BIOGRAPHICAL SKETCH

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NAME: Kei M. Igarashi, Ph.D.

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

POSITION TITLE: Associate Professor

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Tokyo	BS	03/2001	Molecular Biology
University of Tokyo	PhD	03/2007	Neurophysiology
University of Tokyo	Postdoc	04/2009	Neurophysiology
Norwegian University of Science and Technology	Postdoc	12/2015	Systems Neuroscience

A. Personal Statement

Throughout my career, a central direction of my research has been to understand how interactions between multiple brain regions give rise to behavior and how impairment of these interactions results in disease. To this end, I have been pursuing research using the entorhinal-hippocampal circuit as a model system, and investigating cellular and circuit mechanisms that support memory. I have a broad background in systems neuroscience, with extensive training in functional optical imaging (**Igarashi & Mori, *J Neurophys*, 2005**) and single-cell neuroanatomy (**Igarashi et al., *J Neurosci* 2012**) during my PhD with Kensaku Mori at the University of Tokyo, and in high-density electrophysiology from rodents performing memory tasks and spike/local field potential (LFP) analyses (**Igarashi et al., *Nature* 2014**) during my postdoc research in the lab of Edvard Moser and May-Britt Moser at the Norwegian University of Science and Technology. In my lab at the University of California, Irvine (UCI), we investigate (1) cellular and circuit mechanisms of associative memory in healthy subjects (**Lee et al., *Nature* 2021; Jun et al., *Nature* 2024**), and (2) how impairments of memory circuit mechanisms cause memory deficit in Alzheimer's disease (**Jun et al., *Neuron* 2020; Nakagawa et al., *Nat Neuroci* 2026**).

1. Nakagawa T, Xie JL, Park K, Cao K, Savadkohighodjanaki M, Zhang YJ, Jun H, Ichii A, Lee JY, Soma S, Medhat YK, Saido TC, **Igarashi KM*** (2026)
   Early dopamine disruption in the entorhinal cortex of a knock-in model of Alzheimer's disease
   Nature Neuroscience. DOI: 10.1038/s41593-026-02260-w
2. Jun H, Lee JY, Bleza, N, Ichii A, Donohue JD, and **Igarashi KM*** (2024)
   Prefrontal and lateral entorhinal neurons co-dependently learn item-outcome rules.
   Nature 633: 864-871 PMID: 39169188
3. Lee JY, Jun H, Soma S, Nakazono T, Shiraiwa K, Dasgupta A, Nakagawa T, Xie JL, Chavez J, Romo R, Yungblut Y, Hagihara M, Murata K, and **Igarashi KM*** (2021)
   Dopamine facilitates associative memory encoding in the entorhinal cortex.
   Nature 598: 321-326 PMID: 34552245
4. Jun H, Soma S, Saito T, Saido TC, **Igarashi KM*** (2020)
   Disrupted place cell remapping and impaired grid cells in a knock-in model of Alzheimer's disease
   Neuron 107:1095-1112 PMID: 32697942

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2025-present Distinguished Adjunct Professor, Tohoku University School of Medicine, Japan
2023-present Chancellor's Fellow, UC Irvine
2022-present Associate Professor (tenured); 2016- 2022 Assistant Professor,
Department of Anatomy & Neurobiology, UC Irvine
2016-present Fellow, Center for the Neurobiology of Learning & Memory, UC Irvine
2018-present Faculty Member, Institute for Memory Impairments and Neurological Disorders, UC Irvine
2009-2015 Postdoctoral Fellow/Research Associate with Drs. Edvard Moser and May-Britt Moser,
Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology
2007-2009 Postdoctoral Fellow with Drs. Kensaku Mori and Manabu Tanifuji
University of Tokyo School of Medicine/RIKEN Brain Science Institute
2008 Visiting Researcher with Drs. Wei R Chen and Gordon Shepherd, Yale University
2003-2007 PhD student with Dr. Kensaku Mori, University of Tokyo School of Medicine
2001-2003 MS student with Dr. Kensaku Mori, University of Tokyo School of Medicine
2000-2001 Undergraduate research assistant with Dr. Hitoshi Sakano, University of Tokyo

