Supplementary Figures:

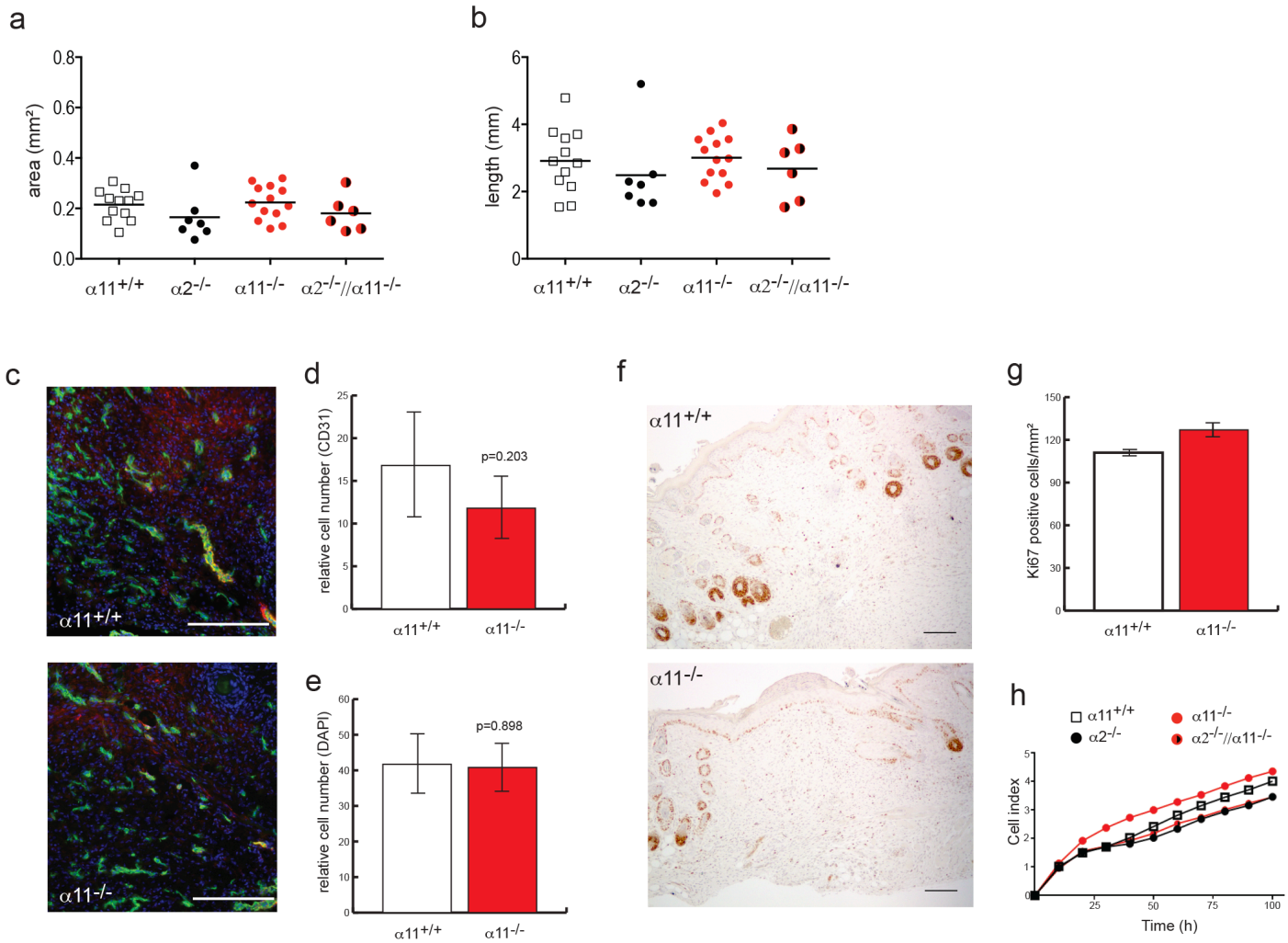

Figure S1: No significant alterations in neo-epidermis, vasculature and cell proliferation in wounds from mice lacking α11β1.

