J Nanopart Res (2012) 14:1211
DOI 10.1007/s11051-012-1211-z

RESEARCH PAPER

DNA complexes with Ni nanoparticles: structural and functional properties

Olga N. Tatarinova · Igor P. Smirnov · Irina V. Safenkova · Anna M. Varizhuk · Galina E. Pozmogova

Received: 17 January 2012 / Accepted: 15 September 2012 / Published online: 29 September 2012

Abstract Supramolecular complexes of biopolymers based on magnetic nanoparticles play an important role in creation of biosensors, implementation of theragnostic and gene therapeutic methods and biosafety evaluation. We investigated the impact of DNA interactions with nanoparticles of nickel (nNi) on the integrity and functionality of DNA. Data obtained by mass spectrometry, electrophoresis, TEM and AFM microscopy techniques, bacterial transformation, and real-time PCR provide evidence that ssDNA and plasmid DNA (pDNA) efficiently form complexes with nNi. AFM data suggest that the complexes are necklace-type structures, in which nanoparticles are randomly distributed along the DNA chains, rather than highly entangled clot-type structures. After desorption, observed DNA characteristics in bioanalytical and biological systems remain unchanged. Only supercoiled pDNA was nicked, but remained, as well as a plasmid–nNi complex, active in expression vector assays. These results are very important for creation of new methods of DNA immobilization and controlled manipulation.

Keywords Nickel nanoparticles · Magnetofection · DNA · Self-assembly

Abbreviations

AFM	Atomic force microscopy
DDS	Drug delivery system
EDTA	Ethylenediaminetetraacetic acid
EGFP	Enhanced green fluorescent protein
FAM	6-Carboxyfluorescein
lpDNA	Linear plasmid DNA
HEX	6-Carboxy-2′,4,4′,5′,7,7′-hexachlorofluorescein
nNi	Nanoscale Ni particles
PBS	Phosphate buffered saline
pDNA	Plasmid DNA
rpDNA	Relaxed plasmid DNA
scpDNA	Supercoiled plasmid DNA
ssDNA	Single stranded DNA
TAE	Tris–acetate–EDTA

Electronic supplementary material The online version of this article (doi:10.1007/s11051-012-1211-z) contains supplementary material, which is available to authorized users.

O. N. Tatarinova · I. P. Smirnov · A. M. Varizhuk · G. E. Pozmogova (✉)
Research Institute for Physico-Chemical Medicine of the Federal Medical-Biological Agency of the Russian Federation, Malaya Pirogovskaya str. 1a, 119435 Moscow, Russian Federation
e-mail: pozmge@gmail.com

I. P. Smirnov
A.N. Belozersky Institute of Physico-Chemical Biology, Leninskie Gory 1, Bldg. 40, 119899 Moscow, Russian Federation

I. V. Safenkova
A.N. Bach Institute of Biochemistry, Leninskii Avenue, 33, 119071 Moscow, Russian Federation

A. M. Varizhuk
Engelhardt Institute of Molecular Biology, Vavilov str. 32, 119991 Moscow, Russian Federation

Introduction

Nanoparticles have vast, unquestionable, potential for the future development of biosensors, diagnosticums, therapeutically important allogenic DNA carriers, drug carriers, novel theragnostic agents, investigative tools, and molecular biology and medical applications (Fang and Zhang 2010; de Dios and Diaz-Garcia 2010; Shubayev et al. 2009; Becerril et al. 2005; Naqvi et al. 2009; Ma et al. 2011; Tang et al. 2011).

Application of magnetic nanoparticles as DNA carriers is a promising alternative to well-known drug delivery systems (DDS) based on microcapsules, liposomes, lipoproteins, and micelles (Ye and Yang 2009). The basic principle underlying DDS is employing carriers to enhance efficacy of a therapeutic agent by controlling its uptake, release, and trafficking in biological environment.

Nanoparticles are usually efficiently taken up by cells and therefore hold significant potential as DDS (Yokoyama 2005), in particular DNA delivery systems (Hosseinkhani 2006). One impediment to the widespread use of nanoparticles as drug carriers stems from the toxic effects of nanoscale corpuscles. Some of these particles have been shown to cause DNA damage (Petersen and Nelson 2010). Due to this damage potential, it is particularly important to analyze the influence of nanoparticles on biopolymer structure and properties when designing biofunctional nanocomplexes.

