Direct translocation through lipid bilayers: design challenges and solutions

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Abstract

The development of nanomaterials that are capable of crossing lipid bilayers presents a significant challenge in the field of nanotechnology. To overcome this barrier, a diverse range of shapes, sizes, and surface coatings have been employed in the design of nanomaterials. The potential barrier for nano-objects to cross the lipid bilayer by thermal motion is too high for objects with a size greater than 5 nm. It is generally accepted that small hydrophobic nanoparticles are covered by the lipid bilayer and accumulate in the bilayer core, while nanoparticles larger than 5 nm can only penetrate cells through slow, energy-dependent processes such as endocytosis, which lasts for several minutes.

Here, we present several examples demonstrating how physico-chemical properties of nanoparticles can impact their ability to translocate passively through the lipid bilayer. In one case, variation of the hydrophobicity of nanoparticles induced reversible destabilization of the bilayer structure, leading to enhanced permeability for water and small solutes. In the other example, we show that lipid-covered hydrophobic nanoparticles can translocate through lipid membranes by direct penetration within milliseconds. Our results reveal that nanoparticles with diameters smaller than 5 nm remain trapped in the bilayer, while nanoparticles larger than 5 nm insert into the bilayer, opening transient pores in the bilayer. Another example demonstrates whow cholesterol present in a lipid membrane can facilitate the translocation of nano-objects. A new type of nanodomain was discovered around ultra-short carbon nanotubes (USCNTs) in a two-component lipid bilayer containing cholesterol. This nanodomain weakens the attachment between USCNTs and the lipid bilayer, leading to detachment through pore formation, suggesting the role of cholesterol in the function of membrane ion channels and biophysics of membrane proteins with inserted nanoobjects.

References

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