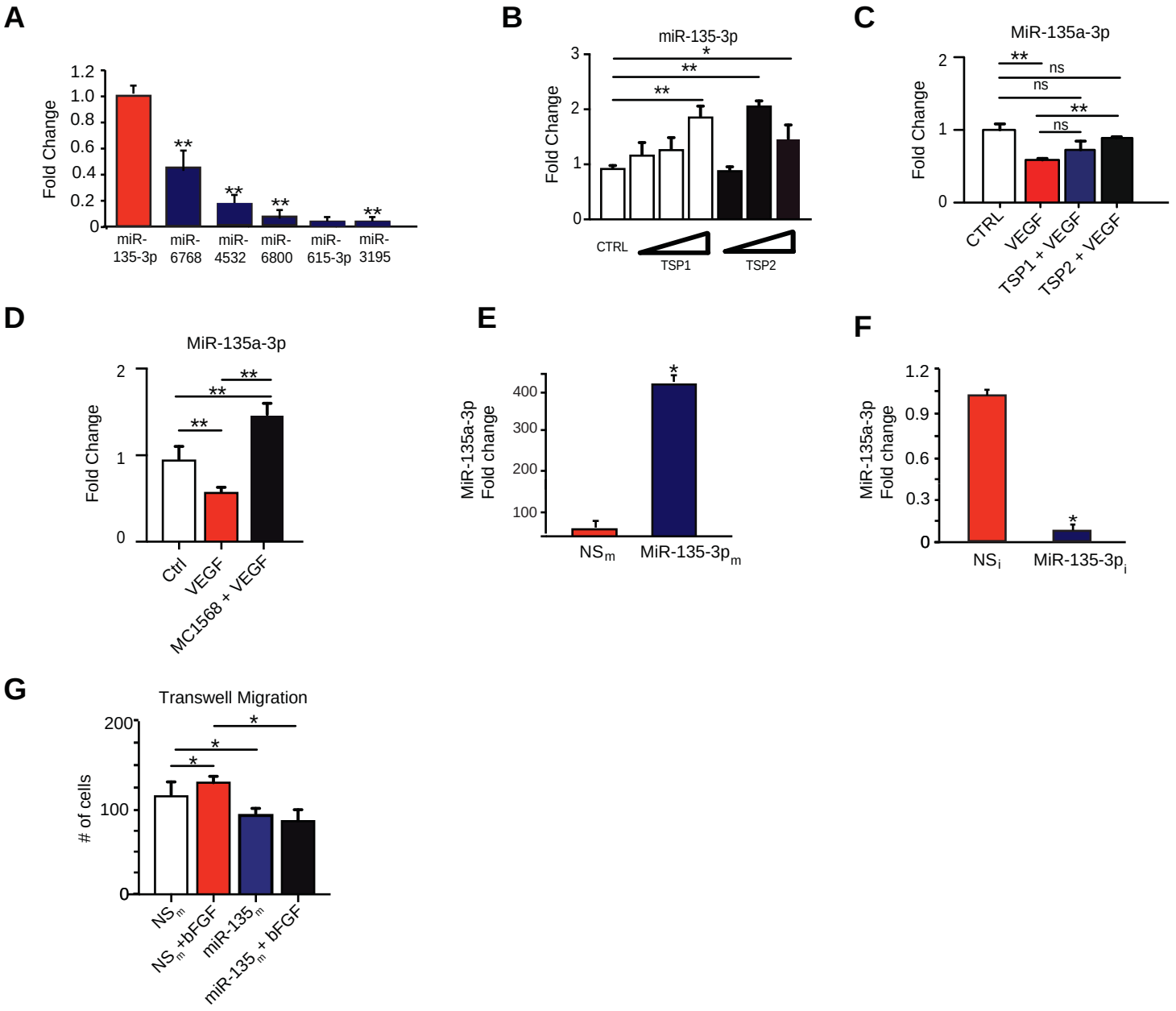
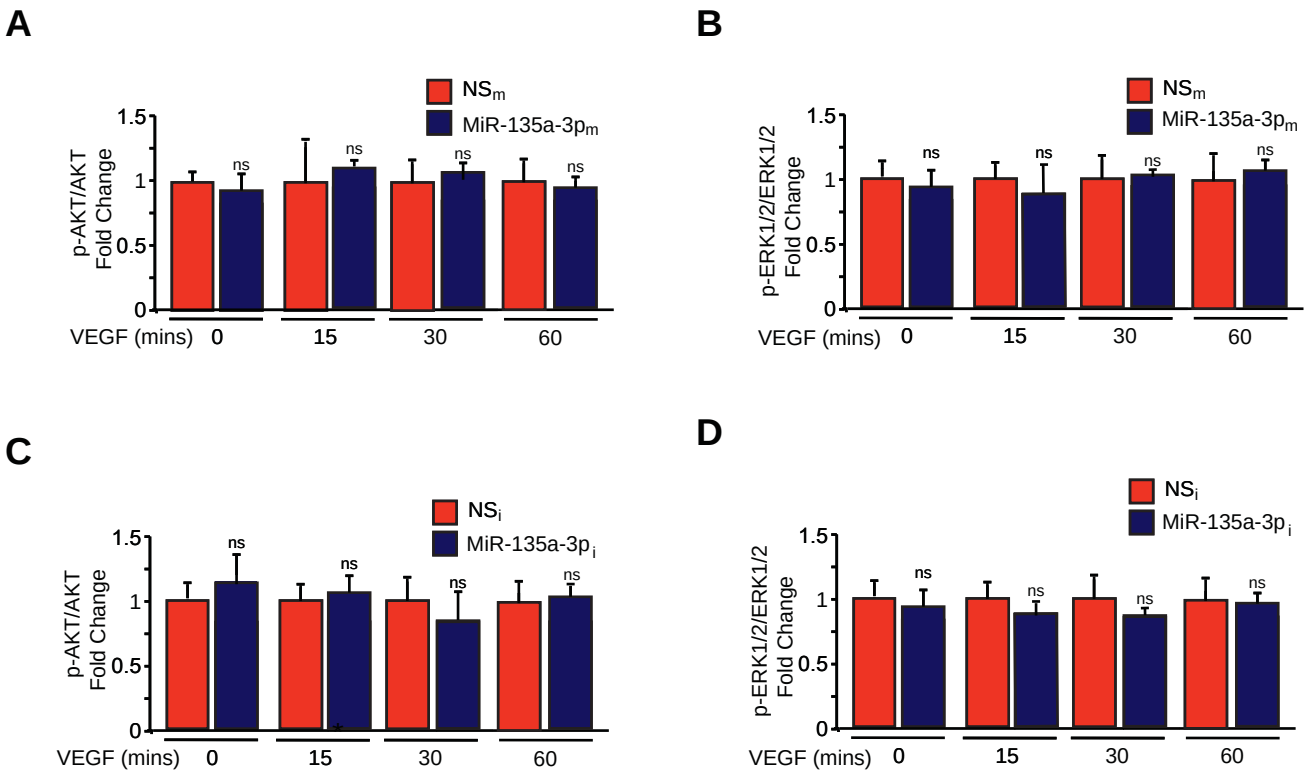
Online Figure 1



Online Figure 1. MiR-135a-3p expression and function in ECs. (A) MiR-135a-3p expression in ECs in comparison to other miRNAs by RT-qPCR. **(B-D)** HUVECs were stimulated with VEGF (50ng/ml), TSP1 (0.1, 1, 10 ug/ml respectively) or TSP2 (0.1, 1, 10 ug/ml respectively) or **(C-D)** costimulated with VEGF (50ng/ml), TSP1 (10ug/ml) or TSP2 (10ug/ml) for 12 hours (**C),** or prestimulated with MC1568 (10ng/ml) for 1 hr followed by VEGF (50ng/ml) stimulation **(D).** MiR135-3p expression was analyzed by RT-qPCR. **(E-F)** HUVECs transfected with **(E)** miR negative control (NS_m) or miR-135a-3p mimics (miR-135a-$3p_m$) or **(F)** miR inhibitor negative control (NS_i) or miR-135a-3p inhibitor (miR-135a-$3p_i$) were subjected to RT-qPCR. **(G)** HUVECs transfected with NS_m or miR-135-$3p_m$ were subjected to Transwell Boyden Chamber Assay with and without bFGF (50 ng/mL). ns, non-significant. All data represent mean ± s.e.m. * P < 0.05 compared to controls, ** P<0.01 compared to vehicle controls.

Online Figure 2



Online Figure 2. MiR-135a-3p has no effect on AKT or ERK signaling in ECs. HUVECs transfected with **(A-B)** miR negative control (NS_m) or miR-135a-3p mimics (miR-135a-3p_m) or **(C-D)** miR inhibitor negative control (NS_i) or miR-135a-3p inhibitor (miR-135a-3p_i) and treated with VEGF (50 ng/mL) were subjected to Western analysis using antibodies to p-AKT, AKT, p-ERK1/2, ERK1/2 and β-actin (n = 3 to 5 experiments). All data represent mean ± s.e.m. * $P < 0.05$ compared to controls.

