Electronic Supporting information for:

Identifying DNA Mismatches at Single-Nucleotide Resolution by Probing Individual Surface Potentials of DNA-Capped Nanoparticles

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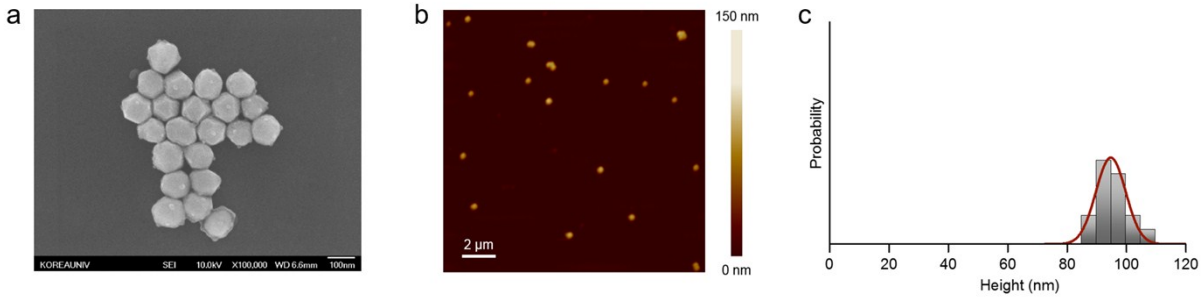

Fig. S1 SEM and AFM analysis of the bare GNP (~100 nm in diameter). (a) SEM image of GNP (100 nm in diameter), (b) An AFM topography image (scan size: 10 μm ×10 μm) and (c) the corresponding height distribution of the bare GNP, extracted from the topography image (b).

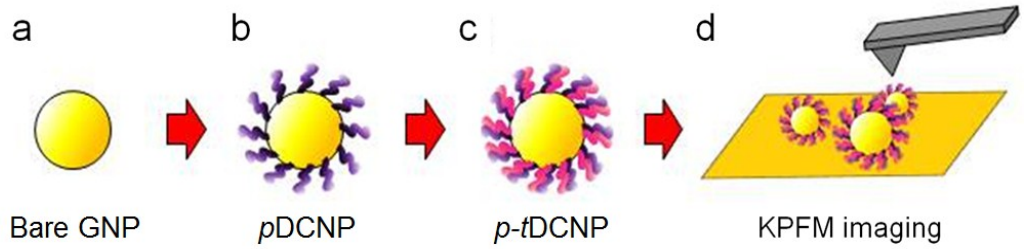

Fig. S2 A schematic describing our experimental procedure. (a) The bare GNP (100 nm, Sigma-Aldrich) was diluted to 0.1 mM in PBS with 3.45 - 4.22 × 10^9 particles in 1 mL. (b) The *p*DNAs (16 mer) are immobilized on the bare GNP, which is called *p*DCNP. (c) The *t*DNAs with 1 to 5 nucleotide mismatches are hybridized with the *p*DCNP. (d) Topography and surface potential images of each sample are obtained by KPFM.