Scientific Appointments

2026 Founding Chair, Gordon Research Conference on Entorhinal-Hippocampal Memory Circuit
2025-present NIH Learning, Memory and Decision Neuroscience (LMDN) study section, standing member
2024 NIH Chronic Dysfunction & Integrative Neurodegeneration (CDIN) study section, Ad-hoc reviewer
2023 External Review Member, Pasteur Institute, France
2022-present Society for Neuroscience, Diversity and Inclusion Working Group
2022-present Society for Neuroscience, Program Committee (Theme I Chair)
2020-present Japan Neuroscience Society, Diversity Committee
2019-present Japan Neuroscience Society, International Collaboration Affairs Committee
2022, 2023 NIH Learning, Memory and Decision Neuroscience (LMDN) study section, Ad-hoc reviewer
2022, 2023 European Research Council (ERC), Ad-hoc reviewer
2022 NIH Special Emphasis study section on Alzheimer's disease (ZRG1 IFCN-J), Ad-hoc reviewer
2020 NIH Brain Initiative study section (ZRG1 IFCN-T(55)), Ad-hoc reviewer
2020, 2025 Wellcome Trust (UK), Ad-hoc reviewer
2019, 2022 Israel Science Foundation, Ad-hoc reviewer
2019, 2020 NIH Neurobiology of Learning and Memory (LAM) study section, Ad-hoc reviewer
2017 – present Alzheimer's Association, standing grant reviewer

Member: Cajal Club (2019 –), Federation of European Neuroscience Societies (2010 –), Norwegian Neuroscience Society (2010 –), Society for Neuroscience (2005 –), Japan Neuroscience Society (2001 –)

Reviewer for Journals: *Nature, Science, Cell, Nat Neurosci, Neuron, Sci Adv, Mol Psych, J Neurosci, eLife, Frontier journals, Cell Reports, Scientific Reports, PLoS Biology, J Neurophysiol, Curr Opin Neurobiol*

Honors

2025 Inoue Prize for Science
2023 Japan Academy Medal
2023 Japan Society for Promotion of Science (JSPS) Prize
2023 Silver Beaker Award for Excellence in Teaching, UC Irvine School of Medicine
2022, 2023 Medical Education Excellence Award in Teaching, UC Irvine School of Medicine
2022 Robert & Sylvia Mapel Research Endowment, UC Irvine School of Medicine
2022 Outstanding Early-Career Faculty Research Award, UC Irvine School of Medicine
2019 Alzheimer's Disease Research Award, BrightFocus Foundation
2019 New Vision Award for Alzheimer's Disease Research, Donors Cure Foundation
2017 Mishima Kaiun Prize, Mishima Kaiun Memorial Foundation
2016 Fay/Frank Seed Grant, Brain Research Foundation
2016 PRESTO Career Development Award, Japan Science and Technology Agency
2014 Young Investigator Award, Japan Neuroscience Society
2012 Norwegian Research Council Postdoctoral Fellowship
2007 – 2009 Postdoctoral Fellowship, Japan Society for the Promotion of Science
2004 – 2007 Predoctoral Fellowship, Japan Society for the Promotion of Science

C. Contributions to Science

1. In the current learning and memory research, one of the most important and outstanding questions is to understand **circuit mechanisms underlying associative memory**, which is the most common form of memory in our daily life. In the past 30 years, neuronal circuits underlying *spatial* memory and navigation have been identified by O'Keefe, Moser, and Moser (2014 Nobel Prize). Despite these findings, mechanisms for episodic memory remain unclear. During my postdoc, I showed that the lateral entorhinal cortex (LEC) plays a major role in associative memory (**Igarashi et al., *Nature* 2014**). To summarize the function of the entorhinal cortex, I wrote a review paper (**Igarashi, *Brain Res*, 2016**). However, my previous study was a correlational recording study of LEC spike activities from rats. This type of correlational recording study has been from the classical tradition in electrophysiology research over the decades, and subsequent correlational recording studies from other labs further implicated roles of the LEC in various functions. Our views on the function of the LEC have thus been significantly divided in the past 10 years, hampering advancement of the field. A major reason for this discordance was that these studies, including ours, were merely correlational, without any circuit interventions, and recordings were collected from unknown neuronal populations. Since I started my lab, I have investigated the role of the LEC using cell-type-specific intervention and recording to challenge the status quo in the field. After a long-term effort, we recently obtained compelling results demonstrating that neurons in the LEC play a critical role in associative memory, a fast-type associative learning between newly-learned information and pre-learned memory (**Lee, Jun et al., *Nature*, 2021**). We also found that dopamine input to the LEC plays a critical role in associative memory. Our results provide a breakthrough in the field of learning and memory research, demonstrating that the LEC is the brain area that achieves associative memory. Furthermore, our novel discovery about how dopamine controls the LEC will bring a major conceptual breakthrough in that two previously independent fields of neuroscience, memory research and reinforcement learning, can be now unified.

