## SUPPLEMENTARY EXPERIMENTAL PROCEDURE

## SUPPLEMENTARY METHODS

### *RT-PCR*

CB-LEPCs ($1\times10^5$ cells) were seeded on gelatin-coated 6 well plates in EGM2-MV medium, while HUVECs ($1\times10^5$ cells) were seeded in EGM-2 medium. After 24 h, the cells were starved in 1% FBS and growth factor free-EBM-2 for 6~12 h and then incubated with COMP-Ang1 (200 ng/mL) for 0, 10, 30, and 60 min. Total RNA was isolated using Trizol (Invitrogen). Subsequently, 3 μg of RNA from each sample was reverse transcribed into cDNA and subjected to conventional PCR. The primer sequences were as follows:

ITGα4 forward, 5'-AATGGATGAGACTTCAGCACT-3', and reverse, 5'-CTCTTCTGTTTTCTTCTTGTAGG-3'; ITGαV forward, 5'-GGAGCACATTTAGTTGAGGTAT-3', and reverse, 5'-ACTGTTGCTAGGTGGTAAAACT-3'; ITGβ3 forward, 5'-CTGCTGTAGACATTTGCTATGA-3', and reverse, 5'-GCCAAGAGGTAGAAGGTAAATA-3'. PCR was performed, and the expression of GAPDH was monitored as a control.

### *Immunofluorescence staining and confocal microscopy*

CB-LEPCs ($1\times10^5$ cells) were seeded on gelatin-coated glass coverslips in EGM2-MV medium, whereas HUVECs ($1\times10^5$ cells) were seeded in EGM-2 medium. After 24 h, the cells were starved in 1% FBS and growth factor free-EBM-2 for 6~12 h and incubated with COMP-Ang1 (200 ng/mL) for 0, 10, 30, and 60 min. The cells were fixed and permeabilized. After blocking, immunofluorescent staining was performed using the following primary antibodies: anti-ITGαvβ3 and anti-ITGα4 (Chemicon, Temecula, CA, USA). Subsequently, coverslips were incubated with a fluorescent-labeled secondary antibody, anti-FITC (Jackson ImmunoResearch Laboratories) and mounted with Vectashield medium containing DAPI (Vector Laboratories). Fluorescence staining was evaluated using the aforementioned confocal laser scanning microscope.

## SUPPLEMENTARY RESULTS

### *COMP-Ang1 increased the FAK/ITGβ1 interaction*

The FAK and ITGβ1 interactions before and after COMP-Ang1 treatment were investigated to identify the molecular mechanism of Tie2-FAK signaling after COMP-Ang1 treatment in EPC. Interaction of FAK and ITGβ1, as measured using PLA, increased approximately 5.5 times by COMP-Ang1 treatment in EPCs (Fig. S1A, B).

### *COMP-Ang1 increased expression of the ITG complexes*

We tested how an ITG-dependent mechanism enhanced the migratory effects of COMP-Ang1 in EPCs and in HUVECs. Expressions of ITGs α4, αV, and β3 were investigated in COMP-Ang1-treated EPCs and HUVECs using RT-PCR (Fig. S2A). Immunofluorescence revealed that ITGα4 expression increased time dependently more in the EPCs compared with that in the HUVECs (Fig. S2B). The expression of ITGαvβ3, a receptor for both fibronectin and vironectin, also markedly increased in time dependent manner in EPCs after COMP-Ang1 treatment (Fig. S2C). Therefore, the increase in ITGs αvβ3 and α4 expressions appeared to be directly responsible for the increase in vascular migration following COMP-Ang1 treatment.

### *The ITG complexes did not control CXCR4 expression level*

We investigated CXCR4 expression after silencing ITGα4 or ITGαV in EPCs after COMP-Ang1 treatment. No change in CXCR4 expression was observed (Fig. S3).

