*: 9 – 11.

9. **Chen, S.X.,** Haas, K. (2011). Function directs form of neuronal architecture. ***BioArchitecture*** *1*, 2-4.

10. **Chen, S.X.,** Tari, P.K., She, K., and Haas, K. (2010). Neurexin-neuroligin cell adhesion complexes contribute to synaptotropic dendritogenesis via growth stabilization mechanisms in vivo. ***Neuron*** *67*, 967-983.

11. Hewapathirane, D.S., Dunfield, D., Yen, W., **Chen, S.,** and Haas, K. (2008). In vivo imaging of seizure activity in a novel developmental seizure model. ***Exp Neurol*** *211*, 480-488.

D. Research Support

1. Principal Investigator – Canadian Institute of Health Research (CIHR)
   Project Grant (2022 – 2027)
   Amount: $850,000

2. Principal Investigator – Brain Canada Future Leader (2021 – 2023)
   Amount: $100,000

3. Principal Investigator – Scottish Rite Foundation (2020 – 2023)
   Amount: $120,000

4. Principal Investigator – NARSAD Young Investigator Award (2019 – 2021)
   Amount: $75,000 USD

5. Co- Principal Investigator – KREMBIL Group Grant (2018 – 2021)

Amount: $162,000

6. Principal Investigator – Canadian Institute of Health Research (CIHR) Project Grant (2017 – 2022)
   Amount: $918,000

7. Principal Investigator - Natural Sciences and Engineering Research Council of Canada (NSERC) Discover Grant (2017 – 2022)
   Amount: $150,000

8. Principal Investigator – Simons Foundation Explorer Grant (2017 – 2018)
   Amount: $100,000 USD

9. Principal Investigator – Canada Foundation for Innovation (2016 – 2017)
   Amount: $750,000

10. Principal Investigator – Canada Research Chair (2016 – 2021)
    Amount: $500,000