

**Steven R. Shuken, Ph.D.**  
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I. Education and Training

**Harvard Medical School:** Postdoctoral Research Fellowship

*Sept 2021 – Present*

- Research advisor: Prof. Steven P. Gygi
- Research area: Multiplexed mass spectrometry-based proteomic methods for chemical biology

**Stanford University:** Ph.D. in Chemistry

*Aug 2014 – Aug 2021*

- Thesis advisor: Prof. Tony Wyss-Coray (Jan 2017 – Aug 2021)
- Thesis title: “Studies on Brain Aging and Alzheimer’s Disease Using Mass Spectrometry, Organic Synthesis, and Biostatistics”

**Stanford University:** M.S. in Chemistry

*Aug 2014 – Sept 2017*

- Thesis advisor: Prof. Noah Z. Burns (Aug 2014 – Sept 2017)
- Thesis title: “Biophysical Studies on Noncanonical Membrane Lipids Using Synthetic Chemical Tools”

**University of California, Berkeley:** B.S. in Chemistry

*Sept 2010 – Dec 2013*

- Research advisors: Prof. Richmond Sarpong, Prof. Sarah Reisman
- Research area: Natural product total synthesis and synthetic methodology development

II. Honors

- *Journal of Proteome Research* Rising Star, one of 33 trainees and independent investigators selected (01/2024)
- Robin Reed Memorial Travel Award, \$2000 to attend ACS Spring 2024 (06/2023)
- University of Chicago Future Faculty Conference, one of 7 selected speakers (03/2023)
- Systems Aging Gordon Research Conference (GRC) Poster Award, full conference registration and travel expenses, awarded to the top 6 of 60 posters (06/2022)
- Stanford Schwab Learning Center Tutor of the Quarter, awarded to the top 1 tutor of the quarter based on student testimonials (11/2020)
- Stanford Center for Molecular Analysis and Design (CMAD) Fellowship, \$70,000 over 1 year – full graduate salary and tuition (09/2020)
- Stanford University Mass Spectrometry (SUMS) Symposium Poster Award, awarded to the top 2 posters (10/2019)
- BioX Stanford Interdisciplinary Graduate Fellowship (SIGF), \$210,000 over 3 years – full graduate salary and tuition (05/2017)
- NSF Graduate Research Fellowship Program (GRFP), \$195,000 over 3 years – full graduate salary and tuition (05/2014)
- Hypercube Award for Organic Synthesis, awarded to the 1 top student in synthetic organic chemistry in the UC Berkeley College of Chemistry graduating class (12/2013)
- Dean’s Honor List, College of Chemistry, UC Berkeley (12/2012, 12/2013)
- UC Berkeley Chemistry Dept. Honors, awarded for academic performance all semesters enrolled (12/2010, 05/2011, 12/2011, 05/2012, 12/2012, 05/2013, 12/2013)
- UT Southwestern McKnight Prize in Chemistry Research, semifinalist (10/2013)
- Caltech Amgen Scholars Award, \$8200 for 10 weeks of research–Reisman lab (05/2013)
- Honor Societies: Phi Beta Kappa (03/2013); National Society of Collegiate Scholars (02/2012); Golden Key Honour Society (11/2011)

