Advances in Mass Spectrometry for Membrane Protein Pharmacology

This manuscript (permalink) was automatically generated from dschust-r/review_ms_mem_prot@ea88482 on May 21, 2025.

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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 methods for the identification of drug targets and binding sites

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

2. Selective probing of membrane proteins with chemoproteomics

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 & 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: 10.1038/s41592-020-01022-1 · PMID: 33398190

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: 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 & Cellular Proteomics (2022-05) https://doi.org/g9ks7r
DOI: 10.1016/j.mcpro.2022.100206 · PMID: 35085786 · PMCID: PMC9062332