(**a**) Histomorphometric quantification of HE-stained mid-wound sections from α11β1 controls ($\alpha11^{+/+}$) and mice deficient for integrin α2β1 ($\alpha2^{-/-}$), α11β1 ($\alpha11^{-/-}$) and both integrins ($\alpha2^{-/-}//\alpha11^{-/-}$) at d7 after wounding (representative images shown in Figure 4a). No significant differences were observed regarding area (**a**) or length (**b**) of the newly formed epithelium covering the wounds. Each symbol represents one wound, 3-5 sections per wound were analyzed. Data were evaluated by one-way ANOVA and a Tukey's multiple comparison test. (**c**) Immunofluorescence images of mid-wound sections from control ($\alpha11^{+/+}$) and α11β1-null mice ($\alpha11^{-/-}$) at 7 days after injury were stained with DAPI to visualize cell nuclei (blue) and double-stained with CD31 antibodies to illustrate blood vessel endothelium (green) and αSMA antibodies depicting myofibroblasts and capillary walls (red). Scale bar = 200μm. (**d**) Histomorphometric analysis revealed no significant differences in either overall cell density per unit area of granulation tissue (**e**) or in area occupied by blood vessels (d). N=4 α11-null and N=5 control mice were analyzed. (**f**) Proliferative cells in wound sections from control ($\alpha11^{+/+}$) and α11β1-null mice ($\alpha11^{-/-}$) at 7 days after injury were detected by immunostaining of Ki-67. Scale bar = 250μm. (**g**) Histomorphometric analysis showed no significant differences in cell proliferation per unit area of granulation tissue. (**h**) $\alpha11^{+/+}$, $\alpha11^{-/-}$, $\alpha2^{-/-}$ and $\alpha2^{-/-}//\alpha11^{-/-}$ were seeded and the occupied area was measured over time, using the xCelligence system. Increase of cell index over time was similar in all samples, indicating a similar proliferation rate.