### III. Publications

- **Shuken, S.R.**; Yu, Q.; Gygi, S. P. “Inserting Pre-Analytical Chromatographic Priming Runs Significantly Improves Targeted Pathway Proteomics With Sample Multiplexing.” *Submitted*.
  - BioRxiv preprint: <https://doi.org/10.1101/2024.02.08.579551>
- **Shuken, S.R.**; McAlister, G. C.; Barshop, W. D.; Canterbury, J. D.; Bergen, D.; Huang, J.; Huguet, R.; Paulo, J.; Zabrouskov, V.; Gygi, S. P.; Yu, Q. “Deep Proteomic Compound Profiling with the Orbitrap Ascend Tribrid Mass Spectrometer Using Tandem Mass Tags and Real-Time Search.” *Analytical Chem.* **2023**, *95*, 15180–15188. Link: <https://doi.org/10.1021/acs.analchem.3c01701>
- **Shuken, S. R.** “An Introduction to Mass Spectrometry-Based Proteomics.” *J. Proteome Res.* **2023**, *22*, 2151–2171. Link: <https://doi.org/10.1021/acs.jproteome.2c00838>
  - Included in the *J. Proteome Res.* “Rising Stars in Proteomics and Metabolomics 2024” collection: <https://pubs.acs.org/page/jprobs/vi/risingstars2024>
- Yu, Q.; Liu, X.; Keller, M. P.; Navarrete-Perea, J.; Zhang, T.; Fu, S.; Vaites, L. P.; **Shuken, S. R.**; Gygi, S. P.; et al. “Sample multiplexing-based targeted pathway proteomics with real-time analytics reveals the impact of genetic variation on protein expression.” *Nature Comm.* **2023**, *14*, 555. Link: <https://doi.org/10.1038/s41467-023-36269-7>
- **Shuken, S. R.**; McNerney, M. W. “Costs and Benefits of Popular P-Value Correction Methods in Realistic Models of Quantitative Omic Experiments.” *Analytical Chem.* **2023**, *95*, 2732–2740. Link: <https://doi.org/10.1021/acs.analchem.2c03719>
- Kaur, A.; **Shuken, S. R.**; Yang, A.; Iram, T. “A protocol for collection and infusion of cerebrospinal fluid.” *STAR Protocols* **2023**, *4*, 102015, 1–19. Link: <https://doi.org/10.1016/j.xpro.2022.102015>
- Iram, T.; Kern, F.; Kaur, A.; Myneni, S.; Morningstar, A. R.; Shin, H.; Garcia, M. A.; Yerra, L.; Palovics, R.; Yang, A. C.; Hahn, O.; Lu, N.; **Shuken, S. R.**; Haney, M.; Lehallier, B.; Iyer, M.; Luo, J.; Zetterberg, H.; Keller, A.; Zuchero, J. B.; Wyss-Coray, T. “Young CSF restores oligodendrogenesis and memory in aged mice via Fgf17.” *Nature* **2022**, *2*, 379–388. Link: <https://doi.org/10.1038/s41586-022-04722-0>
- **Shuken, S. R.**; Wyss-Coray, T. “Structural changes in cerebrospinal fluid proteins are associated with brain aging.” *Nature Aging* **2022**, *1*, 375–376. Link: <https://doi.org/10.1038/s43587-022-00213-z>
- **Shuken, S. R.**; Rutledge, J.; Iram, T.; Losada, P. M.; Wilson, E. N.; Andreasson, K. I.; Leib, R. D.; Wyss-Coray, T. “Limited proteolysis-mass spectrometry reveals aging-associated changes in cerebrospinal fluid protein abundances and structures.” *Nature Aging* **2022**, *2*, 379–388. Link: <https://doi.org/10.1038/s43587-022-00196-x>
- Vest, R. T.; Chou, C.-C.; Zhang, H.; Haney, M. S.; Li, L.; Laqtom, N. N.; Chang, B.; **Shuken, S. R.**; Nguyen, A.; Yerra, L.; Green, C.; Tanga, M.; Abu-Remaileh, M.; Bassik, M. C.; Frydman, J.; Luo, J.; Wyss-Coray, T. “Small molecule C381 targets the lysosome to reduce inflammation and ameliorate disease in models of neurodegeneration.” *Proc. Nat. Acad. Sci.* **2022**, *119*, e2121609119. Link: <https://doi.org/10.1073/pnas.2121609119>
- Moss, F. R. III; Cabrera, G. E.; McKenna, G. M.; Salerno, G. J.; **Shuken, S. R.**; Landry, M. L.; Weiss, T. M.; Burns, N. Z.; Boxer, S. G. “Halogenation-Dependent Effects of the Chlorosulfolipids of *Ochromonas danica* on Lipid Bilayers.” *ACS Chem. Biol.* **2020**, *15*, 2986–2995. Link: <https://doi.org/10.1021/acschembio.0c00624>
- Pluvinaige, J. V.; Haney, M. S.; Smith, B. A. H.; Sun, J.; Iram, T.; Bonanno, L.; Li, L.; Lee, D. P.; Morgens, D. W.; Yang, A. C.; **Shuken, S. R.**; Gate, D.; Scott, M.; Khatri, P.; Luo, J.; Bertozzi, C. R.; Bassik, M. C.; Wyss-

Coray, T. “CD22 blockade restores homeostatic microglial phagocytosis in ageing brains.” *Nature* **2019**, 568, 187–192.

