Figure S1. Patterns of DSC1 fragmented forms in the SC of patients with NE. In Fig. 2(c), the intact forms of DSC1 were shown clearly; however, the signals of the fragmented forms of DSC1 were too overexposed to distinguish their multi-band cleavage patterns, due to focusing on the detection of DSC1 intact forms in the SC of patients with NE. Therefore, the representative images which were focused on the detection of DSC1 fragmented forms were shown. (a) Western blot results with weaker signals of DSC1 fragmented forms performed using the same samples with Fig. 2(c). (b) Western blot results with weaker signals of DSC1 fragmented forms with samples of other patients with NE. The strongest bands of DSC1 fragmented forms were detected at slightly below 50 kDa, and the other fragments were detected at slightly above 50 to around 75 kDa.

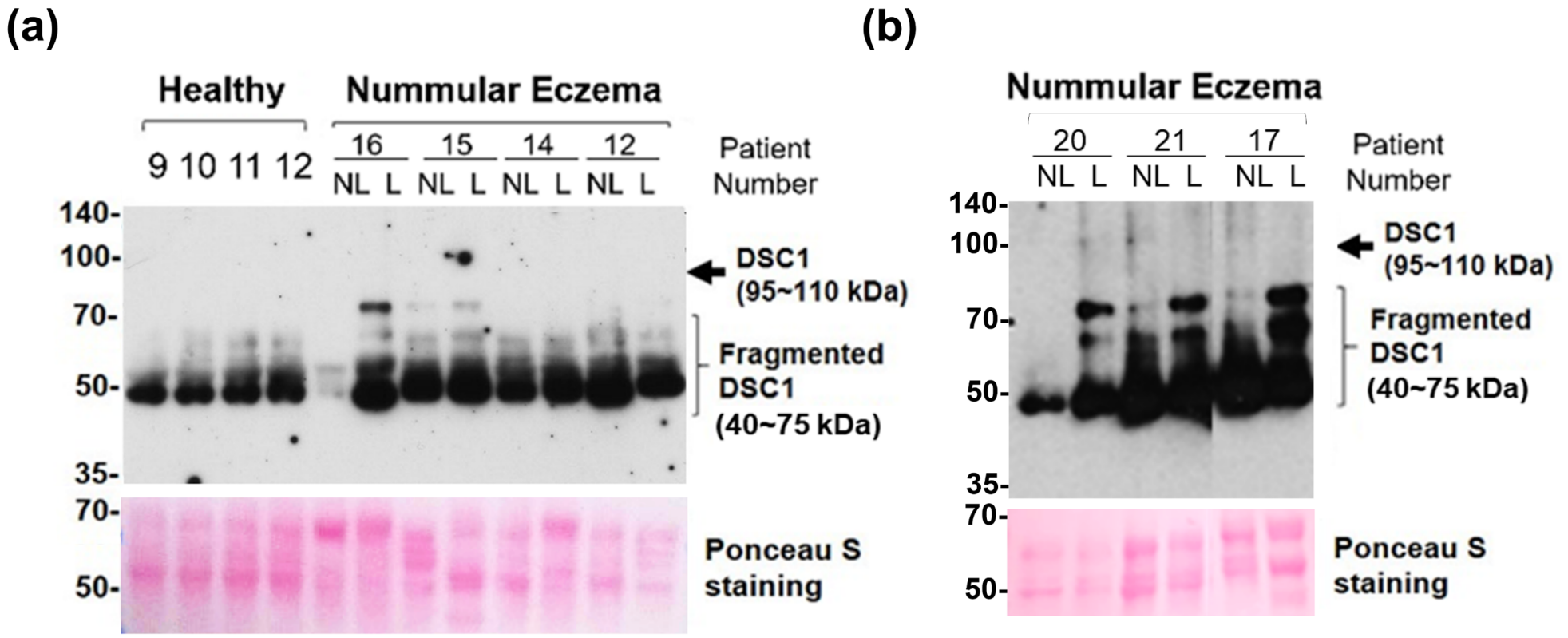