Nanoparticles currently considered as promising DNA and protein carriers may contain metals/metal oxides or water-soluble biodegradable synthetic as well as natural polymers including cationic ones (Hosseinkhani and Tabata 2006; Midoux et al. 2009; Hosseinkhani 2006). Metal nanoparticles, particularly nanoscale Ni (nNi), have a number of advantages as platforms for the assembly of supramolecular complexes for DDS due to their electrical conductivity and magnetic properties (Becerril et al. 2006; Bliznyuk et al. 2009; Chang and Su 2008; Chen et al. 2007; Dong et al. 1998; Duan and Li 2004; Gu et al. 2006; Prabakaran and Athappan 2010; Ramírez-Meneses et al. 2011). One important advantage of nickel nanoparticles is that they can efficiently and selectively capture histidine-tagged proteins. It should be noted that no destruction of polypeptides is observed when they are complexed to nNi of various sizes. Moreover, proteins isolated from Ni associations retain their biological properties (Becerril et al. 2006; Lazarev et al. 2007; Pozmogova et al. 2008).

Oligonucleotides are also capable of binding reversibly to nNi. This occurs presumably via formation of ion and coordination bonds. Thiophosphoryl analogs of oligomers exhibit the highest binding affinity. Specific DNA load, estimated based on the analysis of oligonucleotide-nickel association curves (nickel particle size: $\sim$20 nm), was approximately 5–6 molecules per particle for 15–20-mers and 3–4 molecules per particle for 30-mers (Pozmogova et al. 2008). These data suggest that ssDNA forms a tight coating on the particles and almost completely modifies their surface.

The goal of this work was to analyze the effect of nickel particle ($\sim$20 nm) interaction on the structural and functional properties of ssDNA; therapeutically and diagnostically significant oligonucleotide derivatives; and plasmid DNA (pDNA) in supercoiled, relaxed, and linear forms.

Experimental

Nickel nanoparticles

Nickel nanoparticles (20 nm) were obtained from Skyspring Nanomaterials Inc. (USA) and the Institute of Energy Problems of Chemical Physics, Russian Academy of Sciences (Russia). Nickel particle preparations were found to be similar in their particle size and adsorption properties (see Online Resource 1). The use of fluorescently labeled DNA derivatives provided a mechanism for the control of oligonucleotide sorption and release from nNi complexes.

Oligonucleotides

Oligonucleotides were synthesized by the solid-phase phosphoramidite method on an automated ASM-800 synthesizer (Biosset, Russia) with the use of commercially available reagents: nucleoside phosphoramidite derivatives and fluorophores (6-FAM), nucleoside polymers and 3H-1,2-benzodithiol-3-one-1,1-dioxide (Glen Research, USA), and solvents (Lekbiopharm, Russia, and Panreac, Spain).

RT-PCR

Fluoropol-Chl.tr. EP diagnostic kits were obtained from Lytech (Russia). The DNA used for RT-PCR was extracted from a urogenital scrape specimen.

Accumulation kinetic curves were obtained using iQ5 real-time PCR detection systems (Bio-Rad Laboratories, Inc., USA). FAM-fluorescence ($\lambda_{ex} = 485$, $\lambda_{em} = 520$) of the probe (FAM-A11C13G7T6-BHQ1) was measured after each amplification cycle. Data analysis and curve plotting was performed using the bundled software (BioRad Laboratories, Inc., USA).

Plasmid vectors

The pGEM vector was purchased from Promega Inc. (USA). Linear pGEM/*Sca*I was derived from circular plasmid pGEM digested by *Sca*I enzyme.

The plasmid vector pEGFP-C1 with *E. coli* promoter was provided courtesy of Dr. V.N. Lazarev (Research Institute for Physico-Chemical Medicine, Russia).

Transmission electron microscopy

Suspensions of Ni nanoparticles were placed onto copper gauze (300 mesh, Pelco International, USA), coated with a polyvinyl formal film. Images were recorded on a JEM-100CX/SEG electron microscope (Jeol, Japan) at an acceleration voltage of 80 kV.

Preparation of associates of ssDNA and pDNA with nickel nanoparticles

A suspension of Ni nanoparticle powder (10–15 mg) in 1 mL of 0.1 M sulfuric acid was shaken (30 min, 20 °C) and sonicated (22 kHz, 15 min), then particles were separated by centrifugation or magnetic separation. After removal of the acid, the residue was washed with water until neutral. The nickel particles thus prepared were kept as a suspension in 25 % aqueous glycerol in helium or argon atmosphere. The suspensions after shaking and sonication were stable for 1 h.

For preparation of nNi associates with oligonucleotides, aqueous solutions of oligonucleotides in ammonium-containing buffers (pH 7.0) were added to a nanoparticle suspension, and the mixture was shaken vigorously for 40 min. Excess oligonucleotides were removed by washing with phosphate buffered saline (PBS: 0.01 M phosphate buffer, 0.0027 M potassium chloride, and 0.137 M sodium chloride, pH 7.4). Concentrated PBS (10× PBS) or 0.5 M imidazole solutions were used for oligonucleotide desorption from nanoparticle surface. Oligonucleotide complexes with nNi and desorbed oligonucleotides were analyzed using MALDI TOF MS. Interaction between pDNA and nNi particles was studied in suspensions containing 0.5–10 μg of Ni, 0.05–0.1 μg of pGEM plasmid, and various concentrations of glycerol in a total volume of 20 μL. To a solution of pDNA, nNi suspension and glycerol were added, and the mixture was incubated for 10 min to 3 h and occasionally stirred gently. The integrity of pDNA in thus obtained suspensions was analyzed in 1 % agarose gel. Oligonucleotide and pDNA complexes with nNi were stable under physiological conditions (0.01 M phosphate buffer, 0.0027 M potassium chloride, and 0.137 M sodium chloride, pH 7.4) for at least several days (Pozmogova et al. 2008).

