Supporting Information

Improved Intracellular Delivery of Exosome by Surface Modification with Fluorinated Peptide Dendrimers for Promoting Angiogenesis and Migration of HUVECs

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The synthesis of polyhedral oligomeric silsesquioxane (POSS)

The polyhedral oligomeric silsesquioxane (POSS) was synthesized according to the previous reports. Briefly, 45 mL of hydrochloric acid was dropwise added into 500 mL of anhydrous methanol preheated to 50 °C under stirring. The temperature was continuously increased to 90 °C, followed by the addition of (3-aminopropyl) triethoxysilane (22.5 mL, 90 mmol) and stirred at 90 °C for 24 h. The reaction solution was concentrated to 250 mL by evaporating CH_3OH under reduced pressure using a rotary evaporator. Next, it was poured into THF (300 mL) to precipitate the product. The white solid was obtained by centrifugation at 2500 rpm for 3 minutes and then washed with THF and dried under vacuum. The structure of the obtained compound (POSS·8HCl) was confirmed by mass spectrometry.

The synthesis of generation 1 poly(L-lysine) dendrons (PG1).

Then, under a nitrogen atmosphere, POSS·8HCl (2.0 g, 1.69 mmol), Boc-Lys (Boc)-OH (6.93 g, 20.67 mmol), HBTU (7.71 g, 20.67 mmol) and HOBT (2.27 g, 16.25 mmol) were dissolved in DMF (60 mL). The solution was stirred with ice bath for 30 min followed by addition of DIPEA (9.0 mL, 54.18 mmol). After stirring at 30 °C for 48 h, the reaction solution was diluted with chloroform (250 mL). It was further washed three times with saturated $NaHCO_3$ solution, HCl (1M) and saturated NaCl solution. The obtained organic phase was dried overnight with anhydrous $MgSO_4$. After removal of excess organic solvents using vacuum rotary evaporation, the concentrated solution was

added into cold acetonitrile for recrystallization to obtain white precipitate. The preliminary Boc-protected POSS-G1 dendrimer (PG1-Boc) obtained by centrifugation was washed with acetonitrile. Then, the product was placed in vacuum oven to dry, which was characterized by nuclear magnetic resonance (NMR). Then, the Boc-protected POSS-G1 (2.0 g) dissolved in anhydrous dichloromethane (6 mL) was treated with TFA (7 mL) and stirred for 8 h to remove tert-butyl esters. The reaction solution was concentrated using the rotational evaporation, added to anhydrous diethyl ether for precipitation. The white solid of PG1 was obtained by centrifugation and washed with diethyl ether. The desiccative PG1 were characterized by mass spectrometry.

The synthesis of generation 2 poly(L-lysine) dendrons (PG2).

Next, in a nitrogen environment, PG1 (2.0 g, 1.1 mmol), Boc-Lys (Boc)-OH (8.7 g, 25.2 mmol), HBTU (9.6 g, 25.2 mmol) and HOBT (2.7 g, 20.3 mmol) were dissolved in DMF (60 mL), which was stirred 30 min under the ice bath. DIPEA (11.1 mL, 67.2 mmol) was added to the above solution. The reaction was proceeded for 48 h at room temperature. Then, the purification of product was performed as the same as Boc-protected PG1 dendrimer. The structure of Boc-protected POSS-G2 dendrimer (PG2-Boc) was characterized by nuclear magnetic resonance. Ten molar ratios of TFA to the protected group was used to put off the tert-butyl ester, and the obtained PG2 was characterized by mass spectrometry.

The synthesis of generation 3 poly(L-lysine) dendrons (PG3).

Then, PG2 (2.0 g, 0.5 mmol), Boc-Lys (Boc)-OH (8.3 g, 24.0 mmol), HBTU (9.1 g, 24.0 mmol) and HOBT (2.59 g, 19.2 mmol) was dissolved in 55 mL DMF, followed by a stir for 30 min in ice bath. After the addition of DIPEA (10.57 mL, 64 mmol) into the flask, the reaction was continued for 48 h at room temperature. The purification process and characterization of Boc-protected POSS-G3 (PG3-Boc) was as same as the PG1-Boc. Tert-butyl ester of POSS-G3 (4.0 g) was removed by ten times equivalent of TFA (13.6 mL). After precipitation, washing and drying, the white solid of PG3 was gained and analyzed by mass spectrometry.

