# Delivery of Cyclodextrin-based Polyplexes from Solid Surfaces

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**Statement of Purpose:**
Localized, nucleic acid delivery from solid surfaces is an important technology for biomedical research, with applications ranging from gene therapy to tissue engineering to functional genomics [1]. Non-viral gene delivery vehicles have been immobilized to solid surfaces by physical absorption, biotin-streptavidin interaction, and chemical conjugation [1]. Here, we present a new approach for surface-mediated gene delivery based on inclusion complex formation between the solid surface and delivery vehicles. Cyclodextrins (CD), cyclic oligomers of glucose, form inclusion complexes with small, hydrophobic compounds such as adamantane. In this work, nanoparticle composites of cyclodextrin polycations and nucleic acids were specifically immobilized on adamantane-coated surfaces. The interaction was characterized by surface plasmon resonance (SPR) spectroscopy and by atomic force microscopy (AFM).

**Methods:**
CD–modified polyethylenimine (CD-PEI) was synthesized according to previous reports [2]. Adamantane (AD)-conjugated self-assembled monolayers (SAM) was prepared by tethering the NHS-activated ADs to amine-terminal SAM on a gold-coated glass. Briefly, mixed SAM was formed by soaking a cleaned gold-coated glass in a total 2 mM ethanolic solution of amine- and hydroxyl-terminal thiols for 24 h, followed by the grafting of β- CD onto the monolayered amino groups. CD-PEI and PEI-based nanoparticles were formed by complexation between CD-PEI and PEI, respectively, with plasmid DNA. The AD-SAM-coated glass chip was placed against a glass prism, and solutions containing CD-PEI- and PEI-based nanoparticles were injected into the flow cell at a flow rate of 0.05 mL/min by means of a peristaltic pump. The change (nm) in the resonant wavelength was detected by SPR instrument. The competition of bound CD-PEI with free cyclodextrin was performed to investigate the specific binding of CD-PEI polyplex onto AD-SAM surface. The morphology of bound CD-PEI polyplex was examined by atomic force microscopy.

**Results / Discussion:**
Cyclodextrin molecules form high-affinity inclusion complexes with adamantane. This complexation ability was used to specifically immobilize CD-PEI nanoparticles on the AD-modified surfaces as shown in Fig. 1. To investigate the nanoparticle/surface interaction, CD-PEI-based nanoparticles and PEI-based nanoparticles were passed through an SPR flow cell containing the adamantane-modified chip. Adsorption of the nanoparticles to the chip surface was determined by monitoring the wavelength shift as a function of time.

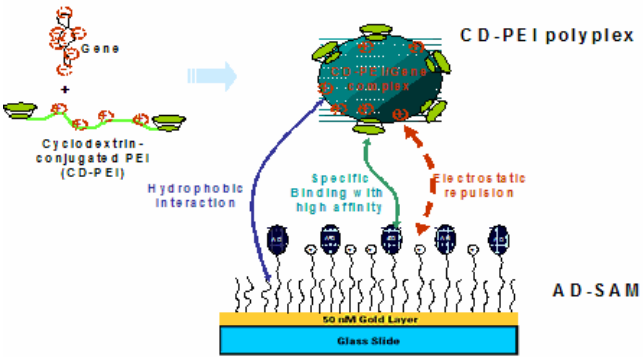


**Figure 1.** Schematic illustration of specific interaction between CD-PEI polyplex and adamantane-modified surface.

As shown in Figure 2, PEI-based nanoparticles do not absorb to the chip surface due to electrostatic repulsion between the cationic particles and unreacted amines. CD-PEI nanoparticles are specifically immobilized on the chip surface by cyclodextrin-adamantane inclusion complex formation.

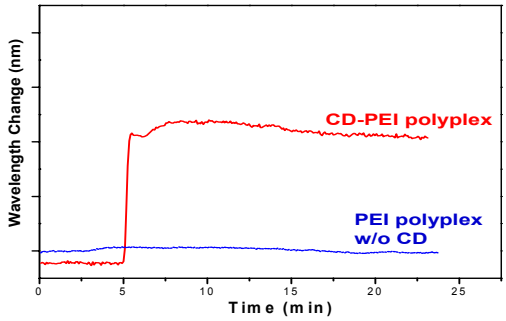


**Figure 2.** Investigation of the specific interaction between CD-PEI polyplex and AD by SPR

The multiple interactions between a single CD-PEI nanoparticle and the adamantane-surface results in significantly higher binding affinity than single cyclodextrin: adamantane complexes.

**Conclusions:**
We have demonstrated a new method for immobilizing gene delivery vehicles to solid surfaces by inclusion complex formation. CD-PEI nanoparticles demonstrated significantly higher adsorption on adamantane surfaces than PEI nanoparticles. Thus, the ability of CD-PEI nanoparticles to form inclusion complexes can be exploited to attain specific, high affinity loading of delivery vehicles onto solid surfaces.

**References:**
1. Pannier and Shea. (2004) *Molecular Therapy* v10:19-
2. Pun, et al. (2004) *Bioconjugate Chemistry* v15:831-840.