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研究期間：2016～2018

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研究課題名(和文) マイコプラズマ細胞膜糖脂質の生物機能解析に関する研究

研究課題名(英文) Bioorganic chemical study on Mycoplasma glycolipids

研究代表者

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交付決定額(研究期間全体)：(直接経費) 3,600,000円

研究成果の概要(和文)：マイコプラズマ肺炎菌が細胞膜に発現するグリセロ糖脂質(GGLs)の三次元構造を独自のプロトンNMR-Karplus法で解析した。その結果、1)同糖脂質の二糖結合は、水中で折り返し構造をとること、2)二糖結合付近に複数の酸素原子が局所的に集中した極性ドメインを形成すること、3)糖の非還元末端につながる連続した疎水面がグリセロ脂質部位から広がっていることを明らかにした。また、糖水酸基と脂肪酸エステル間に分子内水素結合が形成され、これが脂質部位の動的挙動を制御していることを明らかにした。GGLsは細胞膜内で独自の糖脂質ラフトを形成して、ホスト細胞と「何らかのやり取り」をしていると考えられた。

研究成果の学術的意義や社会的意義

細胞膜GGLsはマイコプラズマ肺炎菌に特有の糖脂質抗原であり、マイコプラズマ感染症対策の切り札である。本研究ではGGLsに結合した「糖」の意味を、独自の立体化学解析法を用いて検証した。その結果、GGLsの二糖部分にこれまで確認されていない特異な極性構造が存在すること、細胞膜脂質としてリン脂質と異なる動的配座挙動を示すことを明らかにした。「糖」は極性基として細胞膜の安定化に寄与すると同時に、分子内水素結合を介して脂質部位の動的配座挙動を制御していることを明らかにした。GGLsが細胞膜内でマイクロドメインを形成する分子機構を提案した。

研究成果の概要(英文)：Mycoplasma pneumoniae produces mono- and di-Gal glycerolipids (GGLs) in cytoplasmic membranes. We applied our established ¹H-NMR-Karplus method to examine their biological roles. The analysis indicated that the conformational behaviors of these glycolipids are regulated by the sugar residue. The Gal brings a unique conformational behavior, which is advantageous for the formation of lipid bilayer membranes. The sugar residue makes intramolecular hydrogen bonds in several ways over the glycosyl linkage. M. pneumoniae GGLs possess a unique three dimensional structure when located in aqueous solvents. They possess a polar domain containing six to seven oxygen atoms in a narrow space. They possess a hydrophobic domain also in the sugar moiety extending from the glycerolipid moiety. They seem to have an instinct for making a microdomain in cytoplasmic membranes. The glycolipid microdomain should play an essential role like those for importing fatty acids from the host.

研究分野：生物有機化学

キーワード：マイコプラズマ 細胞膜 糖脂質 グリセロ脂質 立体配座 糖 NMR マイコプラズマ肺炎

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$$^3J_{H1S,H2} \text{ (Hz)} = 2.5gt(+) + 2.3gg(-) + 10.6tg \quad \text{--- (1)}$$

$$^3J_{H1R,H2} \text{ (Hz)} = 10.2gt(+) + 1.3gg(-) + 5.8tg \quad \text{--- (2)}$$

$$gt(+) + gg(-) + tg = 100 \quad \text{--- (3)}$$

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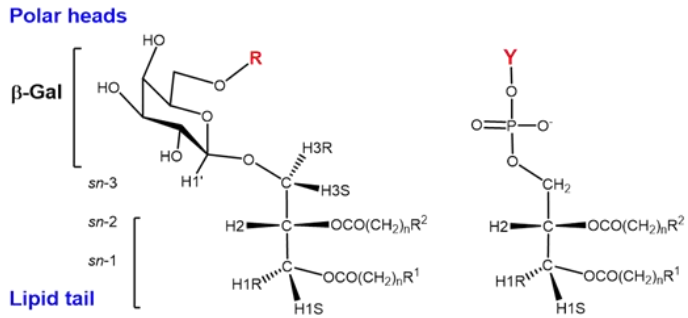
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(DNS) #2A# sn-3) (#

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Mycoplasma pneumoniae (β-GGLs): R = H, β-Glc, or β-Gal

マイコプラズマ肺炎菌が作る細胞膜糖脂質 (β-GGLs)

