SALK INSTITUTE
FOR BIOLOGICAL STUDIES

MEMORANDUM

TO: APPOINTMENTS COMMITTEE CHAIR

FROM: RUSTY GAGE, CHRISTIAN METALLO, AXEL NIMMERJAHN AND TATYANA SHARPEE

SUBJECT: ADJUNCT ASSISTANT PROFESSOR APPOINTMENT OF DR. SIMON SCHAFER

DATE: JUNE 4, 2025

We are pleased to offer our strongest support for the appointment of Dr. Simon Schäfer as an Adjunct Assistant Professor at the Salk Institute. Simon is an exceptionally talented and visionary scientist whose appointment would be a significant asset to the Institute. Over the years, he has maintained deep, productive ties with the Salk community and continues to contribute innovative expertise and collaborative energy that directly benefit our faculty, trainees, and scientific mission.

Simon is currently an Assistant Professor at the Technical University of Munich (TUM), where he leads a research group focused on engineering next-generation human stem cell models to uncover mechanisms of brain development and disease. His interdisciplinary work spans molecular neuroscience, neuroimmunology, and tissue engineering, and is based within the Munich Institute for Biomedical Engineering. He is a founding member of TUM's new Center for Organoid Systems, a faculty member of the International Max Planck Research School for Translational Psychiatry, and a principal investigator within the Excellence Cluster *SyNergy* (Munich Cluster for Systems Neurology). *SyNergy* is a multi-institutional consortium that investigates the origins of complex neurological conditions using a systems neurology approach. The cluster brings together leading institutions across Munich, including TUM, LMU, several Max Planck Institutes, DZNE, and Helmholtz Munich. Recently renewed and expanded, *SyNergy* is preparing to launch new international collaborations, including with the NOMIS Foundation.

Simon's appointment would strongly align with the Salk Institute's mission to support transformative science and foster international collaboration. He has longstanding and active collaborations with the Gage, Glass, and Nimmerjahn laboratories and is a key contributor to a recently submitted NIH Program Project Grant (P01) focused on aging and neuroimmune interactions. As a key consultant to the P01 leadership team, he contributes to multiple project components as well as to Core 2, which focuses on *in vivo* organoid transplantation. His lab's pioneering work on human microglia biology and engineered organoid platforms offers a powerful and complementary framework to existing efforts across the Institute.

In addition to his research contributions, Simon is deeply committed to mentorship and training. He co-supervises graduate student Lisa Mitchell in collaboration with Salk faculty through the UCSD Neurosciences Graduate Program. He also played a central role in integrating Dr. Rusty Gage as a Mercator Fellow in the German Collaborative Research Center (CRC) "NeuroMac" – a major initiative funded by the German Research Foundation (DFG) that focuses on microglia and other brain-resident myeloid cells. These CRCs are long-term research consortia designed to foster interdisciplinary and cross-institutional research efforts over up to 12 years. Simon's role in bringing Salk faculty into this international effort reflects his unique ability to build scientific bridges and foster high-impact, cross-border collaborations.

Simon's ongoing and future engagement clearly meets – and in many respects exceeds – the expectations

for an Adjunct Professor at Salk. He has already co-supervised a Salk/UCSD-based PhD student, co-led collaborative experiments and manuscript development with Salk investigators, and played a pivotal role in the development and submission of a multi-PI NIH Program Grant. He has also facilitated institutional partnerships and initiated researcher exchanges between Munich and Salk.

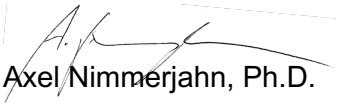
Looking ahead, Simon will continue to co-mentor graduate students jointly advised by Munich and Salk investigators, serve on thesis committees through UCSD, and regularly visit the Institute to advance collaborative projects, contribute to seminars, and support bidirectional training exchanges. He will also remain a key contributor to the implementation of the proposed P01 and continue to enrich the scientific community at Salk.

