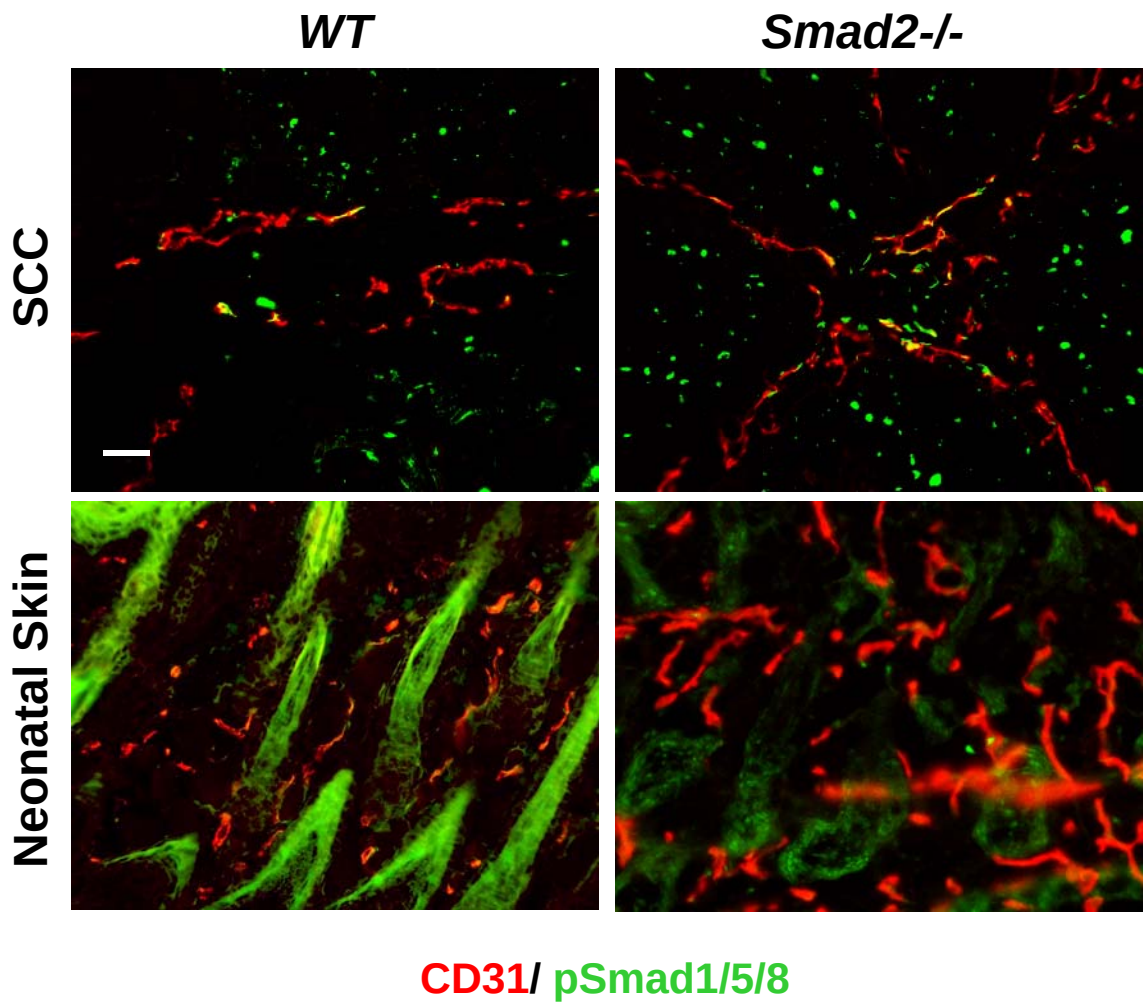
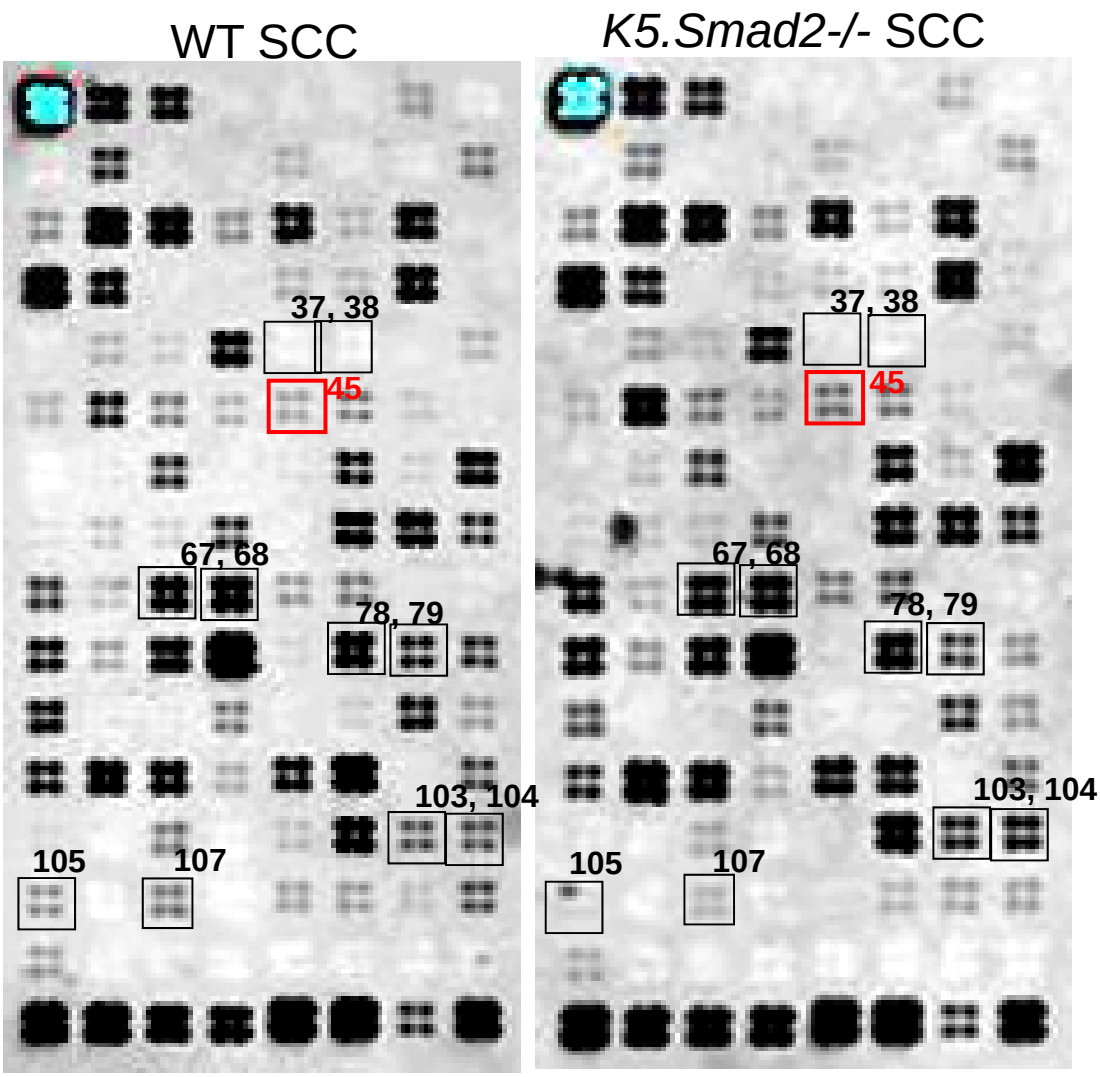
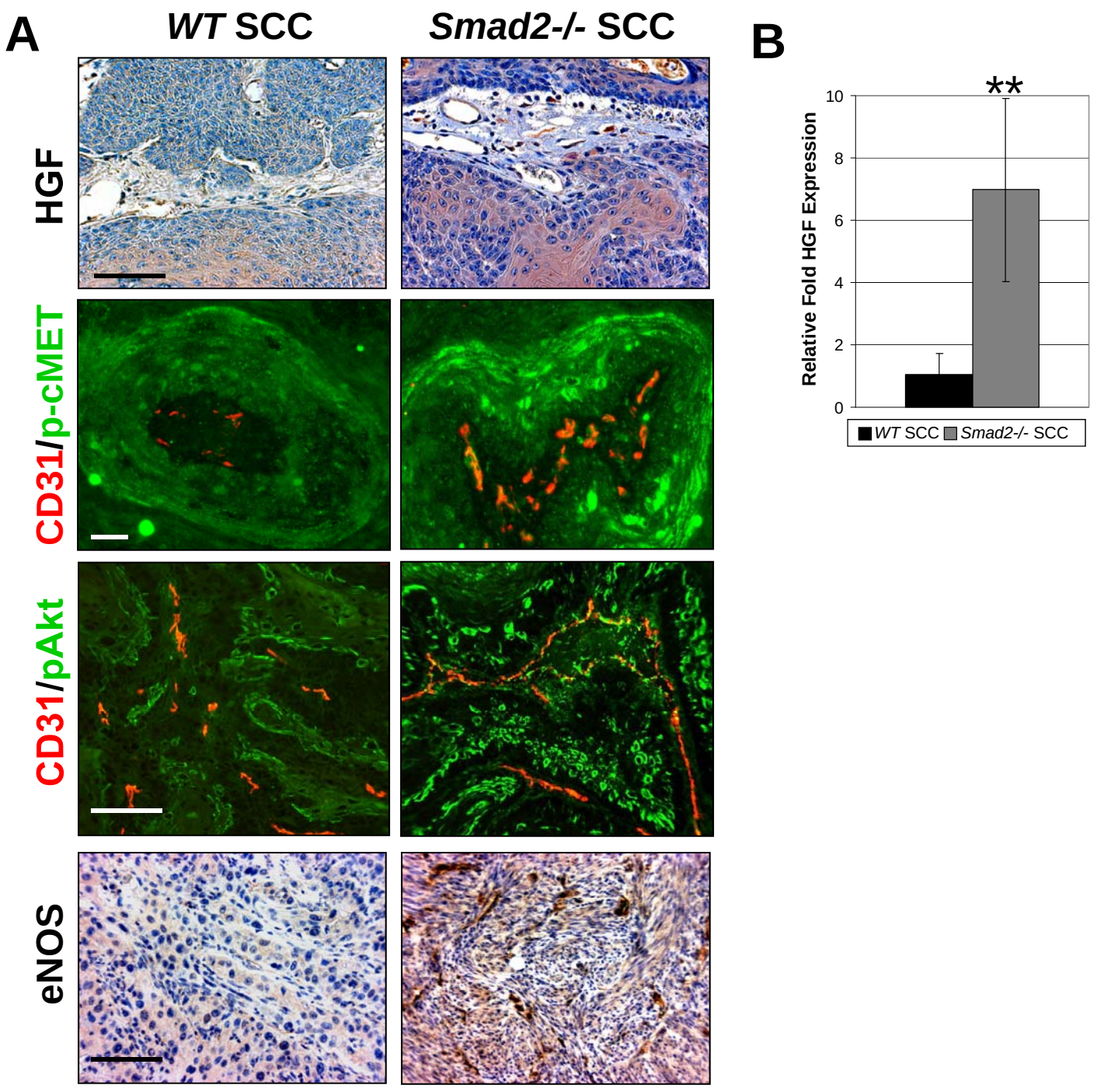


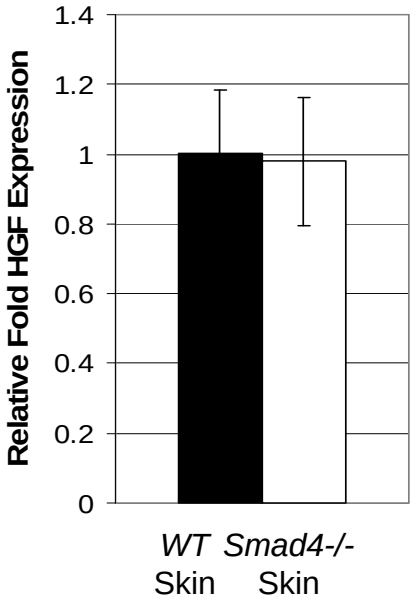
Supplemental Figure 1. ***K5.Smad2-/-*** **SCCs and neonatal skin lack TGFβ-mediated mediated angiogenesis.** Smad2 deficient mice lacked activation of TGFβ-downstream mediators pSmad1, -5, and -8 (CD31 in red, pSmad1/5/8 in green) in endothelial cells. Scale bar in the first panel represents 100μm for all panels.



