Rapid Reversible Photoswitching of Integrin-mediated Adhesion at the Single-Cell Level

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Cells have the ability to adjust their adhesion behavior to different environments and physiological situations through modulation of their cellular adhesion machinery.\textsuperscript{[1, 2]} The involved processes are highly dynamic and exhibit remarkable switchability, which enable cell migration and differential cell-matrix adhesion.\textsuperscript{[3, 4]} Being able to dynamically control adhesion by switching surface properties between adhesion promoting and impeding conditions is of supreme relevance for the development of novel biomaterials, having applications in tissue engineering and implant design. In order to create such dynamic adhesion environments, unidirectional and irreversible switching of integrin-mediated adhesion has been achieved by light-triggered activation of caged molecules and by electrochemical switching.\textsuperscript{[5-7]} Studies using this approach revealed that the time point of cell exposure to adhesion ligands and their density significantly influences cell differentiation\textsuperscript{[8]} and guides vascularization \textit{in vivo}.\textsuperscript{[9]} This shows that cells keep track of their adhesion history and that dynamic changes in adhesion signals are imperative in controlling cell functions.

However, in order to explore the influence of dynamic adhesion environments on cell behavior and to enable exploitation of this mechanism in biomedical applications, biointerfaces with reversibly switchable properties are required. Reversible control of cell adhesion has so far mainly been limited to switching adhesion by use of thermoresponsive
materials, such as poly(\(N\)-isopropylacrylamide),\(^{10,11}\) which are ill-suited for local and rapid switching at high spatial resolution. In contrast, light-induced switching of cell adhesion could prove to be powerful in controlling cell adhesion at high spatial and temporal resolution.

Azobenzenes are reversibly photoswitchable molecules that have been shown to be highly suitable for photoswitching applications ranging from optical devices to polymers and surfaces.\(^{12}\) They can be toggled between two isomerization states, i.e. a \(cis\) and a \(trans\) configuration with light resulting in two distinctively different surface conditions. For specific control of cell adhesion, azobenzenes can be biofunctionalized with bioactive molecules such as RGD (Arginine-Glycine-Aspartate) peptides that bind members of the integrin cell adhesion receptor family.\(^{13}\)

Several studies have employed RGD-functionalized azobenzenes for controlling adhesion with promising results, but more than one hour of illumination with UV light was required for switching.\(^{14-16}\) Extended UV exposure is not suitable for bioapplications due to severe phototoxic damage to living cells,\(^{17}\) whereas short UV exposure has proven successful in irreversible photoswitching approaches.\(^{5}\) Here, we demonstrate a versatile approach that overcomes previous limitations and achieves rapid reversible photoswitching of cell adhesion by biofunctionalized azobenzene surfaces. In order to generate a widely applicable surface coating, we have chosen a covalent binding approach based on generating a coupling layer that is further functionalized with click-chemistry. This surface coating strategy can be applied to many different biomaterial types, including Ti and NiTi.\(^{18,19}\)

Azobenzenes were functionalized with the integrin ligand c(RGDfK)\(^{20}\) and covalently coupled to glass surfaces together with a biologically inert polyethylene glycol (PEG) layer (Figure 1A). The molar ratio of c(RGDfK)-azobenzene and PEG2000 was adjusted to 1:99, which has recently been reported to offer adequate adhesion conditions for fibroblast cells.\(^{21}\) It corresponds to a c(RGDfK)-azobenzene packing density of around 0.5 molecules/nm\(^2\), as determined with UV/Vis spectroscopy. Figure 1B illustrates the working hypothesis of the
mixed c(RGDfK)-azobenzene/PEG2000 monolayer. Short irradiation with monochromatic UV light of 365 nm for only 20 s changes the configuration from trans to cis (Figure 1C). In consequence the c(RGDfK) headgroup is forced to dip into the non-adhesive PEG2000 background. Illumination with visible light of 440 nm switches the azobenzenes back to the trans configuration, making c(RGDfK) again available to integrin binding. This process is reversible, as confirmed by UV/Vis spectroscopy (Figure 1C). Comparison of the UV/Vis spectra before and after illumination with 365 nm from four independent experiments shows that on average 47 % of azobenzene molecules are switched to the cis configuration under the assumption that the cis isomer does not absorb at the π−π* transition (λ = 359.6 nm).