Simon embodies the creativity, rigor, and collaborative spirit that define the Salk faculty. His ongoing engagement has already enriched several programs across the Institute. His Adjunct appointment would not only formalize a productive and longstanding relationship but would also help catalyze new avenues of discovery and international collaboration. We are confident that Simon will remain a highly engaged and visible member of our community, and we enthusiastically recommend his appointment.

Thank you for your consideration.

Fred H. Gage, Ph.D.

Christian M. Metallo, Ph.D



Axel Nimmerjahn, Ph.D.

Tatyana Sharpee, Ph.D.

Attached: Schafer Biosketch, Adjunct Service Form

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Schafer, Simon T.

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

POSITION TITLE: Assistant 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 Greifswald, Germany	B.Sc.	10/2010	Biomedical Sciences
Medical School, University of Greifswald, Germany	Cand.med.	09/2009	Medicine
University of Greifswald, Germany	Ph.D. (*Summa Cum Laude*)	03/2015	Neuroscience
The Salk Institute for Biological Studies, La Jolla, CA	Postdoctoral	05/2022	Neuroscience

A. Personal Statement

I trained in both medicine and biomedical sciences, with a longstanding interest in the molecular logic of brain development and disease. During my graduate studies, I investigated dynamic signaling pathways that regulate neuronal fate decisions in the adult brain. As a postdoctoral researcher in the laboratory of Fred H. Gage at the Salk Institute, I applied personalized stem cell systems to uncover molecular mechanisms underlying clinically stratifiable endophenotypes in autism spectrum disorder (ASD). These studies revealed that cell-type-specific vulnerabilities in ASD are programmed very early in development and helped establish a conceptual foundation for using individualized in vitro models to gain mechanistic insights into human brain disorders. This work was recognized with a NARSAD Young Investigator Award from the Brain and Behavior Research Foundation. In parallel, I pioneered a xenotransplantation platform that enables long-term integration of human microglia into vascularized, brain-like tissue environments in vivo. This technology now provides a powerful tool to model human-specific neuroimmune interactions in both physiological and pathological contexts and serves as a core platform for the proposed P01 program.

I am currently Assistant Professor of Advanced Organoid Systems for Mental Health Research at the Technical University of Munich (TUM), affiliated with the Department of Psychiatry and the Munich Institute for Biomedical Engineering. I lead a research group at the newly established TUM Center for Organoid Systems and serve as faculty at the International Max Planck Research School for Translational Psychiatry. I am also associated with the Munich Cluster for Systems Neurology (SyNergy), an Excellence Cluster funded by the German federal and state governments. My lab develops next-generation stem cell technologies to advance personalized research on human brain disorders and brain repair. We combine developmental biology, gene editing, and bioengineering to create advanced organoid-based model platforms. Our research focuses on how immune activation shapes brain development and circuit formation and on mapping the regulatory programs guiding microglial function across brain niches. A central aim is to identify molecular targets that modulate maladaptive immune states in neurodevelopmental and neurodegenerative disorders.

Within this P01, I will serve as a consultant to the leadership team, contributing to both Project 1 and Core 2 (In Vivo Organoid Transplantation Core). I bring expertise in human microglia biology, brain organoid systems, and xenotransplantation-based in vivo models. For Project 1, I will advise on experimental design and data interpretation to redirect maladaptive microglial states in vivo, including CRISPR-based perturbation, selection and functional analysis of microglial populations, and integration of single-cell genomics to identify therapeutic

targets. In Core 2, I will collaborate to refine and standardize protocols for xenotransplanting human microglia into vascularized brain organoids, ensuring technical rigor and reproducibility.

I am committed to cross-disciplinary collaboration, mentorship, and the development of human-specific platforms that advance precision medicine in brain disorders. This P01 brings together a uniquely qualified team, and I look forward to contributing to research that could transform our understanding of inflammation-driven neurodegeneration and open new therapeutic avenues.

