Advances in Mass Spectrometry for Membrane Protein Pharmacology

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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]; DOI:10.1021/acschembio.3c00781]

Accessibility approaches

[4,5,10,11,12,13,14]

Thermal proteome profiling

[3,15]

Proximity-based approaches and chemical cross-linking

[16,17,18,19,20,21,22,23]

Native and intact mass spectrometry of membrane proteins

[[24]; [25]; [26]; [27]; [28]; [29]; [30]; [31]; [32]; [33]; DOI; [34]; [35]]

2. Selective probing of membrane proteins with chemoproteomics

[36,37,38,39,40,41]

3. Mass spectrometry reveals the cell surface organization

[2,3,18,19,24,37,42,43]

4. Insights into G protein-coupled receptors

[3,7,24,27,29,30,32,33,44]

5. Remaining challenges and outlook

[8,33,45,46,47]

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