Synthesis and immunomodulatory function of lipid-modified α-GalCer derivatives having nitrogen-containing functional groups

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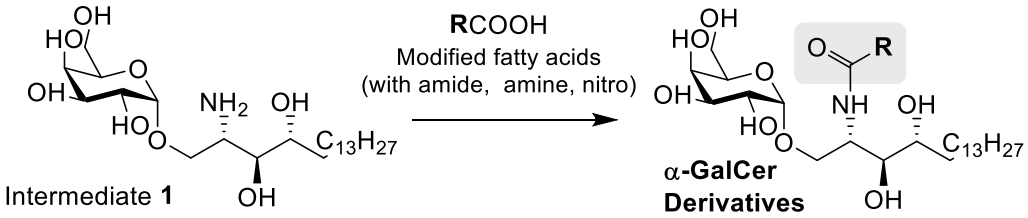
On antigen presenting cells, CD1d recognizes lipid antigens to form complexes, leading to the activation of NKT cells and secretion of various cytokines. We have previously revealed that the lipid moiety of the CD1d ligand (α-GalCer) strongly affects the binding affinity and balance of the immunological activities.[1] To further explore the functions of CD1d and the ligands, various derivatives of α-GalCer with distinctive lipid structures containing nitrogen functional groups (amide, amine and nitro groups) were designed and prepared, and their immunomodulatory activities were analyzed.

The target α-GalCer derivatives were synthesized with introducing modified fatty acids (having nitrogen functional groups such as amide, amine and nitro groups) to an intermediate **1**, which was prepared from D-galactose and phytosphingosine with previously reported methods.[1,2] The biological activities of the synthesized α-GalCer derivatives were then evaluated, which include competitive binding affinity assay with CD1d protein, antigen presenting cell (APC)-free assay and cytokine secretion assay using mouse splenocytes. The results showed that the introduction of nitrogen-containing functional groups to a certain position of the lipid section leads to the increase of binding and cytokine induction ability of the ligands.



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