Citations:

1. Toda, T.*, Bedrosian, T. A.*, **Schafer S.T.***, Cuoco, M. S., Linker, S. B., Ghassemzadeh, S., Mitchell, L., Whiteley, J. T., Novaresi, N., McDonald, A. H., Gallina, I. S., Yoon, H., Hester, M. E., Pena, M., Lim, C., Suljic, E., Mansour, A. A., Boulard, M., Parylak, S. L. & Gage, F. H. (2024) Long interspersed nuclear elements safeguard neural progenitors from precocious differentiation. ***Cell Reports*** 43, 113774. PMCID: PMC10948021. (*equal contribution).
2. **Schafer S.T.[#]***, Mansour A.A.*, Schlachetzki J.C.M., Pena M., … Gage F.H.* (2023) An *in vivo* neuroimmune organoid model to study human microglia phenotypes. ***Cell*** 186, 2111-2126. PMCID: PMC10948021. [#]Lead contact and *co-corresponding author.
3. **Schafer, S.T.**, Paquola, A.C.M., Stern, S., Gosselin, D., Ku, M., Pena, M., Kuret, T.J.M., Liyanage, M., Mansour, A.A., Jaeger, B.N., Marchetto, M.C., Glass, C.K., Mertens, J. & Gage, F.H. (2019) Pathological priming causes developmental gene network heterochronicity in autistic subject-derived neurons. ***Nature Neuroscience*** 22, 243. PMCID: PMC6402576.
4. **Schafer, S.T.**, Han, J., Pena, M., von Bohlen und Halbach, O., Peters, J. & Gage, F. H. (2015) The Wnt Adaptor Protein ATP6AP2 Regulates Multiple Stages of Adult Hippocampal Neurogenesis. ***J Neurosci*** 35, 4983–4998. PMCID: PMC4389597.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 - *Present*	Assistant Professor, Center for Organoid Systems, Munich Institute for Biomedical Engineering & School of Medicine and Health, Department of Psychiatry and Psychotherapy, Technical University Munich, Germany
2023 - *Present*	Faculty Member, International Max Planck Research School for Translational Psychiatry
2023 - *Present*	Faculty Member and Member of the Selection Committee, TUM Graduate School *Medical Life Science and Technology*
2021 - 2022	Senior Research Associate, with Fred H. Gage, The Salk Institute for Biological Studies, La Jolla, CA
2015 - 2021	Research Associate, with Fred H. Gage, The Salk Institute for Biological Studies, La Jolla, CA
2015 - *Present*	Ad Hoc Reviewer *Journals:* Nature Neuroscience, Cell Reports, Science Advances, Molecular Psychiatry, Biological Psychiatry, Frontiers in Cellular Neuroscience *Grant Agencies:* Wellcome Trust (United Kingdom), Austrian Science Fund (FWF), Carl Zeiss Foundation, (Germany), Swiss National Science Foundation (SNSF)
2011 - 2015	Graduate Student, with Prof. Dr. Rettig, Prof. Dr. Peters, and Prof. Dr. Oliver von Bohlen und Halbach, Greifswald Graduate School in Science, University of Greifswald, Germany
2008 - 2010	Bachelor Student, University of Greifswald, Germany
2007 - 2011	Medical Student, Medical School, University of Greifswald, Germany; First state examination (2009), Clinical training (2009 - 2011)

Honors

2023 Early Excellence Academy Member, Cluster for Systems Neurology Munich
2022 Rudolf Mößbauer Fellowship, Technical University of Munich
2022 NARSAD Young Investigator Award, Brain & Behavior Research Foundation
2021 MRC Career Development Award, Medical Research Council, UK (offer)
2021 King's Prize Fellowship, King's College London, UK (offer)
2019 NARSAD Young Investigator Award, Brain & Behavior Research Foundation