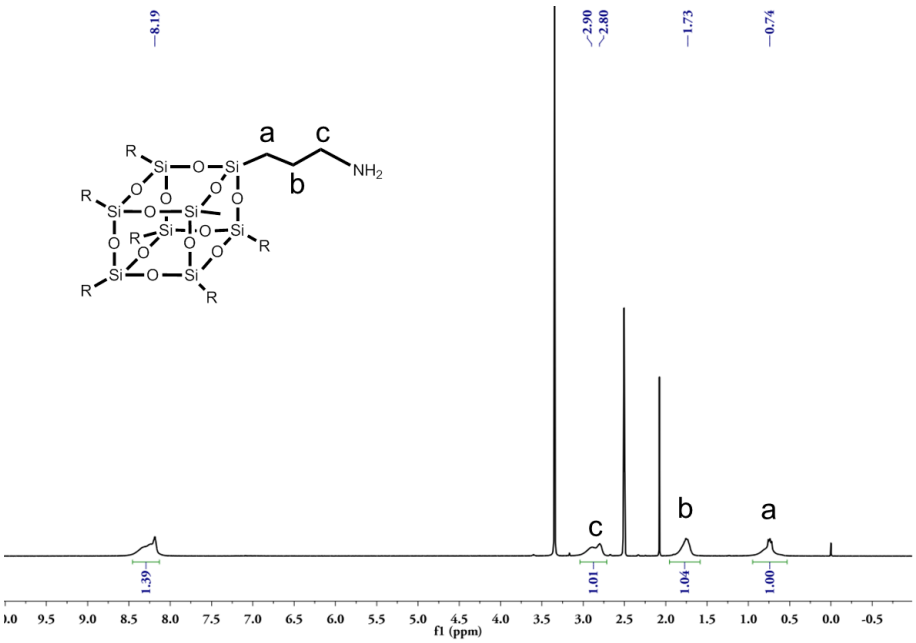

Figure S1. ^{1}H NMR spectra of POSS in DMSO-d6.

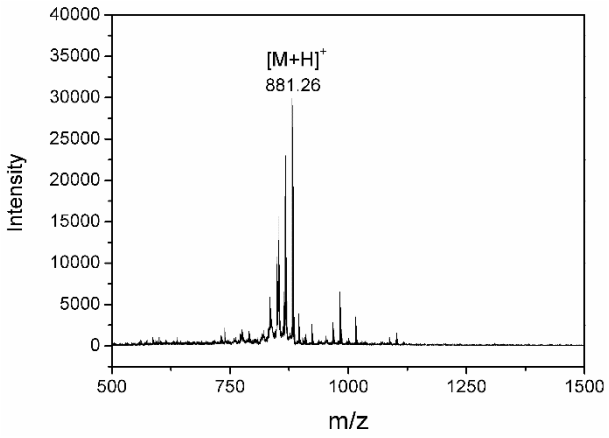

Figure S2. Mass spectra of POSS.

