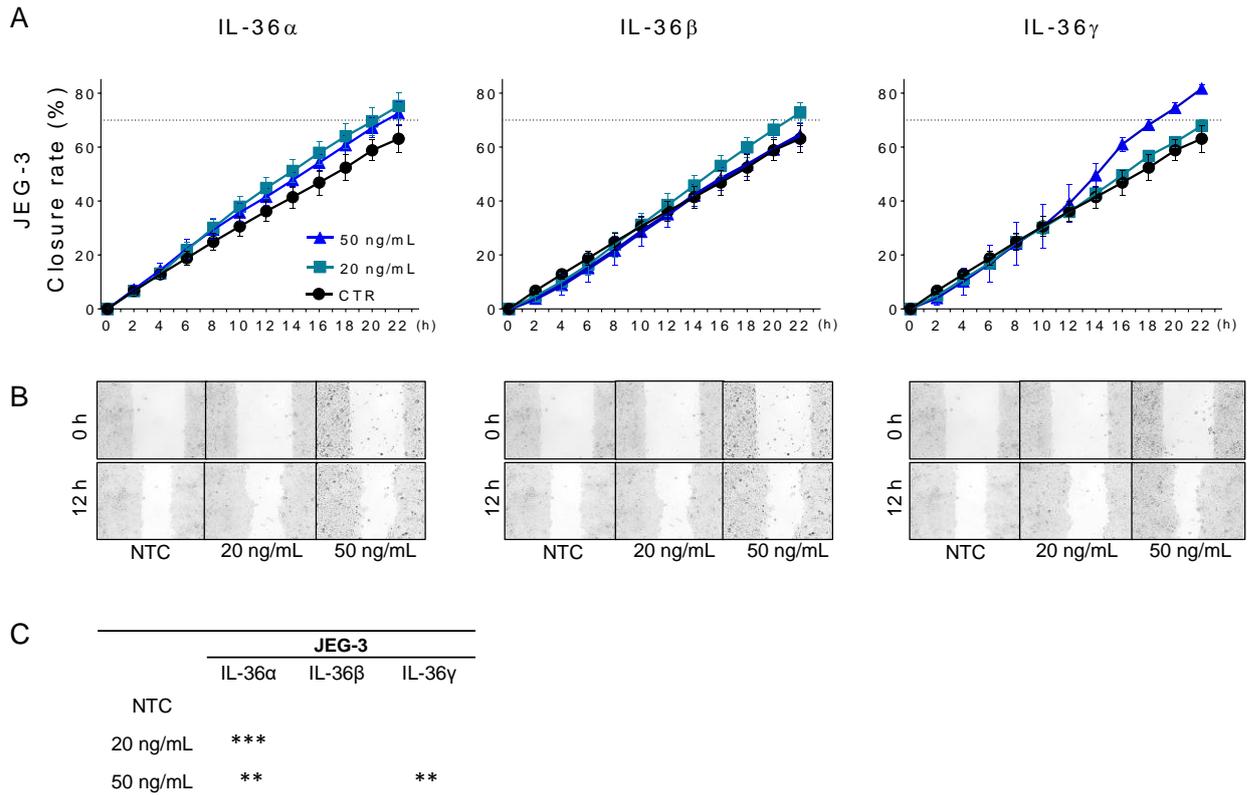
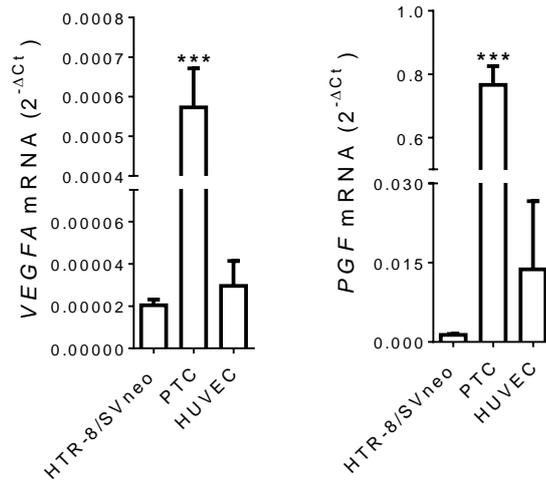


