OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Kinnebrew, Maia

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-7344-8231

Position Title: Stanford Distinguished Fellow

Organization and Location: Stanford University, School of Medicine, Stanford, California, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Stanford University, School of Medicine, Stanford Universtiy, California, United States	Postdoctoral Fellow	10/2021	11/2023	Biochemistry
Stanford University, School of Medicine, Stanford University, California, United States	Doctor of Philosophy (PHD)	09/2014	08/2021	Biochemistry
University of California, Santa Barbara,, Santa Barbara, California, United States	Bachelor of Arts (BA)	09/2010	06/2014	Biology

Appointments and Positions

2024 - present	Stanford Distinguished Fellow, Stanford University, School of Medicine, Stanford, California, United States
2025 - 2026	Section leader for Graduate Advanced Cell Biology course, Stanford University, School of Medicine, Stanford, California, United States
2023 - present	NIH Director's Early Independence Awardee (DP5), National Institutes of Health, Bethesda, Maryland, United States
2023 - present	HHMI Hanna H. Gray Fellow, Howard Hughes Medical Institute, Chevy Chase, Maryland, United States
2023 - 2024	Member of the Pathways to Neuroscience Program, Stanford University, School of Medicine, Stanford, California, United States
2021 - 2023	Postdoctoral Researcher in Dr. Rajat Rohatgi’s research laboratory, Stanford University, School of Medicine, Stanford, California, United States
2021 - 2023	Member of the Stanford Work-Life Office Dependent Care Working Group, Stanford University, School of Medicine, Stanford , California, United States
2019 - 2022	Member of the Biochemistry Advocacy Coalition, Stanford University, School of Medicine, Stanford, California, United States
2019 - 2022	Member of the Student Advocate Support Network, Stanford University, School of Medicine, Stanford, California, United States
2019 - 2020	Vice President for the Biomedical Association for the Interest of Minority Students, Stanford University, School of Medicine, Stanford, California, United States
2019 - 2019	Member of The American Society for Cell Biology, The American Society for Cell Biology, Rockville, MD, United States
2018 - 2019	Communication Chair for the Biomedical Association for the Interest of Minority Students, Stanford University, School of Medicine, Stanford, California, United States
2016 - 2019	Programming coordinator of the Awesome Science Symposium Series, Stanford University, School of Medicine, Stanford, California, United States
2016 - 2017	Teaching assistant for graduate level Macromolecules course, Biochemistry Dept, Stanford University, Stanford, California, United States
2014 - 2021	Graduate Researcher in Dr. Rajat Rohatgi’s research laboratory, Stanford University, School of Medicine, Stanford, California, United States
2014 - 2017	Member of the NSF Graduate Research Fellowship Mentoring Program , Stanford University, School of Medicine, Stanford, California, United States
2014 - 2014	Member of Stanford ADVANCE Program, Stanford University, School of Medicine, Stanford, California, United States

2012 - 2013	Member of the California Nanosystems Institute at Girls Incorporated, Univ of California, Santa Barbara, Santa Barbara, California, United States
2012 - 2012	Mentor for the Materials Research Laboratory Educational Isla Vista Youth Project, Univ of California, Santa Barbara, Santa Barbara, California, United States
2011 - 2012	Member of the Society for the Advancement of Chicanos and Native Americans in Science, Univ of California, Santa Barbara, Santa Barbara, California, United States
2011 - 2012	Associated Students Representative for the College of Creative Studies, Univ of California, Santa Barbara, Santa Barbara, California, United States
2010 - 2014	Member of the Biophysical Society, Stanford University, School of Medicine, Stanford, California, United States
2010 - 2014	Undergraduate Researcher in Dr. Songi Han's research laboratory, Univ of California, Santa Barbara, Santa Barbara, California, United States
2010 - 2014	Undergraduate Student in the College of Creative Studies, Univ of California, Santa Barbara, Santa Barbara, California, United States
2010 - 2012	Undergraduate Researcher in Dr. Armand Kuris's research laboratory, Univ of California, Santa Barbara, Santa Barbara, California, United States

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

Certified by Kinnebrew, Maia in SciENcv on 2026-05-15 19:33:23

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Kinnebrew, Maia

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-7344-8231

Position Title: Stanford Distinguished Fellow

Organization and Location: Stanford University, School of Medicine, Stanford, California, United States

