INHIBITION OF NF-κB ACTIVATION BY DECOY ODN RELEASED FROM LIPOSOMES IN ACTIVATED MACROPHAGES

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Nuclear factor-κB (NF-κB) transcription factor regulates the expression of genes involved in immune response and inflammation. In the present study we investigated the potential of liposomes based on the cationic lipid (2,3-didodecyloxypropyl) (2-hydroxyethyl) dimethylammonium bromide (DE) as delivery system for an ODN against NF-κB in RAW 264.7 macrophages stimulated with lipopolysaccharide (LPS; 1 μg/ml) for 24 h. We prepared liposomes with DE alone or associated to helper lipids, such as cholesterol and 1,2-dioleil-sn-glicero-3-phosphoethanolamine (DOPE). Liposomes were complexed with the decoy ODN at different +/- charge ratios. Naked decoy ODN, naked Mut ODN, decoy ODN/liposome complexes and Mut ODN/liposome complexes were added on the cells at a final ODN concentration of 0.4 μM. Stimulation of cells with LPS caused an increase of nitrite production, inducible nitric oxide synthase protein expression (iNOS) as well as NF-κB/DNA binding activity which were significantly inhibited by ODN complexed with DE/Chol liposomes at a high +/- charge ratio. Naked ODN, naked Mut ODN and Mut ODN complexed with DE/Chol did not exhibit any effect. Our results suggest that DE-based liposomes could be an useful tool to improve pharmacokinetics of a ODN decoy to NF-κB and may represent a promising strategy to effectively inhibit the transcriptional activity of NF-κB in inflammatory process.