2016 DFG Postdoctoral Fellowship German Research Foundation (Deutsche Forschungsgemeinschaft)
2015 Postdoctoral Fellowship James S. McDonnell Foundation (JSMF) for Understanding Human Cognition
2013 Research Fellowship, German National Merit Foundation (Studienstiftung des deutschen Volkes)
2008 Student Scholarship, German National Merit Foundation (Studienstiftung des deutschen Volkes)

C. Contributions to Science

1. Adult Neurogenesis in the Hippocampus: My early research focused on elucidating the molecular mechanisms regulating adult hippocampal neurogenesis, with an emphasis on how newborn neurons integrate into pre-existing circuits. I demonstrated that context-dependent Wnt signaling governs distinct, stage-specific processes in adult neurogenesis, including dendritic refinement and neuronal integration. In collaborative studies, we decoded the role of specific microRNAs as key modulators of newborn neuron migration, linking post-transcriptional regulation to structural plasticity in the adult brain. I also contributed to the first in vivo imaging of dendritic pruning in adult-born dentate granule cells, providing functional evidence that Wnt pathway components orchestrate phase-specific dendrite remodeling. These findings culminated in a comprehensive and widely cited review highlighting adult hippocampal neurogenesis and its relevance to cognition.

a. **Schafer, S.T.**, Han, J., Pena, M., von Bohlen und Halbach, O., Peters, J. & Gage, F. H. (2015) The Wnt Adaptor Protein ATP6AP2 Regulates Multiple Stages of Adult Hippocampal Neurogenesis. ***J Neurosci*** 35, 4983–4998. PMCID: PMC4389597
b. **Schafer, S.T.**, Peters J. & von Bohlen Und Halbach O. (2013) The (pro)renin receptor / ATP6ap2 is expressed in the murine hippocampus by adult and newly generated neurons. ***Restor. Neurol. Neurosci.*** 31, 225–231. PMID: 23357953
c. Han, J., Kim, H.J.*, **Schafer, S.T.***, Paquola, A., Clemenson, G.D., Toda, T., Oh, J., Pankonin, A.R., Lee, B.S., Johnston, S.T., Sarkar, A., Denli, A.M. & Gage, F.H. (2016) Functional Implications of miR-19 in the Migration of Newborn Neurons in the Adult Brain. ***Neuron*** 91, 79–89 PMID: 27387650 [*Authors contributed equally]
d. Gonçalves, J.T.*, **Schafer, S.T.*** & Gage, F.H. (2016) Adult Neurogenesis in the Hippocampus: From Stem Cells to Behavior. ***Cell*** 167, 897–914 PMID: 27814520 [*Authors contributed equally]

2. Modeling Human Brain Development and Disease Using Stem Cell Technologies: During my postdoctoral training, I established human iPSC- and induced neuron (iN)-based models to study human brain development and neurodevelopmental disorders. While numerous studies have described phenotypes associated with neuropsychiatric diseases, fewer have addressed whether such changes represent consequences of ongoing, dynamically aberrant developmental processes. Genetic and phenotypic heterogeneity complicate the search for common biological substrates. To address this, I worked on one of the first iPSC models of autism spectrum disorder (ASD) derived from clinically stratified, high-risk individuals exhibiting early accelerated brain growth. I pioneered the application of pattern recognition algorithms – originally developed for speech recognition – to reconstruct the dynamic progression of cellular developmental programs in these models. This work provided evidence that ASD-associated phenotypes arise from an ongoing developmental process primed early in life. It demonstrated how modeling system dynamics can reveal mechanistic disease states and their temporal unfolding. The study was featured as Editor's Choice in Science Translational Medicine, recommended by F1000Prime, and is highly cited. More recently, I co-led a study revealing that LINE-1 retrotransposons protect neural progenitors from premature differentiation, uncovering a novel role for mobile genetic elements in early human neurogenesis. To enhance direct reprogramming methods, we also developed protocols that modulate transcriptionally enriched signaling pathways, improving the conversion of human fibroblasts into functional neurons. These strategies were applied to generate age-equivalent models of a large cohort from patients with Alzheimer's Disease, providing new insights into mechanisms of neuronal degeneration.