Link: <https://doi.org/10.1038/s41586-019-1088-4>

- **Moss, F. R. III; \* Shuken, S. R.;** Mercer, J. A. M.; Cohen, C. M.; Weiss, T.; Boxer, S. G.; Burns, N. Z. “Ladderane phospholipids form a densely packed membrane with normal hydrazine and anomalously low proton/hydroxide permeability.” *Proc. Nat. Acad. Sci.* **2018**, 115, 9098–9103.
  - \*These authors contributed equally.Link: <https://doi.org/10.1073/pnas.1810706115>
- Mercer, J. A. M.; Cohen, C. M.; **Shuken, S. R.;** Boxer, S. G.; Burns, N. Z.; et al. “Chemical Synthesis and Self-Assembly of a Ladderane Phospholipid.” *J. Am. Chem. Soc.* **2016**, 138, 15845–15848.  
Link: <https://doi.org/10.1021/jacs.6b10706>

#### IV. Patents

- Burns, N.; Shuken, S. R. “Fluorogenic Water Soluble Hydrazine Sensors.”
  - **Patent granted 08/04/2020**
  - US National Patent App. Pub. No. US 2019/0033215 A1 Pub. 01/31/2019
  - US National Patent App. No. 16/046,772 filed 06/26/2018
  - Provisional Patent App. No. 62/538,589 filed 06/28/2017
  - Link: <https://patentimages.storage.googleapis.com/f9/64/b4/0e1a6033d2a5f7/US20190033215A1.pdf>
- Burns, N.; Shuken, S. R.; Mercer, J. A. M.; Cohen, C. M. “Ladderane Lipid Compounds and Liposomes and Methods of Preparing and Using the Same.”
  - **Patent granted 08/18/2020**
  - US National Patent App. Pub. No. US 2019/0177347 A1 Pub. 06/13/2019
  - US National Patent App. No. 16/327,735 filed 08/30/2017
  - Provisional Patent App. No. 62/381,857 filed 08/31/2016
  - Link: <https://patentimages.storage.googleapis.com/82/12/d9/6bec7f33b33933/US20190177347A1.pdf>

#### V. Selected Presentations and Posters

- **Presentation.** “Mass Spectrometry-Based Proteomics with an Enzymatic Probe Reveals Aging-Associated Changes in Protein Abundances and Structures in Cerebrospinal Fluid.” *30 min.* Invited oral presentation at the Future Faculty Conference, Department of Chemistry, University of Chicago, Chicago, IL. (06/2023)
- **Poster.** “Targeted Whole-Pathway Proteomic Assays with Sample Multiplexing: Data Visualization-Guided Optimization.” American Society for Mass Spectrometry (ASMS) Meeting, Houston, TX. (06/2023)
- **Poster.** “High-Depth Multiplexed Compound Profiling with the Orbitrap Ascend Tribid Mass Spectrometer.” American Society for Mass Spectrometry (ASMS) Meeting, Houston, TX. [Officially presented by Amanda E. Lee, Thermo Fisher Scientific.] (06/2023)
- **Presentation.** “Data Visualization Software for GoDig Optimization and Development.” *10 min.* Invited oral presentation at the Thermo Fisher Scientific Instrument API Power-User Meeting in Houston, TX. (06/2023)
- **Presentation.** “Deep Proteomic Compound Profiling with Sample Multiplexing on the Orbitrap Ascend.” *55 min.* Oral presentation at the Thermo Fisher Scientific Mass Spec Users Meeting in Bethesda, MD. (11/2022)
- **Presentation.** “High-Depth Multiplexed Drug Profiling with a Modified Tribid Mass Spectrometer.” *16 min.* Oral presentation at International Mass Spectrometry Conference (IMSC) 2022 in Maastricht, Netherlands. (09/2022)
- **Poster.** “Aging-Associated Changes in Cerebrospinal Fluid Complexes Revealed by Limited Proteolysis-Mass Spectrometry (LiP-MS).” Presented at Systems Aging Gordon Research Conference (GRC) in Newry, Maine. **Poster award winner.** (06/2022)
- **Presentation.** “Limited Proteolysis-Mass Spec (LiP-MS) Reveals Age-Associated Changes in the Cerebrospinal Fluid Proteome.” *30 min.* American Chemical Society (ACS) Spring Meeting, public oral presentation. (04/2021)

- *Poster.* “Simultaneous Unbiased Structural Analysis of Cerebrospinal Fluid Proteins in N-Glycosylation and Aging Using Limited Proteolysis-Mass Spectrometry (LiP-MS).” Stanford University Mass Spectrometry (SUMS) Research Applications Symposium. **Poster award winner. (10/2019)**
- *Presentation.* “Phospholipid Structure and Membrane Function: Self-Assembly and Permeability of Ladderane Bilayers.” 30 min. Stanford Summer Student Seminar, delivered to Stanford Chemistry Department and open to public. (08/2017)
- *Presentation.* “Effects of Bis(oxazoline) Ligands in Asymmetric Catalytic Reductive Cross-Coupling Reactions.” 20 min. Caltech Student-Faculty Programs Seminar Day. Delivered to Caltech Department of Chemistry and Chemical Biology and open to public. (08/2013)
- *Poster.* “Toward the Total Synthesis of (–)-complanadine A and analogs.” Presented at Berkeley Chemistry Undergraduate Research Symposium and open to public. (05/2013)