**Figure 1.** A) Structure of the c(RGDfK)-azobenzene and covalent immobilization on glass. B) Mixed monolayer of polyethylene glycol (PEG) and c(RGDfK)-azobenzenes. UV illumination switches the azobenzene from the trans to the cis isomer and the c(RGDfK) headgroup (black circle) is immersed into the non-adhesive PEG background. C) UV/Vis spectra verify reversible photoswitching of the mixed monolayer.
We used two complementary approaches to assess reversible switching of cell adhesion: cell culture assays and single cell force spectroscopy (SCFS). In cell culture assays, fibroblasts (REF52 wt) were seeded for 15 min onto sterilized azobenzene surfaces that were either stored in the dark (trans configuration) or illuminated with UV light of 365 nm (cis configuration). Non-adhering cells were removed by rinsing with buffer (Figure 2A) and the number of adhered cells was determined (Figures 2C and 2D). About 50 % fewer cells adhered to surfaces with c(RGDfK)-azobenzene in cis configuration than in trans configuration (Figure 2B).

![Figure 2](image)

**Figure 2.** A) Illustration of the cell culture assay. Cells are seeded onto substrates that were stored in the dark (trans) and illuminated with UV light (cis). 15 min after cell seeding, the number of adhered cells was determined. B) Result of the assay. In cis configuration adhesion of fibroblasts was reduced to about 50 % compared to the trans configuration. Error bars denote standard deviations. C) Phase contrast images of cells after 15 min adhesion on a surfaces in the trans and D) cis configuration. Scalebars: 50 µm.

Next we employed SCFS to measure cell adhesion forces\[^{22}\] in response to reversible photoswitching of the mixed c(RGDfK)-azobenzene/PEG2000 monolayer. SCFS facilitates qualitative and quantitative verification of true reversibility of photoswitching in situ on the single-cell level on the same surface spot with one and the same cell (Figure 3A), as a cell is attached to a cantilever and repeatedly brought into contact with the surface. The cantilever deflection is a measure of the force acting on the cell and is plotted against the distance of the
cantilever from the surface (Figure 3B). Figure 3B shows retract parts of force-distance curves for a cell interacting with a substrate in trans (black) and cis (red) configuration. Initially, the cell is held down by the cantilever and is in full contact with the surface. Upon withdrawal from the surface, the cell is stretched and the cantilever is bent downwards, thus experiencing an increasingly attractive (negative) force. With further retraction a critical value is reached, termed the cell detachment force $F_{\text{det}}$, at which the cell starts to successively release from the substrate. Under continued retraction individual cell-substrate bonds dissociate (rupture events in Figure 3B) until the cell is completely freed (baseline). For quantitative and qualitative evaluation of adhesion as a function of isomeric state, $F_{\text{det}}$ as well as the number of single rupture events are key parameters. $F_{\text{det}}$ characterizes adhesion at the level of the whole cell, whereas the number of single rupture events is a measure for available binding sites on the surface. As shown in Figure 3B, $F_{\text{det}}$ and number of single rupture events are noticeably decreased for the cis configuration compared to trans.

In order to prove the reversibility of cell adhesion, several cycles of photoswitching were carried out in situ commencing with c(RGDfK)-azobenzenes in trans configuration. 20 force curves were taken at each of four different positions on the substrate. Then, the azobenzenes were switched into the cis configuration by UV irradiation from below for around 20 s. Again, force curves were recorded at the identical positions and the azobenzenes were switched back into trans configuration using visible light (470 nm). This switching cycle was repeated with the same cell (Figure 3C). In trans configuration, the average cell detachment force ranged between $F_{\text{det}} = (0.74 \pm 0.03)$ nN before illumination and $F_{\text{det}} = (0.92 \pm 0.04)$ nN in the final switching cycle with a mean of $F_{\text{det}} = (0.83 \pm 0.04)$ nN. In cis state the average detachment force was significantly decreased to $F_{\text{det}} = (0.65 \pm 0.03)$ nN, corresponding to a reduction by more than 20%. Analysis of five independent cell experiments confirmed consistently lower mean cell detachment forces in cis than in trans state with a significance level of 0.001 (Student’s t test, number of forces curves: 1186 (trans) and 796 (cis)). Likewise, the number
of rupture events per force curve was reduced in cis configuration (Figure 3D), showing that fewer binding sites were available. The SCFS results are well in agreement with our cell culture assays that have demonstrated 50% reduction in adhered cells by switching to cis configuration. Furthermore, they are also consistent with UV/Vis spectrometry data, showing a switching efficiency of 47%. Cells can sense tiny variations in their environment\[23\] and their adhesion structures exhibit extremely fast molecular turnover rates of a few minutes,\[24\] so that our switching efficiency should modulate cell adhesion at many different timescales.

