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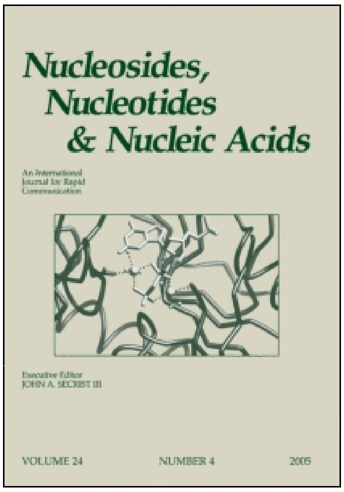

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Ph-Dependent Assembly of DNA-Gold Nanoparticles Based on the i-Motif

Frank Seela[ab]; Simone Budow[ab]
[a] Laboratory of Bioorganic Chemistry and Chemical Biology, Center for Nanotechnology, Münster, Germany [b] Laboratorium für Organische und Bioorganische Chemie, Universität Osnabrück, Osnabrück, Germany

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pH-DEPENDENT ASSEMBLY OF DNA-GOLD NANOPARTICLES BASED ON THE i-MOTIF

Frank Seela and Simone Budow □ *Laboratory of Bioorganic Chemistry and Chemical Biology, Center for Nanotechnology, Münster, Germany, and Laboratorium für Organische und Bioorganische Chemie, Universität Osnabrück, Osnabrück, Germany*

□ *Oligonucleotides containing stretches of 2′-deoxycytidine residues were immobilized on 15 nm gold nanoparticles. Under acidic pH conditions a reversible supramolecular assembly is formed, induced by the formation of the tetrameric i-motif structure. The replacement of 2′-deoxycytidine by 5-propynyl-2′-deoxycytidine (dC*) leads to novel i-motif structures. Oligonucleotides incorporating multiple residues of dC* were immobilized on 15 nm gold nanoparticles and are able to aggregate into i-motif structures even at non-optimal pH values.*

Keywords DNA; i-motif; 5-propynyl-2′-deoxycytidine; gold nanoparticles; self-assembly

INTRODUCTION

One of the most successful approaches in the field of nanobiotechnology are the DNA gold nanoparticle conjugates which have been utilized to construct a variety of highly ordered nanoassemblies and colorimetric screening assays.[1] The DNA gold conjugate concept is based on a visible color change from red to blue induced by a controlled aggregation of DNA-functionalized gold nanoparticles. Thus, the assembling of the DNA gold nanoparticle conjugates is not limited to duplex formation. Also, higher ordered DNA structures such as triplexes and quadruplexes have been used to create networks of gold nanoparticles.[2] Recently, our laboratory reported on the immobilization of cytosine-rich oligonucleotides on 15 nm gold nanoparticles.[3] Cytosine-rich oligonucleotides form a complex tetrameric structure (i-motif) under weak acidic conditions that is stabilized by the intercalation of two parallel duplexes and hemiprotonated base pairs

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Address correspondence to Frank Seela, Laboratory of Bioorganic Chemistry and Chemical Biology, Center for Nanotechnology, Heisenbergstraße 11, 48149 Münster, Germany, and Laboratorium für Organische und Bioorganische Chemie, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany. E-mail: frank.seela@uni-osnabrueck.de

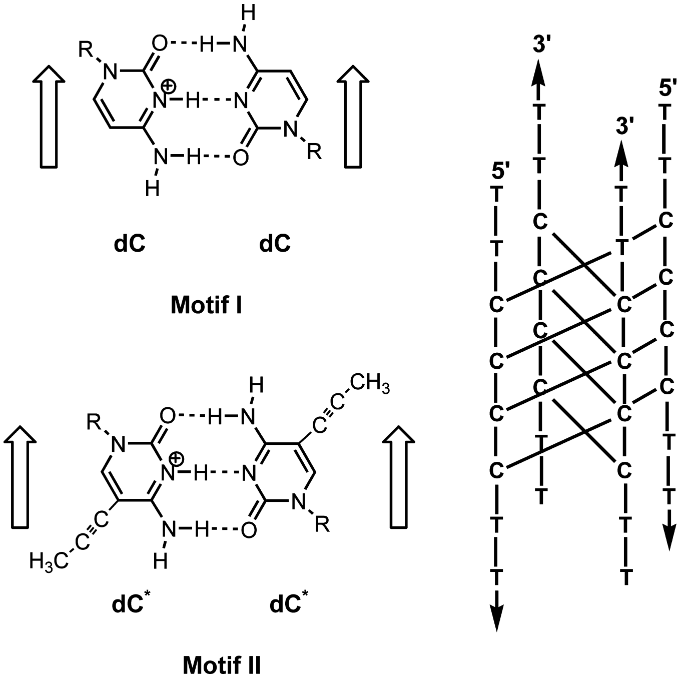


FIGURE 1 i-motif assembly of dC or dC* is stabilized by intercalation and hemiprotonated base pairs; T = dT, C = dC, and dC* = 5-propynyl-2′-deoxycytidine; R = sugar residue.