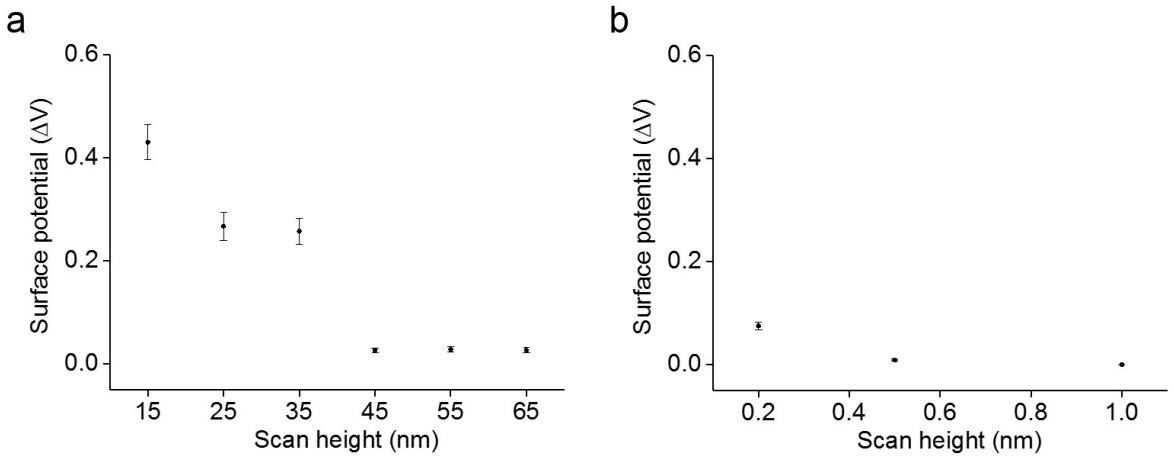

Fig. S3 Optimization of KPFM imaging of the bare GNP. The measured surface potentials of the bare GNP with different lift scan heights (a) and with different drive amplitudes (b).

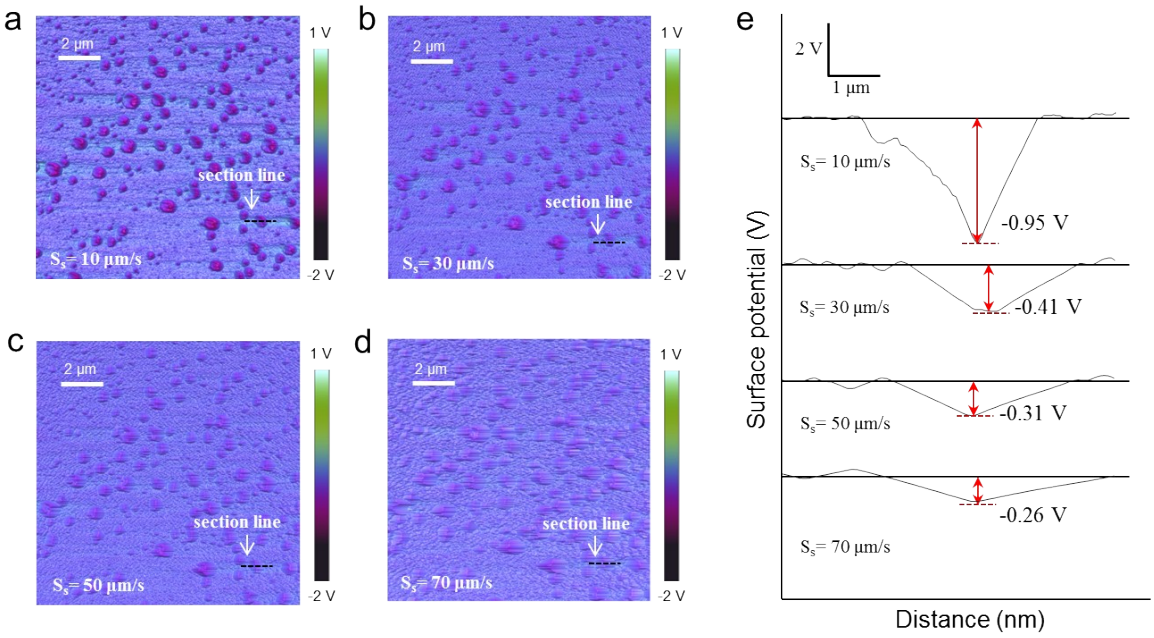

Fig. S4 Surface potential images of the *p*DCNPs with respect to four different scanning speeds. The surface potential mapping images by KPFM (scan size: 10 μm × 10 μm) were obtained at the scan speeds of 10 μm/s (a), 30 μm/s (b), 50 μm/s (c), and 70 μm/s (d), respectively. (e) Cross-sectional views of the surface potentials measured at the different scan speeds, obtained by performing line scans (black dot line) in each image.