Mass spectrometry

Mass spectra were recorded on a MicroFlex MALDI TOF mass spectrometer (Bruker, USA) using a standard MSP polished steel target (Bruker, USA). A 0.25 M solution of 3-hydroxypicolinic acid (Fluka, USA) was used as a matrix in analyzing the oligonucleotide component. In order to record the mass spectra of proteins incorporated in nickel nanocomplexes, the latter were washed twice with 0.1 M ammonium acetate in 1 % acetonitrile and water, and resuspended in a 0.022 M solution of the matrix (3,5-dimethoxy-4-hydroxycinnamic acid, Aldrich) in 50 % aqueous acetonitrile containing 0.1 % trifluoroacetic acid. The resulting suspension was applied to a target and dried in air.

Agarose gel electrophoresis

Electrophoresis was through a horizontal, 1–2.5 % agarose gel in Tris–acetate–ethylenediaminetetraacetic acid (TAE) buffer (40 mM Tris–acetate, 1 mM EDTA, pH 7.4). DNA bands were visualized by staining with ethidium bromide after electrophoresis.

Denaturing gel electrophoresis

Electrophoretic analysis of proteins was performed on a 12 % denaturing polyacrylamide gel in Tris–glycine

buffer (25 mM Tris–HCl, 250 mM glycine, and 0.1 % SDS, pH 8.3), and run for 30 min with a field of 150 V at room temperature. The gel was subsequently stained by Coomassie brilliant.

Atomic force microscopy

Preparations of pDNA/nNi complexes were placed onto a freshly cleaved mica surface (SPI Supplies, Structure Probe, USA). Scanning was performed on a Ntegra Prima atomic-force microscope (NT-MDT, Russia) using fpN01HR cantilevers (Nanotuning, Russia) with the radius curvature <10 nm. The images obtained were analyzed using the Gwiddion software (Czech Metrology Institute, Czech Republic).

Results and discussion

In our previous work we have shown that oligonucleotides of various length and composition, including thiophosphoryl antisense oligomers (Tatarinova et al. 2010; Pozmogova and Chuvilin 2007; Gryaznov 2010), retain their integrity upon association with nNi. Here we provide further evidence of the intactness of ssDNA complexed to and desorbed from nNi and report the results of the first studies of pDNA/nNi complexes.

Associates of ssDNA with nickel nanoparticles were prepared as described in our previous work (Pozmogova et al. 2008). Interaction of nNi with ssDNA over an extended period of time (more than 48 h) caused no degradation in the DNA. HPLC profiles, PAGE electrophoregrams (data not shown), and mass spectra of desorbed and nNi-complexed oligonucleotides (Online Resource 2) contained no signals corresponding to oligonucleotide chain degradation products. Differences in MS-spectra of initial and desorbed oligonucleotides are related to the slight increase in the intensity of cationic adduct signals but not to the appearance of the lower mass peaks.

The effect of nickel particles on the functional properties of oligonucleotides employed in bioanalytical in vitro methods was assessed using oligomers included in a standard real-time PCR kit for clamidiosis diagnostics (two 25-mer primers and a fluorescent probe, FAM-$A_{11}C_{13}G_7T_6$-BHQ1) that were fixed on magnetic nNi. Oligonucleotide sorption on nickel particles was followed by washing the carrier with PBS. The primers and the probe were eluted (2 M aqueous ammonium acetate, 50 mM EDTA, pH 6.5), desalted and reused as components of the Fluoropol-Chl.tr. EP/after nNi diagnostic kit. Figure 1 displays accumulation kinetic curves for the products of the DNA amplification reaction during real-time PCR and electrophoretic analysis of the resulting reaction contents using Fluoropol-Chl.tr. EP (tracks 1 and 2, black curves) and Fluoropol-Chl.tr. EP/after nNi (tracks 3 and 4, red curves) kits.

As evident from Fig. 1, the differences between the curves obtained for the two kits are insignificant. The results of the analyses agree within the method's acceptable error. The oligonucleotides have retained their functionality as primers in the DNA amplification reaction after desorption from Ni nanoparticles. The example above illustrates that sorption of wild-type and modified oligonucleotides on nNi can be used in biochemical systems. This result sheds light on exciting new possibilities in the development of bioanalytical methods.