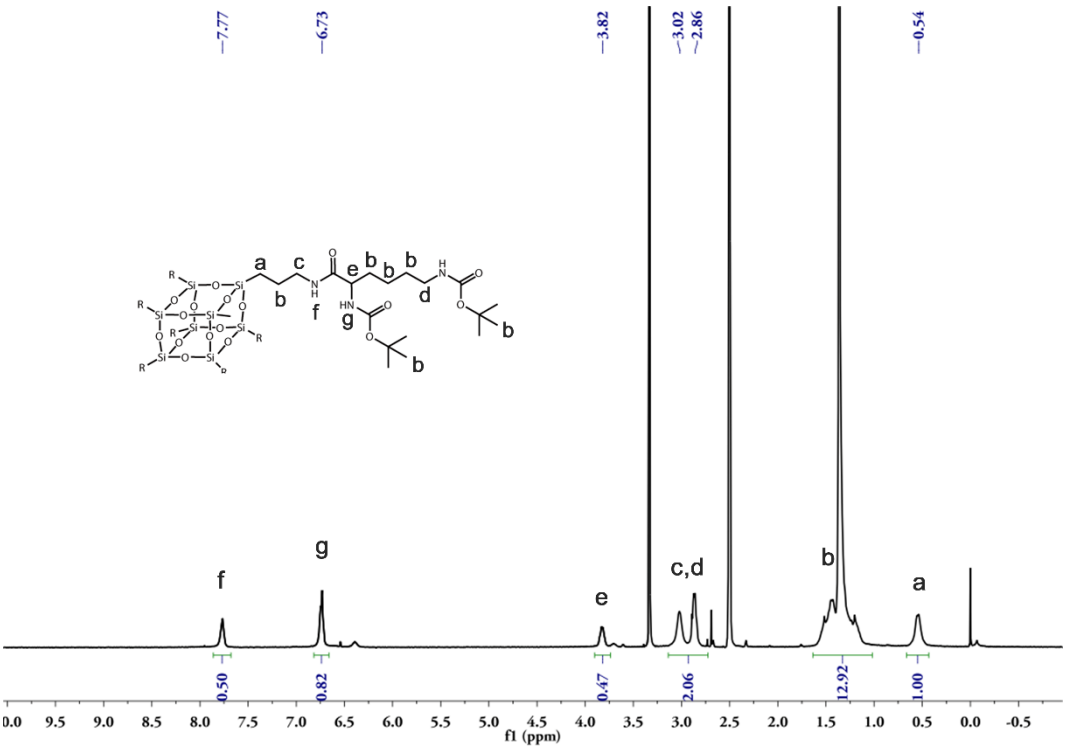

Figure S3. ^{1}H NMR spectra of PG1-Boc in DMSO-d6.

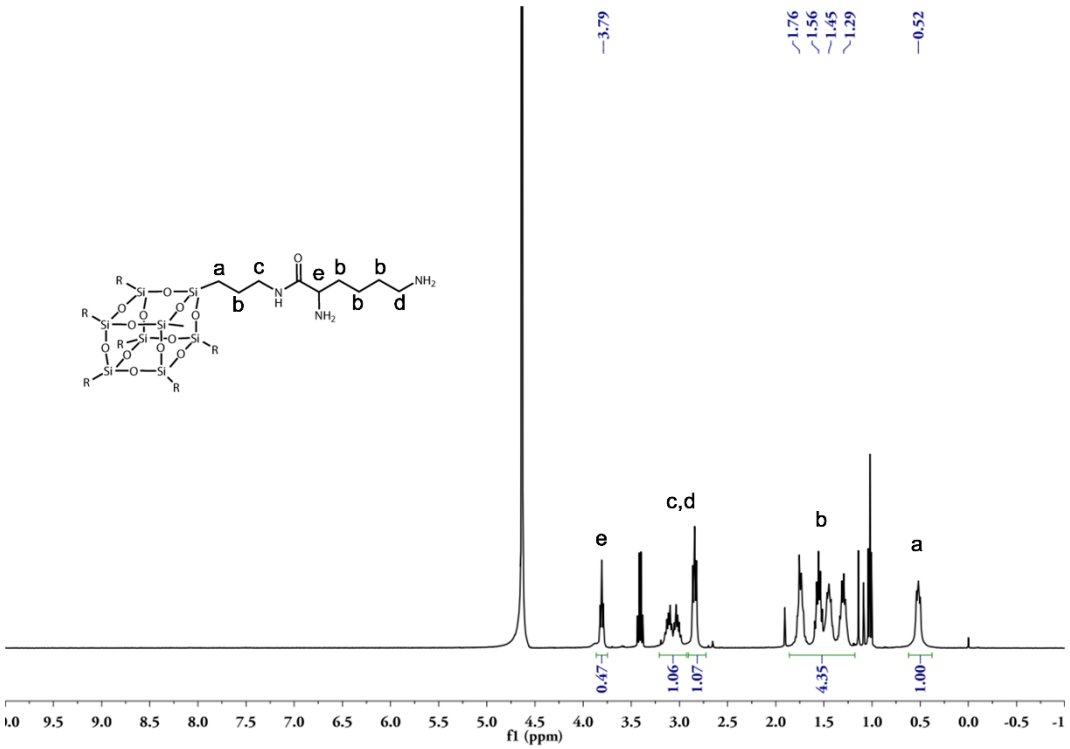

Figure S4. ^{1}H NMR spectra of PG1 in D_2O.

