Orientation of the Ganglioside GM3 Glycan in Lipid Bilayers as Elucidated by Solid-State NMR

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Keywords: Ganglioside; Lipid Raft; Model Membrane; Solid-State NMR; Conformational Analysis

Gangliosides are one of the important components in the bio-functional membrane domains, so called lipid rafts. Gangliosides generally consist of hydrophobic ceramide and hydrophilic sialo-glycan moieties. This amphiphilic feature is involved in various biological functions; one of which is binding activity for exogeneous proteins like viral spike-proteins and bacterial toxins.

Cholesterol-ganglioside interaction occurring at the lipid rafts has been considered to regulate the ganglioside interplay with proteins by altering the orientation of the ganglioside headgroup [1]. We previously elucidate the conformational change of the sphingomyelin headgroup induced by cholesterol [2]. For gangliosides, however, there are few lines of experimental evidence supporting glycan conformational difference [3].

We here examined the conformational difference in the glycan moiety of ganglioside GM3 by solid-state NMR experiments using isotope-labeled GM3 probes (Fig.1). A series of probes labeled on each sugar residue was synthesized, and incorporated in the model membrane mimicking the rafts or the non-rafts. The parameters obtained by solid-state NMR were compared with the theoretical predictions, in which all conformations were comprehensively considered. As a result, the orientation of the sialic acid moiety was remarkably altered depending on the presence or absence of cholesterol, while that of the glucose moiety was not significantly changed. In this presentation, we will also discuss about the whole structure of GM3 glycan moiety on the membrane surface.

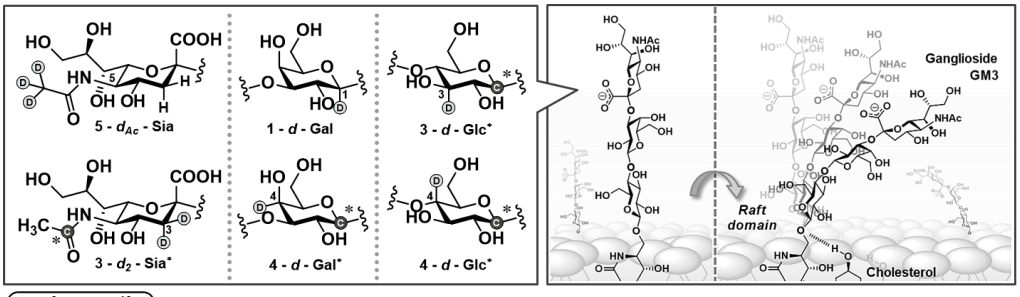

Fig.1 Schematic illustration of conformational analysis using isotope-labeled GM3 probes

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