The possibility of using nNi to deliver therapeutically significant genetic material to cell cultures and tissues has not been shown thus far due to the

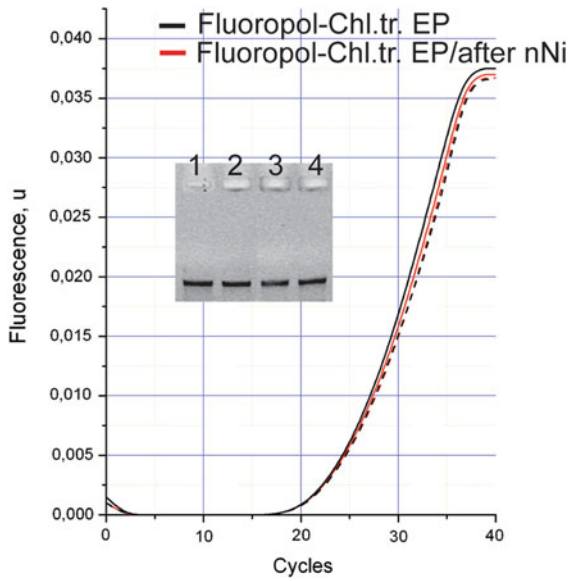

Fig. 1 Accumulation kinetic curves for the products of DNA amplification during real-time PCR and electrophoretic analysis (2 % agarose, ethidium bromide) of the resulting reaction contents using Fluoropol-Chl.tr. EP (tracks 1 and 2, *black curves*) and Fluoropol-Chl.tr. EP/after nNi (tracks 3 and 4, *red curves*) kits. (Color figure online)

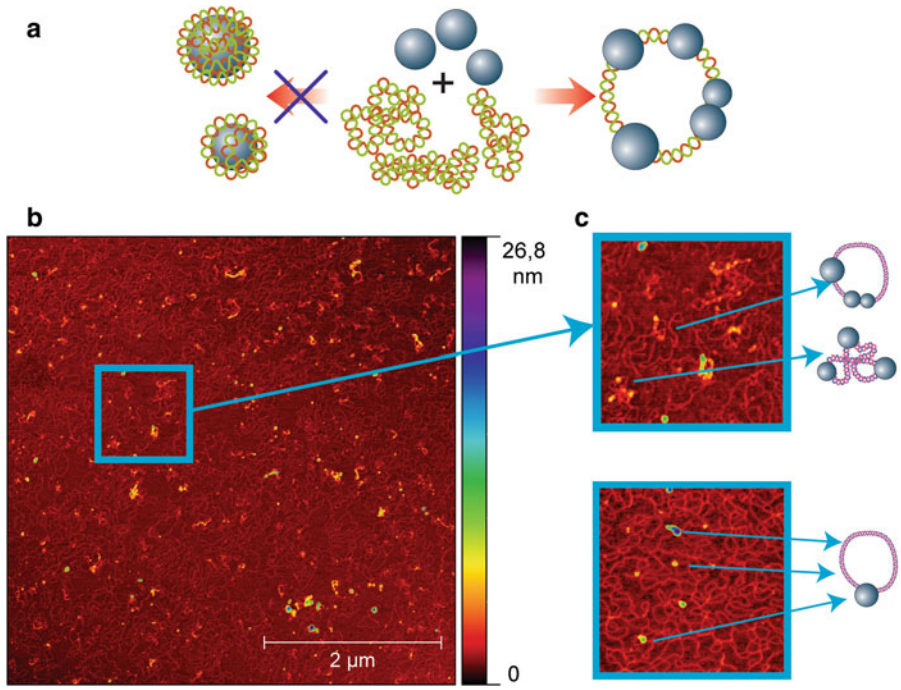

Fig. 2 Scheme representing the formation of pDNA/nNi (**a**) complexes and their AFM images at different component ratios: ~5 nNi particles per pDNA molecule (**b**) and ~1 nNi particle per pDNA molecule (**c**)

destructive effect of the free radicals produced during the process (Zhang et al. 1998). The impact of nNi on pDNA functionality and the possibility of pDNA/nNi complex formation have not been studied in sufficient detail.

In the present work, we report the impact of nNi on linear, relaxed, and supercoiled pDNA (pGEM). The three forms of pDNA were separated and studied individually in several experiments. All pDNA forms associated effectively with nickel particles from aqueous media and 5–50 % (m/m) glycerol in water.

Based on structural data available for nNi biocomplexes, particularly the ability of one particle to bind with several oligonucleotide molecules (Pozmogova et al. 2008), it could be predicted that lengthy DNA adsorbed onto the nNi surface would form clot-type structures (scheme in Fig. 2a). However, atomic-force microscopy (AFM) scans of pDNA/nNi complexes revealed no such structures. Depending on the pDNA:nNi ratio, pDNA/nNi biocomplexes contained one or more particles attached via relaxed circular DNA (Fig. 2b, c). In AFM images, pDNA appeared mainly in a relaxed form. Supercoiled and linear DNA forms were rare. Their abundance did not exceed a tenth of a percent. However, to confirm the hypothesis that interaction with nNi is the principal reason for DNA nicking, special experiments are required. A great number of factors are known to induce relaxed pDNA (rpDNA) formation; one such factor is plasmid immobilization on mica (Lyubchenko et al. 2011; Zheng et al. 2003).

