Development of Ligand for Targeted Delivery to Murine Langerin

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Multivalent ligand-based targeted delivery can improve selectivity and efficacy of drugs or vaccines. Here, we develop targeting ligands that could specifically bind murine Langerin, a carbohydrate binding protein mainly expressed on Langerhans cells (LCs). LCs are skin-resident dendritic cells responsible for antigen presentation. Since many vaccines are delivered via skin, conjugating these ligands on nanoparticles could therefore reduce the side-effect and required dose. To develop molecules into targeting ligand,

(I): SAR study were carried out based on the HSQC data. The SAR analysis provided information about optimal linker sites and replacements to improve solubility and affinity.

(II): their binding sites were validated through solvent Paramagnetic Relaxation Enhancement (sPRE) NMR.

(III): the problem that hydrophobic ligands are inserting into the lipid bilayer of the liposome was addressed by conjugating a hydrophilic peptide spacer, which is composed of lysine and aspartic acid.

The outlook on this project is combining these ligands including the carbohydrate ligand that we developed based on the previous reported structure on the nanoparticle which yield multivalency that could provide better selectivity and affinity.

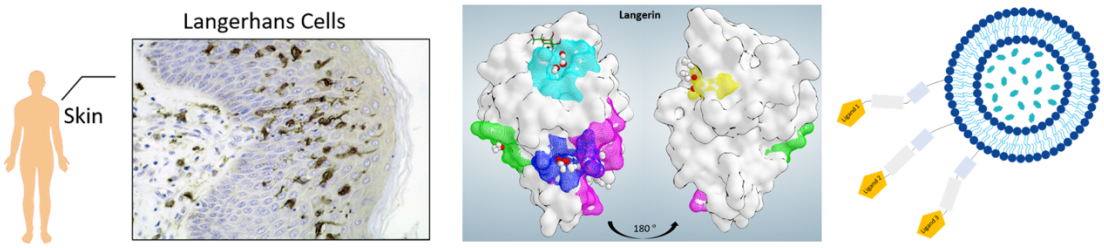

Figure 1. (a) Neoglycolipids. (b) Supramolecular characterization. (c) Heteromultivalency.

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