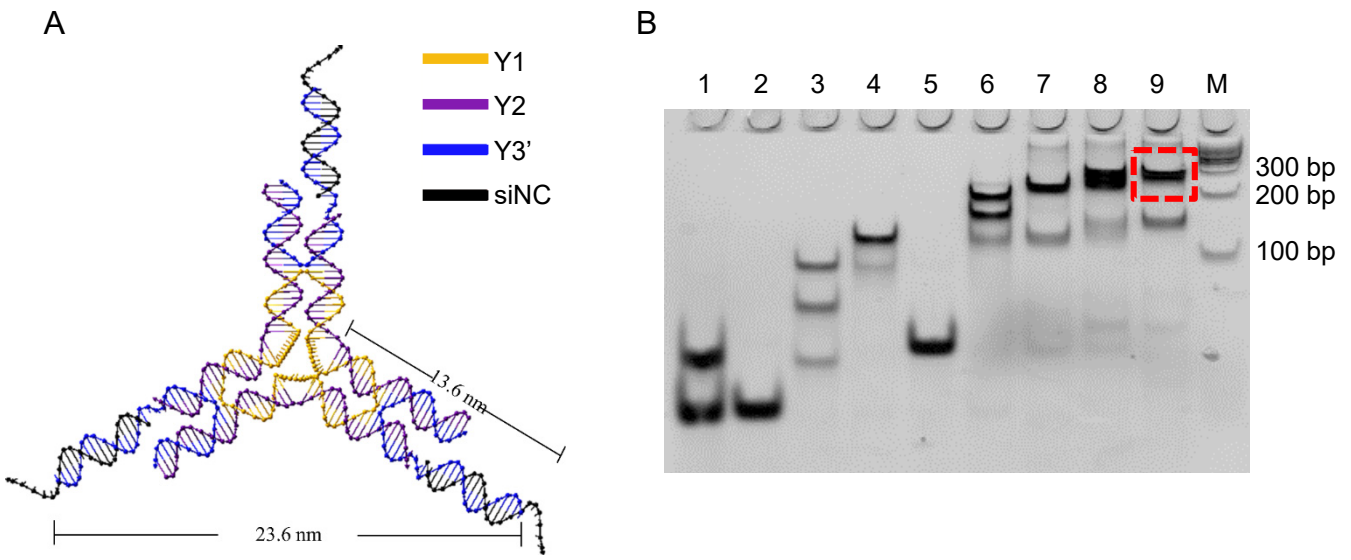

Fig. S1 DNA Y-motif complexes loaded with scramble single-stranded siRNA (siNC-DYM). A. Schematic representation of siNC-DYM. The siNC-DYM consist of three DNA strands and one negative control single stranded siRNA (blank): one central strand Y1 (yellow), three copies of edge strands Y2 (purple) and three copies of peripheral strands Y3' (blue). B. Native polyacrylamide gel electrophoresis (PAGE, 8%) analysis of the formation of siNC-DYM complexes. The RNA oligo strands, DNA strands and their molar ratios are indicated as follows: lane "1" - Y1 and Y3', lane "2" - Y2, lane "3" - 1:1 molar ratio of Y1 to Y2, lane "4" - 1:3 molar ratio of Y1 to Y2, lane "5" - 1:1 molar ratio of Y2 to Y3', lane "6" - 1:3:1.5 molar ratio of Y1 to Y2 to Y3', lane "7" - 1:3:3 molar ratio of Y1 to Y2 to Y3', lane "8" - 1:3:3:1.5 molar ratio of Y1 to Y2 to Y3' to siNC, lane "9" - 1:3:3:3 molar ratio of Y1 to Y2 to Y3' to siNC, and lane "M" - 100 bp ladder-DNA duplex markers. Dashed frame indicates siNC-DYM product.