Investigation of pDNA conformational changes in the presence of nNi was performed using electrophoresis. This method allowed precise discrimination between the pDNA forms (Fig. 3). For adequate data interpretation one must understand that DNA/nickel associates may partially or completely degrade during the electrophoretic separation. Partial oligonucleotide desorption was observed when ssDNA/nNi complexes were analyzed (Fig. 3a, track 11). In the case of pDNA this process was less pronounced. As a result, we observed no significant differences between the electrophoregrams of desorbed pDNA (Fig. 3a, track 8) and pDNA/nNi complexes (Fig. 3a, track 6).

Linear pDNA (lpDNA) and circular DNA associated with nNi in a wide ratio range. Prolonged DNA analysis (more than a day, 4 °C) did not reveal any changes in their electrophoretic behavior or any signs of degradation (Fig. 3a). Simultaneously, a pronounced transition from supercoiled pDNA (scpDNA) to the relaxed form was observed (Fig. 3a, tracks 3 and 6). Suppression of pDNA/nNi complex formation (for instance, with EDTA) blocked the scpDNA conformational transition (Fig. 3a, tracks 6–8), which

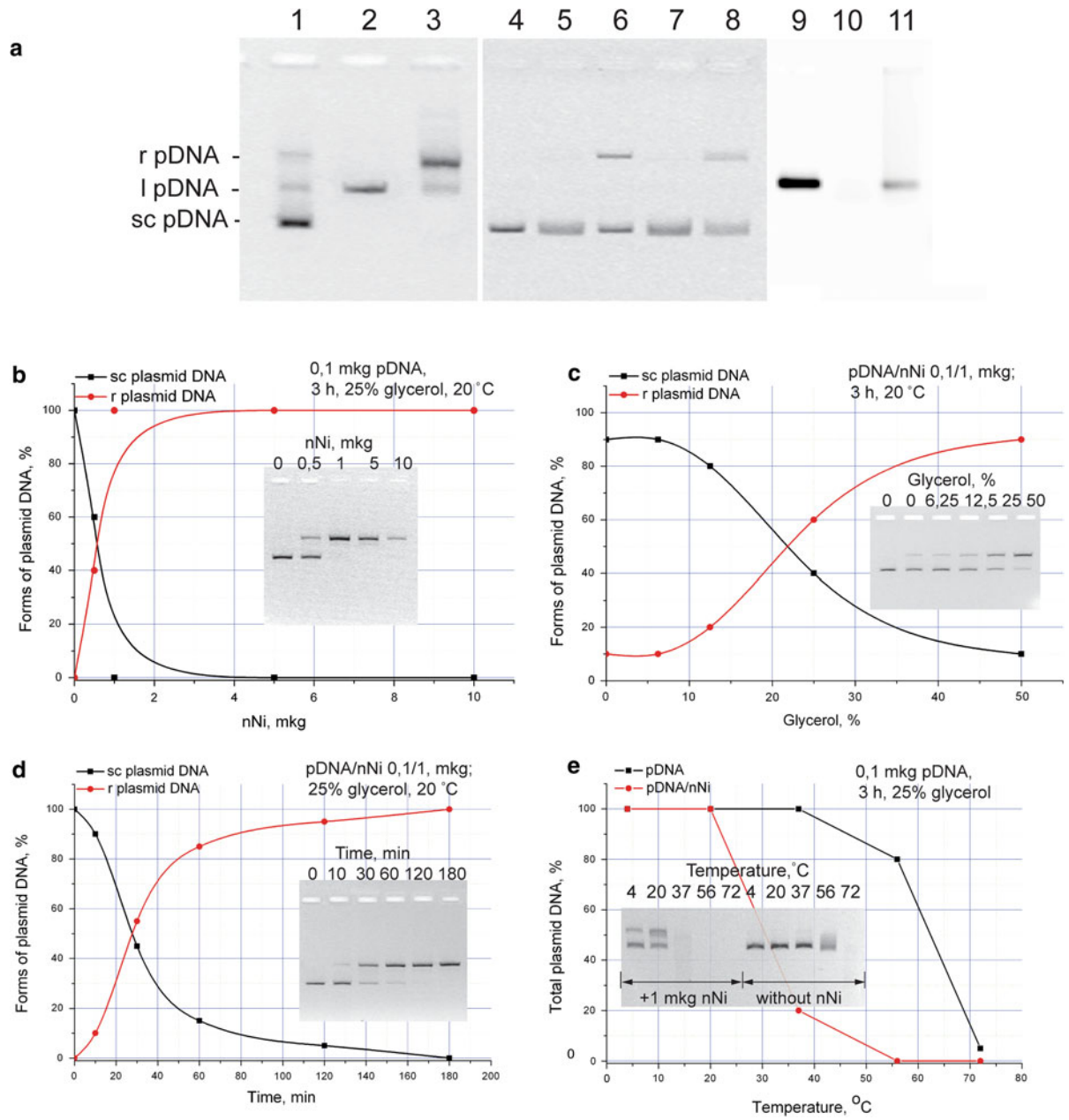

Fig. 3 Electrophoretic analysis of the impact of nNi on pDNA structure. **a** Electrophoregrams of pDNA (tracks 1–8, 1 % agarose, ethidium bromide) and oligonucleotide HEX-$A_{14}C_{11}G_9T_7$ (tracks 9–11, 2.5 % agarose, $\lambda_{ex} = 535$ nm, $\lambda_{em} = 553$ nm). *1* pDNA preparation; *2* lpDNA/nNi complex, 24 h, 4 °C; *3* scpDNA/nNi complex, 24 h, 4 °C; *4* scpDNA; *5* scpDNA in the presence of 50 mM EDTA; *6* scpDNA/nNi, 1/10 (m/m), 25 % aqueous glycerol, 1 h, 20 °C; *7* scpDNA/nNi, 1/10 (m/m), 25 % aqueous glycerol, 50 mM EDTA, 1 h, 20 °C; *8* EDTA eluate of scpDNA/nNi (1/10, m/m, 25 % aqueous glycerol), 1 h, 20 °C; *9* HEX-$A_{14}C_{11}G_9T_7$; *10* supernatant obtained after magnetic separation of nNi/HEX-$A_{14}C_{11}G_9T_7$ associate; *11* nNi/HEX-$A_{14}C_{11}G_9T_7$. **b–e** Electrophoregrams and curves representing the dependence of conformational and structural changes in scpDNA on the excess of nNi (**b**), glycerol content in the reaction medium (**c**), time of scpDNA incubation with nNi, 1/10, m/m (**d**) and temperature (**e**). *lpDNA* linear plasmid DNA; *rpDNA* relaxed plasmid DNA; *scpDNA* supercoiled plasmid DNA

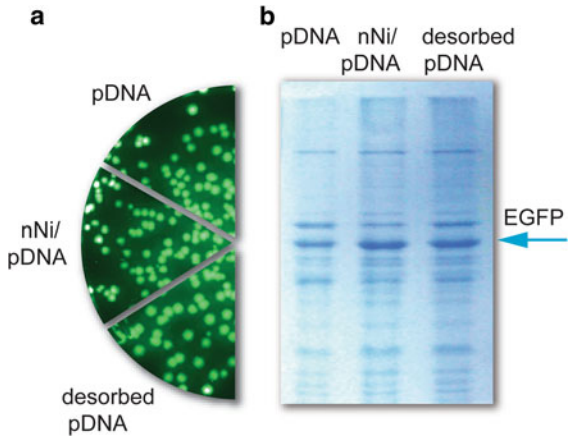

Fig. 4 Results of *E. coli* strain transfection with a pEGFP-C1 expression vector. Fluorescent photographs ($\lambda_{ex} = 495$ nm, $\lambda_{em} = 521$ nm) of *E. coli* colonies (**a**) and electrophoretic analysis of the protein fractions of strains (**b**) transfected with pDNA, pDNA/nNi, and pDNA isolated from the complexes (desorbed pDNA)

confirms that the latter is conditioned by the presence of nNi.

Nicking was dose-dependent over the weight ratio range 1/5–1/100 (scpDNA/nNi) (Fig. 3b). Further increasing metal particle content resulted in the formation of massive aggregates that impeded the analysis.

Extending the duration of scpDNA incubation with nanoparticles also led to rpDNA accumulation (Fig. 3d).

Glycerol addition during nNi suspension preparation resulted in more stable suspensions than those mixed with water. Increasing the glycerol content from 6 to 50 % noticeably favored nicking (Fig. 3c) in the nNi/scpDNA interactions. This may be due to the prolonged existence of nickel nanoparticle surfaces accessible for sorption, presumably because of the slower aggregation of nNi.

Interestingly, the presence of nickel significantly decreased pDNA thermostability (red curve in Fig. 3e). When pDNA/nNi complexes were incubated, DNA destruction products (shorter fragments with higher PAAG mobility) were found after only 3 h of incubation at 37 °C (Fig. 3e, red curve). The scpDNA was stable under these conditions (Fig. 3e, black curve).

