A153

**A LIPOSOME-BASED NANOCARRIER FOR PREFERENTIAL
TARGETING OF THE MONONUCLEAR PHAGOCYTE
SYSTEM IN ARTHRITIC MICE**

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Cells from the mononuclear phagocyte system (MPS) play a key role in the systemic and local progression as well as in the chronicity of rheumatoid arthritis (RA). MPS cells produce many molecules which participate in the inflammatory and catabolic events of RA pathogenesis. Thus, engineering of vectors tailored to selectively target both tissue resident and circulating MPS cells is certainly one of the most promising research tracks for gene therapy-based intervention in RA. The objective of the present study was to develop a vehicle that targets MPS cells in vivo following intravenous administration. The cationic liposome RPR209120/DOPE was formulated with red fluorescent nucleic acids and the so-called lipoplexes were injected intravenously into collagen-induced arthritic mice during the acute phase of inflammation. To increase the selectivity for the MPS cells, the formulation was mannosylated. The blood, spleen, liver, draining lymph nodes (DLNs) and arthritic joints were collected at 4h and/or 24h, freshly isolated cells were stained for F4/80 (monocytes/macrophages), CD11c (dendritic cells, DCs), B220 (B cells) and CD3 (T cells) cell surface markers and analysed by flow cytometry. Lipoplexes were detected in all of the investigated tissues and were preferentially entrapped after intravenous injection by cells from the myeloid lineage, reaching 10–20% of F4-80-positive and CD11c-positive cells in the spleen and liver. Importantly, flow cytometric analysis of the joints from arthritic DBA1 mice injected 24h earlier with fluorescent lipoplexes showed that 4% of the F4-80-positive cells and >20% of the CD11c-positive cells were targeted by the formulation, respectively, compared with control mice. Although the addition of mannose residues at the surface of the lipoplexes does not increase the percentage of transduced phagocytic cells, the amount of genetic material loaded per cell was markedly improved. These data highlight a preferential uptake of our lipoplex formulation by phagocytic cells and suggest that it might represent an efficient tool for screening of novel target genes implicated in RA pathogenesis.