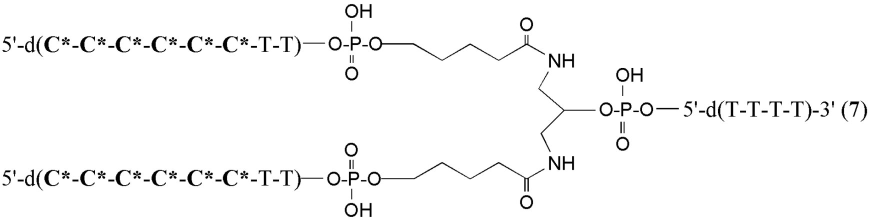
(dC·dCH$^+$) (Figure 1, motif I).[4] The construction of a DNA gold nanoparticle sytem based on the pH-dependent four strand assembly of the i-motif generates a switchable nanoscopic device. The replacement of the canonical 2′-deoxycytidine residues by 5-propynyl-2′-deoxycytidine (dC*) leads to novel i-motif structures. Their ability to form i-motif structures was recently proved by CD spectroscopy and ion-exchange chromatography.[5] Oligonucleotides incorporating multiple residues of dC* were now immobilized on 15 nm gold nanoparticles and their ability to form pH-dependent i-motif gold nanoparticle aggregates was investigated.

RESULTS AND DISCUSSION

Functionalization of Gold Nanoparticles

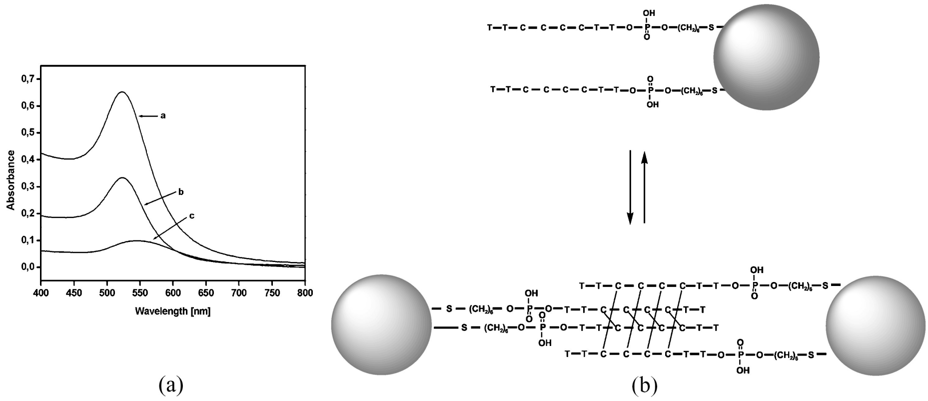
The oligonucleotides **1–3** (Table 1) were synthesized in an automated DNA synthesizer by solid phase synthesis employing a 5′-thiol-modifer-C6-phosphoaramidite (Glen Research, USA) and the phosphoramidite of 5-propynyl-2′-deoxycytidine for **3**. For the synthesis of the branched oligonucleotide **7** a dendrimeric branching residue (Glen Research, USA) was used.[6] The oligonucleotides **1–3** were immobilized on the surface of 15 nm gold nanoparticles according to the procedure

TABLE 1 Thiol-modified oligonucleotides **1–3** utilized for the immobilization on gold nanoparticles, DNA gold nanoparticle conjugates **4–6**, and the branched oligonucleotide **7**

Oligonucleotides
5' -Trityl-S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C-C-C-C-T-T) (**1**)
5' -Trityl-S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C-C-C-C-C-C-T-T) (**2**)
5' -Trityl-S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C*-C*-C*-C*-C*-C*-T-T) (**3**)
5' ●-[S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C-C-C-C-T-T)]$_n$ (**4**)
5' ●-[S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C-C-C-C-C-C-T-T)]$_n$ (**5**)
5' ●-[S-$(CH_2)_6$-O(PO_2H)O-d(T-T-C^*-C^*-C^*-C^*-C^*-C^*-T-T)]$_n$ (**6**)


● = 15 nm diameter gold nanoparticle.
C^* = 5-propynyl-2'-deoxycytidine.

described previously.[3] The resulting DNA gold nanoparticle conjugates **4–6** (Table 1) show the expected plasmon resonance at around 525 nm under alkaline conditions (Figure 2A) indicating a non-aggregated state. The number of oligonucleotides immobilized on each individual gold nanoparticle is abritary.



