Targeted delivery of peptidoglycan immunomodulators using liposomal carriers: NMR study of the lipid encapsulation

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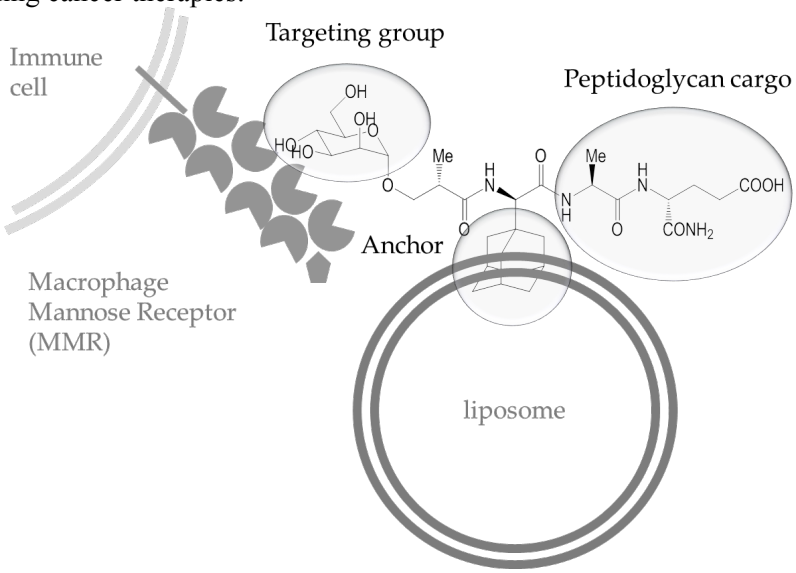
Abstract

Peptidoglycan (PGN) as well as fragments and substances derived from it, have well-documented immunomodulating properties[1] exerted by interaction with innate immune receptors. Such immunomodulators are urgently needed in many medical interventions[2], such as adjuvants in vaccines or in aiding cancer therapies.



In order to selectively modulate immune cells using PGN fragments, we developed actively targeted delivery of PGN-based immunomodulators using liposomes as carriers. We investigated the encapsulation of targeting compounds into lipid bilayers and the interaction between them on a molecular level using NMR spectroscopy. We show that the PGN derivatives are incorporated in the studied lipid bilayers by the change of the sign and intensity of the NOE as well as by the observation of slower translational diffusion in PFG-NMR spectra. We determined the encapsulation efficiency and found that the adamantylated parent compounds are incorporated more efficiently, while the chirality of the adamantly group attachment have a minor influence on the entrapment efficiency. We utilised STD experiments for the characterisation of the orientation of the studied derivatives in the bilayer. We found that the adamantylated derivatives are positioned on the surface of the bilayer, while the mannosylated compounds penetrate deeper. We also determined membrane associated conformations using transferred NOEs. With help of the experimental observations, we were able to propose a model of the interactions that provides an explanation for the observed encapsulation efficiencies.

References

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