![Diagrams](image)

**Figure 3.** Single-cell force spectroscopy on a c(RGDfK)-azobenzene/PEG2000 surface. A) Illustration of SCFS adhesion experiments. A cell is immobilized on a tipless cantilever and brought into contact with the surface. Photoswitching is achieved by illumination from below. B) Force curves of cell detachment for surfaces in cis (red) and trans state (black). $F_{\text{det}}$, is defined as the force needed to initiate cell detachment and corresponds to the minimum of the force curves (red, black arrows). Distinct steps in the curve denote single rupture events (grey arrows). C) Detachment forces of a cell in several subsequent switching cycles (average of >76 force curves from four different surface locations). D) Average number of rupture events per force curve due to the cis/trans isomerization. Error bars: standard deviation. Both, $F_{\text{det}}$ and the number of rupture events, are consistently lower in cis configuration.
In summary our data demonstrate efficient cell adhesion switching at considerably shorter UV illumination times of only a few tens of seconds compared to previous studies. Most importantly, our SCFS-based approach demonstrates the true reversibility of cell adhesion switching by our approach. To date, the dynamic control of cell adhesion properties is still a highly challenging task, but could revolutionize biointerface research and many biomaterials applications.\textsuperscript{[25]} Thus our strategy to generate rapid and reversible photoswitching holds significant potential for \textit{in vitro} and \textit{in vivo} applications, particularly in order to control cellular behavior and adhesion temporally and spatially. The surface coating strategy presented here can be easily applied to many different metallic materials that contain a silanizable oxide layer, including Ti and NiTi. Thus, in the long run we expect that it will open doors towards novel ways to investigate and apply the reversible and dynamic presentation of cell adhesion ligands in biomaterial systems.

5. Experimental Section

\textit{Photoswitchable surfaces:} The synthesis of azobenzene compound 4-(2-(4-(Prop-2-yn-1-yloxy)phenyl)diazenyl)benzoic acid AB\textsubscript{3}, preparation of mixed azobenzene and polyethylene glycol (CH\textsubscript{3}-O-PEG-C≡CH, PEG-MW: 2000 Dalton) monolayers, and subsequent functionalization with cyclic RGD peptide (cRGDfK)\textsuperscript{[26]} are detailed in the Supporting Information. We have chosen the cRGDfK as headgroup to the azobenzene because it guarantees both specific and also high affinity binding of the azobenzene to the integrins in cell membrane. Packing densities of the mixed monolayers were determined through UV/Vis spectroscopy (Perkin-Elmer Lambda 14 spectrometer).\textsuperscript{[27, 28]} Photoswitching between azobenzene isomers was done with a UV LED combination assembled by Sahlmann Photochemical Solutions. Switching from \textit{trans}- to \textit{cis} configuration was induced by UV light of 365 nm (Nichia LED, NCSU033, 350 mW). Switching back from \textit{cis} to \textit{trans} configuration
was done by irradiation with visible (VIS) light of 440 nm (Roithner LED, VL440-EMITTER, 300 mW).

Cell culture: Rat embryonic fibroblast 52 wild type cells (Ref52 wt) were maintained in Dulbecco’s Modified Eagle’s Medium (DMEM, Biochrom) supplemented with 10 % fetal bovine serum (FBS, Biochrom) at 37 ºC, 5 % CO₂ and about 90 % humidity.

Cell adhesion assay: The cell adhesion assay was carried out in four independent experiments each in duplicate. Azobenzene samples were treated by rinsing with 70 % ethanol (Walter CMP) and sterilized phosphate buffered saline (PBS, Sigma-Aldrich, P5493) and either in \textit{trans} or \textit{cis} configuration prior to cell seeding (Figure 2A). The \textit{cis} configuration was generated by 20 s UV illumination. Cells were trypsinized (0.25 % trypsin/ 0.05 % ethylenediamine tetraacetic acid, Biochrom), and suspended in Hank’s balanced salt solution (HBSS, Sigma-Aldrich, H6648). \(2 \times 10^4\) cells were seeded onto each sample and incubated for 15 min at room temperature, followed by washing with PBS and fixation with 4 % paraformaldehyde (Sigma-Aldrich) for 25 min. Afterwards, samples were washed twice with PBS and the number of adhered cells was counted on a phase contrast microscope (CKX41, Olympus) at 10x magnification (CACHN 10x 0.25, Olympus).