a. **Schafer, S.T.**, Paquola, A.C.M., Stern, S., Gosselin, D., Ku, M., Pena, M., Kuret, T.J.M., Liyanage, M., Mansour, A.A., Jaeger, B.N., Marchetto, M.C., Glass, C.K., Mertens, J. & Gage, F.H. (2019) Pathological priming causes developmental gene network heterochronicity in autistic subject-derived neurons. ***Nature Neuroscience*** 22, 243. PMCID: PMC6402576.

- Toda, T.*, Bedrosian, T. A.*, **Schafer S.T.***, Cuoco, M. S., Linker, S. B., Ghassemzadeh, S., Mitchell, L., Whiteley, J. T., Novaresi, N., McDonald, A. H., Gallina, I. S., Yoon, H., Hester, M. E., Pena, M., Lim, C., Suljic, E., Mansour, A. A., Boulard, M., Parylak, S. L. & Gage, F. H. (2024) Long interspersed nuclear elements safeguard neural progenitors from precocious differentiation. ***Cell Reports*** 43, 113774 PMCID: PMC10948021. [*Authors contributed equally]

b. Herdy, J., **Schafer, S.T.**, Kim, Y., Ansari, Z., Zangwill, D., Ku, M., Paquola, A., Lee, H., Mertens, J. & Gage, F.H. (2019) Chemical modulation of transcriptionally enriched signaling pathways to optimize the conversion of fibroblasts into neurons. ***eLife*** 8, e41356. PMCID: PMC6524968.

c. Mertens, J., Herdy, J.R., Traxler, L., **Schafer, S.T.**, Schlachetzki, J.C.M., Böhnke, L., Reid, D.A., Lee, H., Zangwill, D., Fernandes, D.P., Agarwal, R.K., Lucciola, R., Zhou-Yang, L., Karbacher, L., Edenhofer, F., Stern, S., Horvath, S., Paquola, A.C.M., Glass, C.K., Yuan, S.H., Ku, M., Szücs, A., Goldstein, L.S.B., Galasko, D., Gage, F.H. (2021) Age-dependent instability of mature neuronal fate in induced neurons from Alzheimer's patients. ***Cell Stem Cell*** 28, 1533-48. PMCID: PMC8423435.

3. Establishing Humanized Platforms to Study Microglia Function: Microglia are central regulators of brain development and disease, yet conventional in vitro models fail to preserve their identity and physiological functions. To overcome these limitations, I developed an immunocompetent human brain organoid platform in which microglia naturally integrate and mature during development. Upon xenotransplantation into mouse cortex, these neuroimmune organoids support human microglial maturation, generating cells with transcriptional and functional profiles closely resembling primary microglia in vivo. These microglia demonstrate dynamic immune surveillance, injury responses, and inflammatory reactivity within a humanized brain-like environment. Additionally, I contributed to the generation of a high-resolution enhancer–promoter interactome map across brain cell types by validating non-coding regulatory elements in human iPSC-derived neuron and microglia models.

a. **Schafer, S.T.**[#*], Mansour, A.A.[*], Schlachetzki, J.C.M., Pena, M., Ghassemzadeh, S., Mitchell, L., Mar, A., Quang, D., Stumpf, S., Ortiz, I.S., Lana, A.J., Baek, C., Zaghal, R., Glass, C.K., Nimmerjahn, A., Gage, F.H.[*] (2023) An *in vivo* neuroimmune organoid model to study human microglia phenotypes. ***Cell*** 186, 2111-2126. PMID: 37172564. PMCID: PMC10284271. [[#]Lead contact and *co-corresponding author]