The ability of genetic material to retain its functional properties in complex with nNi was studied using a plasmid vector capable of expressing a reporter protein (EGFP, enhanced green fluorescent protein) in *E. coli*. Preparations of a pEGFP-C1 plasmid containing a *E. coli* promoter, pDNA/nNi complexes, and isolated pDNA were used for the transfection of the competent cell culture strain B834(DE3). Recombinant strain colonies grown on selective media fluoresced intensely in all three cases (Fig. 4a, $\lambda_{ex} = 495$ nm, $\lambda_{em} = 521$ nm). Analysis of proteins isolated from the transformant biomasses and the control strain transformed by pDNA that had not been subjected to nNi exposure (control) confirmed equally high levels of EGFP expression in all cases (Fig. 4b). Our data provide evidence that interaction with nickel particles does not affect DNA function in *E. coli*. These results are of significant interest with respect to the development magnetic DNA delivery systems (Ma et al. 2011) for gene therapy, production of transgenic organisms, and tissue engineering (Salvay and Shea 2006; Hosseinkhani et al. 2008).

Conclusion

The effect of nanoscale nickel particles on the structural and functional properties of associated DNA has been investigated through microscopy, mass spectrometry, HPLC, electrophoresis, and biochemical in vitro tests. DNA stability in complexes with nNi has been examined. Structures of nNi complexes with linear and pDNAs appeared to differ from those of the ssDNA/nNi complexes. AFM data suggest that pDNA/nNi do not form highly entangled clot-type structures as may be assumed based on data reported for nNi complexes with oligonucleotides (Pozmogova et al. 2008). The pDNA–nNi complexes are necklace-type structures, in which nanoparticles are randomly distributed along the DNA chains.

The fact that oligonucleotides, linear pDNAs, and rpDNAs desorbed from the nNi surface are intact leads us to conclude that sorption on nNi can be used in biochemical methods, for diagnostic analysis, and in the development of novel bioanalytical systems.

As we have shown in the experiments with *E. coli*, both isolated pDNA and pDNA/nNi complexes retain their transfection ability and result in the same level of reporter protein expression as the initial plasmid vector. These findings indicate the potential benefits of employing nNi for constructing functional biopolymer-nickel nanostructures in the development of biosensors or medical diagnostic kits and they are of particular interest with respect to novel physical gene transfection technologies, such as magnetofection.

Acknowledgments The authors thank V. Karpov for oligonucleotide synthesis and A. Urusov for his help with material presentation. This work was supported by Russian Foundation for Basic Research [11-04-12155-ofi-m-2011].

References

Becerril HA, Stoltenberg RM, Wheeler DR, Davis RC, Harb JN, Woolley AT (2005) DNA-templated three-branched nanostructures for nanoelectronic devices. J Am Chem Soc 127(9):2828–2829. doi:10.1021/ja043314l

Becerril HA, Ludtke P, Willardson BM, Woolley AT (2006) DNA-templated nickel nanostructures and protein assemblies. Langmuir 22(24):10140–10144. doi:10.1021/la061740+

Bliznyuk V, Singamaneni S, Sahoo S, Polisetty S, He X, Binek C (2009) Self-assembly of magnetic Ni nanoparticles into 1D arrays with antiferromagnetic order. Nanotechnology 20(10):105606. doi:10.1088/0957-4484/20/10/105606

Chang H, Su H-T (2008) Synthesis and magnetic properties of Ni nanoparticles. Rev Adv Mater Sci 7(18):667–675

Chen L, Chen J, Zhou H, Zhang D, Wan H (2007) Synthesis of dodecanethiol monolayer-stabilized nickel nanoparticles. Mater Sci Eng A 452–453:262–266

de Dios AS, Diaz-Garcia ME (2010) Multifunctional nanoparticles: analytical prospects. Anal Chim Acta 666(1–2): 1–22. doi:10.1016/j.aca.2010.03.038

Dong XL, Zhang ZD, Jin SR, Sun WM, Chuang YC (1998) Surface characterizations of ultrafine Ni particles. Nanostruct Mater 10(4):585–592

Duan Y, Li J (2004) Structure study of nickel nanoparticles. Mater Chem Phys 87(2–3):452–454

Fang C, Zhang M (2010) Nanoparticle-based theragnostics: integrating diagnostic and therapeutic potentials in nanomedicine. J Control Release 146(1):2–5. doi:10.1016/j.jconrel.2010.05.013

Gryaznov SM (2010) Oligonucleotide n3′–>p5′ phosphoramidates and thio-phoshoramidates as potential therapeutic agents. Chem Biodivers 7(3):477–493. doi:10.1002/cbdv.200900187

Gu Q, Cheng C, Suryanarayanan S, Dai K, Haynie DT (2006) DNA-templated fabrication of nickel nanocluster chains. Physica E 33(1):92–98

Hosseinkhani H (2006) DNA nanoparticles for gene delivery to cells and tissue. Int J Nanotechnol 3(4):416–461

