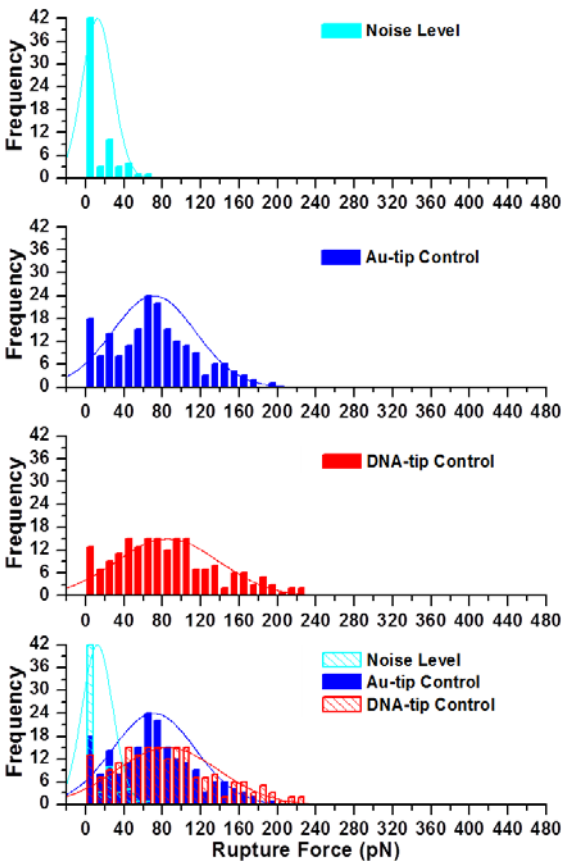
Electric Supplement Information

Preparation of DNA-AuNPs

Thiol-modified oligonucleotide (5'-Cy5-ATCTCGGCTCTGCTAGCGAAAAAAAAAA-(C3H6)-SH-3', 15.5 OD) was added to 13 nm citrate-stabilized AuNPs (~3 nmol oligonucleotide per 1 ml of 10 nM colloid). After two hours, sodium phosphate buffer (1.0 M; pH 7.0) was added to balance to 0.1 M phosphate, and 2.0 M sodium chloride was added to produce 0.1 M NaCl. The resulting mixture was incubated for six hours, after which two more additions of 2.0 M NaCl were added in six-hour intervals to achieve a final concentration of 0.3 M NaCl. This final mixture was incubated for 24 hours, and the particles were centrifuged (12,000 rpm, 20 min.; 3x) and resuspended.

Preparation of the fluorescent protein

Fetal bovine serum (FBS) was centrifuged overnight at 7,000×g and 4°C using a centrifugal device with a 3 kDa molecular weight cutoff. The filtrate was removed, and the concentrate was resuspended in PBS. The resulting protein was labeled with the Alexa Fluor® 488 Microscale Protein Labeling Kit (Invitrogen) according to the manufacturer's instructions.



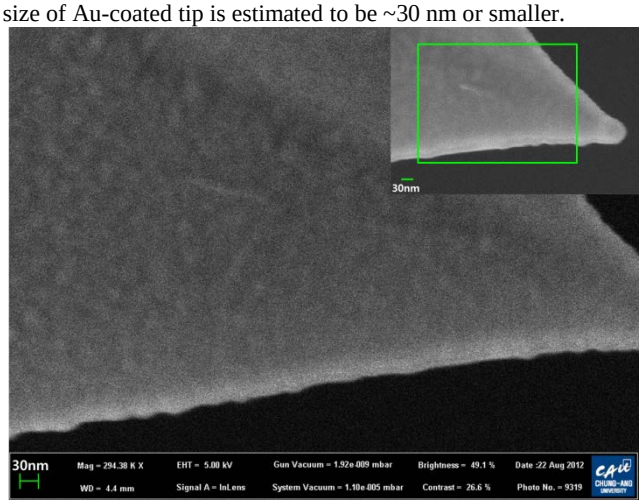
E. S. I. Fig. 1 Noise level investigation

Noise level investigation in rupture force analysis

The noise level in rupture force was investigated for analytical accuracy. After removing the cells, we performed a preliminary test to measure the force distance curve of the DNA tip to the bottom of the culture dish. Most of the frequency of rupture forces were in the range of 0~30 pN, which was set to the noise level. Thus, rupture events in the range of 0~30 pN were discarded.

