Usage Report for Fiscal Year 2024

Project Title:

Ligand-Protein, Protein-Lipid and Lipid-Lipid Interactions

Name:

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1. Background and purpose of the project, relationship of the project with other projects

The cellular membrane serves as the fundamental boundary that separates the intracellular environment from the external surroundings. Additionally, lipid membranes partition the cell into distinct compartments, contributing to cellular specialization. Collectively, lipid membranes safeguard the integrity and function of cellular processes, making them the most critical boundary in the biological realm. While biological membranes are densely populated with proteins, their primary components are a diverse array of lipids.

A protective barrier requires specific mechanisms for the exchange of nutrients and information between the interior and the external environment. Within the cellular context, this function is carried out by membrane-embedded proteins, such as receptors and transporters, which facilitate signal transduction and nutrient transport across the membrane. The pre-assembly of transport and signaling complexes within the membrane is facilitated through specific lipid-protein interactions.

2. Specific usage status of the system and calculation method

Quantum mechanics (QM) simulations utilizing the Gaussian 09 and Gaussian 16 software package have been performed. Molecular dynamics simulations were performed utilizing the NAMD software package and results were visualized with VMD.

3. Result & Conclusion

Ginsenoside Rh2 (Rh2), a ginseng saponin, has garnered attention for its diverse biological activities. Rh2's interactions with membrane lipids in both liquid-disordered (Ld) and liquid-ordered (Lo) phases were correlated between MD simulation and small-angle X-ray diffraction, solid-state NMR, fluorescence microscopy. The findings revealed that Rh2 preferentially localizes in the shallow interior of the bilayer in the Ld phase and less so in the Lo phase, reducing the order of lipid acyl chains in the Ld phase. The molecular structure of Rh2, including its dihydroxy group and glucose moiety, causes tilting of the triterpene core, potentially enhancing membrane permeability without exhibiting the strong membrane-disrupting effects seen with steroidal saponins like digitonin and dioscin. [1]

4. Schedule and prospect for the future

From an atomistic point of view, the specifics of the lipid-lipid and lipid-protein interaction remains poorly understood. For example, the detailed mechanism of lipid flip-flopas well as the conformation of lyso-phospholipids solubilized by methyl-β-cyclodextrine remains to be resolved. To gain a more complete atomistic understanding, we employ QM and MD simulations and correlate our results with experimental observation.

Fiscal Year 2024 List of Publications Resulting from the Use of the supercomputer

[Paper accepted by a journal]

1. “Mode of molecular interaction of triterpenoid saponin ginsenoside Rh2 with membrane lipids in liquid-disordered phases”
   Garza-Miyazato D, Hanashima S, Umegawa Y, Murata M, Kinoshita M, Matsumori N, Greimel P; B*iochim Biophys Acta Biomembr*. **2024**, 1866(7):184366. doi: 10.1016/j.bbamem.2024.184366.

[Conference Proceedings]

[Oral presentation]

[Poster presentation]

[Others (Book, Press release, etc.)]