(a) (b)

FIGURE 2 A: UV/VIS spectra of (a) the alkaline solution (pH = 9) of 15 nm diameter gold nanoparticles. Gold nanoparticle conjugates **6** measured in 10 mM phosphate buffer containing 0.1 M NaCl at (b) pH = 8.0 as disperse system and (c) at pH = 5 after i-motif formation leading to aggregation. B: Schematic representation of the assembly of gold nanoparticle assembly **4**; T = dT, C = dC.

pH-Dependent Self-Assembly of Gold Nanoparticles

As the formation of the i-motif structure requires acidic conditions, it was expected that the same is valid for the i-motif formation of the DNA gold nanoparticle conjugates **4** and **5**. Accordingly, it was shown that at acidic pH values a reversible self-assembly of the gold nanoparticle conjugates occured which was indicated by a red shift of the plasmon resonance from 525 nm to 549 nm accompanied by a color change of the solution from red to blue. The addition of an alkaline phosphate buffer led to the disassembly of the aggregates (Figure 2B).

Properties of Modified Gold Nanoparticles

The replacement of the 2′-deoxycytidine residues of **1** and **2** by 5-propynyl-2′-deoxycytidine strongly effects the formation of the i-motif structure. Due to the introduction of the propynyl group at position C5 of the pyrimidine ring, the pK_a value of the heterocycle is lowered from 4.5 to 3.3.[5] As a consequence, oligonucleotide **3** requires a lower pH value for the protonation of N-3, which contributes to the formation of the hemiprotonated tridentate ($dC^{*}\cdot dC^{*}H^{+}$) base pair (Figure 1, motif II). However, on the surface of gold nanoparticles the immobilized oligonucleotides are forced into close proximity, leading to a steric situation similar to that of branched oligonucleotides with a parallel strand orientation (**7**). The branched oligonucleotide **7** forms an i-motif structure even at non-optimal pH-values ($pH = 5$) which is away from the pK_a value of the 5-propynyl-2′-deoxycytidine nucleoside. The formation of i-motif structures formed by **7** was proved by CD measurements and ion-exchange chromatography. As a consequence, it can be expected that the i-motif formation of DNA-gold nanoparticle conjugates incorporating multiple residues of dC^{*} is possible at pH 5. Consequently, the DNA gold nanoparticle conjugate **6** was incubated in a phosphate buffer at pH 5. Within 24 h, i-motif formation occured which was indicated by a red shift of the plasmon resonance from 525 nm to 545 nm accompanied by a color change of the solution from red to blue (Figure 2A).

In conclusion, we have shown that the immobilization of oligonucleotides incorporating stretches of 2′-deoxycytidine on 15 nm gold nanoparticles generates pH-sensitive nanoscopic devices. The replacement of 2′-deoxycytidine by 5-propynyl-2′-deoxycytidine leads to novel i-motif structures. The immobilization of oligonucleotides incorporating multiple residues of dC^{*} on 15 nm gold nanoparticles leads to DNA gold nanoparticle conjugates which are able to aggregate into i-motif structures even at non-optimal pH-values.

REFERENCES

1. Mirkin, C.A.; Letsinger, R.L.; Mucic, R.C.; Storhoff, J.J.A.; DNA-based method for rationally assembling nanoparticles into macroscopic materials. *Nature* **1996**, 382, 607–609.

2. a) Han, M.S.; Lytton-Jean, A.K.R.; Oh, B.-K.; Heo, J.; Mirkin, C.A. Colorimetric screening of DNA binding molecules with gold nanoparticle probes. *Angew. Chem. Int. Ed.* **2006**, 45, 1807–1810. b) Chah, S.; Hammond, M.R.; Zare, R.N. Gold nanoparticles as a colorimetric. sensor for protein conformational changes. *Chemistry and Biology* **2005**, 12, 323–328. c) Seela, F.; Jawalekar, A.M.; Chi, L.; Zhong, D. Ion-specific aggregation of gold-DNA nanoparticles using the dG quartet hairpin 5′-d($G_4T_4G_4$). *Chem. Biodiv.* **2005**, 2, 84–91.
3. Seela, F.; Budow, S. pH-dependent assembly of DNA-gold nanoparticles based on the i-motif: A switchable device with the potential of a nanomachine. *Helv. Chim. Acta* **2006**, 89, 1978–1985.
4. Guéron, M.; Leroy, J.-L.The i-motif in nucleic acids. *Curr. Opin. Struc. Biol.* **2000**, 10, 326–331.
5. Robles, J.; Grandas, A.; Pedroso, E.; Luque, F.J.; Eritja, R.; Orozco, M. Nucleic acid triple helices: Stability effects of nucleobase modifications. *Curr. Org. Chem.* **2002**, 6, 1333–1368.
6. Seela, F.; Budow, S.; Leonard, P. Oligonucleotides forming an i-motif: The pH-dependent assembly of individual strands and branched structures containing 2′-deoxy-5-propynylcytidine. *Org. Biomol. Chem.* **2007**, 5, 1858–1872.