CARBON NANOTUBES DECORATED WITH CATIONIC CARBOSILANE DENDRONS AND THEIR HYBRIDS WITH siRNA

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Carbon nanotubes (CNTs) are extensively used as carriers nucleic acid therapeutics, including small interfering RNA (siRNA) [1]. A versatile approach commonly used to construct hybrids of siRNA with single-walled and multi-walled carbon nanotubes (SWCNTs and MWCNTs) presumes the electrostatic interactions between nucleic acid backbone and cationic groups on the CNT surface. Cationic SWCNTs and MWCNTs can be easily obtained by grafting of amino-bearing compounds to CNT surface. The use of dendritic compounds to functionalize CNTs is highly promising due to the increase of the surface charge that leads to more efficient siRNA binding and better biocompatibility of hybrid constructions [2]. Due to their structure and properties, carbosilane dendrimers are prospective carriers for siRNA [3, 4]. In this work, multicomponent hybrid nanoparticles for siRNA delivery built of CNTs and carbosilane dendritic molecules were designed.

A series of cationic carbosilane dendrons of generations 1 to 3 bearing pyrene residues in focal point (fig. 1) has been synthesized and characterized. Pyrene is known as a good anchor group to immobilize macromolecules on the CNT surface. Meanwhile, cationic groups of dendrons can bind siRNA in the complex with nanoparticles.

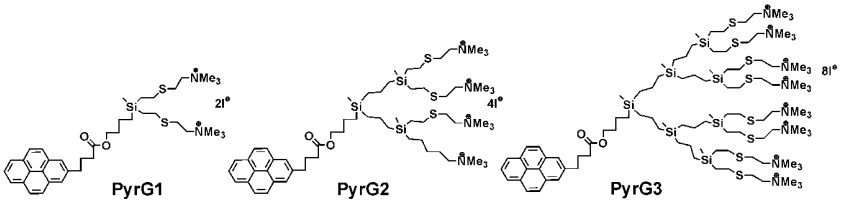

Figure 1 – Structures of pyrene-modified carbosilane dendrons

Cationic SWCNTs and MWCNTs have been obtained by grafting of diamines to the carboxy-modified CNTs as described in [5, 6]. Amino-modified CNTs were non-covalently functionalized with pyrene-modified cationic carbosilane dendrons (fig. 2). To quantify the affinity of dendrons to CNTs and to estimate the density of functionalization, the isotherms of adsorption were plotted. The quantity of dendron adsorbed was calculated from the data on pyrene fluorescence quenching upon its adsorption onto the CNTs [6].

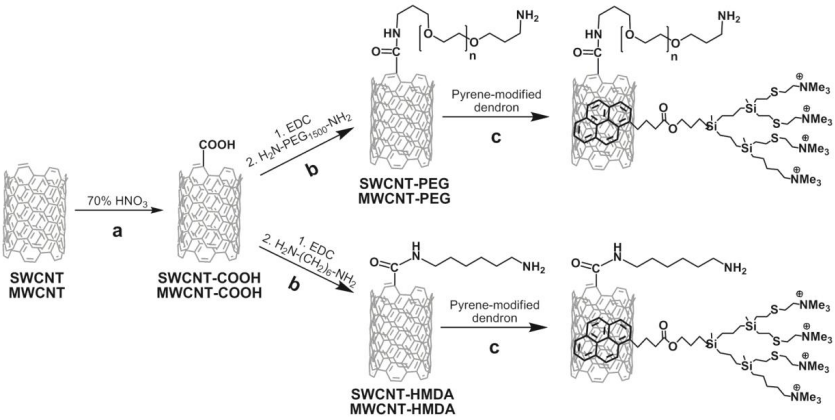

Figure 2 – Scheme of CNT functionalization

Dendron-decorated CNTs are able to bind siRNA efficiently. As shown on fig. 3, SWCNTs bind siRNA better, than MWCNTs. The positive dendritic effect on siRNA binding (G1<G2<G3) has been also observed. The formation of hybrid nanoparticles can be observed by TEM.

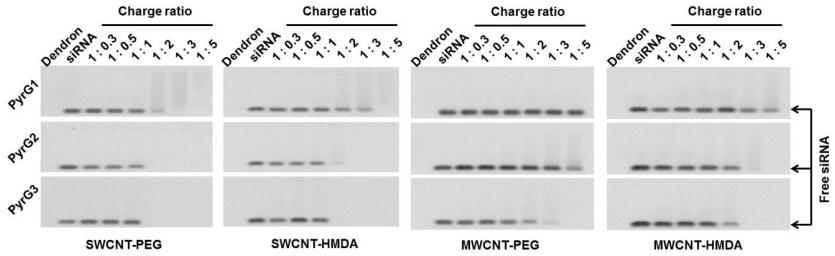

Figure 3 – siRNA binding by dendron-decorated CNTs

The obtained data suggest that both SWCNTs and MWCNTs decorated with pyrene-modified cationic carbosilane dendrons can be prospective carriers for therapeutic nucleic acids, including siRNA.

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References

1. Apartsin E.K., Buyanova M.Yu., Novopashina D.S., Venyaminova A.G. Hybrids of siRNA with carbon nanotubes as RNA interference instruments / Karachevtsev V.A. (ed.). Nanobiophysics: fundamentals and applications // Singapore: Pan Stanford Publishing. 2015. P. 33-57.
2. Al-Jamal K., Toma F., Yilmazer A., Ali-Boucetta H., Nunes A., Herrero M., Tian B., Eddaoudi A., Al-Jamal W., Bianco A., et al. (2010) Enhanced cellular internalization and gene silencing with a series of cationic dendron-multiwalled carbon nanotube:siRNA complexes // FASEB J. – 2010. – V. 24. – P. 4354-4365.
3. Ionov M., Lazniewska J., Dzmitruk V., Halets I., Loznikova S., Novopashina D., Apartsin E., Krasheninina O., Venyaminova A., Milowska K., Nowacka O., Gomez Ramirez R., de la Mata F.J., Majoral J.-P., Shcharbin D., Bryszewska M. Anticancer siRNA cocktails as a novel tool to treat cancer cells. Part (A). Mechanisms of interaction // Int. J. Pharm. – 2015. – V. 485. – N. 1-2. – P. 261-269.
4. Dzmitruk V., Szulc A., Shcharbin D., Janaszewska A., Shcharbina N., Lazniewska J., Novopashina D., Buyanova M., Ionov M., Klajnert-Maculewicz B., Gómez Ramirez R., Mignani S., Majoral J.-P., Muñoz-Fernández M.A., Bryszewska M. Anticancer siRNA cocktails as a novel tool to treat cancer cells. Part (A). Efficiency of pharmacological action // Int. J. Pharm. – 2015. – V. 485. – N. 1-2. – P. 288-294.
5. Apartsin E.K., Novopashina D.S., Nastaushev Yu.V., Venyaminova A.G. Fluorescently labeled single-walled carbon nanotubes and their hybrids with oligonucleotides // Nanotechnol. Russ. – 2012. – V. 7. – N. 3-4. – P. 99-109.
6. Apartsin E.K., Buyanova M.Yu., Novopashina D.S., Ryabchikova E.I., Filatov A.V., Zenkova M.A., Venyaminova A.G. Novel multifunctional hybrids of single-walled carbon nanotubes with nucleic acids: synthesis and interactions with living cells // ACS Appl. Mater. Interfaces – 2014. – V. 6. – N. 3. – P. 1454-1461.