Supplementary information

Experimental Section

Functionalized silica aggregates: All chemicals used were purchased from Sigma-Aldrich (St Louis, MO, USA); and all reagents involved in cell culture were from Gibco, Invitrogen (Carlsbad, CA, USA) – unless otherwise noted. The raw fumed silica nanoparticles (SiR, R711) were provided by Degussa (Germany) and their average particle size is ~ 10 nm. SiR particles were suspended into the 1:1 (v/v) mixture of concentrated H_2SO_4 and 30% (v/v) H_2O_2 for 2 hours, and rinsed in de-ionized water (DI-water) for at least five times with centrifuge at 15,000 g x 5 min. Then, the particles were resuspended into 10% (v/v) 3-aminopropyltriethoxysilane (APS) for 2 hours at room temperature, centrifuged again and placed into 1% (v/v) glutaraldehyde for another 2 hours. After washing to remove excess glutaraldehyde, these samples containing aldehyde groups (SiA) were immersed in various protein solutions, namely bovine serum albumin (BSA), calf skin collagen (Col, Type I), or human FN, at 4 ^{o}C for 24 hours with occasional shaking, to prepare functionalized SiB, SiC and SiF, respectively. The immobilization of proteins onto the silica particles was characterized by Fourier Transform Infrared Spectroscopy (FT-IR), and the zeta potential of samples in DI-water, phosphate buffer saline (PBS) and cell culture medium (DMEM/FBS: Dulbecco's Modified Eagle Medium containing fetal bovine serum) was detected.

Cell-laden silica aggregates: The silica particles for cell culture experiments were sterilized before being functionalized with proteins: SiR and SiA were soaked in 75% ethanol for 48 hours and the subsequent treatments were conducted in cell culture hood. Four types of sample, namely SiR, SiB, SiC and SiF, were pre-equilibrated with cultural medium in cell-non-adhesive 24-well plate for overnight before cell seeding. Human mesenchymal stem cells (hMSCs, Passage 2) were purchased from Cambrex (North Brunswick, NJ, USA), and

expanded over multiple passages in mesenchymal stem cell growth medium (MSCGM, Cambrex) to prevent unexpected differentiation before induction. One-to-three million hMSCs in 0.5 ml were seeded onto the silica aggregates in each well. Half of the supernatant was changed the next day for removing the unattached cells and 1 ml of fresh medium was supplemented.

Cell biology: The cell viability at various time-points was examined with Live-specific staining and determined with WST-1 assay. For the qualitative Live-specific staining (Calcein-AM, Molecular Probes, Invitrogen), living cells (green) were observed under fluorescent microscopy after 30-minute incubation and sufficient PBS rinse. For the quantitative WST-1 (4-[3-(4-Iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate, Roche Diagnostics, Basel, Switzerland) colorimetric assay, 10% (v/v) WST reagent was added into culture medium, followed by a 2-hour incubation and the measurement of absorbance at 450 nm with reference to 620 nm in a microplate reader. For certain groups, cell attachment was observed by field emission scanning electron microscopy (FESEM, JSM-6700F, JEOL Ltd., Tokyo, Japan). Briefly, the samples were fixed with 2.5% glutaraldehyde and subsequently 1% OsO_4, dehydrated in gradient ethanol solutions (30% ~ 100 %) and further dried in vacuum overnight. Platinum was sputtered for SEM contrasting. The activity of reactive oxygen species (ROS) was determined with DCFH-DA (2',7'-dichlorofluorescin diacetate) staining, and the fluorescent absorbance (excitation: 485 nm; emission: 530 nm) was acquired on a microplate-based fluorescent reader. Besides, the expression of integrins was investigated by RT-PCR and immunofluorescent staining. RNA was extracted following the TRIzol (Invitrogen) protocol, normalized and converted to cDNA for the subsequent real-time quantitative polymerase chain reaction (PCR) analysis. Relative gene expression values (human integrin $\alpha5$, αv, $\beta1$, $\beta3$) were obtained from iQ^{TM} qPCR system (Bio-Rad, Hercules, CA, USA) and calculated with the comparative $\Delta\Delta C_T$ (threshold

cycle) method. All the primers used are listed in **Table S1**, and all the oligonucleotides were synthesised by AIT Biotech (Singapore).

Table S1. PCR primers used in this study.

Genes	Primer sequence (both 5' – 3') [a]
β-actin	F: GTGGGGCGCCCCAGGCACCA; R: CTCCTTAATGTCACGCACGATTTC
Integrin-α5	F: CATTTCCGAGTCTGGGCCAA; R: TGGAGGCTTGAGCTGAGCTT
Integrin-αv	F: GTTGGGAGATTAGACAGAGGA; R: CAAAACAGCCAGTAGCAACAA
Integrin-β1	F: TGTTCAGTGCAGAGCCTTCA; R: CCTCATACTTCGGATTGACC
Integrin-β3	F: GTGACCTGAAGGAGAATCTGC; R: TTCTTCGAATCATCTGGCC

[a] F and R stand for 'forward' and 'reverse' sequence, respectively. The primer design was referred to:

S. Roux, F. Pichaud, J. Quinn, A. Lalande, C. Morieux, A. Jullienne, M.C. de Vernejoul, *Endocrinol* **1997**, *138*, 1476.