Single-cell force spectroscopy: Cell detachment forces were measured with an atomic force microscope (Nanowizard III, JPK Instruments) mounted on an inverted light microscope (IX71, Olympus). Experiments were carried out in HBSS buffer at room temperature. Tipless Si₃N₄ cantilevers with Au reflective coating and nominal spring constants between 0.06 and 0.35 N/m (NP-O10, Bruker) were first calibrated by the thermal noise method implemented in the JPK AFM software and then functionalized with concanavalin A (conA,
Sigma-Aldrich, C2272) for immobilization of single REF52 wt cells according to standard procedures.\textsuperscript{[22, 29, 30]} For cell capture a small number of freshly trypsinized cells was injected into the sample chamber. Immediately, the cantilever was approached to a cell up to a contact force of a few nN and held at constant height for about 8 s, followed by careful lift-off from the surface and 12 min resting to ensure stable attachment at the cantilever.\textsuperscript{[22, 29, 30]}

Force-distance curves were recorded using an approach/retract speed of 30 µm/s. Contact between cell and surface was held at a constant force of 500 pN for 1 s. For each azobenzene configuration, 20 force curves were recorded on each of four different positions on the surface as defined by the vertices of a 10 µm x 10 µm square. For switching of the surface between isomeric configurations, the cell was retracted and the surface was illuminated for 30 s from below using an LED combination mounted on objective slots. Irradiation periods were followed by a 3 min waiting period before commencing with new force measurements to let the cell recover from previously taken force curves. Each cell was used for at least two complete cycles of trans - cis - trans isomerization. Control experiments were carried out on glass cover slips in order to demonstrate that cells are not influenced by the irradiation (Figure S3, Supporting Information).

Force curve analysis was done using JPK Instruments data processing software. Statistical significance was tested with Origin 9.0 (OriginLab).

**Supporting Information**

Supporting Information are available from the Wiley Online Library or from the author.

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Rapid and reversible photoswitching of cell adhesion is achieved by c(RGDfK)-azobenzenes embedded in a polyethylene glycol background on surfaces. The light-induced cis-trans-isomerization of the azobenzene enables switching of cell adhesion on the surface. Reversibility of switching over several consecutive switching cycles is demonstrated by single-cell force spectroscopy.

**Keyword** Stimuli-Responsive Materials

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ToC figure
Supporting Information

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1. Preparation of azobenzene compounds

Organic starting materials were purchased from Aldrich, Grüssing, Riedel-de Haën, Alfa Aesar and Merck and used as delivered. Solvents were purified and dried by standard techniques. $^1$H-NMR and $^{13}$C-NMR spectra were recorded using a Bruker DRX 500. Mass spectra were recorded on a Finigan MAT 8200 (EI, 70 eV) / MAT 8230 (CI, Isobutan). Elemental analysis was carried out on a Euro Vector EA 3000 Series.