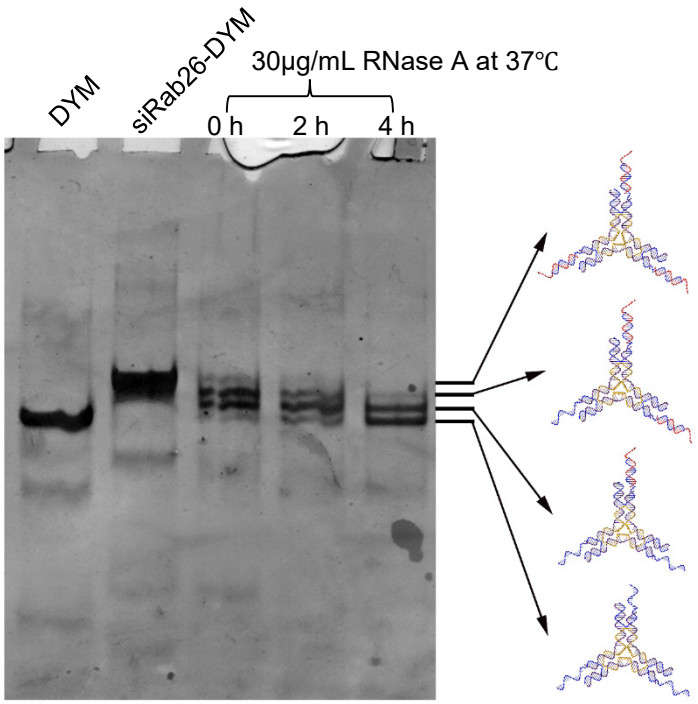

Fig. S2 Evaluating the intracellular stability of siRab26-DYM by a RNase A assay . To elucidate the advantages of siRab26-DYM over siRNA, we conducted an RNase assay to evaluate the intracellular stability of siRab26-DYM. After self-assembly, siRab26-DYM was added into the PBS containing 30 μg/mL RNase A and incubated for different time points (1 h, 2 h and 4 h). Lane "DYM"-bare DNA Y-motif nanoparticles without Rab26 siRNA; Lane "siRab26-DYM"-complete siRab26-DYM nanoparticles. Right three lanes show the degradation of siRab26-DYM after RNase treatment in different times. When subjected to a very high level (extreme) of RNase A, Rab26 siRNA cargo was degraded in a step-wise manner.