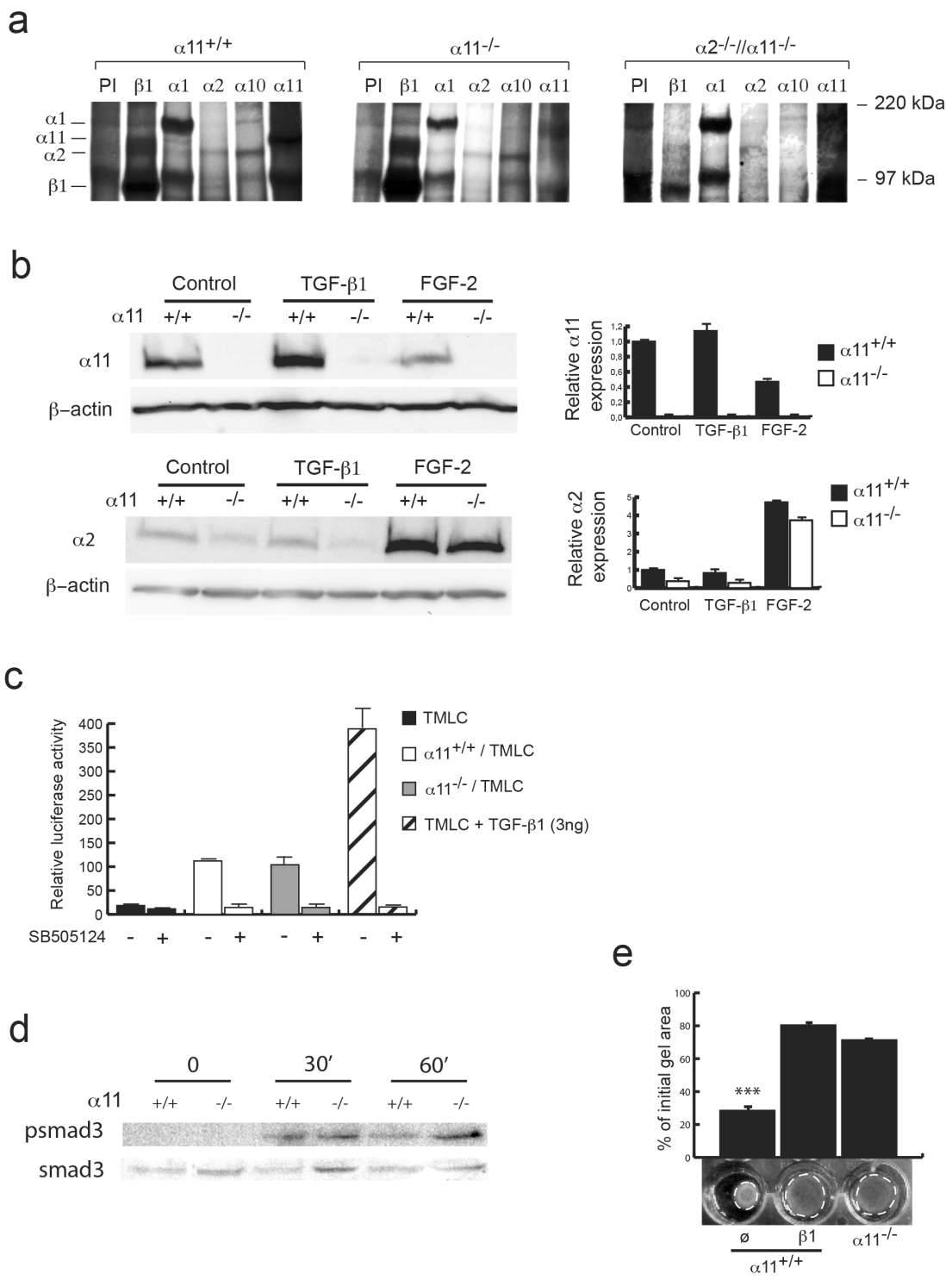

Figure S2: Regulation of α11β1 integrin by TGF-β.

(**a**) Metabolic labeling and immunoprecipitation of integrins in immorto skin fibroblasts. Protein extracts from cultured ^{35}S metabolically labeled $\alpha11^{+/+}$, $\alpha11^{-/-}$ or $\alpha2^{-/-}//\alpha11^{-/-}$ skin fibroblasts were immunoprecipitated with control pre-immune serum (PI) and antibodies to mouse β1, α1, α2, α10 and α11 integrin chains and analyzed by SDS-PAGE followed by fluorography. (**b**) $\alpha11^{+/+}$ and $\alpha11^{-/-}$ primary mouse skin fibroblasts, seeded on collagen I (100μg/ml), were treated with TGF-β1 (5ng/ml) or FGF-2 (20ng/ml) for 24 hours. Protein expression was then analyzed by Western blotting. α11, α2 and αSMA band intensities were normalized to β-actin. (**c**) TMLC cells were co-cultured with $\alpha11^{+/+}$ or $\alpha11^{-/-}$ skin fibroblasts or cultured alone as control, treated with or without SB505124 (10μM). TGF-β1 (3ng/ml) was used as positive control. Luciferase activity was determined after 24h of incubation. (**d**) Primary fibroblasts seeded on collagen were treated with TGF-β1 (5ng/ml). 0, 30 or 60min after treatment, proteins were extracted and analyzed by Western blotting for detection of Smad3 phosphorylation. (**e**) Primary $\alpha11^{+/+}$ and $\alpha11^{-/-}$ fibroblasts were allowed to contract floating collagen gels for 24h in presence of 2% serum. Integrin β1 blocking antibody Ha2/5 (10μg/ml) was added. Contracted gels are depicted with dash lines. (***, $p<0.001$; mean ±SD).