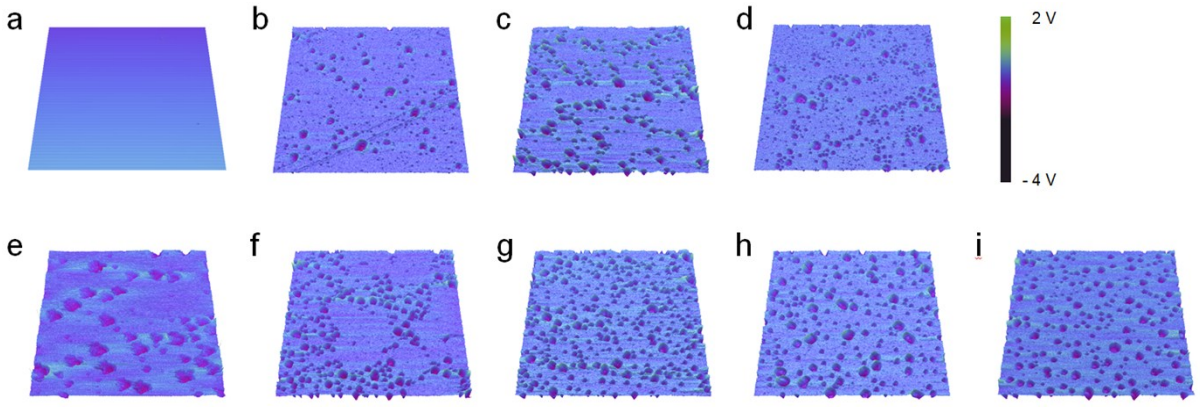

Fig. S5 Top view 3D surface potential images of all the samples. (a-i) 3D images (10 × 10 μm^2) of all the samples with top-view point: (a) the bare GNP (100 nm), (b) the *p*DCNP, (c) the *p-c*DCNP, (d) the *p-nc*DCNP, (e) the *p*-χ_1DCNP, (f) the *p*-χ_2DCNP, (g) the *p*- χ_3DCNP, (h) the *p*-χ_4DCNP, and (i) the *p*-χ_5DCNPs.

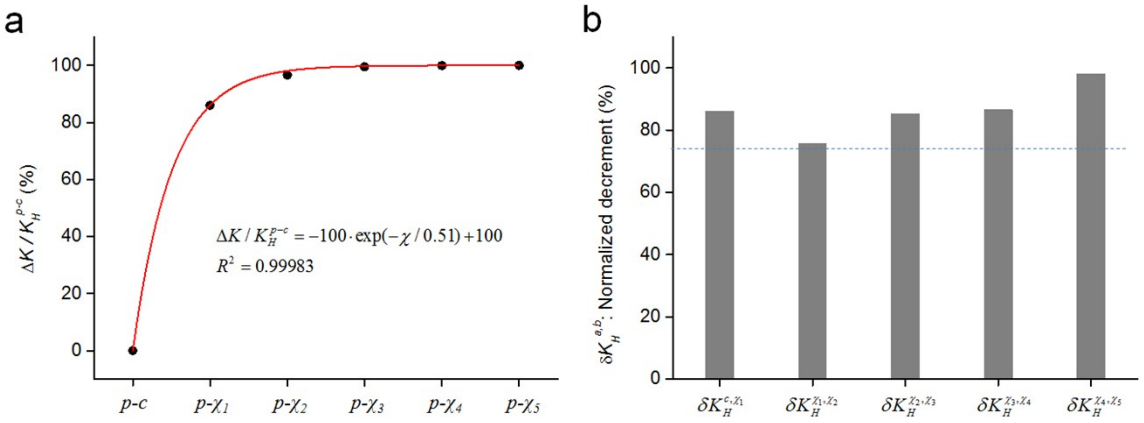

Fig. S6 Comparison between the equilibrium constants for DNA hybridization (K_H). (a) Relative equilibrium constant of each case in comparison with the K_H of the *p*-*c*DNA, (b) Normalized decrement (between two neighboring cases) of the equilibrium constants for DNA hybridization of 1 to 5 mutations. For instance, normalized decrement between *p*-*a*DNA and *p*-*b*DNA is given by:

$$\delta K_H^{a,b}(\%) = \frac{K_H^a - K_H^b}{K_H^a} \times 100$$

Each difference between two neighboring values of the K_H was at least 75%, implying that this system has a capacity for discriminating between any two similar mutations and performing gene analysis with high accuracy and reliability.