Characterization of Au-coated AFM tip

E. S. I. Fig. 2 shows the Au-coated AFM tip characteristics. The radius at the apex of the AFM tip was circa ~60 nm and the grain size of Au-coated tip is estimated to be ~30 nm or smaller.

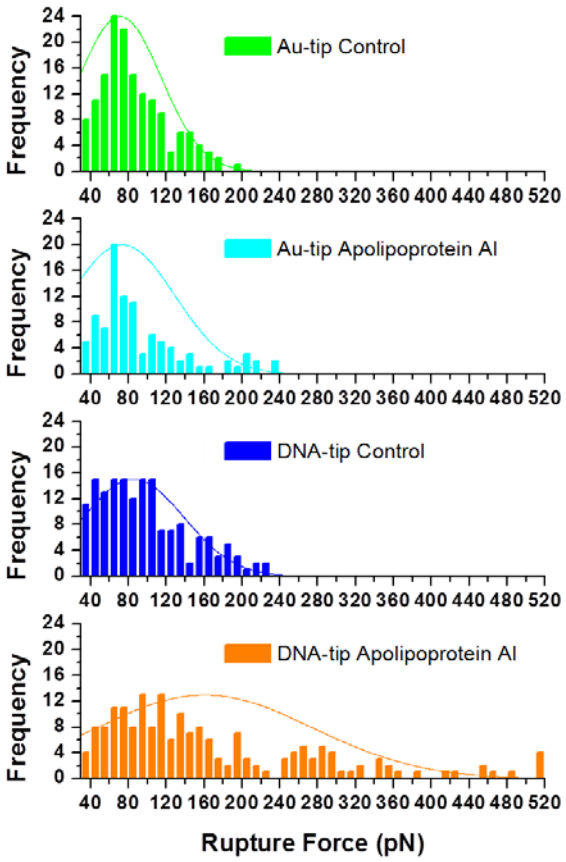


E. S. I. Fig. 2 SEM image of Au-coated AFM tip.

Analogous result using specific protein

Equivalent measurements using apolipoprotein A-I (Sigma)-treated cells were performed to confirm that the strong interaction between the DNA-tip and cell surface was influenced by proteins rather than non-protein factors in FBS.

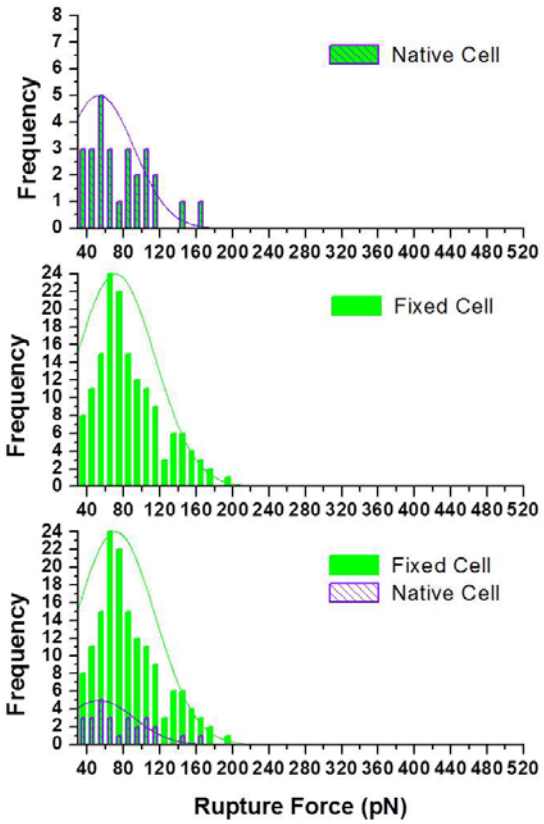
The rupture force histogram shows similar results in the 10% FBS environment. Therefore, the protein exclusively affects the interaction between the DNA-tip and cell surface, and the presence of the protein has limited effect on the interaction between the Au-tip (without DNA attached) and the cell surface.