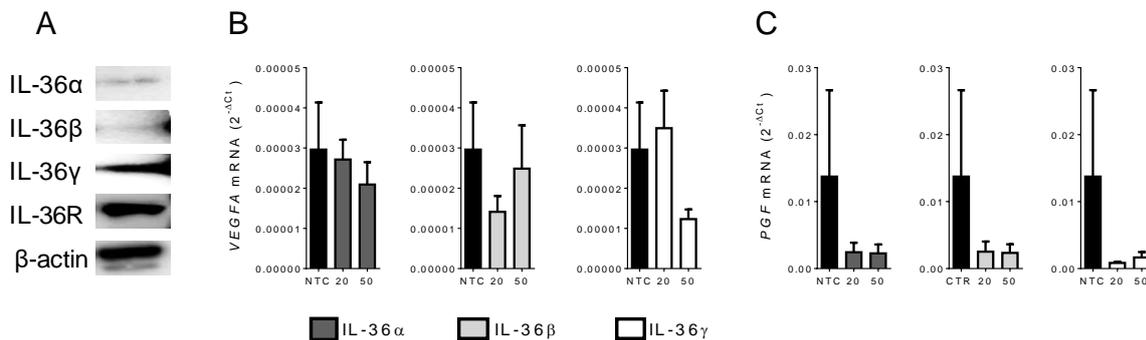
**Supplementary Figure S1. IL-36 expression induced in JEG-3 cells after poly I:C and LPS stimulation.** JEG-3 cells were cultured under standard conditions. Cells were stimulated with 25  $\mu\text{g}/\text{mL}$  of poly I:C, 100  $\text{ng}/\text{mL}$  of LPS, or medium alone as a control for 6, 12 or 24 h. The mRNA levels of *IL36A*, *IL36B*, *IL36G*, *IL36RN*, *IL1RL2* and *IL6* were determined by quantitative real-time PCR and normalized to *GAPDH* using the  $2^{-\Delta\text{Ct}}$  method. PCR results are shown as the mean  $\pm$  SEM ( $n=3$ ). One-way ANOVA with Dunnett's multiple comparisons test.  $*p < 0.05$ ,  $**p < 0.01$  for significant differences to 0 h. B) IL-36 ( $\alpha$ ,  $\beta$ ,  $\gamma$ ), IL-36R and GAPDH proteins were detected by Western blotting using 20  $\mu\text{g}$  of cell lysate from JEG-3 cells stimulated for 12h with poly I:C or LPS respectively.



**Supplementary Figure S2. Effect of recombinant IL-36 ( $\alpha$ ,  $\beta$  and  $\gamma$ ) on JEG-3 cell migration.** JEG-3 cells were seeded in both chambers of an Ibidi insert separated by a 0.5 mm divider. After 4 h attachment, the insert was removed, and recombinant IL-36 was added. The resultant gap (“wound”) was photographed every hour and closure was expressed as percentage of the initial wound. A) Closure rate curves for HTR-8/SVneo cells treated with different concentrations of IL-36 $\alpha$ , IL-36 $\beta$  or IL-36 $\gamma$ . Dashed lines denote the 70 % closure rate. B) Representative images showing cell distribution at 0 and 12 h. C) Statistical analysis of “wound healing” increase induced by IL-36 ( $\alpha$ ,  $\beta$  and  $\gamma$ ) compared to non-treated cells (NTC). Results are from three independent experiments and shown as mean  $\pm$  SEM. Two-way ANOVA with Tukey’s multiple comparisons test. \*\* $p < 0.01$ , \*\*\* $p < 0.001$  against NTC control.



**Supplementary Figure S3. VEGFA and PGF in non-stimulated cells.** HTR-8/SVneo, PTC and HUVECs were cultured under standard conditions. The mRNA levels of *VEGFA* and *PGF* were determined by quantitative real-time PCR and normalized to *GAPDH* using the 2<sup>-ΔCt</sup> method. PCR results are shown as the mean ± SEM. One-way ANOVA with Dunnett's multiple comparisons test. *p* < 0.001 for significant differences between PTC and other cell types.



**Supplementary Figure S4. HUVECs stimulated with IL-36 (α, β and γ).** A) Western blots showing IL-36 (α, β and γ) and IL-36R protein expression in non-stimulated HUVECs. Further, HUVECs were cultured under standard conditions and were stimulated with 20 and 50 ng/mL of IL-36 (α, β and γ) or medium as a control for 24 h. The mRNA levels of B) *VEGFA* and C) *PGF* were determined by quantitative real-time PCR and normalized to *GAPDH* using the 2<sup>-ΔCt</sup> method. PCR results are shown as the mean ± SEM (n=3). Unpaired two-tailed Student's t-test with Welch's correction.