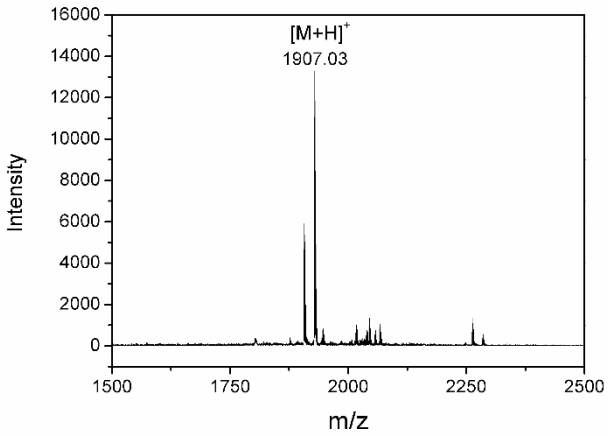

Figure S5. Mass spectra of PG1.

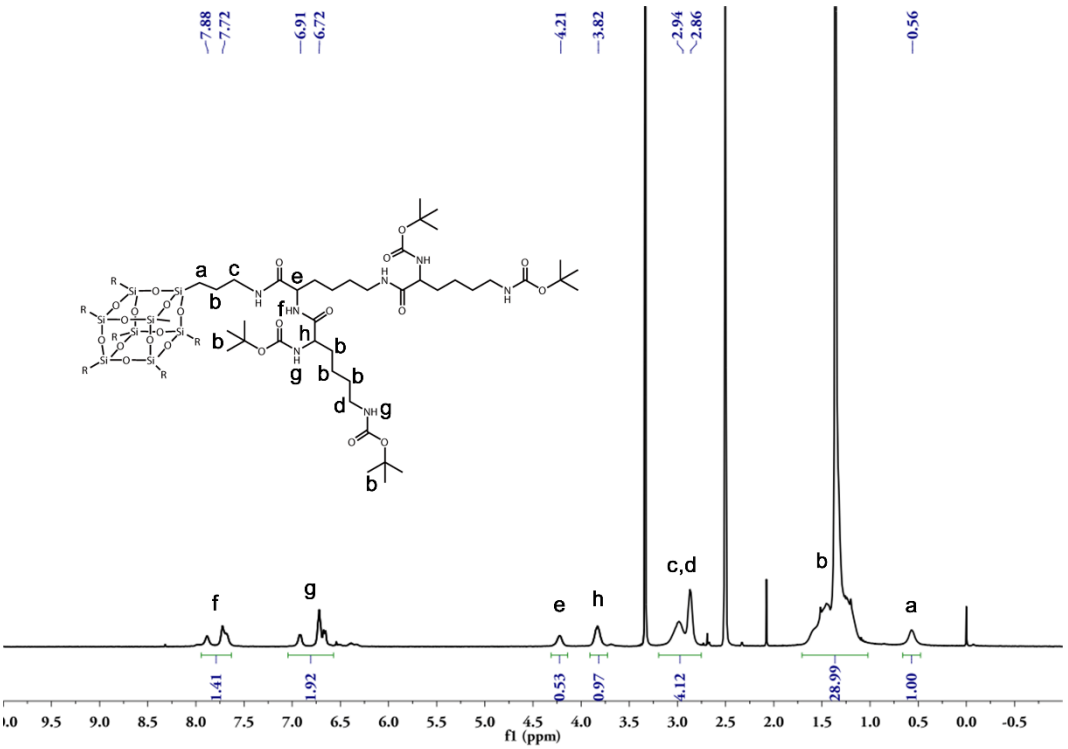

Figure S6. ^{1}H NMR spectra of PG2-Boc in DMSO-d6.