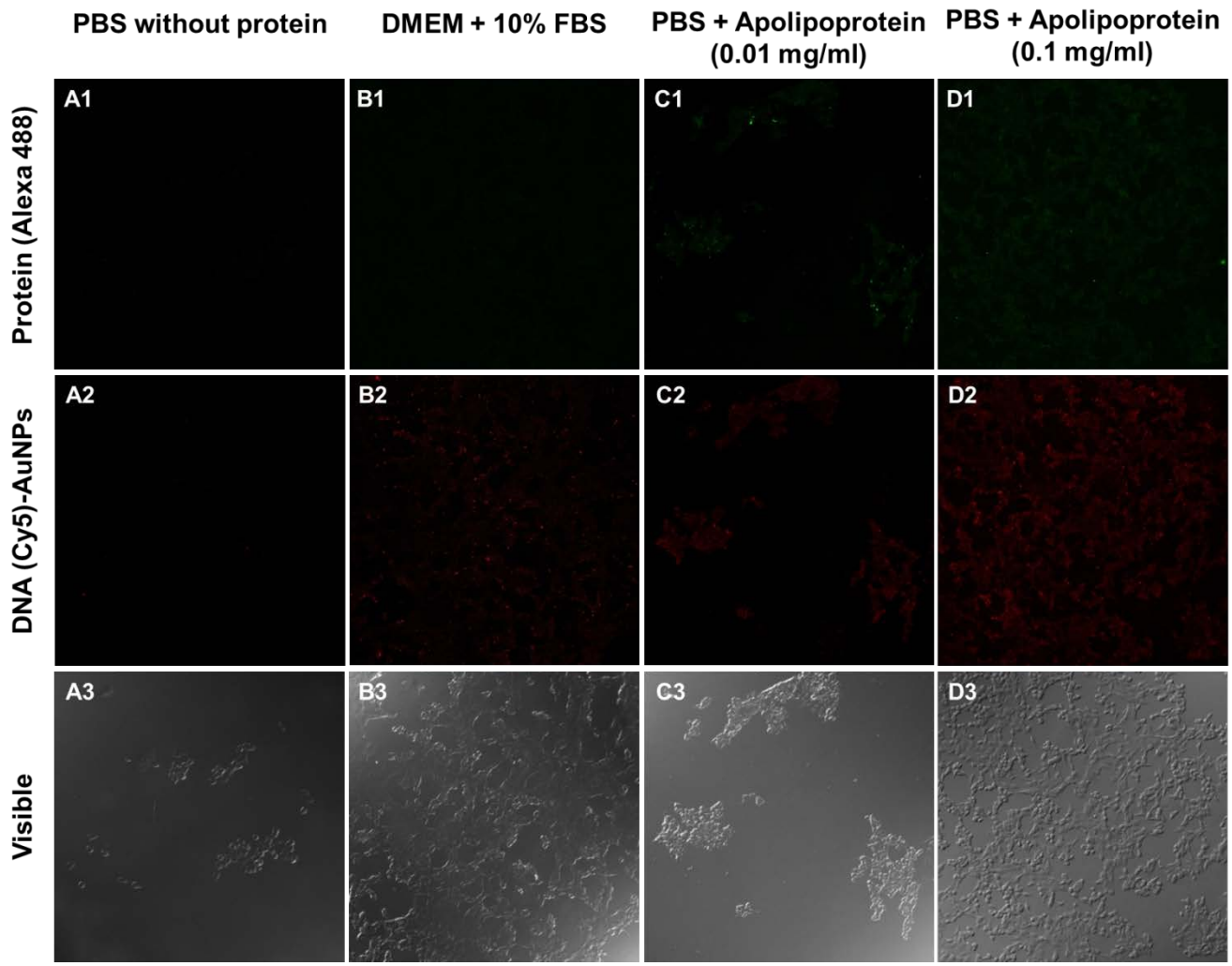
E. S. I. Fig. 3 Distribution of the rupture forces between the AFM tip and apolipoprotein A-I treated MCF7 cell membrane.

