Figure S1: TP blocks loss of trans-interaction of recombinant Dsg3 molecules and prevents loss of binding of Dsg3-coated microspheres on cultured human keratinocytes

By applying force-distance measurements using an AFM setup, we measured binding of recombinant Dsg3-Fc molecules in a cell-free system. Panel (A) shows two example curves of the forces acting on the cantilever recorded during retraction from the mica sheet. The linear part indicates the upward deflection of the cantilever when in contact with the mica. In the lower curve, a Dsg3 interaction occurred, deflecting the cantilever downwards during the retraction course, which finally jumps back in the neutral position upon bond rupture (asterisk). In the upper example curve no interaction occurred.

(B) The number of curves with at least one rupture event per given number of curves (binding frequency) was strongly reduced following addition of AK23 or PV-IgG to the solution. This effect was completely abrogated by pre-application of TP (n=4 tip/mica combinations, yielding ~1,500 force-distance curves).

(C) In a cell-based approach, we used laser tweezers to detect binding of Dsg3-coated microspheres on cultured keratinocytes. Microspheres that could not be displaced by a laser beam

were considered bound. The percentage of bound beads before (control) and after treatment with antibodies and TP were compared and are a measure for changes of Dsg3-mediated adhesion. Both AK23 and PV-IgG reduced number of bound beads on the keratinocyte surface. 30 min pre-incubation with TP prevented the loss of bound beads (n=7).

Figure S2: Control experiments in vivo

(A) Serial skin sections of mice injected with different amounts of AK23 were evaluated for blister length. Each data point represents one animal. (B) TP was applied topically on mouse backskin either unlabeled (upper panels) or tagged with biotin (lower panels). Biotin was detected with fluorescently labeled streptavidin. The white line marks the transition from the granular layer to the corneal layer (unspecifically labeled by streptavidin-Cy3), the dashed red line denotes basement membrane of the epidermis. Bar is 50 µm (left panels) and 20 µm (right panels). (C) Serial sections of mice skin injected with a ten-fold higher amount of TP (200 µmol/L) as compared to the concentration which has shown to be protective (20 µmol/L).

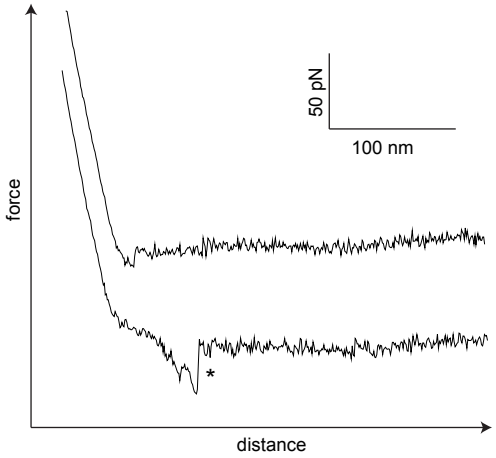
Figure S3: Control experiments in vitro

Dose-dependent effects of TP (A), tryptophan (B), and phenylalanine (C) on cell adhesion measured by dispase-based dissociation assays. n=9.

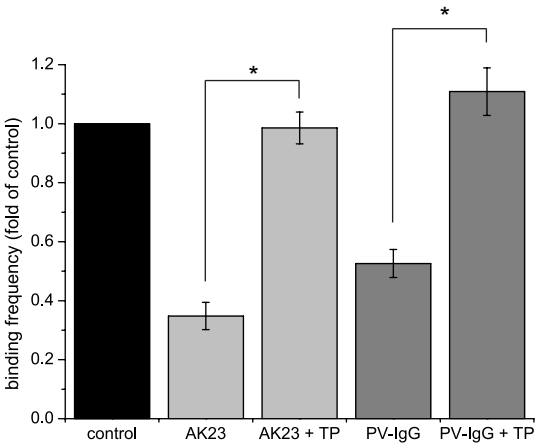
Figure S4: TP does not prevent depletion of Dsg3 in HaCaT

Depletion of HaCaT keratinocytes maintained for 3d in high Ca^{2+} media induced by 24 h and 48 h incubation with PV1-IgG (upper panels) and PV2-IgG (lower panels) was not prevented by simultaneous treatment with TP. n=3.