Hosseinkhani H, Tabata Y (2006) Self assembly of DNA nanoparticles with polycations for the delivery of genetic materials into cells. J Nanosci Nanotechnol 6(8):2320–2328

Hosseinkhani H, Hosseinkhani M, Gabrielson NP, Pack DW, Khademhosseini A, Kobayashi H (2008) DNA nanoparticles encapsulated in 3D tissue-engineered scaffolds enhance osteogenic differentiation of mesenchymal stem cells. J Biomed Mater Res A 85(1):47–60. doi:10.1002/jbm.a.31327

Lazarev VN, Filatova EV, Levitskiy SA, Nikilaev EN, Leypunskiy IO, Zhigach AN, Kuskov ML, Govorun VM (2007) Development of the method for purification of recombinant proteins with the use of nickel nanoparticles. Nanotechnol Russ 2(5–6):131–138

Lyubchenko YL, Shlyakhtenko LS, Ando T (2011) Imaging of nucleic acids with atomic force microscopy. Methods 54(2):274–283. doi:10.1016/j.ymeth.2011.02.001

Ma Y, Zhang Z, Wang X, Xia W, Gu H (2011) Insights into the mechanism of magnetofection using MNPs-PEI/pDNA/free PEI magnetofectins. Int J Pharm 419(1–2):247–254. doi:10.1016/j.ijpharm.2011.07.017

Midoux P, Pichon C, Yaouanc JJ, Jaffres PA (2009) Chemical vectors for gene delivery: a current review on polymers, peptides and lipids containing histidine or imidazole as nucleic acids carriers. Br J Pharmacol 157(2):166–178. doi:10.1111/j.1476-5381.2009.00288.x

Naqvi S, Samim M, Dinda AK, Iqbal Z, Telagoanker S, Ahmed FJ, Maitra A (2009) Impact of magnetic nanoparticles in biomedical applications. Recent Pat Drug Deliv Formul 3(2):153–161

Petersen EJ, Nelson BC (2010) Mechanisms and measurements of nanomaterial-induced oxidative damage to DNA. Anal Bioanal Chem 398(2):613–650. doi:10.1007/s00216-010-3881-7

Pozmogova GE, Chuvilin AN (2007) Principles of creation of protein carriers of DNA new derivatives of human epidermal growth factor for gene therapy. Bull Exp Biol Med 144(3):457–463

Pozmogova G, Chuvilin A, Smirnov I, Zaitseva M, Tatarinova O, Govorun V (2008) Preparation and properties of associates of nickel nanoparticles with ss-DNA and proteins. Nanotechnol Russ 3(5):391–396. doi:10.1134/s1995078008050157

Prabakaran N, Athappan P (2010) DNA assisted fragmentation of nickel nanoparticle clusters and their spectral properties. J Inorg Biochem 104(7):712–717. doi:10.1016/j.jinorgbio.2010.03.003

Ramírez-Meneses E, Betancourt I, Morales F, Montiel-Palma V, Villanueva-Alvarado C, Hernández-Rojas M (2011) Superparamagnetic nickel nanoparticles obtained by an organometallic approach. J Nanopart Res 13(1):365–374. doi:10.1007/s11051-010-0039-7

Salvay DM, Shea LD (2006) Inductive tissue engineering with protein and DNA-releasing scaffolds. Mol BioSyst 2(1): 36–48. doi:10.1039/b514174p

Shubayev VI, Pisanic TR 2nd, Jin S (2009) Magnetic nanoparticles for theragnostics. Adv Drug Deliv Rev 61(6): 467–477. doi:10.1016/j.addr.2009.03.007

Tang S, Zheng Z, Vongehr S, Meng X (2011) Facile and rapid synthesis of nickel nanowires and their magnetic properties. J Nanopart Res 13(12):7085–7094. doi:10.1007/s11051-011-0622-6

Tatarinova ON, Gorokhovets NV, Makarov VA, Posypanova GA, Serebriakova MV, Pozmogova GE (2010) [New protein vectors based on an alpha-fetoprotein fragment for targeted DNA delivery into cancer cells]. Vestn Ross Akad Med Nauk 1:3–8

Ye X, Yang D (2009) Recent advances in biological strategies for targeted drug delivery. Cardiovasc Hematol Disord: Drug Targets 9(3):206–221

Yokoyama M (2005) Drug targeting with nano-sized carrier systems. J Artif Organs 8(2):77–84. doi:10.1007/s10047-005-0285-0

Zhang Q, Kusaka Y, Sato K, Nakakuki K, Kohyama N, Donaldson K (1998) Differences in the extent of inflammation caused by intratracheal exposure to three ultrafine metals: role of free radicals. J Toxicol Environ Health A 53(6): 423–438

Zheng J, Li Z, Wu A, Zhou H (2003) AFM studies of DNA structures on mica in the presence of alkaline earth metal ions. Biophys Chem 104(1):37–43