Rupture force measurements on native MCF7 cells

The distribution of 47 data points of the rupture force on native MCF7 cells in PBS, measured by using gold-coated AFM tips, is shown in E. S. I. Figure 4, where it is also compared to the distribution of 192 data points on fixed MCF7 cells. The two distributions are quite similar although there is an extremely small difference, less than 20 pN, between their maxima. Thus, we can conclude that there seems to be extremely small effect of our cell fixation on the rupture force, if any.



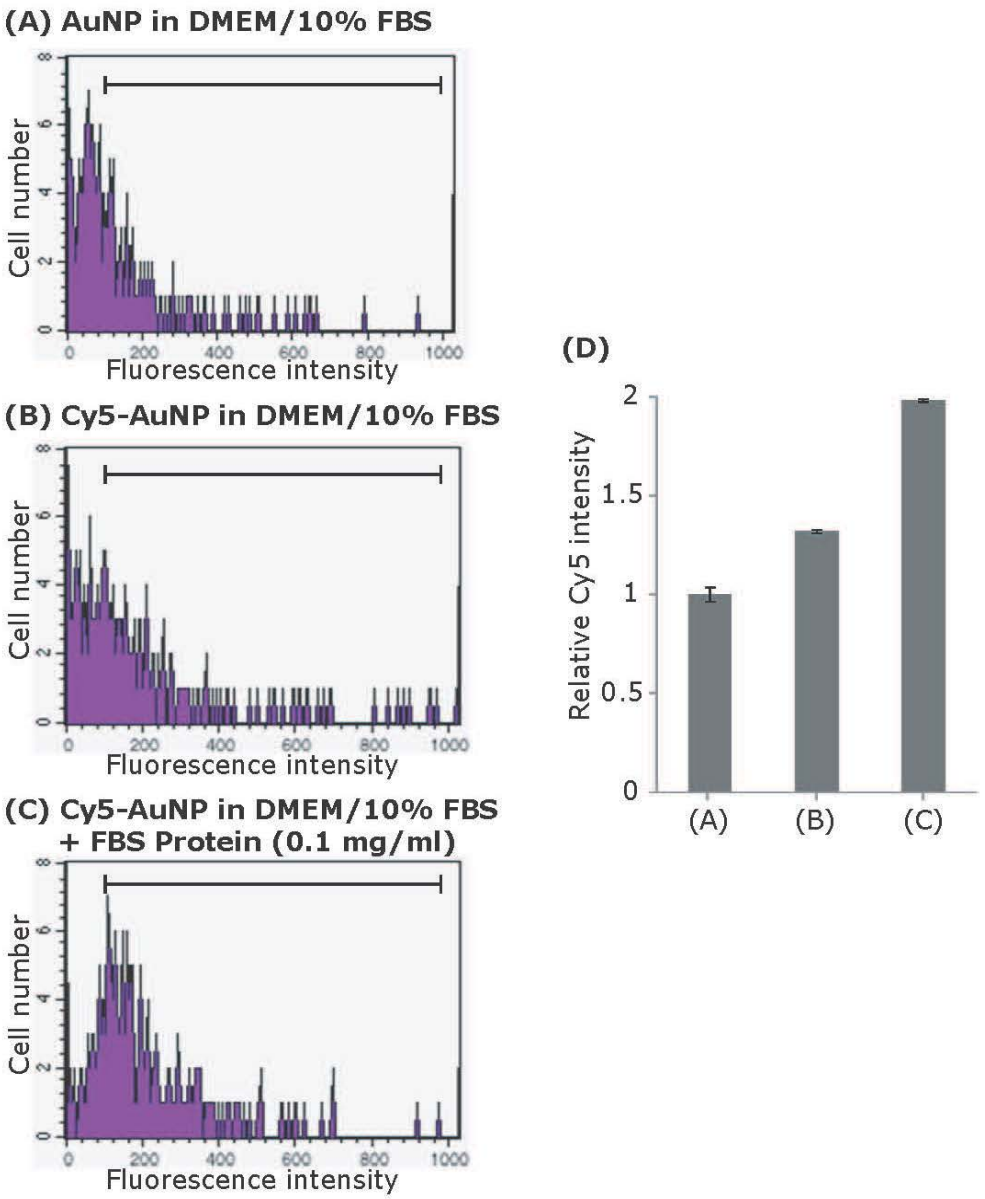
E. S. I. Fig. 4 Distributions of the rupture forces on native MCF7 cells (top), on fixed MCF7 cells (middle), and their compilation (bottom), measured by using gold-coated AFM tips.