## VI. Research Experience

### Harvard Medical School

*Sept 2021 – Present*

Advisor: Steven P. Gygi

- I have developed a new targeted proteomic technology with sample multiplexing that requires neither synthetic standards, manual scheduling, nor pre-assembled data libraries. This method has unprecedented ease of use and flexibility; it may revolutionize studies that currently use low-throughput methods, e.g., Western blot. Applications to drug-protein interactions are underway. Work includes programming and visualizing data in C#.
- In collaboration with the laboratory of Prof. Maria Lehtinen at Boston Children’s Hospital, I am analyzing how the choroid plexus, a major component of the blood-cerebrospinal fluid barrier, changes with aging.
- I implemented a next-generation targeted method based on the GoDig targeted proteomic platform, which enables high-throughput targeted analysis without the use of synthetic standard peptides, with dramatically increased success rates (>95% for targets quantified <40% of the time with untargeted MS) and applied it to a macroautophagy assay as well as assays of somatic mutations in cancer cells. **1<sup>st</sup>-author manuscript submitted (BioRxiv preprint).**
- I worked with Research and Development staff at Thermo Fisher Scientific to develop and optimize methods on the new Orbitrap Ascend tribrid mass spectrometer. Work included optimization of real-time search-synchronous precursor selection-MS3 methods. **1<sup>st</sup>-author publication.**
- I published a 16-page tutorial (21 including references) on mass spectrometry-based proteomics, covering basic details and cutting-edge techniques. The article has been viewed over 20,000 times. **Single-author publication.**

### Stanford School of Medicine Department of Neurology

*Jan 2017 – Aug 2021*

Advisor: Tony Wyss-Coray

- Main project: Studies on cerebrospinal fluid (CSF) protein abundance and structure changes during aging using limited-proteolysis mass spectrometry (LiP-MS). Work involved surgical collection of CSF from mice, LiP-MS protocol modifications, proteomic data analysis, and hit validation by Western blot and enzyme activity assays. **1<sup>st</sup>-author publication and 2<sup>nd</sup>-author publication.**
- Characterization of sensitivity costs and FDR benefits of  $p$ -value correction. I developed theoretical models of quantitative comparative omic experiments, simulated statistical testing, and implemented fast and easy-to-use permutation FDR control software. **1<sup>st</sup>-author publication.**
- I installed a new Q<sub>Exactive</sub> HF-X mass spectrometer (Thermo) and generated and optimized methods. I oversaw the planning and construction of a mass spectrometry room in the ChEM-H/Neuro complex. I maintained and operated this LCMS system for several projects in the Wyss-Coray lab.
- I collected mouse CSF for multiple projects in the Wyss-Coray lab including: novel targets for microglial phagocytosis (**publication**); and rejuvenating the aged mouse brain with young CSF (**publication**).
- I performed organic syntheses of 5 small molecule analogs for a TGF- $\beta$  activation drug development project. **Publication.**

### ETH Zürich Institute of Molecular Systems Biology

*April 2019 – May 2019*

Advisor: Prof. Paola Picotti

- For 6 weeks, I worked in the Picotti lab in Zürich to learn LiP-MS and data-independent acquisition (DIA).

## Stanford University Department of Chemistry

*Aug 2014 – Sept 2017*

Advisor: Prof. Noah Z. Burns

- Main project: biophysical studies on ladderane lipid membranes. Work involved synthesis of a new water-soluble fluorogenic hydrazine sensor, development of a novel hydrazine transmembrane diffusion rate assay, and various biophysical characterization methods. **Co-1<sup>st</sup>-author publication and patent.**
- Self-assembly, isolation from biomass, and absolute configuration assignment of ladderane phospholipids. I collaborated with Stanford Biomaterials and Advanced Drug Delivery (BioADD) to develop liposome drug formulation technology using ladderanes. **Publication and patent.**
- Self-assembly properties of algal chlorosulfolipids. Work involved large-scale algal mixotroph culture, lipid isolation, and cryo-transmission electron microscopy (cryoTEM). **Publication.**
- Synthetic studies toward glycerol dialkyl glycerol tetraether (GDGT) lipids. I discovered a cyclization reaction affording rapid access to 1,3-dialkylcyclopentanes which otherwise require several steps to synthesize.

## UC Berkeley Department of Chemistry

*Aug 2012 – Dec 2013*

Advisor: Richmond Sarpong

- I developed an enantioselective formal synthesis of (–)-complanadine A, member of the *Lycopodium* family of alkaloids. Route involved organic dianion chemistry and an asymmetric organocatalytic Michael addition reaction.