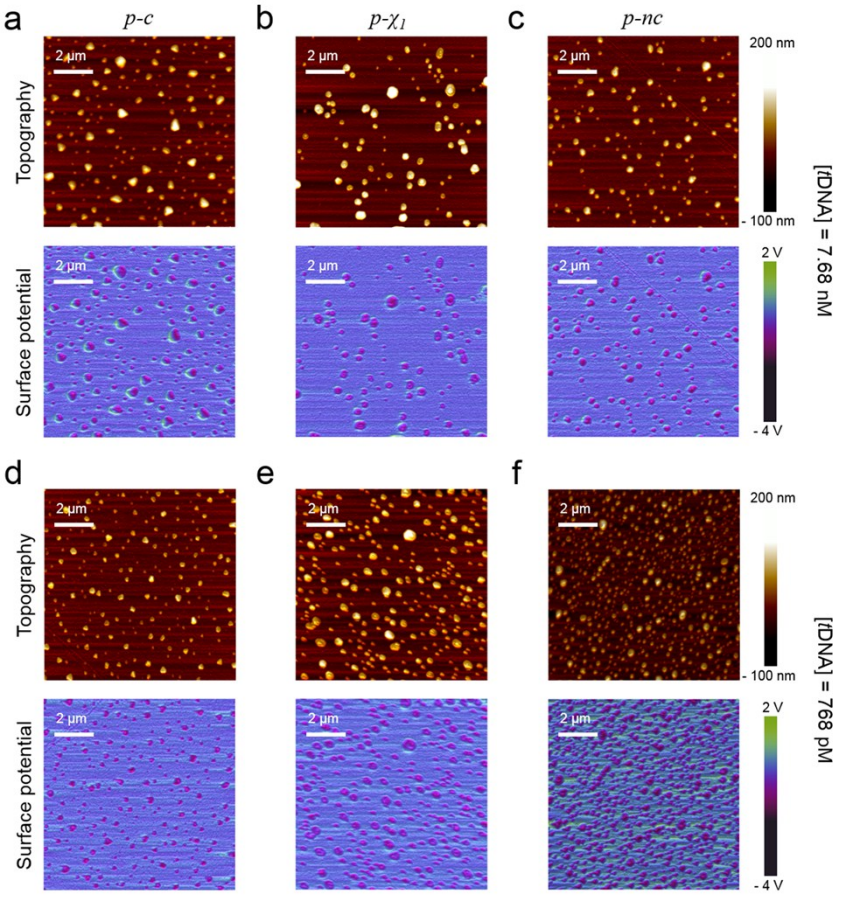

Fig. S7 KPFM analyses at lower concentrations of *t*DNA (7.68 nM and 768 pM). (a-f) Topography and surface potential images (10 × 10 μm^2) of the DCNPs: (a) *p-c*DCNP at 7.68 nM cDNA, (b) *p*-χ_1DCNP at 7.68 nM χ_1DNA, (c) *p-nc*DCNP at 7.68 nM *nc*DNA, (d) *p-c*DCNP at 768 pM *c*DNA, (e) *p*-χ_1DCNP at 768 pM χ_1DNA, (f) *p-nc*DCNP at 768 pM *nc*DNA, respectively.