E. S. I. Fig. 5 Confocal fluorescence microscopy images showing enhancement of AuNPs absorption based on increasing apolipoprotein concentration. Column (A) is the untreated control of MCF7 cells, and Column (B) is FBS and the DNA-AuNP-treated experimental group. (C and D) Cells treated with DNA-AuNPs and apolipoprotein. The top row of each column shows the detection of proteins (Alexa 488 labeling, emission at 519 nm); the middle row shows detection of oligonucleotides on the AuNP (Cy-5 labeling, emission at 670 nm); bottom row shows a transmission image of the cells. The result shows enhanced cellular uptake of DNA-AuNP in the presence of apolipoprotein.

Flow cytometry analysis

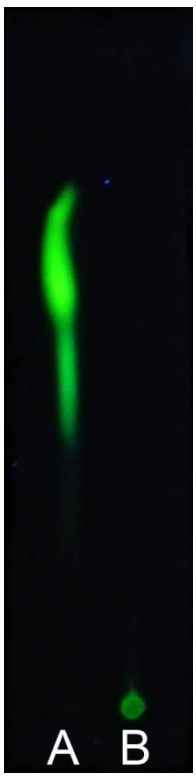
To detect Cy5-labeled AuNPs in MCF7 cells, the MCF7 cells were incubated for 1 hr with or without 0.1 mg/ml protein in the DMEM/FBS culture condition. The labeled cells were analyzed by a FACS Calibur flow cytometer (BD Biosciences, Franklin Lakes, NJ, USA).



E. S. I. Fig. 6 Flow cytometry analysis showing enhancement of AuNPs absorption by addition of FBS protein. (A)-(C) are cell numbers as a function of fluorescence intensity. (A) Cells treated with unlabeled AuNP as a negative control. (B) Cells treated with Cy5-labeled AuNP in DMEM/10% FBS and no additional FBS protein. (C) Cells treated with Cy5-labeled AuNP in DMEM/10% FBS and additional FBS protein (0.1 mg/ml). Bars in the graphs (A-C) indicate the range of fluorescence intensity that was used to measure relative Cy5 intensity in graph (D). (D) is the relative Cy5 fluorescence intensity of (A), (B), and (C). Three independent experiments were performed in triplicate.

Degree of free dye separation from labelled species

We have measured the residual amount of free dye that remained in protein labelled with Alexa Fluor® 488, by using thin layered chromatography as suggested in the manual of labelling kit purchased from Molecular Probes®. As shown in E. S. I. Fig. 7, no residual free dye was found in FBS proteins labelled with Alexa Fluor® 488.



E. S. I. Fig. 7 Picture of silica-gel thin layer chromatography with eluent of chloroform: methanol (1:1). A) Alexa Fluor® 488 TFP ester, B) Alexa Fluor® 488-fluorescence-labeled FBS proteins made by using Alexa Fluor® 488 microscale protein labelling kit (catalog number: A30006) purchased from Molecular Probes®.