Small Poly-L-Lysines Improve Cationic Lipid-Mediated Gene Transfer in Vascular Cells in vitro and in vivo

Abstract:
The potential of two small poly-L-lysines (sPLLs), low molecular weight sPLL (LMW-L) containing 7–30 lysine residues and L18 with 18 lysine repeats, to enhance the efficiency of liposome-mediated gene transfer (GT) with cationic lipid DOCSPER [1,3-dioleoyloxy-2-(N5-carbamoyl-spermine)-propane] in vascular smooth muscle cells (SMCs) was investigated. Dynamic light scattering was used for determination of particle size. Confocal microscopy was applied for colocalization studies of sPLLs and plasmid DNA inside cells. GT was performed in proliferating and quiescent primary porcine SMCs in vitro and in vivo in porcine femoral arteries. At low ionic strength, sPLLs formed small complexes with DNA (50–100 nm). At high ionic strength, large complexes (>1 µm) were observed without any significant differences in particle size between lipoplexes (DOCSPER/DNA) and lipopolyplexes (DOCSPER/sPLL/DNA). Both sPLLs were colocalized with DNA inside cells 24 h after transfection, protecting DNA against degradation. DOCSPER/sPLL/DNA formulations enhanced GT in vitro up to 5-fold, in a porcine model using local periadventitial application up to 1.5-fold. Both sPLLs significantly increased liposome-mediated GT. Poly-L-lysine L18 was superior to LMW-L since it enabled maximal GT at a 10-fold lower concentration. Thus, sPLLs may serve as enhancers for GT applications in SMCs in vitro.
and in vivo using local delivery.

**Stichworte:**
Gene transfer; Lipopolyplexes; Poly-L-lysine; Cationic lipid; Smooth muscle cells

**Zeitschriftentitel:**
Journal of Vascular Research

**Jahr:**
2007

**Band:**
44

**Heft / Issue:**
4

**Seiten:**
273--282

**Volltext / DOI:**
http://doi.org/10.1159/000101449

**Verlag / Institution:**
S. Karger AG

**Verlagsort:**
Basel, Switzerland

**Print-ISSN:**
1423-0135

**E-ISSN:**
1423-0135

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**Occurences:**
- Kollektionen > Open Access Publikationen > Verlage > Karger
- Kollektionen > Open Access Publikationen > 2007

**entries:**