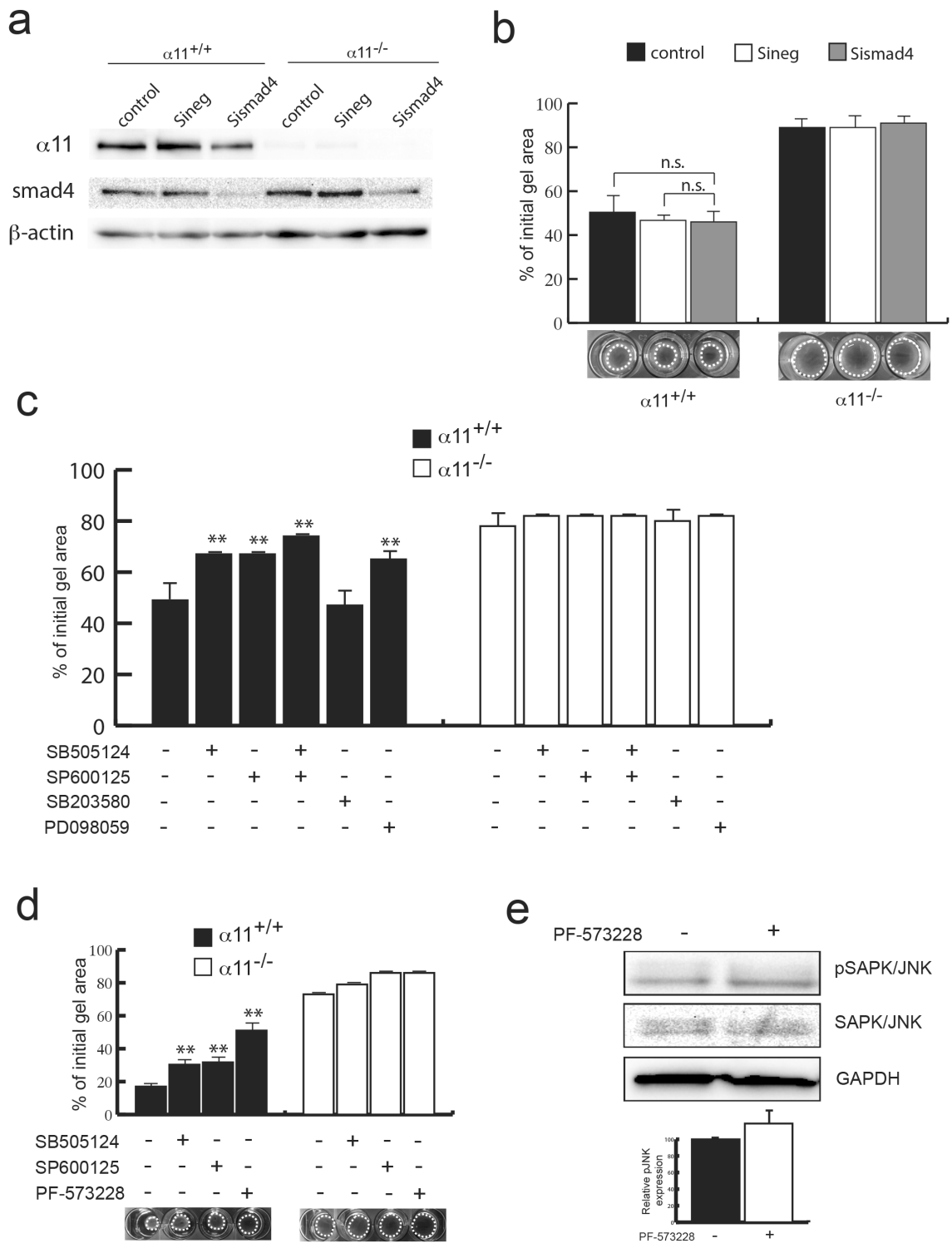

Figure S3: Signaling pathways involved during collagen reorganization.
(**a**) Primary fibroblasts were transfected with non-targeting siRNA (sineg) or Smad4 siRNA (sismad4). Untransfected cells are used as another control. Efficiency of Smad4 knock-down were analysed by Western blotting 72h after transfection. (**b**) Impact of Smad4 knock-down on collagen remodeling. Primary siRNA-transfected fibroblasts were allowed to contract floating collagen gels for 24h in presence of 2% serum. Contraction was assessed photographically. (**c**) Effect of signaling inhibitors on collagen gel remodeling stimulated with 2% serum. Analysis was performed using SB505124 (10µM), SP600125 (25µM), SB203580 (10µM) and PD098059 (5µM). (**d**) Impact of FAK inhibitor PF-573228 (10µM) on collagen gel remodeling. Contraction was assessed photographically. The contracted gels are depicted with dash lines. (**e**) Effect of PF-573228 on JNK phosphorylation in a11$^{+/+}$ fibroblasts during collagen gel contraction. (**, p<0.001; n.s., not significant; mean ±SD).

Supplementary Material and methods:

Preparation of protein lysates and immunoblotting

A 4mm punch biopsy from GTs or collagen lattices were mechanically homogenized (2min at 30Hz, Mixer Mill, Retsch) in RIPA buffer (150mM NaCl, 50mM Tris base, 0.1% sodium dodecyl sulfate, 12mM deoxycholate, 1% Nonidet-P40, 1% Triton X-100, pH 8), supplemented with protease inhibitors (Roche Diagnostics). Debris was removed by centrifugation and protein concentration was determined by BCA assay (BioRad) according to manufacturer's protocol. Of cleared lysates, 20µg were analyzed by SDS-PAGEand blotted onto PVDF membranes (Millipore).