   a. Jun H, Lee JY, Bleza, N, Ichii A, Donohue JD, and **Igarashi KM*** (2024) Prefrontal and lateral entorhinal neurons co-dependently learn item-outcome rules. ***Nature*** 633: 864-871 PMID: 39169188

   b. **Igarashi KM***, Lee JY, Jun H (2022) Reconciling neuronal representations of schema, abstract task structure, and categorization under cognitive maps in the entorhinal-hippocampal-frontal circuits ***Curr Opin Neurobiol*** 77:102641 PMID: 36219950

   c. Lee JY, Jun H, Soma S, Nakazono T, Shiraiwa K, Dasgupta A, Nakagawa T, Xie JL, Chavez J, Romo R, Yungblut Y, Hagihara M, Murata K, and **Igarashi KM*** (2021) Dopamine facilitates associative memory encoding in the entorhinal cortex. ***Nature*** 598: 321-326 PMID: 34552245

   d. **Igarashi KM***, Lu L, Colgin LL, Moser MB, Moser EI* (2014). Coordination of entorhinal-hippocampal ensemble activity during associative learning. ***Nature*** 510: 143-7 PMID: 24739966

2. Alzheimer's disease (AD) currently affects 50 million people worldwide, but no cure exists. Although previous studies are shedding light on molecular and cellular mechanisms of AD, it remains unclear what type of impairment in neuronal activity causes memory impairment in AD subjects. This is a critical gap in knowledge in current AD research: If we can clearly identify such mechanisms, we may be able to develop a therapeutic treatment to prevent the deterioration of memory circuits in AD patients. To fill this critical gap, I have been striving to elucidate **circuit mechanisms of AD** that cause memory impairment using in vivo circuit analysis and electrophysiological methods applied to a mouse model of AD. My specific focus is the role of the **entorhinal cortex** in AD pathogenesis. Although it has long been known that the entorhinal cortex is the primary brain area showing functional and cellular degeneration in the early phase of AD, little has been known about the entorhinal cortex in AD because AD research has emphasized the hippocampus. We first focused on gamma oscillations, a network activity essential for the communication between the entorhinal cortex and hippocampus. We provided the first evidence that in vivo gamma oscillations are impaired in the entorhinal cortex of an AD mouse model (**Nakazono et al., *Front Syst Neurosci*, 2017**). This finding was also summarized in our review (**Nakazono et al., *Neurosci Res*, 2018**). To determine what circuit activity is causing memory impairment, we recently provided the first evidence that the impairment of place cell remapping, a network activity for distinguishing different environments, is disrupted in an AD mouse model (**Jun et al., *Neuron* 2020**). We showed that the remapping deficit emerges together with memory impairment over the course of pathogenesis, whereas the impairment of grid cells in the entorhinal cortex precedes the remapping/memory impairment. Our results suggest that remapping impairment is a circuit mechanism underlying spatial memory impairment in AD, and grid cell degeneration can be a primary cause of remapping

impairment in the hippocampus. Our finding is expected to lead to future therapeutic methods that slow the rate of spatial memory decline in AD patients. Since the publication of the *Neuron* paper we have received an increasing number of requests to provide experimental methods. To share the methods with a larger community, we published a protocol paper (**Jun et al., *STAR Protocols*, 2021**). Recently we further showed that sharp-wave ripples are impaired in our AD mouse model (**Funane et al., *Front Syst Neurosci*, 2022**). I recently reviewed current knowledge about activity dysfunctions of the entorhinal cortex (**Igarashi, *Trends Neurosci*, 2023**).

