Advances in Mass Spectrometry for Membrane Protein Pharmacology

This manuscript (<u>permalink</u>) was automatically generated from <u>dschust-r/review ms mem prot@18df3a6</u> on May 21, 2025.

Authors

- Dina Schuster [™]
 - **(D** 0000-0001-6611-8237 · **(7** dschust-r

Sarafan ChEM-H, Stanford University, Stanford, CA, 94305, USA

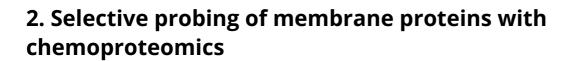
☑ — Correspondence possible via <u>GitHub Issues</u> or email to Dina Schuster <dschust@stanford.edu>.

Abstract

Membrane proteins are important targets for pharmacological research, due to their involvement in various cellular processes, ranging from signal transduction to transport, and cellular communication. While they make up roughly 30% of the human proteome and are the target of more than half of all approved drug products, their hydrophobicity and low abundance pose significant challenges for drug discovery and development. Mass spectrometry has emerged as a powerful tool for studying membrane protein structure, dynamics, regulation, as well as their interaction with proteins, small molecules, and lipids. In this review, we summarize recent findings and methodological advances that facilitate the study of cell surface organization, the discovery of druggable membrane proteins, and the identification of binding sites.

1. Novel mass spectrometric m	ethods for the identification of
drug targets and binding sites	

[1,2,3,4,5,6,7,8,9]



3. Mass spectrometry reveals the cell surface organization		

4. Insights into G protein-coupled receptors			

5. Remaining challenges and outlook			

References

1. Capture of the Mouse Organ Membrane Proteome Specificity in Peptidisc Libraries

Frank Antony, Zora Brough, Zhiyu Zhao, Franck Duong van Hoa *Journal of Proteome Research* (2024-01-17) https://doi.org/g5w3hs DOI: 10.1021/acs.jproteome.3c00825 · PMID: 38232390

2. A Peptidisc-Based Survey of the Plasma Membrane Proteome of a Mammalian Cell

Zhiyu Zhao, Arshdeep Khurana, Frank Antony, John W Young, Keeley G Hewton, Zora Brough, Tianshuang Zhong, Seth J Parker, Franck Duong van Hoa *Molecular & Amp; Cellular Proteomics* (2023-08) https://doi.org/g9ks7s

DOI: 10.1016/j.mcpro.2023.100588 · PMID: 37295717 · PMCID: PMC10416069

3. Cell surface thermal proteome profiling tracks perturbations and drug targets on the plasma membrane

Mathias Kalxdorf, Ina Günthner, Isabelle Becher, Nils Kurzawa, Sascha Knecht, Mikhail M Savitski, HChristian Eberl, Marcus Bantscheff

Nature Methods (2021-01) https://doi.org/ghswc8

DOI: <u>10.1038/s41592-020-01022-1</u> · PMID: <u>33398190</u>

4. Target Deconvolution by Limited Proteolysis Coupled to Mass Spectrometry

Viviane Reber, Matthias Gstaiger

Methods in Molecular Biology (2023) https://doi.org/g9ks7q

DOI: 10.1007/978-1-0716-3397-7 13 · PMID: 37558949

5. High-throughput peptide-centric local stability assay extends protein-ligand identification to membrane proteins, tissues, and bacteria

Kejia Li, Clement M Potel, Isabelle Becher, Nico Hüttmann, Martin Garrido-Rodriguez, Jennifer Schwarz, Mikhail M Savitski

Cold Spring Harbor Laboratory (2025-04-29) https://doi.org/g9ks7v

DOI: 10.1101/2025.04.28.650974

6. Effects of theophylline on ADCY5 activation—From cellular studies to improved therapeutic options for ADCY5-related dyskinesia patients

Dirk Tänzler, Marc Kipping, Marcell Lederer, Wiebke F Günther, Christian Arlt, Stefan Hüttelmaier, Andreas Merkenschlager, Andrea Sinz

PLOS ONE (2023-03-03) https://doi.org/grv9ht

DOI: 10.1371/journal.pone.0282593 · PMID: 36867608 · PMCID: PMC9983822

7. Phosphorylation Sites of the Gastric Inhibitory Polypeptide Receptor (GIPR) Revealed by Trapped-Ion-Mobility Spectrometry Coupled to Time-of-Flight Mass Spectrometry (TIMS-TOF MS)

Kyle A Brown, Rylie K Morris, Samantha J Eckhardt, Ying Ge, Samuel H Gellman *Journal of the American Chemical Society* (2023-12-13) https://doi.org/g9ks7t DOI: 10.1021/jacs.3c09078 · PMID: 38091482 · PMCID: PMCID: PMC10842860

8. Integrative structural modeling of macromolecular complexes using Assembline

Vasileios Rantos, Kai Karius, Jan Kosinski

Nature Protocols (2021-11-29) https://doi.org/gq586q

DOI: 10.1038/s41596-021-00640-z · PMID: 34845384

9. Simple But Efficacious Enrichment of Integral Membrane Proteins and Their Interactions for In-Depth Membrane Proteomics

Pornparn Kongpracha, Pattama Wiriyasermkul, Noriyoshi Isozumi, Satomi Moriyama, Yoshikatsu Kanai, Shushi Nagamori

Molecular & Proteomics (2022-05) https://doi.org/g9ks7r

DOI: <u>10.1016/j.mcpro.2022.100206</u> · PMID: <u>35085786</u> · PMCID: <u>PMC9062332</u>