The following antibodies were used: α11 and α2 integrin (generated as previously described (Popova *et al.*, 2004; Zhang *et al.*, 2006), 1:500), α-SMA 1A4 and β-actin AC15 (Sigma-Aldrich, Oslo, Norway; 1:5000), phospho-smad3, smad3, smad4, phospho-c-jun, c-jun, phospho-SAPK/JNK (Thr183/Tyr185) and SAPK/JNK (Cell Signaling Technology, Lysaker, Norway; 1:1000). Membranes were photographed using the ChemiDoc XRS device and the Quantity One 1-D Analysis Software (Biorad). Band intensities in western blots were quantified using Image J software (Rasband, W.S., ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA, http://rsb.info.nih.gov/ij/, 1997-2008).

Immunoprecipitation

Immunoprecipitation was assessed as previously described (Tiger *et al.*, 2001). The following antibodies were used: α1 integrin Ha 31/8, α2 integrin Ha 1/29 and β1 integrin Ha 2/5 (BD Biosciences, Trondheim, Norway; 10µg/ml), α10 and α11 (generated as previously described (Camper *et al.*, 1998; Popova *et al.*, 2004); 100µg/ml).

Cell attachment & migration

Cell attachment experiments were performed as previously described (Tiger *et al.*, 2001). For inhibition experiments with integrin function-blocking antibodies, integrin β1 Ha2/5 and α2 Ha1/29 (BD Biosciences; 10µg/ml) were used. Adherent cells were quantified as previously reported (Aumailley *et al.*, 1989).

Single cell tracking was performed as previously described (Liu *et al.*, 2010).

Tensile strength measurements

Using the punch shown in Figure 4e, two skin-strips of 25mm length and 5mm central width were harvested 16d after injury, containing the scar at mid-length (white arrow). Tensile strength measurements were performed using a materials testing device (Instron Tensiometer). Tissue strips were preloaded with a force of 0.5N to assess the initial length. Then the skin was stretched (loading rate 0.6mm/second) to failure. Ultimate force (N) and deformation (mm) were obtained from the load-deformation curves.

Dominant negative JNK

pCDNA3 Flag Jnk1a1(apf) and pCDNA3 Flag Jnk2a2(apf) were a gift from Roger Davis (Addgene plasmid # 13846 and # 13761, respectively) (Derijard *et al.*, 1994; Gupta *et al.*, 1996). Both plasmids were used to co-transfect immortalized dermal fibroblasts (Amaxa® Nucleofactor™ system; program U23). Efficiency of DN JNK was appreciated by analysis of c-jun activation, stimulated by UV light (100J/m^2) (Derijard *et al.*, 1994).

Smad4 silencing

Primary dermal fibroblasts were transfected with 1µM Accell SMARTpool mouse Smad4 siRNA (target sequence: 5'GGCACAAGGUUAGUUAUUU, 5'CCUUUGAUUCACAAUGGUU, 5'CUGCUAAAUUCUAUGUUAA and 5'CUGUUAAAAUCAUGUAUGU) in presence of 0.1% FCS. Untransfected cells and fibroblast transfected with Accell non-targetting pool were used as control. 72h after siRNA treatment, a pool of cells was lysed and Smad4 levels were analysed by Western blotting to appreciate efficiency of knock-down. Another pool of cells was subjected to collagen remodeling assay.

TGF-β activity bioassay

Mink lung epithelial cells transfected with a luciferase reporter gene linked to a truncated plasminogen activator inhibitor-1 (PAI-1) promoter (TMLC cells) were used to determine TGF-β activity (Abe *et al.*, 1994). Dermal fibroblasts were co-culture with TMLC cells in presence of 10% serum for 16 hours, with or without SB505124 (10 µM). Recombinant human TGF-β1 was added to TMLC cells monoculture and used as positive control. Luciferase activity was measured using luciferase assay system (Promega) and Wallac 1420 multilabel counter (PerkinElmer).

Image analysis and morphometry

Images of wound sections were acquired of HE- and immunohistochemical stained sections using a DM 4000B microscope (Leica) and a digital KY F75U camera (JVC). Immunohistochemical signals were acquired using a Eclipse 800E microscope with a DS-Qi1Mc camera (Nikon). Image J was used for image analysis.

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