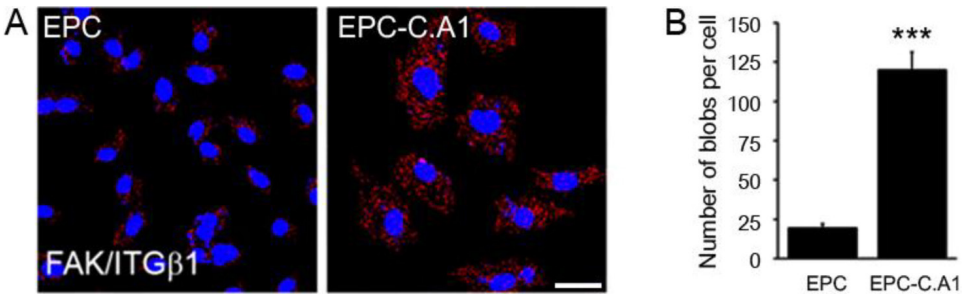


**Fig. S1.** COMP-Ang1 increased the FAK/ITGβ1 interaction. (A, B) Significant interaction between FAK and ITGβ1 with or without COMP-Ang1 treatment in EPCs was observed. A proximity ligation assay (PLA) was used to measure the close physical interactions. Red spots indicate the physical proximity of the corresponding protein pair (A). Significant number of blobs (or interactions) per cell was observed between FAK and ITGβ1 with or without COMP-Ang1 treatment in EPCs (B). The number of interacting pairs between FAK and ITGβ1 increased dramatically after COMP-Ang1 treatment. Scale bar, 200 μm.

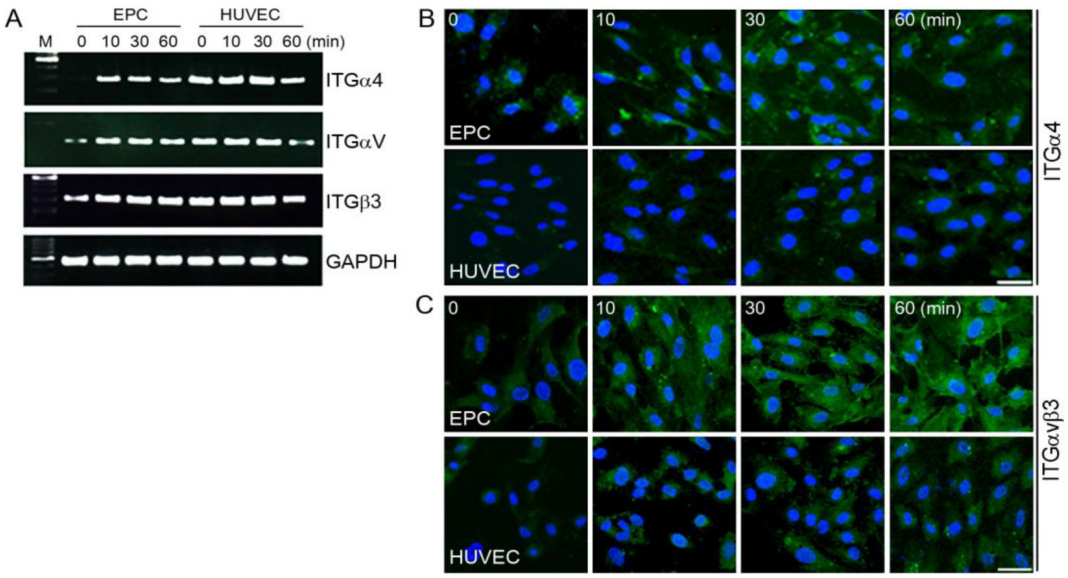


**Fig. S2.** COMP-Ang1 increased ITG complexes expression. (A) The relative mRNA expression level of ITGα4, ITGαV, and ITGβ3 after treatment with 200 ng/mL of COMP-Ang1 for 0, 10, 30 and 60 min in EPC and HUVEC. M: marker (B) Confocal images of ITGα4 (green) with DAPI as a nuclear marker (blue) after treatment with 200 ng/mL COMP-Ang1 for 0, 10, 30, and 60 min in EPCs and HUVECs. Bar, 50 μm. (C) Confocal images of ITGαvβ3 (green) with the DAPI nuclear marker (blue) after treating EPCs and HUVECs with 200 ng/mL COMP-Ang1 for 0, 10, 30 and 60 min. Bar, 50 μm.