b. Wang M, Gage, F.H. & **Schafer, S.T.*** (2023) Transplantation strategies to enhance maturity and cellular complexity in brain organoids. ***Biological Psychiatry*** 93, 616-621. PMID: 36739209 [*corresponding author]

c. Nott, A., Holtman, I.R., Coufal, N.G., Schlachetzki, J.C.M., Yu, M., Hu, R., Han, C. Z., Pena, M., Xiao, J., Wu, Y., Keulen, Z., Pasillas, M.P., O'Connor, C., Nickl, C. K., **Schafer, S.T.**, Shen, Z., Rissman, R.A., Brewer, J.B., Gosselin, D., Gonda, D.D., Levy, M.L., Rosenfeld, M.G., McVicker, G., Gage, F.H., Ren, B. & Glass, C.K. (2019) Brain cell type–specific enhancer–promoter interactome maps and disease-risk association. ***Science*** 366, 1134–1139. PMID: 31727856. PMCID: PMC10662460.

Salk Adjunct Service/Contributions Form

Name: Simon Thomas Schafer **Appointment Start Date:** Nov 3rd 2025
Sponsors: Gage, Nimmerjahn, Metallo

To be eligible for appointment and reappointment in the Adjunct series, appointees are expected to be engaged in **at least two** Institute-related activities outlined below. If you are being considered for your first Adjunct Professor appointment, provide information about your plans to engage in the Salk community and select any of the activities you would be interested in below. If you are being considered for reappointment, select your ongoing activities and give a brief summary of your engagement in each activity during the past appointment period. Also provide a summary of your plans to engage in the Salk activities during the next appointment period.

Salk Activities (list the course/seminar titles, committees, and student names if known)
** Please note research collaborations with a Salk Faculty sponsor(s) do not qualify as Institute-related activities expected for an Adjunct position*

- ☒ Giving Seminars, such as those hosted by Sponsors or by the Institute
- ☐ Teaching in Salk-organized courses
- ☒ Serving on UCSD Student Review committees and/or Thesis Committees in Salk Labs
- ☐ Reviewing Postdoctoral and other Internal Grants
- ☐ Participating in Salk's outreach and educational efforts to recruit underrepresented minority student applicants
- ☒ Consulting on Salk scientific initiatives or multi-PI grants
- ☐ Serving on Faculty Review Committees
- ☐ Promoting award and nomination opportunities for Salk Faculty
- ☐ Organizing or participating on Salk Meetings or Conferences
- ☒ Other

Salk Service Summary & Plans: Describe your plans to engage in the activities marked above during the next appointment period (i.e.: Salk Course or Seminar Titles, names of Student or Faculty review committee, description of contributions to grants, etc. if unable to fit above). If you are being considered for reappointment, also describe your engagement in the Salk activities during the last appointment period. You may attach a supplemental letter with these activities as needed.

During the upcoming appointment period, I will continue and deepen my active engagement with the Salk community through several channels:

• Graduate Training: I co-mentor Lisa Mitchell (UCSD Neurosciences PhD Program) with Salk faculty and plan to serve on additional thesis committees through UCSD.
• Collaborative Research: I collaborate with the Gage, Glass, and Nimmerjahn labs on multiple projects involving human microglia and brain organoid models, and co-develop manuscripts and grant applications.
• NIH P01 Grant: I am a named consultant and contributor to a recently submitted multi-PI NIH P01 focused on aging and neuroimmune interactions, including work on both project-specific aims and the Transplantation Core.
• Institutional Partnerships: I helped integrate Dr. Gage as a Mercator Fellow in Germany's CRC "NeuroMac" and will continue to facilitate collaborative exchange between Salk and leading German research centers.
• Seminar & Campus Engagement: I will visit regularly to participate in seminars, joint project meetings, and mentoring activities with students and postdocs.

These efforts support Salk's mission in research, training, and global collaboration.