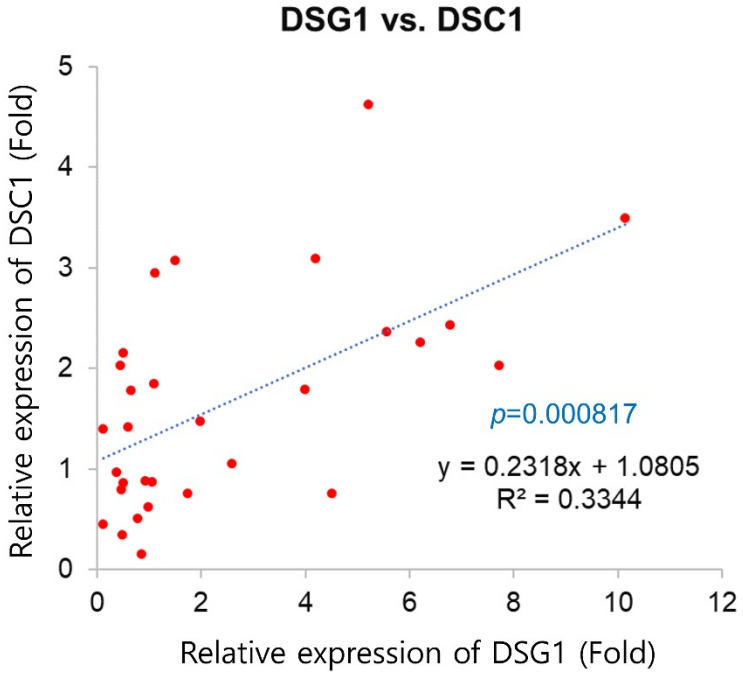
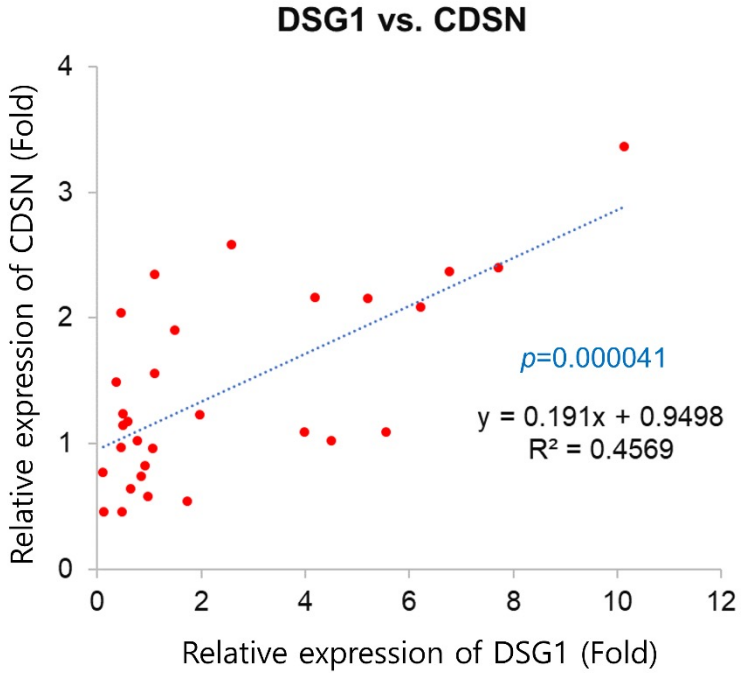


Figure S2. Correlation between corneodesmosomal protein levels in the SC of patients with NE. To examine whether there are any correlations between the levels of DSG1, DSC1, and CDSN, we plotted the graphs for the correlations among DSG1, DSC1, and CDSN with densitometry data of the western blot of lesional and nonlesinal skin of patients with NE (n=15), normalized as relative folds to the mean intensity of nonlesional skin. (a) DSG1 vs. DSC1. (b) DSG1 vs. CDSN. (c) CDSN vs. DSC1. From the linear regression analysis of each pair, there exist significant correlations between the corneodesmosomal protein expression levels; R^2-values and *p*-values for each analysis are shown in the graphs. These results suggest that the increases of the levels of these corneodesmosomal proteins in NE lesional skin seem to occur together.