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M# (##w#2Ab# #c#0188# #E #2Ac(#

$$^3J_{H1S,H2} \text{ (Hz)} = 2.5gt(+) + 2.3gg(-) + 10.6tg \quad \text{--- (1)}$$

$$^3J_{H1R,H2} \text{ (Hz)} = 10.2gt(+) + 1.3gg(-) + 5.8tg \quad \text{--- (2)}$$

$$gt(+) + gg(-) + tg = 100 \quad \text{--- (3)}$$

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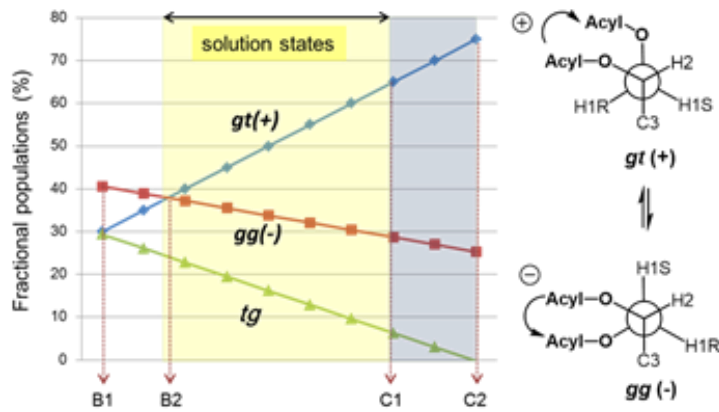
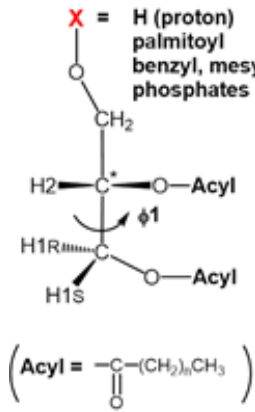
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各種1,2-DAG脂質 sn-1,2炭素軸の動的配座挙動

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1, 2-DAG00

3)487K

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+2A4)b 00 P

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C2 00

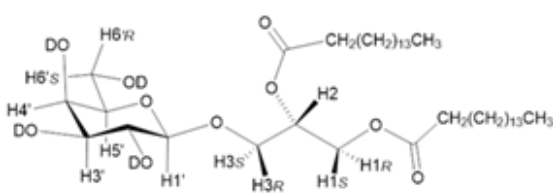
GGL-C2000

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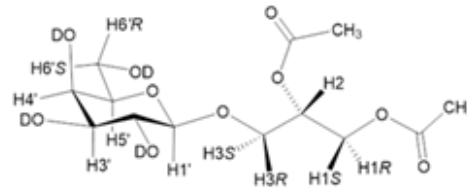
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β-Gal-lipid (βGal-C16)



β-Gal-lipid C2 homologue (βGal-C2)

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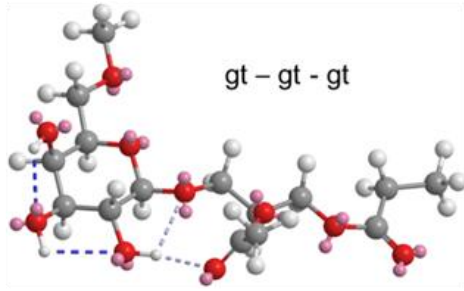
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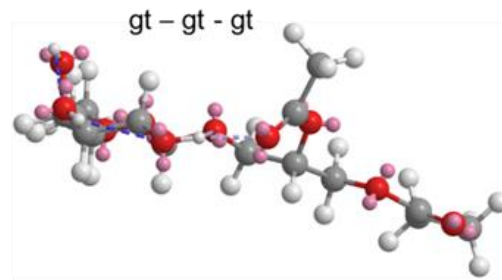
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(a) vertical view



(b) horizontal view



H-bonds : β -Gal 4'-OH \rightarrow 3'-OH \rightarrow 2'-OH \rightarrow sn-1-O and sn-2 carbonyl (-C=O)

β Gal

2A

(7)

(3)

GGLs: 4S4

M. pneumoniae

GGLs 5S4

8Z

GGL-C2b ¹H-NMR-Karpl us 00) Y

0P

p]1KS

(34)c

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SSrSg4

(70

6)40

dSpM

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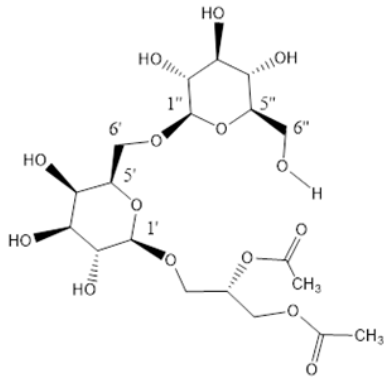
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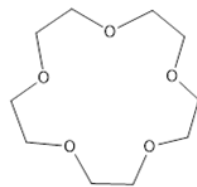
GGLs 9x0+