The synthetic pathways to obtain the azobenzene compounds 1, 2 and 3 (AB 1, AB 2, and AB 3) are schematically depicted in Figure S1. First, ethyl-4-(2-(4-hydroxyphenyl)diazenyl)benzoate (AB 1) was prepared according to a procedure reported in the literature.[S1] Then, 5.00 g (18.5 mmol) of AB 1 and 3.83 g (27.7 mmol) potassium carbonate were dissolved in anhydrous N,N-dimethylformamide (24.0 mL) under nitrogen atmosphere. 2.40 mL (22.2 mmol) 3-bromo-1-propyne (80 % in toluene) was added to the solution. The reaction mixture was stirred at 80 °C for 21 h and then allowed to cool to room temperature. Ethyl acetate (120 mL) was added and the mixture was diluted with water (48 mL). The aqueous layer was extracted with ethyl acetate (3 x 80 mL). The combined organic layer was washed with NaCl saturated solution (80 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The resulting orange solid contained AB 2 (ethyl-4-(2-(4-(prop-2-yn-1-yl)oxy)phenyl)diazenyl)benzoate) and was used without further purification (5.75 g, quant.). $^1$H-NMR (500 MHz, CDCl$_3$): δ = 8.17 (d, 2H, $H_3^\prime$), 7.95 (d, 2H, $H-2$), 7.90 (d, 2H, $H-2$), 7.10 (d, 2H, $H-3$), 4.78 (d, 2H, $H-5$), 4.41 (q, 2H, $CH_2$), 2.57 (t, 1H, $H-7$), 1.42 (t, 3H, $CH_3$) ppm. $^{13}$C-NMR (126 MHz, CDCl$_3$): δ = 166.1 (C q, C−O), 160.4 (Cq, C-4),
155.2 (Cq, C-1'), 147.5 (Cq, C-1), 131.7 (Cq, C-4'), 130.5 (Ct, C-3'), 125.0 (Ct, C-2), 122.3 (Ct, C-2'), 115.2 (Ct, C-3), 77.9 (Cq, C-6), 77.1 (Ct, C-7), 61.2 (Cs, CH2), 56.0 (Cs, C-5), 14.3 (Cp, CH3) ppm. MS(EI): m/z (%) = 308 (71) [M]+. MS(CI): m/z (%) = 309 (100) [M+H]+, 308 (18) [M]+. C_{15}H_{16}N_{2}O_{3} (308.12): calcd. C 70.12, H 5.23, N 9.09; found C 68.96, H 5.19, N 9.06.

2.88 g (10.3 mmol) of AB 2 and 6.46 g (154 mmol) lithium hydroxide monohydrate were dissolved in 33 mL of an aqueous solution of acetonitrile (MeCN:H_{2}O, 3:1). The reaction mixture was stirred and heated at 60 °C for 2 d. The mixture was allowed to cool to room temperature and was neutralized with a solution of hydrochloric acid-water (conc. HCl:H_{2}O, 1:2, 20 mL). The resulting precipitate was filtered off and washed to yield AB 3 (4-(2-(4-(Prop-2-yn-1-yloxy)phenyl)diazenyl)benzoic acid), which was then used without further purification (2.28 g, 79 %). ^1H-NMR (500 MHz, CD_{3}OD): δ = 8.09 (d, 2H, H-3'), 7.93 (d, 2H, H-2), 7.85 (d, 2H, H-2'), 7.15 (d, 2H, H-3'), 4.84 (d, 2H, H-5), 3.01 (t, 1H, H-7) ppm. ^13C-NMR (126 MHz, CD_{3}OD): δ = 174.1 (Cq, C=O), 161.8 (Cq, C-4), 155.2 (Cq, C-1'), 148.8 (Cq, C-1), 140.5 (Cq, C-4'), 131.2 (Ct, C-3'), 125.7 (Ct, C-2), 122.9 (Ct, C-2'), 116.4 (Ct, C-3), 79.3 (Cq, C-6), 77.2 (Cq, C-7), 56.9 (Cs, C-5) ppm. C_{16}H_{12}N_{2}O_{3} (280.08) calcd. C 68.56, H 4.32, N 9.99; found C 66.94, H 3.87, N 9.85.
Figure S1. Synthesis of AB 3. a) NaNO$_2$, 0-5 °C, HCl; b) K$_2$CO$_3$, N$_2$, 80 °C, DMF; c) LiOH·H$_2$O, 60 °C, MeCN, H$_2$O.

2. Preparation of self-assembled azobenzene monolayers

Reagents were purchased from ABCR, Alfa Aesar and Aldrich. CH$_3$-O-PEG-C≡CH (PEG-MW 2000 Dalton) was purchased from Rapp Polymere and c(RGDfK) peptide from Panatecs. All reagents were used as delivered. Self-assembled monolayers were prepared by chemisorptions of bromo-terminated alkyltrichlorosilane on silicon oxide surfaces, i.e. activated quartz or glass slides, which were subsequently functionalized with azobenzene and cyclic RGD peptide.