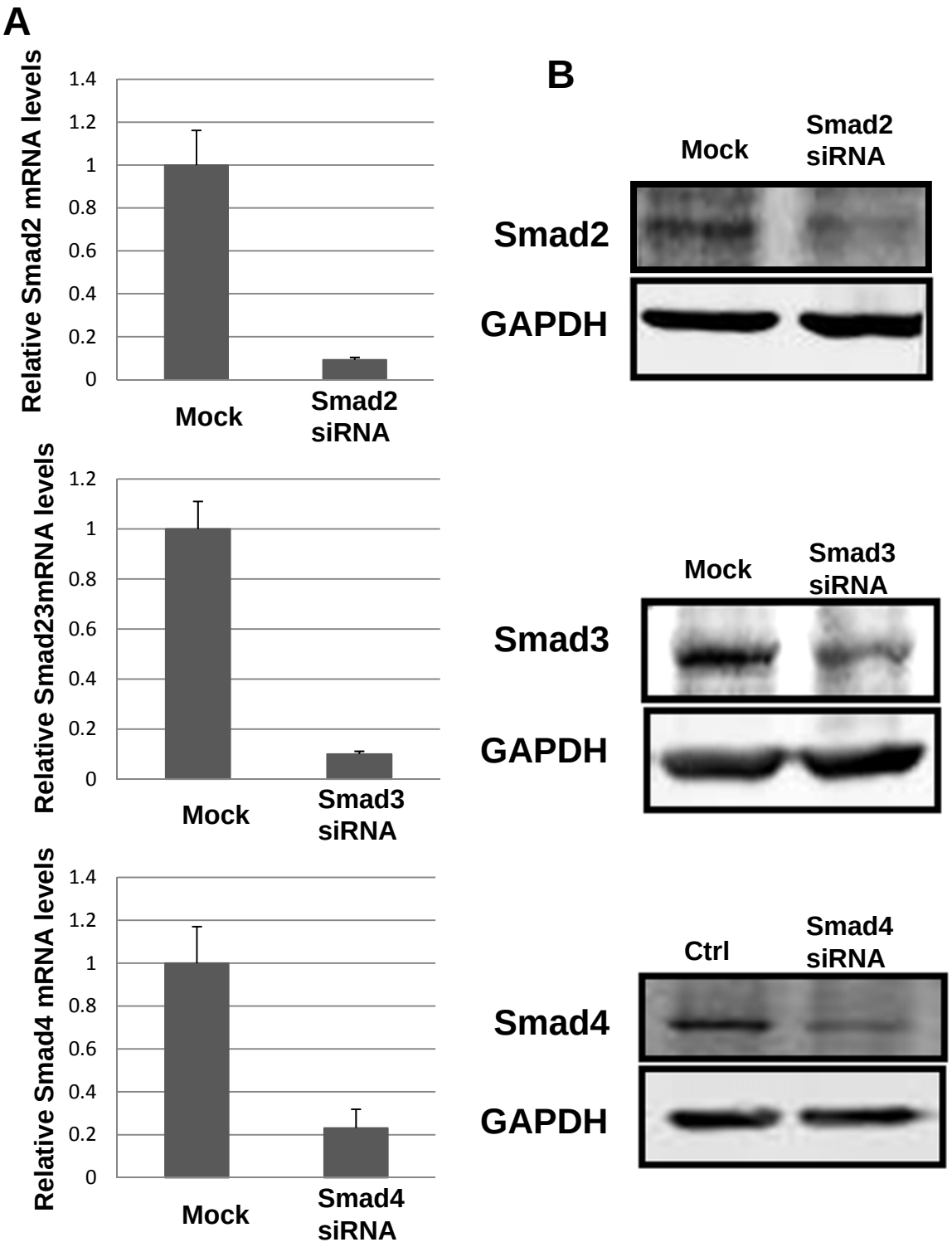
Supplemental Figure 2. Representative cancer pathway superarray with angiogenic markers identified. Markers boxed in black are angiogenesis-related molecules which do not contribute to *K5.Smad2-/-* SCCs when compared to WT SCCs. Upregulated HGF is boxed in red. 107—VEGFa (downregulated), 103, 104–TIMPS (upregulated), 105–TNFα (downregulated), 67--MMP2 (unchanged), 68--MMP9 (unchanged), 37--FGF1 (unchanged), 38-- FGF2 (unchanged), 78–PDGFa (unchanged), 79–PDGFb (downregulated). n=3 samples per group.