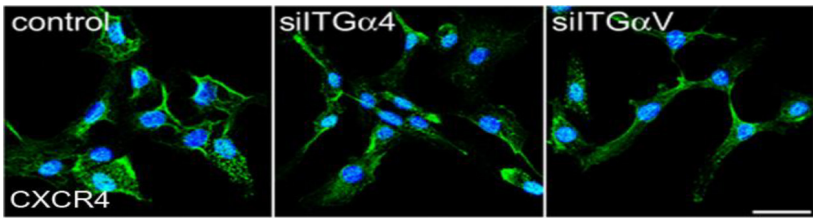


**Fig. S3.** The ITG complexes did not control the CXCR4 expression level. Confocal images of CXCR4 (green) with DAPI as the nuclear marker (blue) before or after ITGα4 and ITGαV silencing after COMP-Ang1 treatment in EPCs. Scale bar, 200 μm.

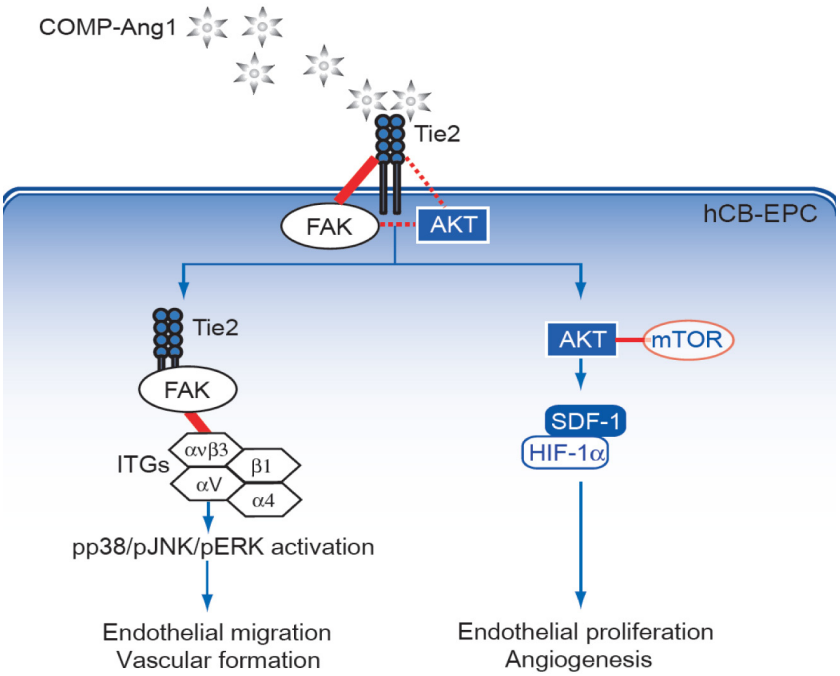


**Fig. S4.** Proposed diagram of how COMP-Ang1-Tie2 signaling is involved in both vascular migration and angiogenesis.

***COMP-Ang1-Tie2 signaling is involved in both vascular migration and angiogenesis***

COMP-Ang1 increased interactions and expressions of Tie2 and FAK and the ITG complexes. These interactions activated MAPK signaling, leading to endothelial migration and vascular formation after COMP-Ang1 treatment. However separated AKT from the Tie2/FAK complex interacted with mTOR, and activated CXCR4, SDF-1 and HIF-1α expression. These interactions and expressions lead to endothelial proliferation and angiogenesis (Fig. S4).