Online Figure 3

A

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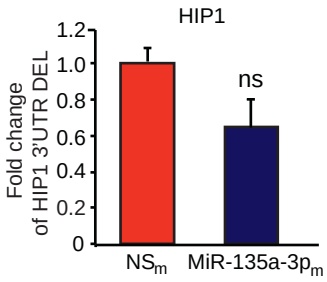
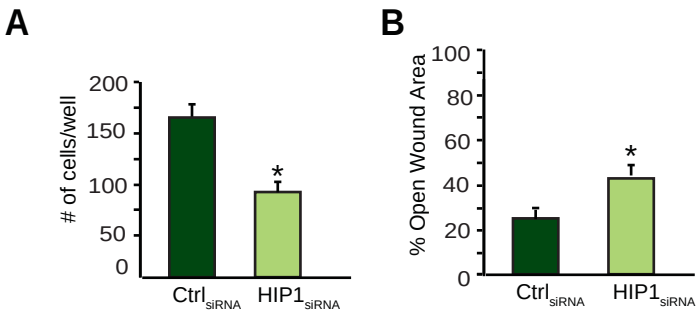
HIP1 3'UTR      TGCCCCAGGCTCTCGCTGCCCTGTG
(1636-1661)     :| ||     | | ||| |:       | ||| |:| :
miR-135a-3p     GCGG-TGCCGAGG--TTAGGGATA T
Deletion site   TGCCCCAGGCTCTCGCTGCCCTGTG
```

B



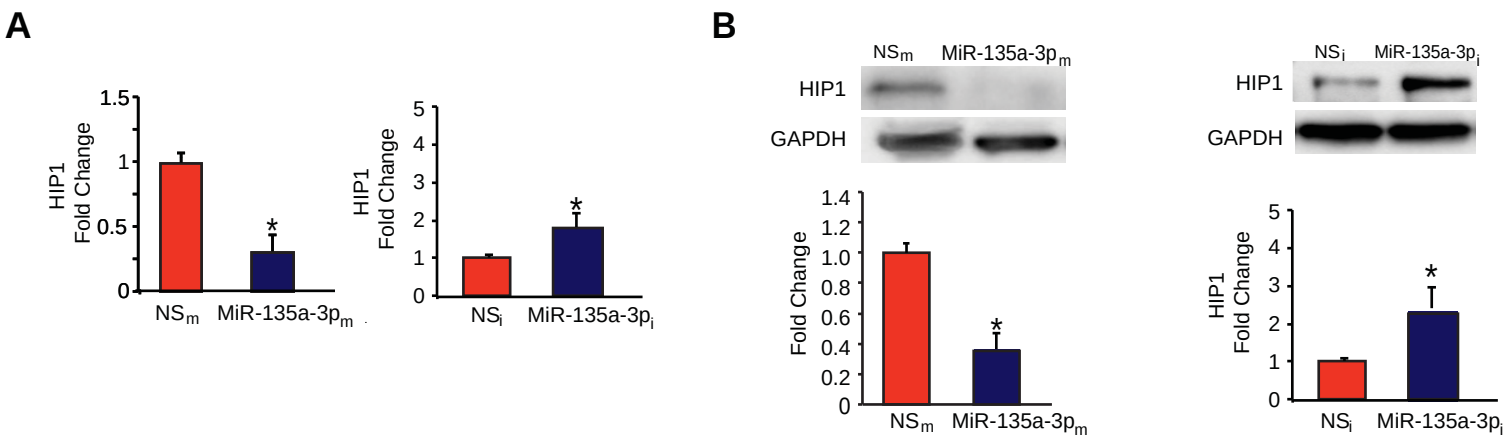
Online Figure 3. MiR-135a-3p targets HIP1 in ECs. (A) Binding sites in HIP1 3'UTR for miR-135-3p were predicted by rna22. The positions of binding sites are indicated as numbers in parentheses. Lines indicate perfect matches, while colons indicate G:U pairs. Nucleotides marked in red were deleted to generate deletion constructs (DEL) of 3'-untranslated region (UTR). **(B)** Luciferase activity of HIP1 3'- UTR deletion constructs (DEL-3'UTR) normalized to total protein was quantified in HUVECs transfected with NS_m or miR-135a-$3p_m$, (n = 3 experiments). Deletion of miR-135a-3p binding site impaired miR-135a-3p's inhibitory effect on HIP1. 3'UTR.All data represent mean ± s.e.m. * $P < 0.05$ compared to controls.