a. Nakagawa T, Xie JL, Park K, Cao K, Savadkohighodjanaki M, Zhang YJ, Jun H, Ichii A, Lee JY, Soma S, Medhat YK, Saido TC, **Igarashi KM*** (2026)
Early dopamine disruption in the entorhinal cortex of a knock-in model of Alzheimer's disease
Nature Neuroscience. DOI: 10.1038/s41593-026-02260-w

b. **Igarashi KM*** (2023)
Entorhinal cortex dysfunction in Alzheimer's disease
Trends in Neuroscience, 46: 124-136 PMID: 36513524

c. Jun H, Soma S, Saito T, Saido TC, **Igarashi KM*** (2020) Disrupted place cell remapping and impaired grid cells in a knock-in model of Alzheimer's disease ***Neuron*** 107:1095-1112 PMID: 32697942

d. Nakazono T, Lam TN, Patel AY, Kitazawa M, Saito T, Saido TC, **Igarashi KM*** (2017). Impaired In Vivo Gamma Oscillations in the Medial Entorhinal Cortex of Knock-in Alzheimer Model. ***Front Syst Neurosci*** 11:48 PMID: 28713250

3. During my postdoctoral work in the Moser lab, I also investigated **pattern separation of place cells and grid cells** in the hippocampus and medial entorhinal cortex during animals' spatial memory. We found that place cells in the CA2 area of the hippocampus show pattern completion (memory filling-in) compared to those in CA3, which showed pattern separation (memory dissociation). I also investigated the roles of gamma oscillations in the spatial representation of grid cells in the medial entorhinal cortex (paper in preparation).

a. **Igarashi KM*** (2016). Entorhinal map of space. ***Brain Research*** 1637:177-87. PMID: 26940561

b. Lu L, **Igarashi KM**, Witter MP, Moser EI, Moser MB (2015). Topography of Place Maps along the CA3-to-CA2 Axis of the Hippocampus. ***Neuron*** 87:1078-92. PMID: 26298277

4. My Ph.D. and successive short postdoc works identified **olfactory brain circuits** that enable rodents to process a wide variety of odor information. These studies were performed in the laboratory of Kensaku Mori at the University of Tokyo. Basic circuitry in the olfactory brain regions, including the olfactory bulb and olfactory cortex, has been long unexplored, and thus it was unclear how the brain processes odor information. I have investigated rodent olfactory circuits, as they share olfactory brain regions of a similar structure to those in humans. In the publications listed below, I used a variety of imaging, electrophysiology, and anatomical techniques to investigate the circuit architecture of the olfactory bulb and cortex. I found that a small, compartmentalized structure in the olfactory bulb (glomeruli) processes information of distinct odor molecules, forming clusters for hydrophilic and hydrophobic odors. I further discovered that individual odor information is decomposed into temporally fast coarse information and slow precise information by two distinct cell types, and conveyed to distinct regions in the olfactory cortex. These results contributed to the foundations of current research on olfactory perception and behaviors, and have been cited as background references in many research papers. I continue working with my long-term collaborators to understand circuit mechanisms for olfactory sensory processing.

a. **Igarashi KM***, Ieki N, An M, Yamaguchi Y, Nagayama S, Kobayakawa K, Kobayakawa R, Tanifuji M, Sakano H, Chen WR, Mori K.* (2012).
Parallel mitral and tufted cell pathways route distinct odor information to different targets in the olfactory cortex. ***Journal of Neuroscience*** 32:7970-85 (*Co-corresponding authors) PMCID: PMC3636718

b. Mori K, Takahashi YK, **Igarashi KM**, Yamaguchi M. (2006). Maps of odorant molecular features in the Mammalian olfactory bulb. ***Physiol Rev*** 86:409-433 PMID: 16601265

c. **Igarashi KM**, Mori K. (2005). Spatial representation of hydrocarbon odorants in the ventrolateral zones of the rat olfactory bulb. ***Journal of Neurophysiology*** 93:1007-1019 PMID: 15385587

Complete list of published work can be found on PubMed
https://pubmed.ncbi.nlm.nih.gov/?term=Igarashi+KM%5Bau%5D&sort=date