Personal Statement

Our lab aims to determine how lipids are organized in cell membranes and how lipids regulate transmembrane receptor signaling events in health and disease. My expertise studying lipids stems from my training with Dr. Songi Han at UC Santa Barbara, where I investigated how protein-protein and protein-lipid interactions tune signaling events in vitro with purified receptors (*Biophysical Journal* 2013, *Cell Press Structure* 2014, *Journal of Molecular Biology* 2015, *Biophysical Journal* 2023). During my PhD training with Dr. Rajat Rohatgi at Stanford University, I investigated the receptor-mediated steps of the Hedgehog pathway, an essential developmental signaling cascade. In the Rohatgi lab I solved a 25-year-old mystery in the Hedgehog field by showing how cholesterol, an abundant cellular lipid, can act as an instructive signal to drive G protein-coupled receptor signaling (*Elife* 2019, *Elife* 2021, *Science Advances* 2022, *Elife* 2026).

Currently, with the support of an HHMI Hanna Gray Fellowship and an NIH Director's Early Independence Award (DP5), I am running an independent lab in the Biochemistry Department at Stanford University. My lab is focused in two areas: first, we aim to understand how cells maintain plasma membrane (PM) lipid organization by utilizing fluorescent lipid binding protein probes, genetic screens, and mechanistic dissection of new membrane regulators. Secondly, we investigate lipoprotein secretion and internalization pathways to better understand human diseases such as Alzheimer's Disease and cardiovascular disease. In both areas, we are particularly excited by cholesterol, which makes up about 40% of PM lipids and also about 40% (esterified and free cholesterol) of low density lipoprotein (LDL), which is a significant source of cholesterol for many cell types. Within cells, we are interested in cholesterol's role in regulating receptor signaling and membrane trafficking events that are vital to cell survival.

Using a genome-wide genetic screen, we recently identified that adipose triacylglycerol lipase (ATGL), a protein known to control energy metabolism via triacylglycerol hydrolysis, has a second function in remodeling the PM lipidome. By reducing the saturation of phospholipid acyl chains, ATGL activation raises the *chemical activity* of cholesterol in the PM, and ATGL inhibition does the opposite (In press, 2026; PMID: 40909529). Our future studies aim to determine how ATGL-dependent lipid remodeling modulates receptor signaling events at the PM. More broadly, we are dissecting the function of chemically active cholesterol for in vivo biology by measuring it across primary cells isolated from animal models of autoinflammation and aging. Altogether, by using unique cell-biological approaches to study lipids, our work will advance our understanding of diseases linked to lipid dysregulation, including neurodegeneration, metabolic syndromes and cardiovascular disease.

Honors

2025 - 2025	Stanford.Berkeley.UCSF Next Generation Faculty Symposium Speaker, Stanford, Berkeley, and UCSF
2023	HHMI Hanna H. Gray Fellow, The Howard Hughes Medical Institute
2023	Stanford Distinguished Fellow, Stanford University
2023	NIH Director’s Early Independence Award, National Institutes of Health
2019 - 2020	Stanford Biosciences Excellence in Service to Graduate Students Award, Stanford University
2014 - 2017	National Science Foundation Graduate Research Fellowship, Stanford University
2014 - 2014	Faculty Executive Committee Commendation of Excellence Award, University of California, Santa Barbara
2013 - 2013	Minority Affairs Committee Travel Awardee, Biophysical Society 57th National Conference, Biophysical Society
2012 - 2013	Beckman Scholar, funded by the Arnold and Mabel Beckman Foundation, University of California, Santa Barbara
2012 - 2012	SACNAS National Conference Travel Scholarship, Society for Advancement of Chicanos/Hispanics & Native Americans in Science.
2012 - 2012	Poster Presentation Award, Society for the Advancement of Chicanos and Native Americans in Science, Society for Advancement of Chicanos/Hispanics and Native Americans in Science

2012 - 2012	Special Merit Award for poster presentation, CAMP Statewide Conference, National Science Foundation California Alliance for Minority Participation (CAMP)
2011 - 2012	California Alliance for Minority Participation (CAMP) Scholar, University of California, Santa Barbara

Contributions to Science

1. *Lipid environment and oligomerization control the function of 7-transmembrane proteins.*

