Magnetic Nanobeads for the Delivery of Therapeautic Nucleic Acids to the Heart

Wenzhong Li[1], Nan Ma[1], Leelee Ong[1], Christof Stamm[1], Alexander Kaminski[1], Peter Lorenz[2], Brigitte M. Pützer[3], Gustav Steinhoff[1]

Department of Cardiac Surgery[1], Department of Immunology[2], Department of Vectorology and Experimental Gene Therapy[3], University Rostock, Germany

Statement of Purpose: The retention problem of vector-gene complexes limits the gene therapy in cardiovascular system. We conjugated polymer vector-gene complexes to magnetic nanobeads (MNB) and employed external magnetic fields to guide MNB/DNA complexes to the target area and induce localized therapeautic nucleic acids expression after intravenous administration.

Methods: The poly-ethyleneimine vector (PEI) was conjugated with MNB using a Sulfo-NHS-LC-Biotin linker. Stability of the MNB/PEI/DNA complex was evaluated by DNase I protection assay. Under magnetic field stimulation, in vitro transfection efficacy of MNB/PEI/DNA was assessed in 4 different cell lines and compared with unconjugated PEI/DNA. In vivo, MNB/PEI/Bcl-2 complexes were injected in the tail vein of mice (n=12) and epicardial magnets were employed to trap circulating MNB/PEI/DNA complexes. Transfection efficacy of therapeautic nucleic acid Bcl-2 was assessed in the hearts by immunostaining.

Results / Discussion: The MNB/PEI/DNA complexes were very stable, biocompatible, and non-toxic. MNB/PEI/DNA complexes had a 36- to 85-fold higher transfection efficiency in magnetic fields compared with PEI/DNA complexes alone. In vivo, the epicardial magnets effectively trapped MNB/PEI/DNA complexes in the heart, resulting in effetive expession of therapeautic nucleic acid Bcl-2.

Conclusions: Magnetic nanobeads conjugated with non-viral polymer vector-gene complexes could induce therapeautic gene expression under magnetic field stimulation. This technique could greatly enhance the prospects of gene therapy in the cardiovascular system.