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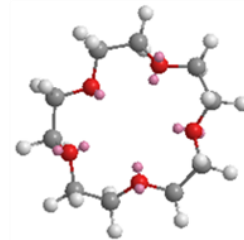
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β -GGL-C2



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M. pneumoniae @ 2A&

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S4G W

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63 2A 7aZ8488

GGLs cMOB M\ 6i-Sp 2A

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A 50KZ8 2A+V k7K

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lipid

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KS+K8

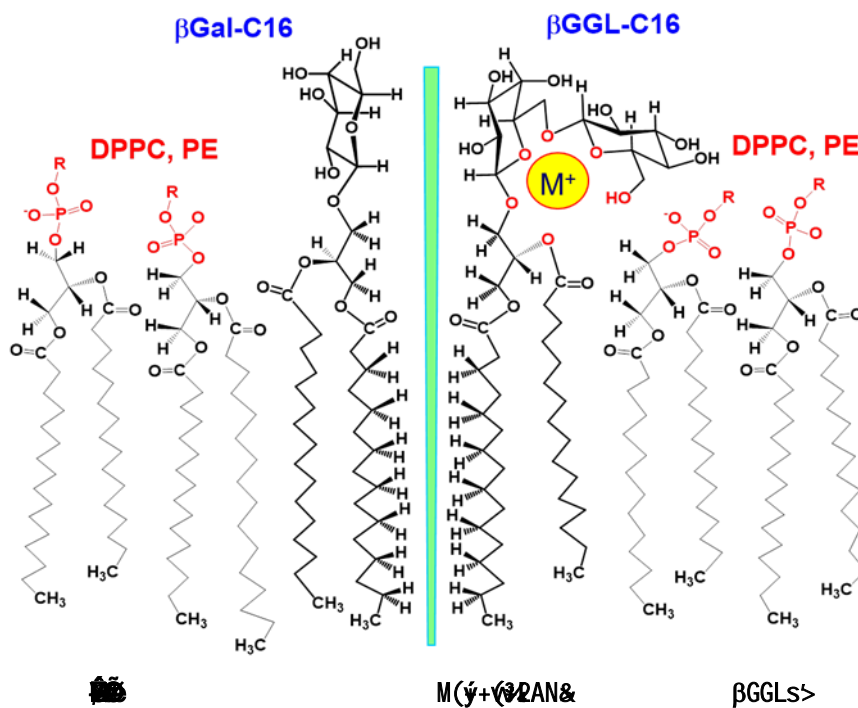
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(1) Kazuo Fukuda, Kazuhiro Matsuda, Sachie Matsuda, Sayaka Kado, Hyuma Masu, Hirofumi Dohi, Yoshihiro Nishida "Chemosynthetic homologues of *Mycoplasma pneumoniae* β -glycolipid antigens for the diagnosis of mycoplasma infectious diseases", *Bioorg. Med. Chem.*, **2018**, *26* (4), 824-832 (doi.org/10.1016/j.bmc.2017.12.046). □ □ □ □

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the diagnosis of mycoplasma infectious diseases' (The Joint congress of the 7th Meeting of the Asian Organization for Mycoplasmology (AOM) and the 45th Meeting of the Japanese Society of Mycoplasmology (JSM), 2018 □ 5 v 18 H □ 20 FgU2dFH □

(2) Kazuhiro Matsuda, Sachie Matsuda, Yoshihiro Nishida, Yuichiro Wasaki, Kunimi Kitada, Mizuho Hosogi, Tooru Araki, 'Mycoplasma pneumoniae and Mycoplasma fermentans-associated psychomotor deterioration, movement disorders without respiratory symptom: A case report' (The Joint congress of the 7th Meeting of the Asian Organization for Mycoplasmology (AOM) and the 45th Meeting of the Japanese Society of Mycoplasmology (JSM), 2018 □ 5 v 18 H □ 20 FgU2dFH □

(3) Yoshihiro Nishida (U\$ OY# / (2ANb 1,2-Y
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(8) Yoshihiro NISHIDA, Mengfei Yuan, Hirofumi Dohi, Akira Matsuura, "Helical conformation properties in cytoplasmic membrane glycerophospholipids and glycolipids in solution states"; (International Molecular Chirality Symposium- 2018 Jan 11-12, Chiba University, Chiba □

(9) Yoshihiro Nishida OY# / (2ANb : U 2ANb
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