Synthesis and Characterization of Polyethylene Glycol-Grafted Rosette Nanotubes as Drug Delivery Vehicles

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Nanomaterials are widely used, beginning with daily life products all the way to highly specialized systems.[1-3] Such materials measure in the range of approximately 1-100 nm. Because of their small dimension, nanomaterials have a wide range of applications. They are used in or as catalysts, electro-devices, biological labels, and as materials for delivery in the areas of biomedical and tissue engineering.[4-6] In the past decades, nanotubes, which have a hollow interior, have become among the most promising classes of materials as tools for drug delivery, tissue engineering and opto-electronics.[7-9] A good example of such materials are self-assembled peptides, [10] which are composed of short sequence of amino acids. Experiments have shown that such self-organized scaffolds can promote cell growth and differentiation (in the area of tissue engineering) [11] and deliver genes (in the area of gene therapy).[12] However, the instability and the difficulty in manipulating the function of such structures strongly hinders their applicability and limits the quality of the materials that can be obtained.

Inspired by the Watson-Crick pairing, nucleic acid-based self-assembled nano-architectures have been reported such as oligonucleotide nanoparticles, [13] DNA nanotubes[14] and rosette nanotubes (RNTs).[15] RNTs are hierarchically self-assembled from synthetic DNA hybrid molecule G∧C motif in which Watson-Crick pairing takes place between the guanine side of the G∧C motif and its cytosine side.[15] The spatial arrangement of these arrays leads them to form a six-membered supermacrocycle. Compared with self-assembled peptides, RNTs exhibit high stability as a result of the extensive H-bond network (18 H-bonds hold each rosette macrocycle) and the inter-rosette π-π stacking interactions. The functional side-groups covalently attached to the G∧C motif offer important physical and chemical properties as well as diverse applications of the RNTs, such as drug delivery, tissue engineering, catalysis and photovoltaic devices.[16-18]

In order to improve the hydrophilicity and biocompatibility of the RNTs as biomaterials, PEGylation can be used as a strategy.[19] PEGylation is a commonly used modification technique consisting in the covalent attachment of polyethylene glycol chains to molecules and supramolecular structures. PEGylation changes the physical and chemical properties of the biomedical molecules and results in improvement in the pharmacokinetic behavior of the

biomedical materials.[20] For example, PEG-grafted single-wall carbon nanotubes (PEG-SWCNTs) showed promise as a drug delivery vehicles with low cytotoxicity and good delivery performance.[21]

My research project consists in conjugating PEG chains to the G∧C motif via reductive amination reactions. As a result, the surfaces of the RNTs will display PEG chains. This modification will enhance the solubility, biocompatibility, and bioavailability of the RNTs. We also expect to reduce the cytotoxicity of the RNTs in applications as drug delivery vehicles. Currently, my work focuses on the synthesis of the G∧C motif and its subsequent PEGyation. I will then investigate the physical properties, cytotoxicity, biodistribution of the resulting RNTs in animal models and the efficiency of paclitaxel/RNT drug formulation in the treatment of cancer.

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