For surface cleaning and activation quartz and glass slides were immersed in a solution containing 98 % H$_2$SO$_4$ and 30 % H$_2$O$_2$ (volume ratio 7:3) for 1 h, rinsed thoroughly with bidest. water and dried under nitrogen gas. Then the slides were immersed in isopropanol and treated with ultrasound for 5 min. This procedure was repeated once with isopropanol and twice with double distilled H$_2$O. Then the slides were dried at 130 °C in an oven for 45 min and finally treated with oxygen plasma (Expanded Plasma Cleaner PDC-002, Harrick Plasma) for another 45 min (29.6 W, 1-1.5x10$^{-1}$ mbar).
Surface coating with a coupling layer and the subsequent click reaction were carried out as reported in literature. In brief, cleaned and activated slides were immersed in a solution of 11-bromoundecyltrichlorosilane (750 µL) in anhydrous toluene (150 mL) for 30 min in a glove box under nitrogen atmosphere. Then the slides were rinsed once with anhydrous toluene under nitrogen atmosphere and were taken out of the glove box and rinsed twice with toluene. Then the slides were immersed in toluene and treated twice with ultrasound for 5 min, followed by two rinsing steps with N,N-dimethylformamide. In order to obtain azide terminal groups on the monolayer, the slides with bromo terminal groups were immersed for 3 d in a saturated solution of sodium azide in anhydrous N,N-dimethylformamide at 70 °C. After 3 d the slides were immersed in fresh N,N-dimethylformamide, treated with ultrasound for 5 min and rinsed with N,N-dimethylformamide one more time. This procedure was repeated with double distilled H₂O and toluene. Afterwards the slides were dried under nitrogen gas.

For the click reaction (Figure S2, a), solutions of 1 · 10⁻³ M AB 3 in ethanol and 1 · 10⁻³ M CH₃-O-PEG-C≡CH (PEG-MW 2000 Dalton) in ethanol were prepared. 1.00 mg Copper(II) sulfate pentahydrate and 1.00 mg sodium ascorbate were suspended in double distilled H₂O (1 mL). 400 µL of the suspension were added to 11 mL of a mixture of the azobenzene solution and the polyethylene glycol CH₃-O-PEG-C≡CH solution (AB 3:PEG, 1:99). The slides were immersed into the reaction mixture and stirred under nitrogen atmosphere at room temperature for 3 d. After 3 d the slides were immersed in ethanol, treated with ultrasound for 5 min and rinsed with ethanol. This procedure was repeated with acetone and isopropanol.
Figure S2. Activation of the carboxylic acid function with N-hydroxysuccinimide (NHS). The NHS-activated acid reacts easily with the lysine amino function of the c(RGDfK) peptide.

3. NHS-activation and cyclic RGD peptide coupling

For NHS-activation (Figure S2, b) of the azobenzene carboxyl terminus a solution of 86.3 mg (750 µmol) N-hydroxysuccinimide (NHS) and 144 mg (750 µmol) 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) in double distilled H2O was cooled to 15 °C and degassed with nitrogen for 15 min. The slides with azobenzene monolayer were immersed in the solution under nitrogen atmosphere at 15 °C for 90 min. Afterwards the slides were rinsed twice with double distilled H2O, immersed in double distilled H2O, treated with ultrasound for 5 min and dried under nitrogen gas.

For coupling of cyclic RGD peptide (Figure S2, c), 2 mg of c(RGDfK) were dissolved in 1 mL phosphate buffered saline (PBS, pH = 7.2). The slides with an activated ester azobenzene monolayer were incubated with c(RGDfK) in PBS (100 µl each) at room temperature. After an immersion time of 2 h, the slides were rinsed twice with double distilled
H$_2$O, then immersed in double distilled H$_2$O and treated with ultrasound for 5 min. After a final rinsing step with acetone, the c(RGDfK) functionalized surfaces were dried under nitrogen gas and stored under nitrogen until further use.

4. Control experiments on glass

As control experiment, we have irradiated adhering cells in a six-well plate several times with light of wavelength 365 nm and 440 nm (same light sources as in the manuscript). No effects of the irradiation on cell conformation have been observed, as shown in figure S3.

![Image](image.png)

**Figure S3.** (A) Cells (REF52 wt) before irradiation. (B) Cells after 30 sec irradiation with 365 nm. (C) Cells after irradiating 30 sec with 365 nm and another 30 sec with 440 nm. No change in cell conformation can be observed. (D) Single-cell force spectroscopy control experiment on blank glass after irradiation at 440 nm and 365 nm (cell-surface contact time: 1 sec, ≥ 80 force-distance curves for each situation).

References for the Supporting Information