Online Figure 4



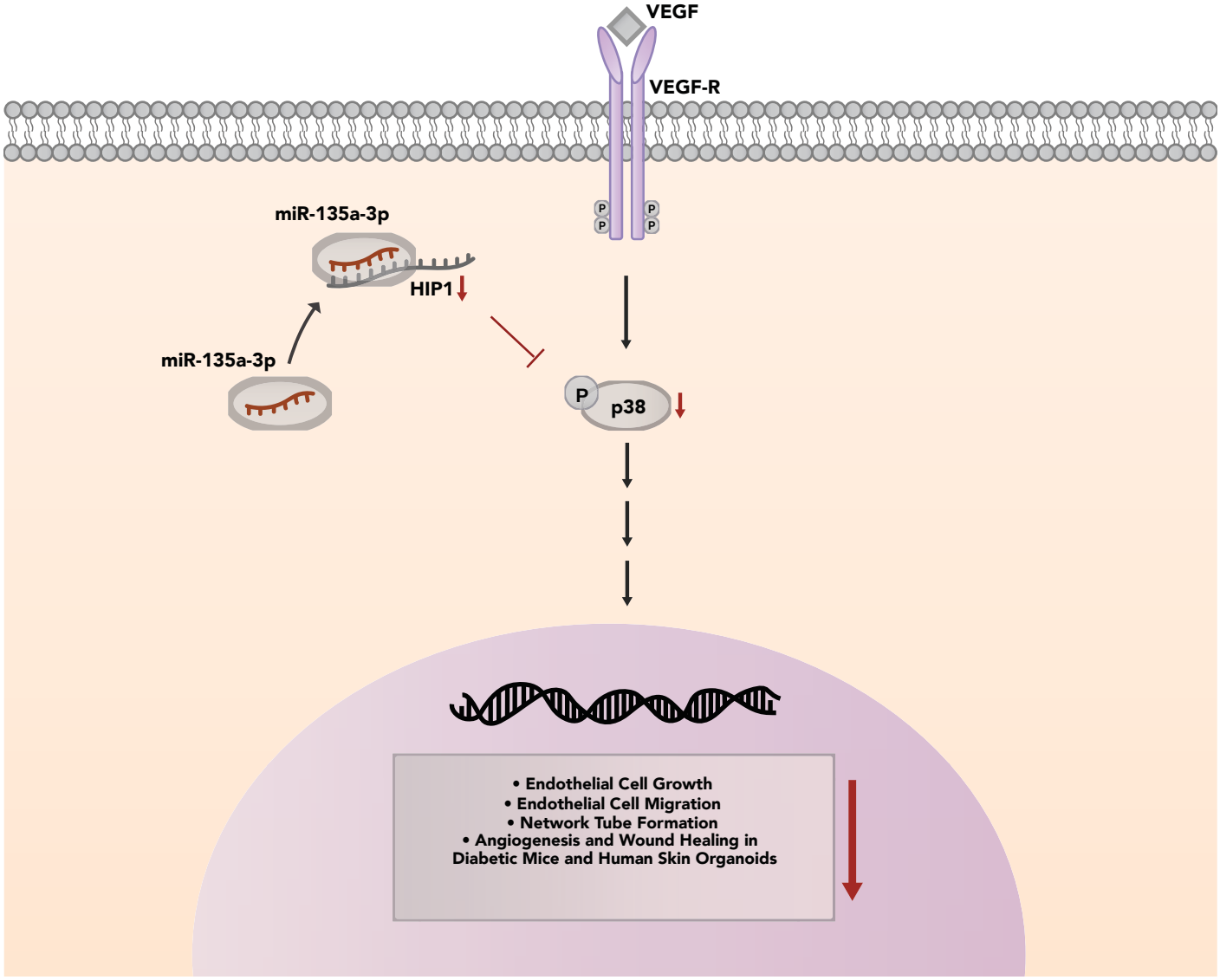
Online Figure 4. siRNA-mediated knockdown of HIP1 reduces endothelial cell (EC) migration. HUVECs were transfected with siRNA to HIP1 **(A-B)**, or scrambled control (ctrl) siRNA. Migration of ECs were quantified by Boyden transwell chamber assay **(A)** or by scratch assay **(B)**. *P < 0.01. Results are representative of n = 3 replicates per group. All data represent means ± s.e.m.

Online Figure 5



Online Figure 5. Validation of miR-135-3p target HIP1 in human skin organoids. Human skin organoids transfected with miR negative control (NS_m), miR-135a-3p mimics (miR-135a-$3p_m$), NS_i, or miR-135a-$3p_i$ were subjected to RT-qPCR analyses for HIP1 **(A)** expression or Western blot analyses using antibody to HIP1 **(B)**, and GAPDH (n = 3 experiments). *P < 0.001; All data represent means ± s.e.m.

Online Figure 6



Online Figure 6. MiR-135a-3p inhibits VEGF activation of p38 signaling by targeting HIP1 in endothelial cells (ECs). Consequently, endothelial cell growth, migration, network tube formation, angiogenesis and wound healing in mouse and human skin models are significantly impaired.