Functionalized lipid bilayer on LbL-microcarriers – mimicking a cell for targeted drug delivery

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Common systemically applied therapeutics may cause side effects due to non-targeted transport and highly dosed amounts of active agents. Therefore, new drug delivery systems are needed which exhibit a targeted transport, time controlled release and are able to transport multiple active agents safely and in a defined dosage in just one carrier system.

One promising approach which provides all these features is based on the combination of the (1) Layer-by-Layer-technique (LbL) with the (2) Liposome-Spreading-technique (LS) and (3) antibody surface modification.

(1) The LbL-technique allows the integration of defined amounts of multiple active agents into specific layer depth and/or the microcarrier core, facilitating a time dependent release within the targeted cell [1,2].

(2) The LS-technique uses the fusion of small unilamellar vesicles on surfaces to create a lipid bilayer, reducing the risk of opsonization and enhancing biocompatibility [3].

(3) Specific functionalized lipids (e.g. biotinylated lipids) can be easily integrated into this lipid bilayer to provide a binding site for specific antibody coupling and targeted cell interaction.

The combination of all three techniques results in a smart drug delivery system with unique features. However, for the fabrication of an effective microcarrier system it is essential to create a homogeneous and regular lipid bilayer on top of the microcarrier to inhibit unspecific serum protein interaction and to reduce microcarrier uptake by non-targeted cells.

Using SiO_2 microparticles and an LbL multilayer consisting of protamine sulfate and dextran sodium sulfate, we could show that the lipid bilayer formation is strongly influenced by the applied lipid mixture as well as the LS coating conditions. For instance, the integration of the functional lipid PE-PEG-biotin into a homogeneous POPS/POPC lipid membrane leads to a concentration dependent disturbance of the lipid bilayer homogeneity [4].

In this study we demonstrate that suitable adjustments of the incubation conditions (e.g. concentration of liposomes, microcarriers and functional lipid PE-PEG-Biotin) can be made in order to obtain a homogenous functionalized lipid bilayer on top of LbL-microcarriers. Such microcarriers exhibit a highly specific steptavidin as well as optimal antibody binding. Cell approaches show the specifity and adaptability of the smart drug delivery system.

Acknowledgements The research was made possible by funding from the German Research Foundation (DFG), the European Union and the Free State of Saxony and was supported by the DFG project RE 2681/2-2 and the DFG graduate school 185 “Leipzig School of Natural Sciences Building with Molecules and Nano-objects” (BuildMoNa).

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