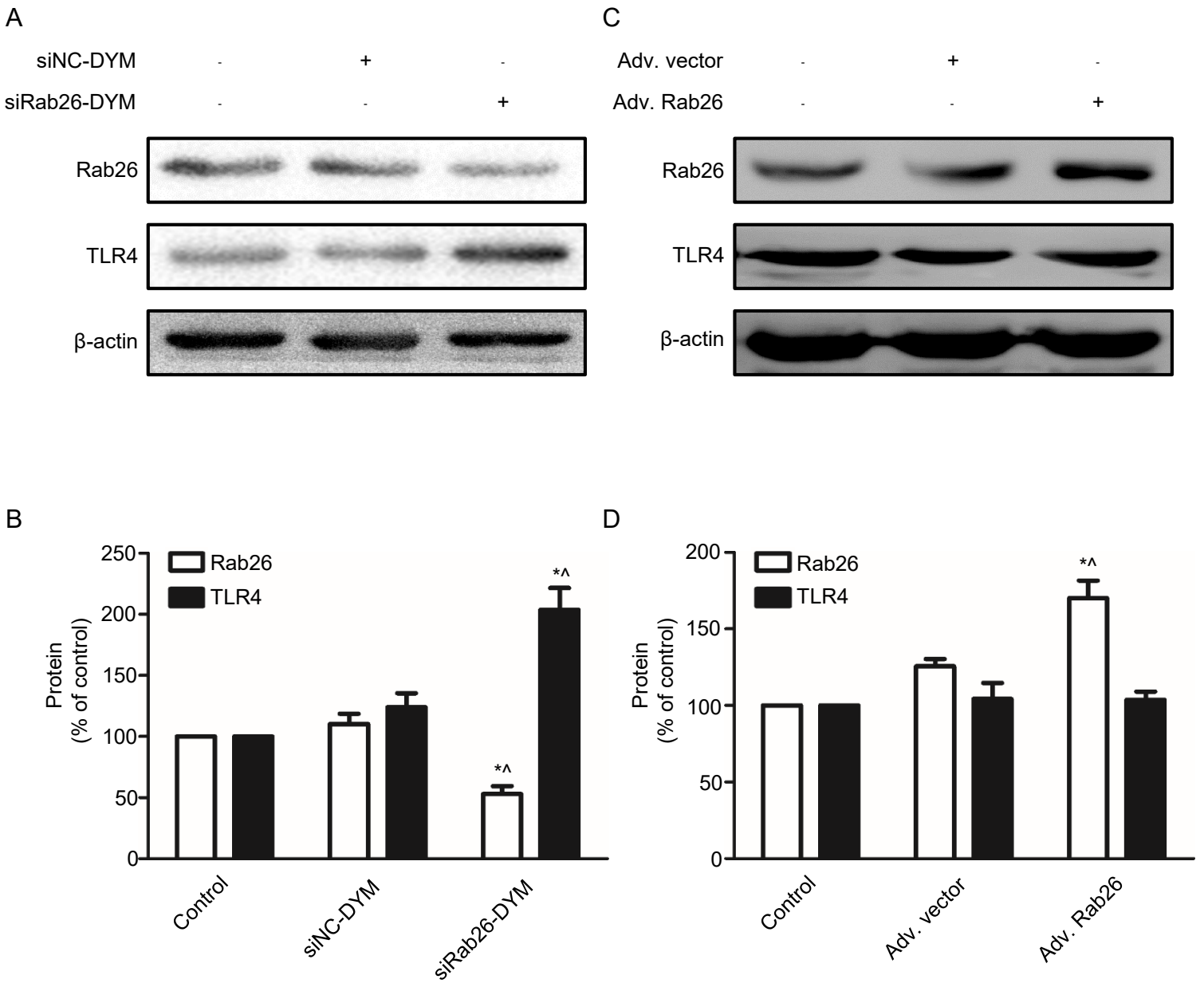

Fig. S3 Rab26 and TLR4 expression in HPMVECs treated with siNC-DYM, siRab26-DYM, Adv. vector or. Adv. Rab26. A. Rab26 and TLR4 protein expression was detected by western blot analyses after HPMVECs were treated with 50 nM siNC-DYM or 50 nM siRab26-DYM. The upper, middle and lower panels show representative bands of Rab26, TLR4 and β-actin. B. The histograms show the quantitative analysis of Rab26 and TLR4 levels, which were normalized to β-actin levels. *, $p< 0.05$ versus the control group. ^, $p< 0.05$ versus the siNC-DYM group. C. Rab26 and TLR4 protein expression was detected after HPMVECs were treated with MOI100 Adv. Rab26 or MOI100 Adv. D. Quantitative analysis of Rab26 and TLR4 levels, which were normalized to β-actin levels. *, $p< 0.05$ versus the control group. ^, $p< 0.05$ versus the Adv. vector group.

