

# Precise chemical synthesis of glycolipid biosurfactants and structure-function relationships for the creation of novel highly functional cosmetic materials

**Daisuke Takahashi**

*Faculty of Science and Technology, Keio University*

Mannosylerythritol lipids (MELs) are a group of amphipathic molecules consisting of a hydrophilic 4-*O*- $\beta$ -D-mannopyranosyl-erythritol core and two hydrophobic fatty acyl chains. Our group has systematically and stereoselectively synthesized 20 variants of *S*-MEL-A-D (C6, C8, C10, C12, C14) with different fatty acid chain lengths and varying acetylation patterns at C4' and C6' of the mannose unit. In addition, we conducted a structure-activity relationship (SAR) study to evaluate their recovery effects on damaged skin cells. The findings revealed that *S*-MELs with a C10 fatty chain length demonstrated the most significant recovery effects. Here, to create potential candidates for new cosmeceuticals, we designed and synthesized four MEL analogues—*R*-MEL-A, *S*-mannosylthreitol lipid (MTL)-A, *R*-MTL-A, and  $\alpha$ -*S*-MEL-A—using our previously established boron-mediated aglycon delivery (BMAD) method along with a neighboring group-assisted glycosylation method. Among these, *R*-MTL-A exhibited the highest selective cytotoxicity against human skin squamous carcinoma cells while also exhibiting an efficient recovery effect on damaged skin cells. These results indicate that *R*-MTL-A holds promise as a lead compound for next-generation cosmeceuticals.