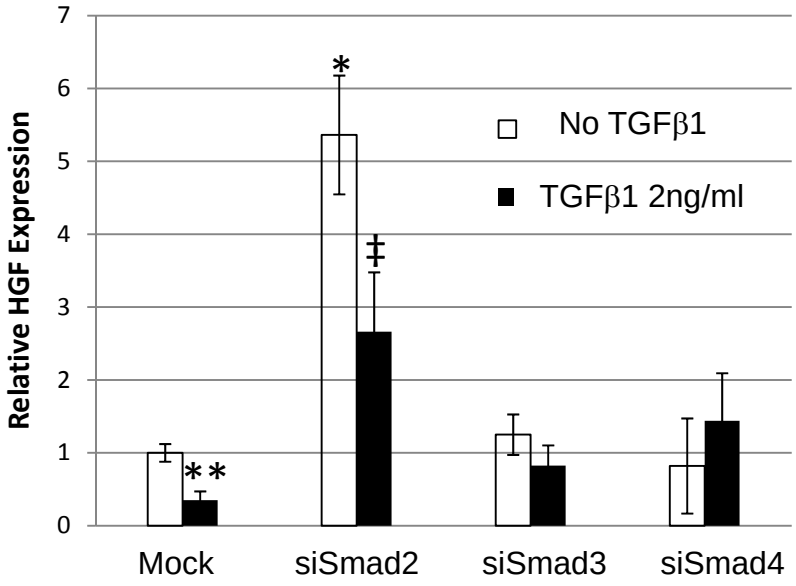
Supplemental Figure 3. Increased HGF with activation of downstream mediators in tumor epithelia and endothelia in *K5.Smad2-/-* SCCs. A: Immunohistochemistry (IHC) of HGF showing stronger HGF staining in a *K5.Smad2-/-* SCC compared to a *wildtype (WT)* SCC primarily in tumor epithelia (first panel). Immunofluorescence (IF) of activated HGF receptor, p-c-Met (Green) an endothelial cell marker CD31 (red) shows that a *K5.Smad2-/-* SCC has increased p-c-Met in both tumor epithelia and vessels compared to a *WT* SCC (second panel). Consistently, HGF downstream targets, pAKT (green by IF, CD31 counterstained in red, third panel) and eNOS (brown by IHC, fourth panel) were increased in tumor epithelia and vessels in a *K5.Smad2-/-* SCC compared to a *WT* SCC. Scale bars represent 100μm. **B**: qRT-PCR revealed that *K5.Smad2-/-* SCCs had 7-fold increase in HGF mRNA level compared to *WT* SCCs. HGF level in *WT* SCCs was arbitrarily assigned as "1". Five SCC samples in each group were used. ** $p<0.01$.



Supplemental Figure 4. Lack of HGF expression in *K5.Smad4-/-* skin. *K5.Smad4-/-* neonatal skin shows normal HGF expression determined by qRT-PCR. HGF level in *WT* skin was arbitrarily assigned as "1". Five skin samples in each group were used.



Supplemental Figure 5. Knockdown of Smads by siRNA 72h after siRNA transfection. **A**: qRT-PCR; **B:** Western analysis. Primary antibodies: rabbit anti-human-Smad2 (Zymed,1:1,000), rabbit anti-human-Smad3 (Santa Cruz Biotechnologies, 1:1,000), mouse monoclonal anti-human-Smad4 (Santa Cruz Biotechnologies, 1:1,000. Anti-human GAPDH (Santa Cruz Biotechnologies, 1:5,000) was used as a loading control.



Supplemental Figure 6. Smad2 knockdown caused increased HGF expression with or with TGFβ1 treatment. Individual Smads were knocked down 72h, and TGFβ1 (final concentration of 2ng/ml) or PBS was added 2h prior to cell harvest. qRT was performed for HGF levels. HGF level in mock-transfected HaCaT cells without TGFβ1 treatment was arbitrarily set as "1". Data are expressed as Mean±SE (n=8). *: $p<0.05$ and **:$p<0.01$, compared to mock-transfected cells; ‡: $p<0.05$ compared to mock-transfected, TGFβ1-treated cells.