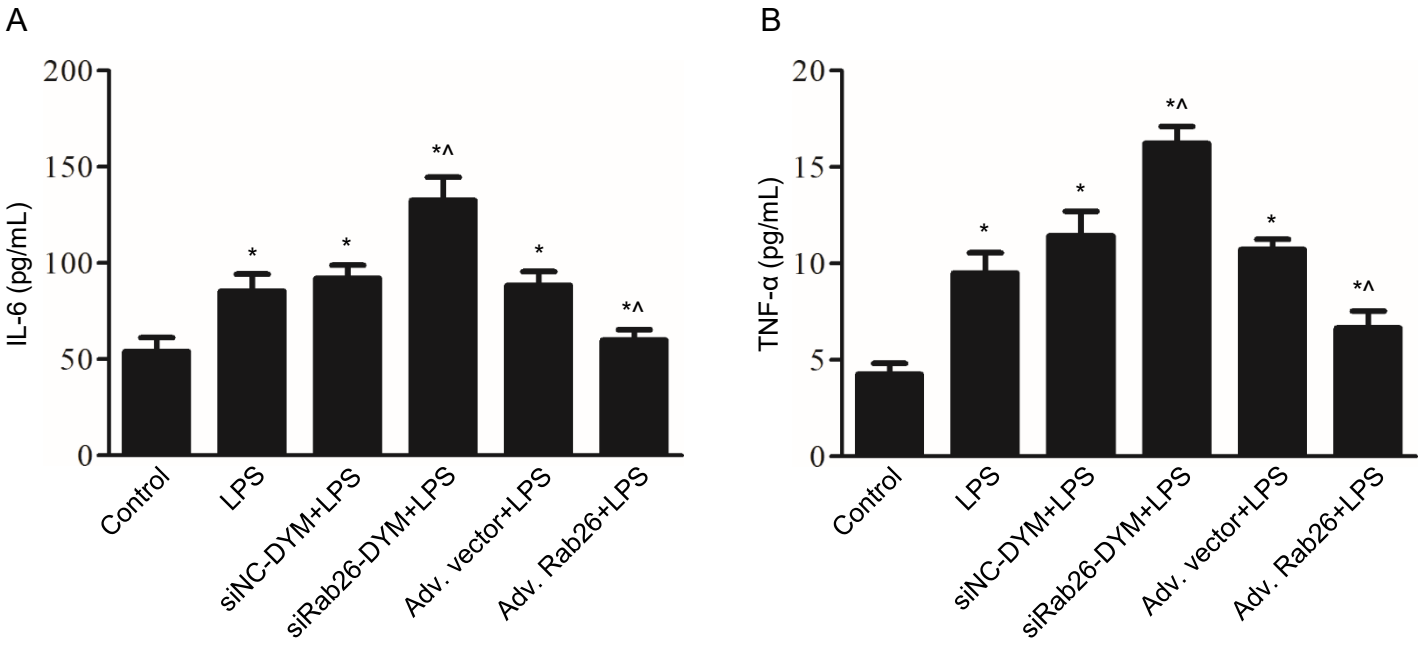

Fig. S4 Effects of Rab26 and LPS on cytokines in HPMVECs. HPMVECs were cultured in 10% serum ECM for 24 h and then divided into six groups. Two groups were cultured in fresh ECM for 36 h and treated with or without 1 μg/mL LPS for additional 24 h. Two groups were transfected with 50 nM siRab26-DYM or 50 nM siNC-DYM for 12 h, then cultured in fresh ECM for another 24 h, and treated with 1 μg/mL LPS for 24 h. Last two groups were infected with MOI100 Adv. Rab26 or MOI 100 Adv. Vector for 6 h, then cultured in fresh ECM for 24 h, and treated with 1 μg/ml LPS for 24 h. A. IL-6 concentration in supernatants of HPMVECs in different treatment groups. The data are presented as the mean ± S.E. of three separate experiments (n = 3) *, $p < 0.05$ versus the control group, ^, $p < 0.05$ versus the LPS group. B. TNF-α concentration in supernatants of HPMVECs in different treatment groups. The data are presented as the mean ± S.E. of three separate experiments (n = 3) *, $p < 0.05$ versus the control group, ^, $p < 0.05$ versus the LPS group.

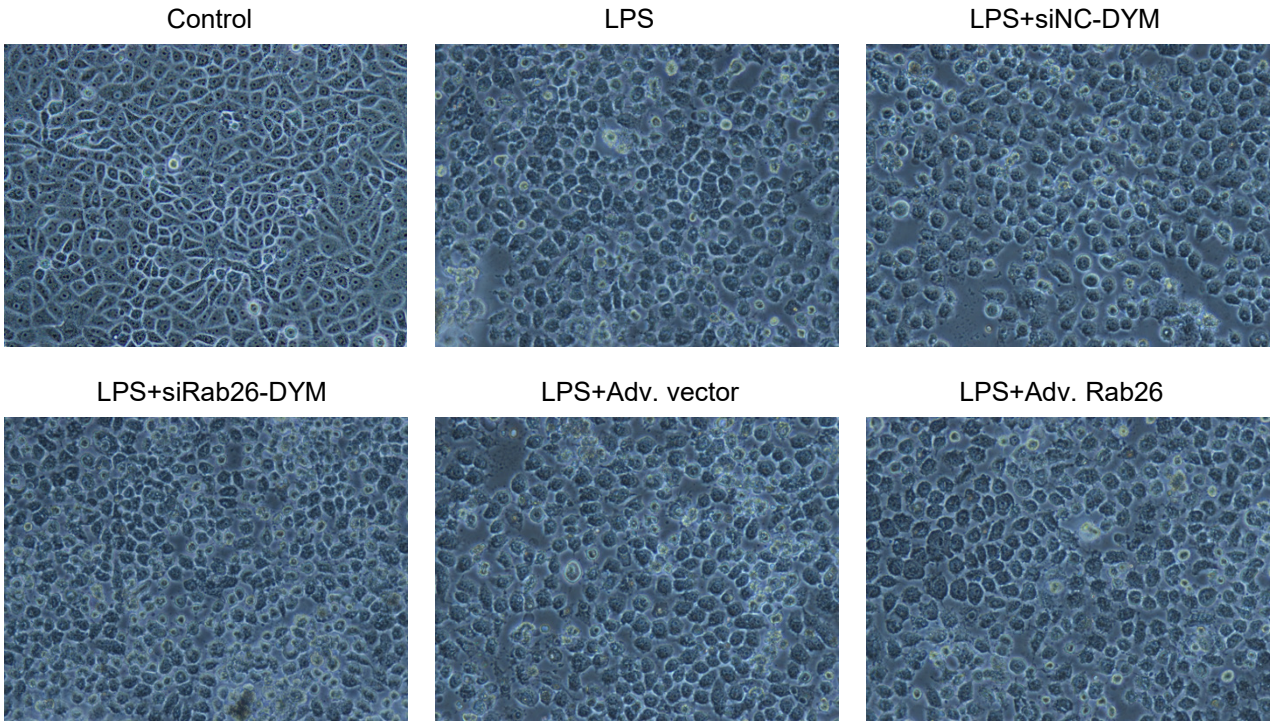

Fig. S5 Effect of Rab26 on cell morphology by optical microscope. HPMVECs were cultured in 10% serum ECM for 24 h and then divided into six groups. Two groups were cultured in fresh ECM for 36 h and treated with or without 1 μg/ml LPS for 24 h. Two groups were transfected with 50 nM siRab26-DYM or 50 nM siNC-DYM for 12 h, then cultured in fresh ECM for another 24 h, and treated with 1 μg/ml LPS for 24 h. Two groups were infected with MOI100 Adv. Rab26 or MOI 100 Adv. Vector for 6 h, then cultured in fresh ECM for 24 h, and treated with 1 μg/mL LPS for 24 h. The condition of cell in every group was observed by optical microscope (magnification: 200×).