Structure and Dynamics of Phospholipid Bilayer Nanodiscs

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Phospholipid bilayer nanodiscs are lipid-protein complexes in which amphipathic helices, such as apolipoprotein A-I (apoA-I) surround the edge of the bilayer. Nanodiscs have been used as a tool to investigate the function of membrane proteins by incorporating them into the bilayer while retaining their native structure. Nanodiscs can be formed by simply mixing apoA-I and lipids (such as dimyristoylphosphatidylcholine (DMPC)) at the gel-liquid crystalline phase transition temperature of the lipid. Their detailed structure and characteristics, especially the dynamic properties of lipids in Nanodiscs, are not well understood.

We previously succeeded in determining the rates of interbilayer exchange of dimyristoylphosphatidylcholine (DMPC) in vesicles [1] and in nanodiscs [2] by small-angle neutron scattering (SANS) technique and found that the exchange rate is 20-fold faster in the latter particles. In the present study, we elucidated the dynamic properties of nanodiscs composed by amphipathic peptide instead of apoA-I.

The amphipathic α-helical peptide 18A (Ac-DWLKAFYDKVAEKLKEAF-NH2) was mixed with DMPC (DMPC:18A = 3:1 (wt/wt)) and incubated at 25 °C. Nanodiscs formed were separated from coexisting vesicles and lipid-free proteins by density gradient ultracentrifugation. Nanodiscs consisting of either d54-DMPC (D-disc) or DMPC (H-disc) were prepared.

Time-resolved SANS measurement was started immediately after mixing an equivalent volume of D-disc and H-disc. Surprisingly, the scattering intensity fell to a baseline level even 3 min after the mixing. It was therefore impossible to determine the decay rate.

We performed fluorescence resonance energy transfer experiments and observed the exchange of fluorescence-labeled lipid between 18A nanodiscs, the rate of which was concentration-dependent. These results suggest that lipid exchange with 18A nanodiscs is mediated by collisions between nanodiscs.

References

[1] M. Nakano, M. Fukuda, T. Kudo, H. Endo, T. Handa, Phys. Rev. Lett. 98 (2007) 238101.
[2] M. Nakano, M. Fukuda, T. Kudo, M. Miyazaki, Y. Wada, N. Matsuzaki, H. Endo, T. Handa, J. Am. Chem. Soc. 131 (2009), 8308.