   Oligomerization is a common strategy for tuning protein signaling. However, proving that oligomeric complexes exist in vivo, and isolating them for biochemical analysis in vitro, can be challenging. We utilized the light-activated proton pump proteorhodopsin (PR) as a model system to test how oligomerization can tune protein function. Early in this project, we made the unexpected discovery that changing the lipid environment surrounding PR had large effects on its oligomeric state and its proton pumping capacity. We showed that hexameric and pentameric PR, compared to monomeric PR, have a decreased rate of proton transport, opening further questions about the role of PR multimers observed in vivo. This work beautifully demonstrates how the local environment surrounding a protein tunes its activity.

   a. CT Han, KDQ Nguyen, MW Berkow, S Hussain, A Kiani, **M Kinnebrew**, MN Idso, N Baxter, E Chang, E Aye, E Winslow, M Rahman, S Seppälä, MA O'Malley, BF Chmelka, B Mertz, S Han. Lipid membrane mimetics and oligomerization tune functional properties of proteorhodopsin. *Biophysical Journal*, 2023. PMID: 36352784.

   b. S Hussain, **M Kinnebrew**, NS Schonenback, E Aye, S Han. Functional consequences of the oligomeric assembly of proteorhodopsin. *Journal of Molecular Biology*, 2015. PMID: 25597999.

   c. DT Edwards, T Huber, S Hussain, K Stone, **M Kinnebrew**, I Kaminker, E Matalon, MS Sherwin, D Goldfarb, S Han. Determining the oligomeric structure of proteorhodopsin by Gd3+- based pulsed dipolar spectroscopy of multiple distances. *Cell Press Structure*, 2014. PMID: 25438671.

   d. KM Stone, J Voska, **M Kinnebrew**, A Pavlova, S Han. Structural insight into proteorhodopsin oligomers.*Biophysical Journal*, 2013. PMID: 23442869.

2. *Partially structured tau oligomers precede the formation of insoluble aggregates.*

   A hallmark of Alzheimer's disease is neurofibrillary tangles formed from misfolded tau protein. Despite the clinical importance of tau aggregation, the process that initiates the formation of these large structures has remained a mystery. Utilizing my skillset in studying protein multimerization, I helped show that prior to tau aggregate formation, partially structured oligomers form. These oligomers, rather than monomers, assemble onto the growing end of long tau fibers, precipitating their growth.

   a. A Pavlova, CY Cheng, **M Kinnebrew**, J Lew, F Dahlquist, S Han. Protein structural and surface water rearrangement constitute major events in the earliest aggregation stages of tau. *Proceedings of the National Academy of Sciences*, 2016. PMID: 26712030.

3. *Accessible cholesterol is the second messenger of the Hedgehog signaling pathway.*

   The Hedgehog (HH) pathway is a cell-cell communication system that is critical for proper animal development. HH signaling is initiated when Sonic Hedgehog (SHH) ligands inhibit the receptor Patched-1 (PTCH1) in the primary cilia (PC) membrane. This relieves the inhibitory effect that PTCH1 has on Smoothened (SMO), which ultimately transmits information across the PC membrane to intracellular effectors. How PTCH1 regulates SMO, and why this occurs at PC, were 25-year-old mysteries in the field. Prior work suggested that PTCH1 controls SMO activity by restricting its access to cholesterol. However, cholesterol makes up 40% of lipids in the plasma membrane (PM), raising the question how PTCH1 could regulate this abundant molecule. I showed that PC membranes have low *accessible* cholesterol compared to the PM. Accessible cholesterol is the minor fraction (5%) of total membrane cholesterol that is not sequestered by other lipids and is available to interact with proteins. I showed that PTCH1 depletes accessible cholesterol from the membrane outer leaflet to regulate SMO. The unique lipid composition of PC likely regulates the function of other membrane proteins, including GPCRs, channels and receptors, that function there.

   a. **M Kinnebrew**, RE Woolley, et al. Patched-1 regulates Smoothened by controlling sterol binding to its extracellular cysteine-rich domain. *Science Advances*, 2022. PMID: 35658032.

b. **M Kinnebrew**[1], KA Johnson[1], et al. Measuring and manipulating membrane cholesterol for the study of Hedgehog signaling. *Methods in Molecular Biology*, 2022. PMID: 34562244.

c. **M Kinnebrew**, G Luchetti, et al. Patched 1 reduces the accessibility of cholesterol in the outer leaflet of membranes.*Elife*, 2021. PMID: 34698632.

d. **M Kinnebrew**[1], EJ Iverson[1], et al. Cholesterol accessibility at the ciliary membrane controls Hedgehog signaling.*Elife*, 2019. PMID: 31657721.