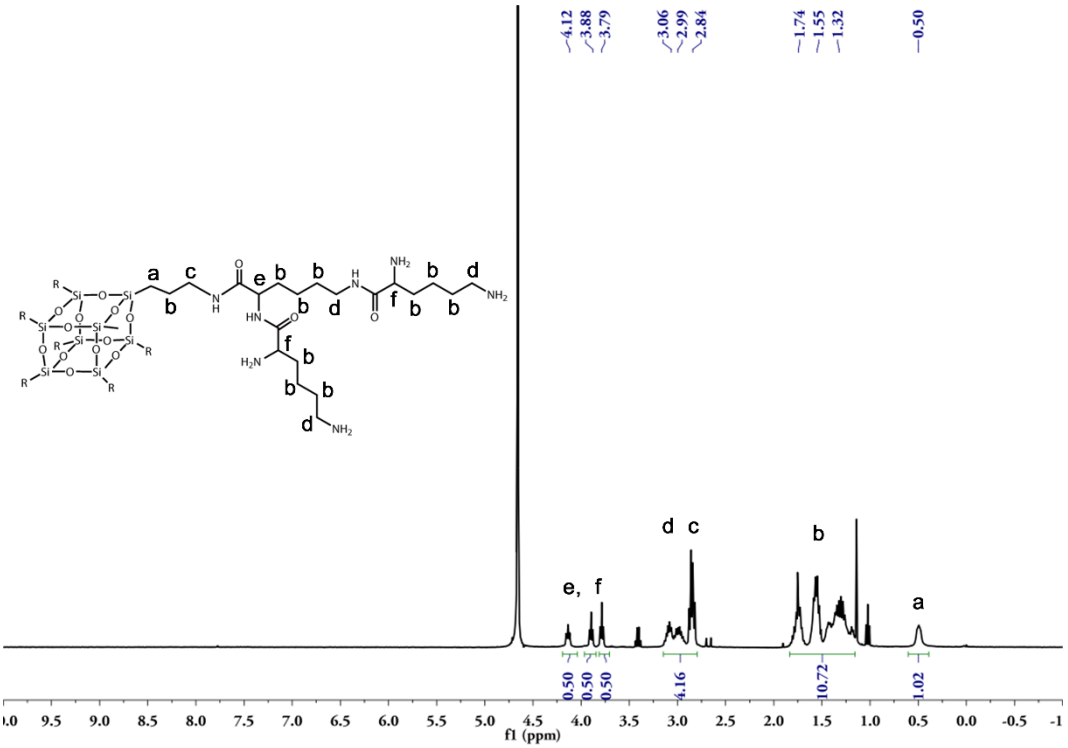

Figure S7. ^{1}H NMR spectra of PG2 in D_2O.

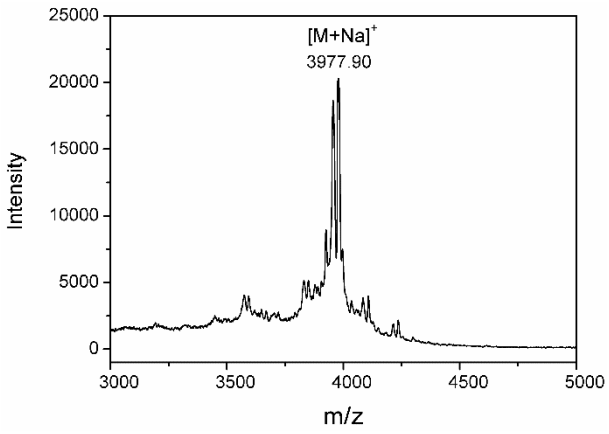

Figure S8. Mass spectra of PG2.

