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Effect of surface chemistry on gene transfer efficiency mediated by surface-induced DNA-doped nanocomposites

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ABSTRACT

Surface-induced biomineralization represents an effective way of immobilizing DNA molecules on biomaterial surfaces to introduce DNA into cells in contact with or at an approximate distance from the biomaterial surfaces. Previous studies have investigated how the composition of mineralizing solutions affects the composition and pH responsiveness of nanocomposites and thus gene transfer efficiency in different cell types. This study investigates how the functional groups of a biomaterial surface affect the induction and crystallographic properties of nanocomposites and thus the gene transfer efficiency. Self-assembled monolayers with different termini were used to control the functional groups of a surface. It is demonstrated that the induction of DNA-doped nanocomposites depends on the surface functional groups, which is consistent with previous studies. The crystallographic properties did not vary significantly with the functional groups. DNA-doped nanocomposites induced by different surface functional groups resulted in different cellular uptake of DNA and thus gene transfer efficiency. The differential cellular uptake may be attributed to the interactions between nanocomposites and functional groups. The weaker inducer resulted in higher cellular uptake, and thus higher gene transfer efficiency. Together with other previous studies, the current results suggest that surface-mediated gene transfer by DNA-doped nanocomposites can be modulated through both mineralizing solutions and surface chemistries.

1. Introduction

Biomineralization is a naturally controlled process which assembles nano- or micro-scale inorganic structures for living organisms. The resulting highly organized structures resemble hard tissues in the human body and have been adapted to two- or three-dimensional biomaterial matrices for bone tissue engineering [1–4]. Matrices with mineral coatings enhance bone bonding on implant surfaces, inhibit resorption of the surrounding bone and promote the attachment and proliferation of cells [5–9]. Previously, it has been shown that DNA can be doped into surface-induced biominerals during the process of biomineralization; these structures were termed DNA-doped nanocomposites. It was demonstrated that these nanocomposites can deliver DNA into a wide range of cells [10,11], and the efficiency of gene transfer can be tuned by manipulating the composition of mineralizing solutions. This approach has great potential in building DNA delivery into tissue engineering constructs for further mediating cellular functions [12,13].

In order for mineralization to occur, the solution must be supersaturated with respect to the precipitating mineral phases [14]. Extensive studies have demonstrated that the nucleation and growth of mineral phases can be precisely controlled not only by the composition of supersaturated aqueous solutions, but also by various biological macromolecules [15,16]. These macromolecules are acidic in nature and usually consist of specific functional groups, such as SO_3^- [17], COO^- [18], $H_2PO_4^-$ [19] and OH [20]. These anionic groups all initiate crystal nucleation and growth. The relative ability to induce apatite formation by anionic groups is in the order of: $H_2PO_4^- > SO_3^- > COO^- > OH$ [21–24]. However, the induction of DNA-doped nanocomposites has been studied mainly on poorly controlled surfaces with OH and/or COO^- functional groups. Three key questions remain to be addressed. First, how do surface functional groups affect the induction of DNA-doped nanocomposites? Second, how do surface functional groups affect the crystallographic properties of DNA-doped nanocomposites? Last, how do surface functional groups affect the detachment of minerals from the surface and the gene transfer efficiency mediated by DNA-doped nanocomposites?

Self-assembled monolayers (SAMs) formed from long-chain alkanethiols ($HS(CH_2)_nX$, $n > 10$, X = a functional group) are well packed and oriented. They are tethered to the surface through the sulfur atom, which forms a covalent bond with the gold surface. The polyethylene chains are *all-trans* and tilted 20–30° from the normal to the surface; and the terminal group X is the predominant group exposed to the monolayer–liquid interface [25]. SAMs have been used to modify the surface of materials [14,26–28]. For

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