results demonstrated that G5 showed the highest gene transfection efficiency both in the medium with or without serum. Peptide dendrimer based drug delivery system was with dual targeting and pH-sensitive functions. Dendrimer–doxorubicin conjugates were synthesized via a pH sensitive bond. The drug release at pH 5.0 was much faster that that at pH 7.4. The sustained release time was as long as 20 hours and more than 90% of the immobilized drugs were released at pH 5.0. The *in vitro* anti-tumor effects of the dendrimer drug delivery system were investigated and it showed that the peptide dendrimer was a promising carrier for drug delivery.

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A31
Pyridylhydrazone-based PEG for pH-reversible lipopolyplex shielding

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PEGylation that is reversed after the therapeutic agent reaches the target cell presents an attractive feature for drug, protein or nucleic acid delivery. Amine-reactive, endosomal pH cleavable ω-2-pyridyldithio poly(ethylene) glycol α-(butyraldehyde)-carboxypridylhydrazone N-hydroxysuccinimide ester (OPSS-PEG-HZN-NHS) was synthesized and applied for bioreversible surface shielding of DNA lipopolyplexes. N1-cholesteryloxycarbonyl-1,2-diaminoethane was reacted with pH-sensitive (OPSS-PEG-HZN-NHS) or the corresponding stable (OPSS-PEG-NHS) reagent. Both types of micelles remained shielded at pH 7.4 as demonstrated by size exclusion column separation after 4 hours of incubation at 37 °C. But only disruption of OPSS-PEG-HZN-Chol micelles was observed at endosomal pH 5 in 30 min, while OPSS-PEG-Chol was almost stable for 8 h in the same conditions. Lipopolyplexes composed of DNA condensed with polyethylenimine (PEI), dioleoyl phosphatidylethanolamine (DOPE) and hydrazone linked pH labile lipid Chol-HZN-PEG were prepared by the ethanol injection technique, with particle size of 160 nm and zeta potential of 8 mV. Pyridylhydrazone-based PEGylated lipopolyplexes was as stable as their non-pH sensitive counterparts at physiological conditions, and had smaller size compared with non-PEGylated variants. At pH 5.4, increasing size was only detectable in pH-reversible lipopolyplexes. Both luciferase and EGFP gene transfections of pH-reversible lipopolyplexes showed an up to 40-fold enhancement in gene expression with reversibly shielded polyplexes compared to stably shielded lipopolyplexes. Investigation of cellular association and uptake by flow cytometry, together with intracellular tracking by CLSM reveal the probability of intracelluar deshielding of PEG. Incorporation of a ligand for transferrin receptor targeting further improved the transfection.

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A32
The 5th generation of poly(L-lysine) dendrimer is a potential carrier for *in vivo* in gene delivery

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Poly(L-lysine) dendrimers have been widely used as reagents for *in vitro* gene transfecion. Here, different generations of dendritic poly(L-lysine)s were synthesized, including G3, onium salt G3 (OG3), G4 and G5, and their characteristics for *in vitro* gene transfection and potentials as *in vivo* gene delivery carriers were evaluated. Gel retardation assays proved that the dendrimers could form complexes with plasmid DNA, and dendrimer G3 could inhibit the migration of pDNA at an N/P ratio of 0.5, G4 and G5 at N/P ratio of 1.0 and onium salt G3 at N/P ratio of 2.0. A DNase I protection assay with G5 showed acquired resistance from combining pDNA with dendrimer; this can resist the nuclease-catalyzed degradation, and the protection capacity of G5 was even stronger than that of PEI. Atomic force microscopy demonstrated that all the 4 generations of dendrimer/DNA complexes showed similar particle size within 100–200 nm. At N/P ratios from 1 to 25, zeta potentials of the 4 dendrimer/pDNA complexes gradually changed from negative to positive with a tendency that the higher generation and higher potential value variants gave a stronger combination potency of the complex with negatively charged cell membranes. *In vitro* cytotoxicity evaluation showed good biocompatibility of each dendrimer within N/P ratios of 1–25. Body weight evaluation of BABL/c mice, together with tissue section observation, blood routine detection and blood biochemistry analysis (liver and kidney function, myocardial enzymes and electrolytes, etc.) of dendrimer G5 also showed good *in vivo* biocompatibility 2 and 7 days after tail vein injection. *In vitro* gene transfection comparison revealed that G5 had an obvious higher efficiency than other dendrimers. Transfection efficiencies of each dendrimer were not influenced by the presence of serum, which is a very important merit for *in vivo*in gene delivery. Quantitative analysis in mRNA and protein level showed that the transfection efficiency of dendrimer G5 was ~60% of PEI's, but PEI had obvious toxicity to cultured cells and its transfection efficiency would be greatly reduced by the presence of serum. Considering that dendrimer G5 had almost the same *in vitro* gene transfection efficiency as G6, we concluded that the fifth generation of poly(L-lysine) dendrimer should be a suitable carrier for *in vitro* gene transfection and, more importantly, a potential carrier to construct *in vivo* gene delivery system.

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A33
Muscle-targeted HIF-1a gene expression system for therapeutic angiogenesis in ischemic limbs

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Therapeutic angiogenesis is expected to be a promising treatment for patients with ischemic disorders such as cardiac and limb ischemia. However, recent clinical trials failed to show much expectant benefits, largely due to suboptimal therapeutic genes and delivery strategies. Herein, we focused on the development of a hypoxia inducible factor-1a (HIF-1a) gene induced muscle-specific angiogenesis strategy that would improve safety and effi-