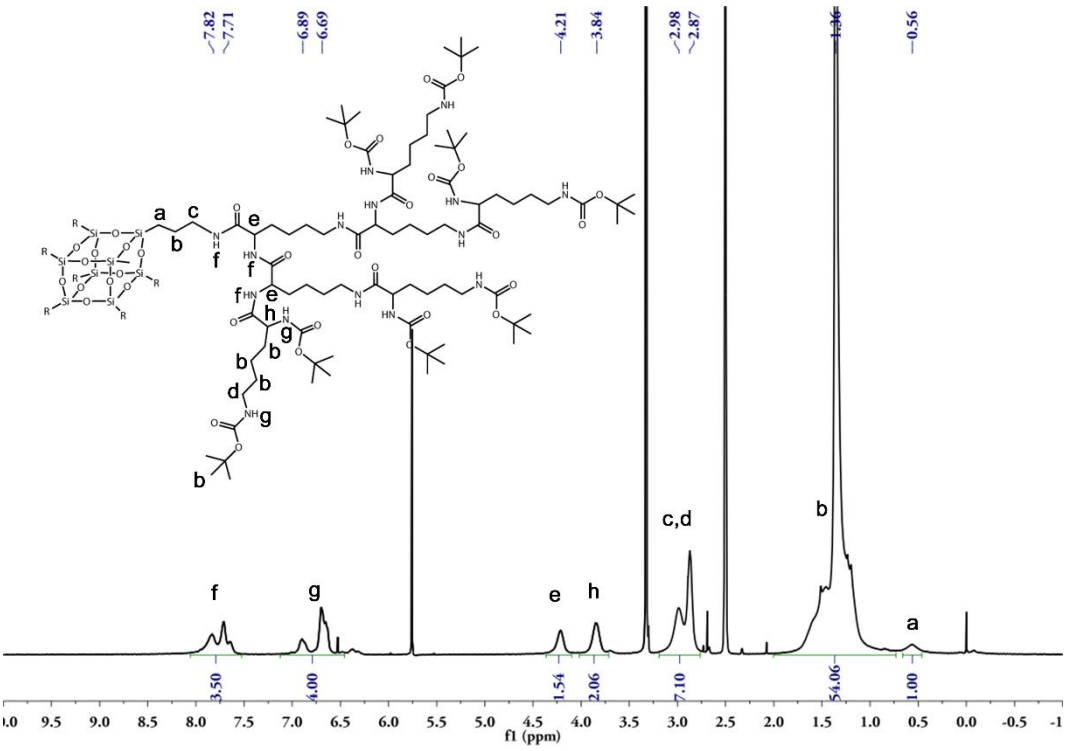

Figure S9. ^{1}H NMR spectra of PG3-Boc in DMSO-d6.

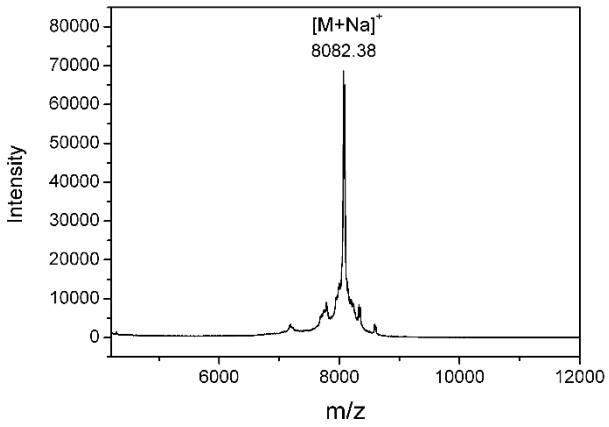

Figure S10. Mass spectra of PG3.

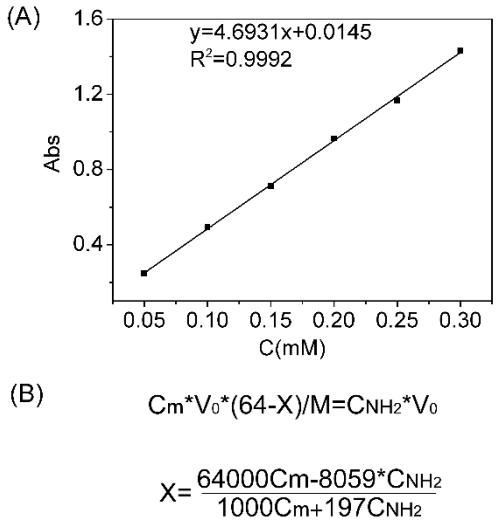

Figure S11. (A) The standard curve of primary amine by ninhydrin assay. (B) The calculation formula for the number (X) of fluoride group on FPG3. The known mass concentration (Cm) of the sample was 1 mg/mL, and the primary amine concentration (C_{NH_2}) was obtained by the standard curve.

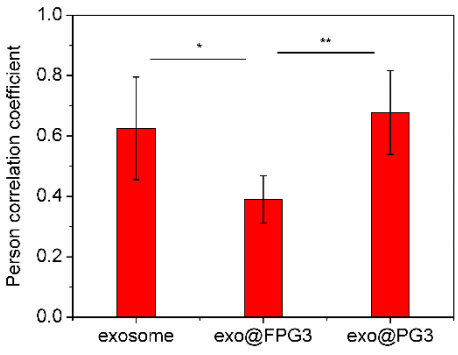

Figure S12. The co-localization ratio of lyso-tracker and DiO-tagged exosome, exo@FPG3 and exo@PG3 in HUVECs after incubation 4 h.