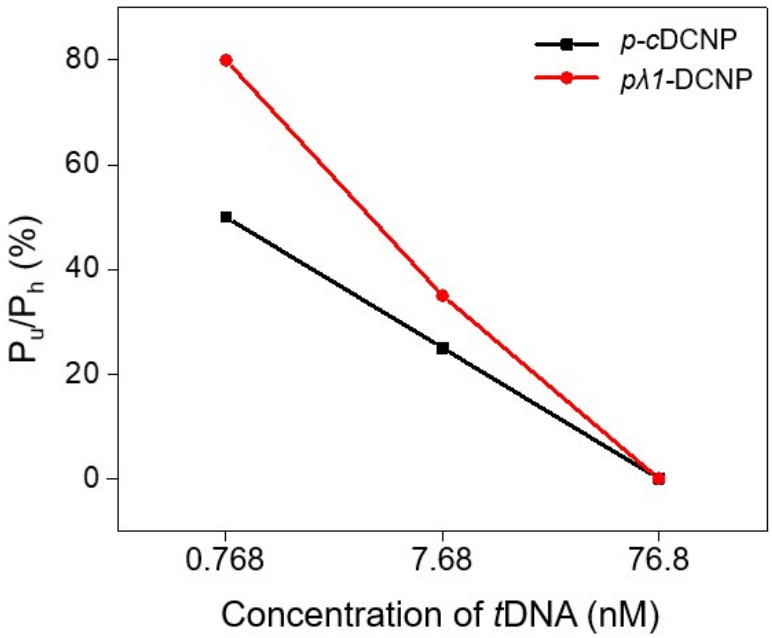

Fig. S8 Population ratio (P_u/P_h) of the unbound to the hybridized DCNPs with concentration of *t*DNA

	ϕ_{pDNA}	Φ	Φ_{ideal} (=2 ϕ_{pDNA})	ϕ'_{pDNA}	$\phi'_{p\text{-}tDNA}$	K_H
p-*c*DNA	0.743	1.455	1.490	0.035	1.420	1502.029
p-χ_1DNA	0.743	1.410	1.490	0.080	1.330	201.089
p-χ_2DNA	0.743	1.334	1.490	0.156	1.177	51.262
p-χ_3DNA	0.743	1.156	1.490	0.334	0.822	7.612
p-χ_4DNA	0.743	0.912	1.490	0.578	0.335	1.031
p-χ_5DNA	0.743	0.748	1.490	0.742	0.006	0.019
p-*nc*DNA	0.743	0.747	1.490	0.743	0.005	0.017

Table S1. Summary of the surface potentials of the *p*-*t*DCNPs, and the calculated equilibrium constants for DNA hybridization (K_H). Table shows the results obtained from the average surface potentials of each *p*-*t*DCNP case (that is, from the *p*-*c*DNA to the *p*-*nc*DNA). ϕ_{pDNA} indicates the measured surface potential of the *p*DCNPs. Φ is a total average potential of each *p*-*t*DCNP case, measured by KPFM, and Φ_{ideal} is an ideal case of the Φ which has double charge of the *p*DNA surface potential. After hybridization, ϕ'_{pDNA} and ϕ'_{dsDNA} reflect the surface potentials of the remaining *p*DNA and the dsDNA (hybridized *p*-*t*DNA). Based on the model (Eq. 3) we calculated the K_H between the *p*DNA and the *t*DNA.

		*p-c*DNA		*p-*χ_1DNA		*p-nc*DNA	
		Average (ΔV)	Probability (%)	Average (ΔV)	Probability (%)	Average (ΔV)	Probability (%)
76.8 nM	ϕ_{ssDNA}	1.455	100.000	1.410	100.000	-	-
	ϕ_{dsDNA}	-	-	-	-	0.743	100.000
7.68 nM	ϕ_{ssDNA}	1.398	76.171	1.320	64.151	-	-
	ϕ_{dsDNA}	0.760	26.829	0.772	35.849	0.741	100.000
768 pM	ϕ_{ssDNA}	1.325	51.667	1.335	18.667	-	-
	ϕ_{dsDNA}	0.765	48.333	0.762	81.333	0.752	100.000

Table S2. Summary of the bimodal distributions in surface potential of the DCNPs at low *t*DNA concentration, and their probability between two different states of each DCNP case. Herein, the ϕ_{ssDNA} represents an average surface potential of the *p*DCNP left not hybridized. The ϕ_{dsDNA} is an average surface potential of the *p-t*DCNP, the hybridization of which is completed.