A.T. Rogojina, W.E. Orr, B.K. Song, E.E. Geisert, Jr., *Mol Vis* **2003**, *9*, 482.

Figure S1

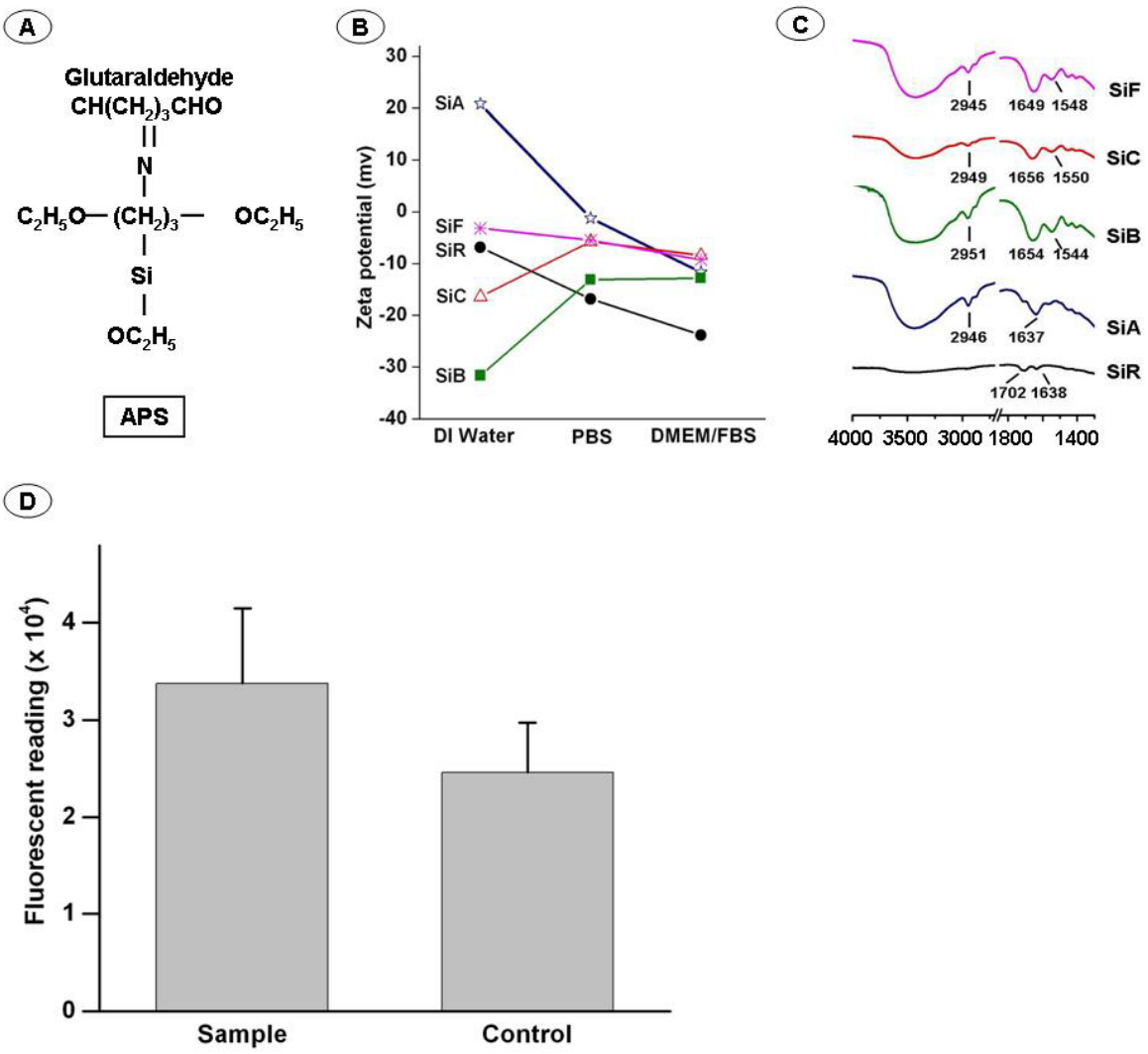

Figure S1. (A) Illustration of APS structure and its reaction with glutaraldehyde; (B) Zeta-potential values of different Si products in various aqueous medium; (C) FT-IR spectra of different Si products; (D) Production of ROS by hMSCs in monolayer in the presence (Sample) or the absence (Control) of SiC suspension.