A



B



C

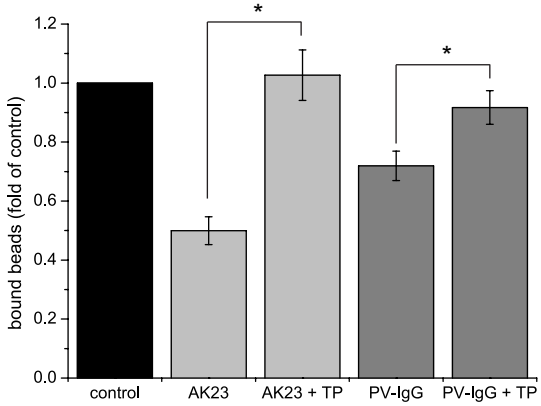


Figure S1

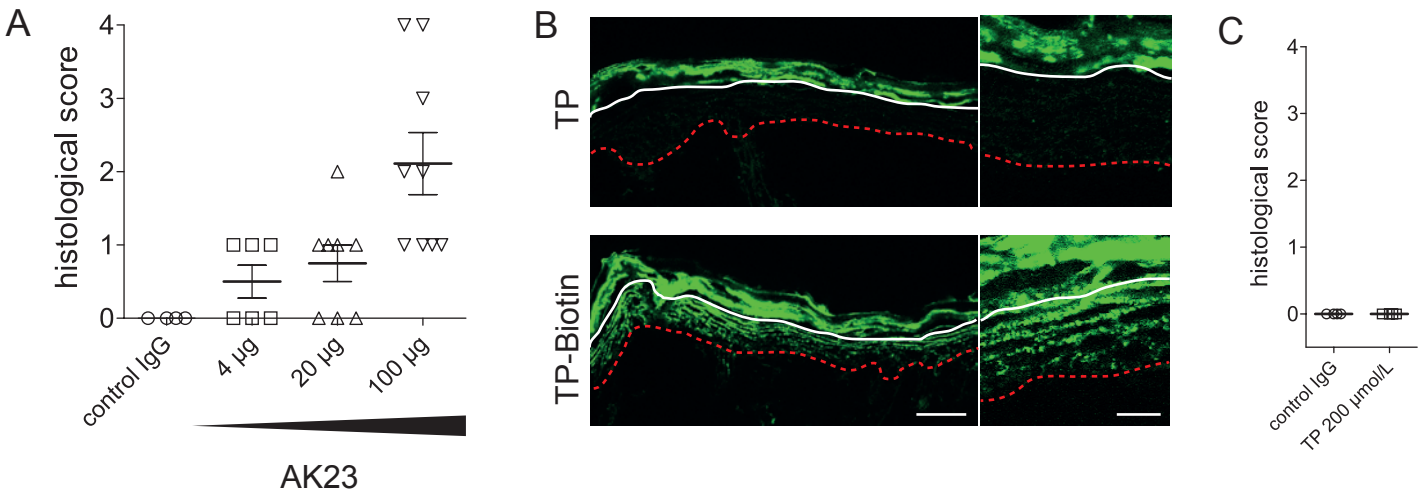

A
histological score
4
3
2
1
0
control IgG
4 µg
20 µg
100 µg
AK23
B
TP
TP-Biotin
C
histological score
4
3
2
1
0
control IgG
TP 200 µmol/L

