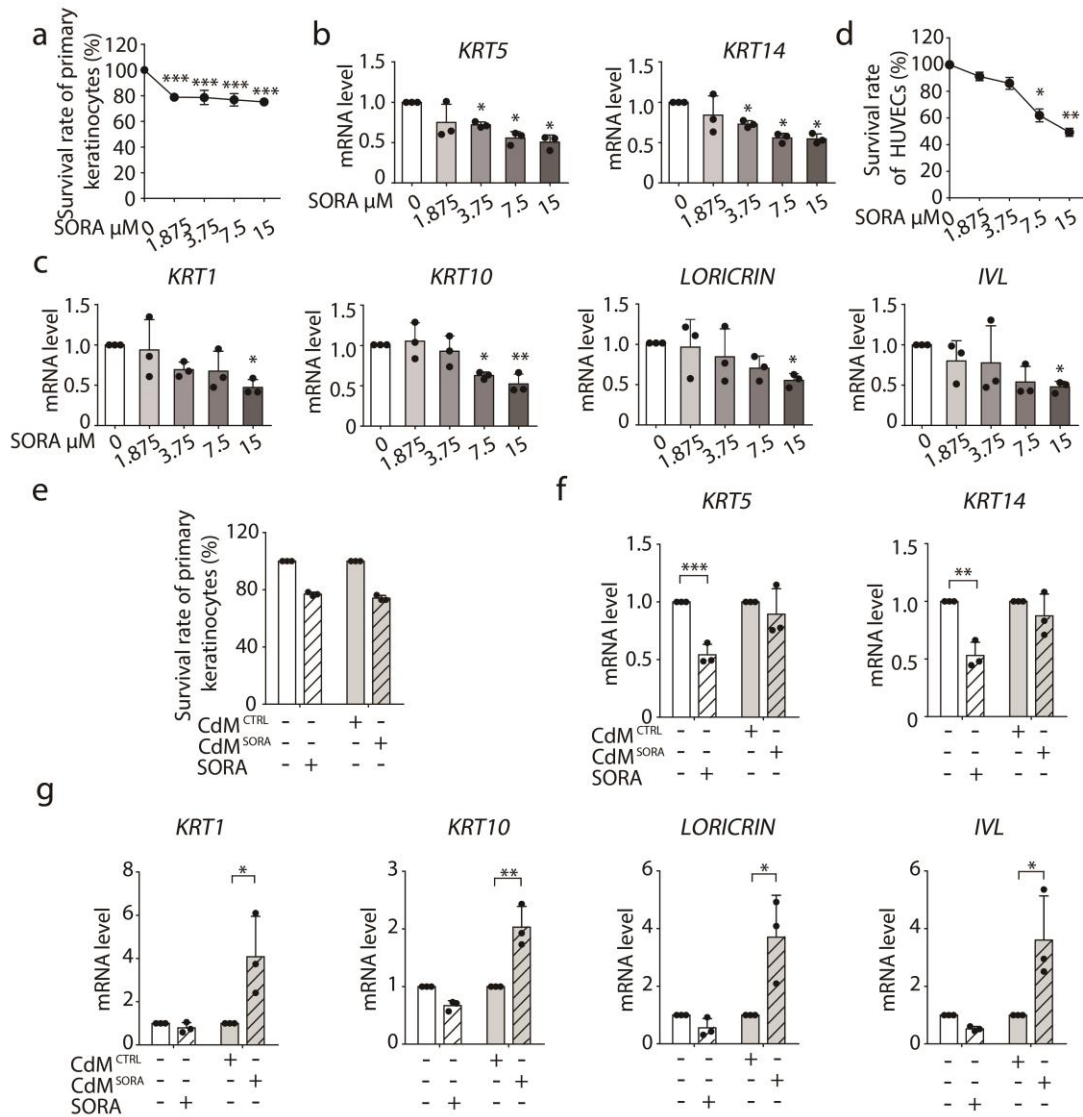


## Supplementary Figure S1



**Fig. S1 Vascular endothelial cells participate in sorafenib-induced hyper-keratosis in human primary keratinocytes.**

**a** Human primary keratinocytes were treated with 0-15  $\mu\text{M}$  sorafenib for 24 h. Cell survival rate was detected by SRB colorimetric assay (N = 3). **b, c** Human primary keratinocytes were treated with 0-15  $\mu\text{M}$  sorafenib for 24 h. The transcription levels of proliferation markers (**b**) and differentiation markers (**c**) were measured by RT-qPCR (N = 3). **d** HUVECs were treated with 0-15  $\mu\text{M}$  sorafenib for 72 h. Cell survival rate was detected by SRB colorimetric assay (N = 3). **e** Human primary keratinocytes were treated with supernatants from HUVECs exposed to 0 or 15  $\mu\text{M}$  sorafenib (CdM<sup>CTRL</sup> or CdM<sup>SORA</sup>) for 24 h. Cell survival rate was

detected by SRB colorimetric assay (N = 3). **f, g** Human primary keratinocytes were treated with supernatants from HUVECs with or without sorafenib exposure (CdM<sup>CTRL</sup> or CdM<sup>SORA</sup>) for 24 h. **(f)** The transcription levels of *KRT5* and *KRT14* were measured by RT-qPCR (N = 3). **(g)** The transcription levels of *KRT1*, *KRT10*, *LORICRIN* and *IVL* were measured by RT-qPCR (N = 3). The results in **(a)**, **(b)**, **(c)**, **(d)**, **(e)**, **(f)** and **(g)** are presented as the mean  $\pm$  SD. Statistical analyses were performed using unpaired two-tailed Student's t-test in **(f)** and **(g)**. Statistical analyses were performed using one-way ANOVA with LSD post hoc test in **(a)** and when comparing the levels of *KRT10* in **(c)** and with Dunn's post hoc test in **(b)**, **(d)** and when comparing the levels of *KRT1*, *LORICRIN* and *IVL* in **(c)**. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . SORA, sorafenib; CdM, HUVECs conditional medium; CTRL, control; SRB, sulforhodamine B.