[1] equal contribution

4. *Mechanisms of receptor signaling at the primary cilia.*

I have collaborated on multiple projects to answer questions about protein trafficking and signaling from primary cilia. GPCRs such as the Hedgehog (HH) signaling transducer Smoothened (SMO) are dynamically trafficked throughout the cilium through ill-defined mechanisms. I studied how SMO trafficking was altered by a ciliary protein complex called EvC, whose loss gives rise to a genetic condition called Ellis-van Creveld syndrome. In collaboration with Hunter Fraser's lab at Stanford, I showed that EvC expression tunes SMO signaling strength in different species, influencing the craniofacial patterning differences seen in humans and chimps.

In a second collaboration with Christian Siebold's lab at Oxford, I provided physiological relevance for the covalent cholesterol modification of the protein Sonic Hedgehog (SHH), which binds and inactivates Patched-1. The cholesterol moiety increases SHH's potency as a morphogenic ligand, providing a rationale for why this modification is conserved as the only example of a protein modified by cholesterol in the human proteome.

a. D Gokham, RM Agoglia, **M Kinnebrew**, et al. Human-chimpanzee fused cells reveal cis-regulatory divergence underlying skeletal evolution. *Nature Genetics*, 2021. PMID: 33731941.

b. AF Rudolf[1], **M Kinnebrew**[1], et al. The morphogen Sonic hedgehog inhibits its receptor Patched by a pincer grasp mechanism. *Nature Chemical Biology*, 2019.

c. GV Pusapati[1], JH Kong[1], BB Patel, A Krishnan, A Sagner, **M Kinnebrew**, et al. CRISPR screens uncover genes that regulate target cell sensitivity to the morphogen Sonic hedgehog. *Developmental Cell*, 2018. PMID:29290584.

d. C Kowatsch[1], RE Woolley[1], **M Kinnebrew**, R Rohatgi, C Siebold. Structures of vertebrate Patched and Smoothened reveal intimate links between cholesterol and hedgehog signaling. *Current Opinion in Structural Biology*, 2019. PMID: 31247512.

[1] equal contribution

5. *Plasma membrane cholesterol is regulated by fatty acyl-CoA availability.*

Accessible cholesterol, the pool of membrane cholesterol with high chemical activity, regulates vital processes including vertebrate development and pathogen evasion. The mechanisms that govern plasma membrane (PM) cholesterol accessibility are incompletely understood. Using a genome-wide screen we find that acetyl-CoA carboxylase alpha (ACC1) loss causes a ~10-fold increase in PM accessible cholesterol in cells and a mouse model. ACC1 inhibition lowers fatty acyl-CoA levels which activates adipose triacylglycerol lipase (ATGL). ATGL activation elevates the abundance of polyunsaturated diacylglycerols through a mechanism that is independent of triacylglycerol hydrolysis. These diacylglycerol species are utilized to generate polyunsaturated phosphatidylcholine and phosphatidylethanolamine, which raises PM fluidity and cholesterol accessibility. Conversely, ATGL inhibition rigidifies the PM, reducing PM accessible cholesterol. Increased PM fluidity impairs cholesterol transport, triggering elevated de novo cholesterol biosynthesis at the ER. This study reveals a surprising link between fatty acid metabolism and cholesterol homeostasis, demonstrating that ATGL can modify the lipidome through a triacylglycerol-independent mechanism.

a. KM Wijesinghe, C Kim, S Chen, EO Shad, E Takeshima, S Li, CB Khandwala, D Calhoon, M Danielewicz, RD Leib, J Garcia-Bermudez, D Tillo, AM Lebensohn, JA Olzmann, R Rohatgi, **M Kinnebrew**. ACC1 inhibits ATGL to regulate plasma membrane fluidity and cholesterol accessibility. In press, 2026. PMID: 40909529.

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