Figure S2

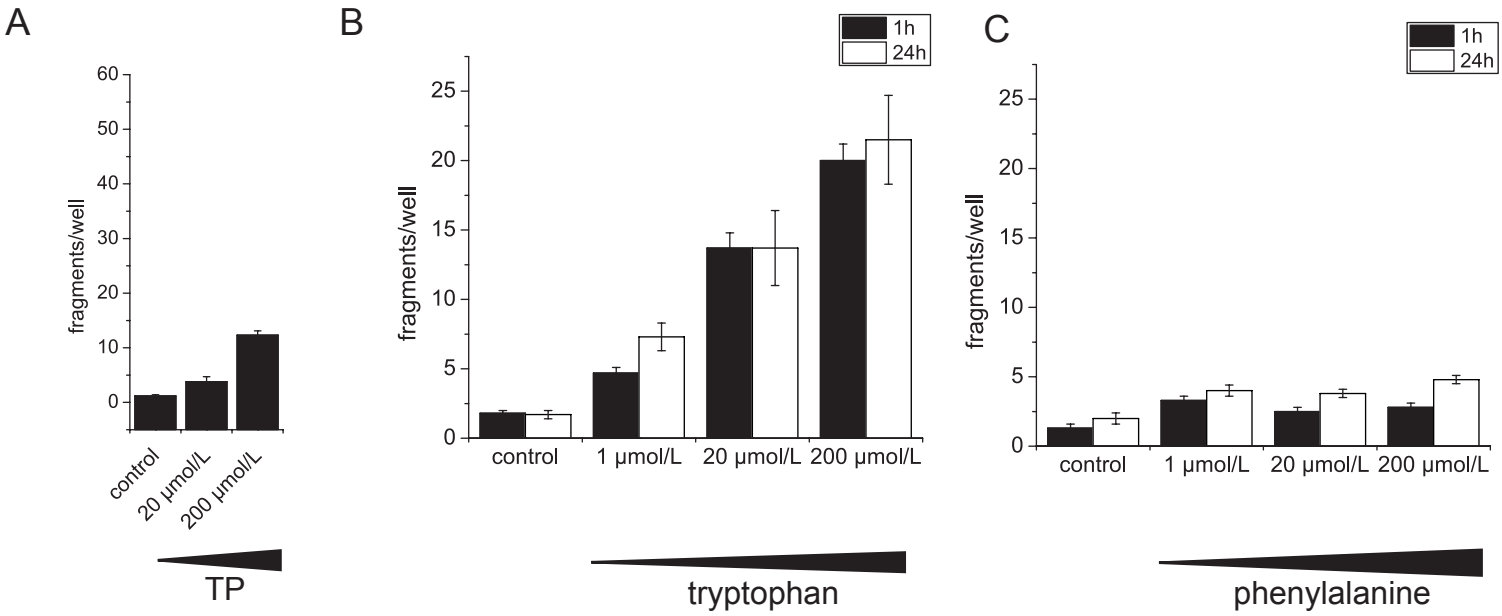
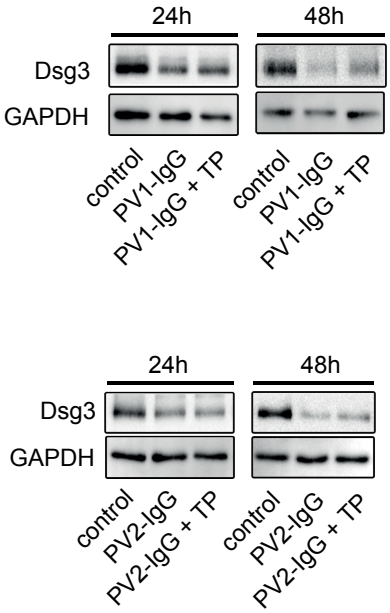

A
B
C
fragments/well
60
50
40
30
20
10
0
control
20 µmol/L
200 µmol/L
TP
25
20
15
10
5
0
1h
24h
control
1 µmol/L
20 µmol/L
200 µmol/L
tryptophan
phenylalanine

Figure S3


24h
48h
Dsg3
GAPDH
control
PV1-IgG
PV1-IgG + TP
control
PV1-IgG
PV1-IgG + TP

24h
48h
Dsg3
GAPDH
control
PV2-IgG
PV2-IgG + TP
control
PV2-IgG
PV2-IgG + TP

Figure S4