## Caltech Department of Chemistry

*June 2013 – Aug 2013*

Advisor: Sarah Reisman

- As an Amgen Scholar, I studied ligand effects in the catalytic asymmetric reductive acyl cross-coupling reaction and related methods. I synthesized bis(oxazoline) ligands; tested the effect of bite angle on yield and enantioselectivity.

## VII. Work Experience

### Impetus Grants

*Boston, MA*

- Grant Application Reviewer

*Sept 2023 – Present*

I review grant applications for Impetus Grants (Norn Group), which funds high-risk, high-reward academic research proposals in aging biology unlikely to be funded by the government. Annual grants total \$10M.

### Inductive Bio

*Boston, MA*

- Consultant

*Feb 2023 – Present*

I consult for the R&D team at Inductive Bio about mass spectrometry-based proteomics. Work involves reading papers and presenting slides to provide an expert's perspective on mass spectrometry.

### GlaxoSmithKline (GSK)

*Collegeville, PA*

- Medicinal Chemistry Intern/Co-op, Oncology R&D

*Jan 2014 – June 2014*

I synthesized drug analogs for biological assessment in Oncology research unit. Presented slides of progress to research unit every month. Multi-step syntheses of 11 compounds and batches of intermediates.

## VIII. Teaching Experience

### Independent / Wyzant, Inc.

- Organic Chemistry Tutor

*Sept 2017 – Present*

Independent tutor for high school and college students in organic chemistry. Work includes lesson planning, one-on-one lesson execution, and writing and grading practice problems and providing feedback.

### Stanford Schwab Learning Center

- Tutor

*Sept 2020 – Dec 2020*

The Schwab Learning Center is a free resource for students with learning differences. I spent 5 hours per week tutoring students in organic chemistry. Included writing and grading practice problems and planning and teaching lessons virtually. **Tutor of the Quarter award 11/2020.**

## Stanford Department of Chemistry

- TA: Advanced Synthetic Organic Chemistry (Chem 223)

*Jan 2016 – April 2016*

I assistant-taught a 10-week class containing 20 1<sup>st</sup>-year graduate students in synthetic organic chemistry. I introduced a weekly seminar-style discussion of total syntheses. I delivered 8 lectures as a substitute for Prof. Burns. I taught a 1-hr discussion section each week. I wrote and graded problem sets and exams.

## UC Berkeley Department of Chemistry

- TA: Organic Chemistry

*Aug 2013 – Dec 2013*

I co-taught with one other instructor a supplementary seminar for 17 undergraduates. 3 hours/week, 1 semester credit. Work included lecture-style review and writing and grading practice problems, quizzes, and worksheets.

- TA: Chemical Structure and Reactivity

*Jan 2013 – May 2013*

Sophomore organic chemistry. I supervised a lab section for 20 undergraduates; held office hours for undergraduates; and graded homework, lab reports, quizzes, and exams.

- Laboratory Assistant: Chemical Structure and Reactivity

*Aug 2012 – Dec 2012*

Sophomore organic chemistry. I assisted a TA in supervising lab section and advising students.

## IX. Peer Review Service

- *Analytical Chemistry*

*June 2023 – Present*

## X. Volunteer Work

### HMS Cell Bio Equity Initiative (Boston, MA)

- Volunteer

*Oct 2022 – Present*

I participate in the ideation, planning, and execution of events focused on fostering a culture of inclusion and equity in the Cell Biology Department at Harvard Medical School.

### Big Brothers Big Sisters of Eastern Massachusetts (Boston, MA)

- Big Brother

*July 2022 – Present*

I mentor a child from a disadvantaged background in Eastern Massachusetts, taking him on an outing every two weeks to do various activities.

### FutureProfits by AbleWorks (East Palo Alto, CA)

- FutureProfits Coach

*Jan 2018 – Mar 2021*

With a co-coach, I taught a weekly 1-hour course about personal finance to high school students from disadvantaged communities in the Bay Area.

### Inspiring Future Scientists with Shadowing (IFSS) (Stanford, CA)

- Mentor

*June 2016 – June 2016*

A high school student from a disadvantaged community in the Bay Area shadowed me daily during June 2016. I involved her in research as much as possible and helped her prepare a final research presentation.

### Bay Area Scientists in Schools (Berkeley, CA)

- Volunteer

*Aug 2013 – Dec 2013*

I did demonstrations for elementary and middle school students in disadvantaged communities in the Bay Area. Work included helping plan and execute scientific demonstrations and facilitate discussions.