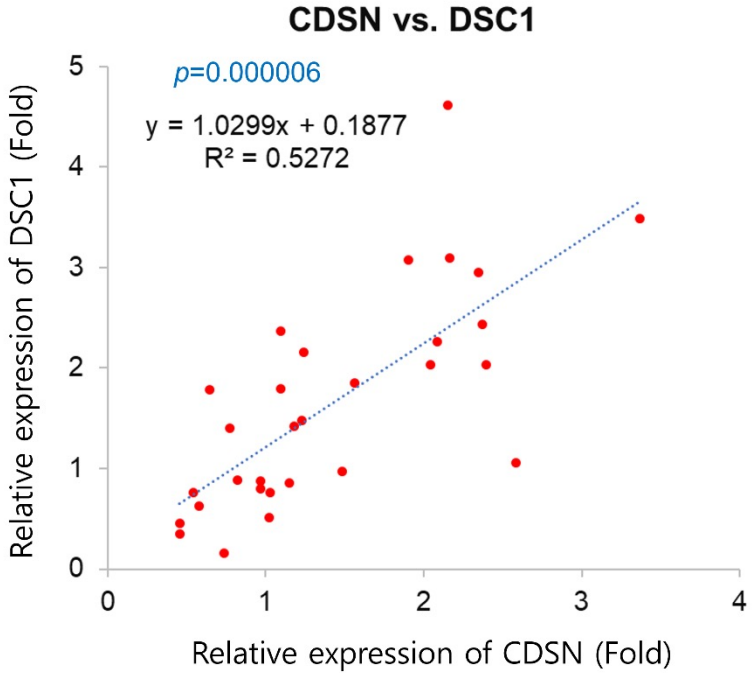
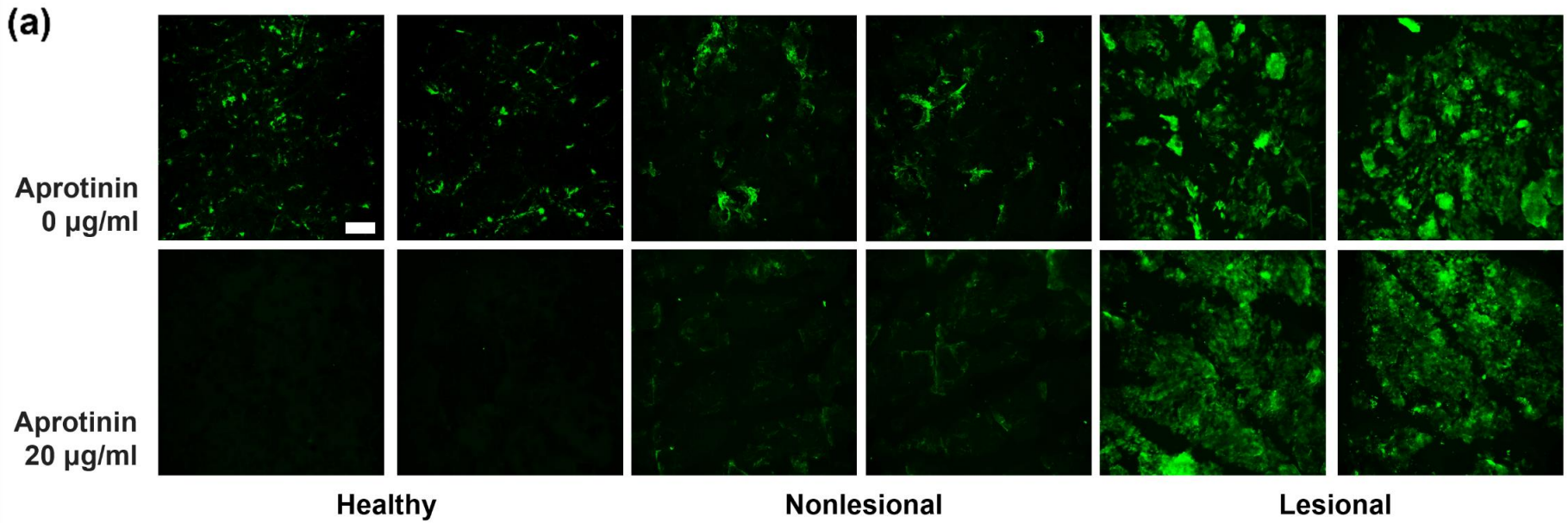
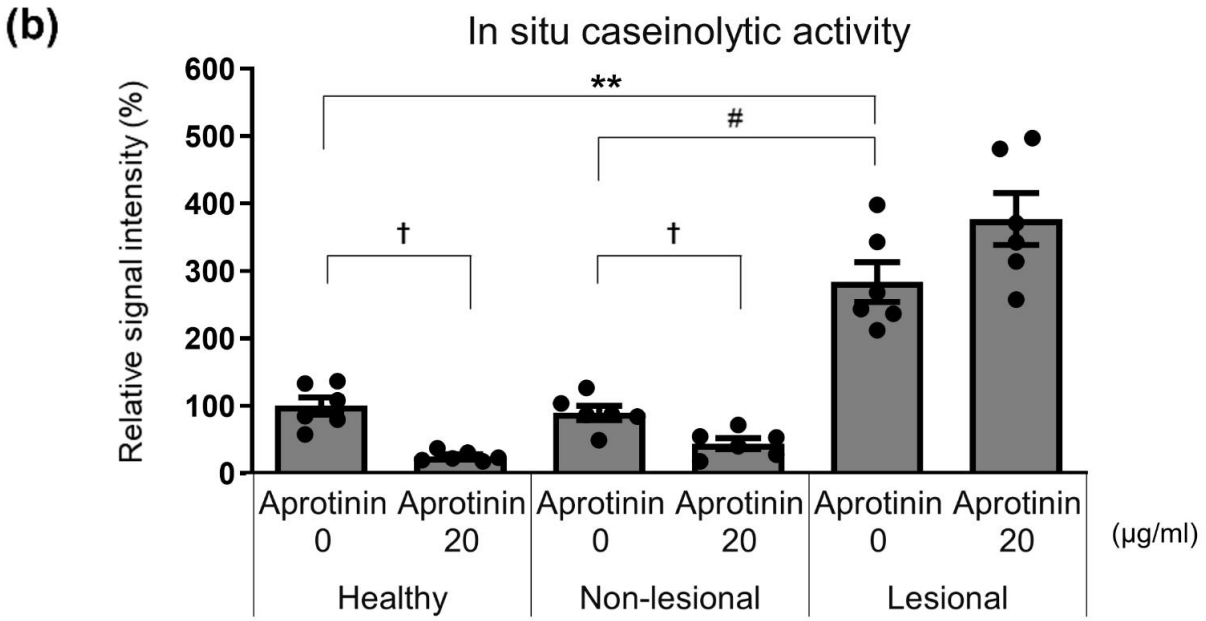


Figure S3. No serine protease activity in the SC of patients with NE (a) In situ casein zymography with aprotinin, a serine protease inhibitor, was performed with the tape-stripped uppermost SC of healthy subject skin and nonlesional and lesional skin of the same patients with NE (n = 6 for each group). To investigate the net serine protease activity in tape-stripped samples, in situ zymography using BODIFY FL casein (EnzChek® Protease Assay kit, E6638, Thermo Fisher Scientific) was performed, as previously reported (13), and to determine the serine protease activity from the caseinolytic activity of the samples, aprotinin was used as an inhibitor of serine proteases. Differences between the samples treated with aprotinin 0 and 20 μg/ml mean net serine protease activity in each group. Results of each 2 representative of healthy and NE samples were shown. Scale bar = 100 μm. (b) Relative signal intensity of fluorescence signal was quantified using ImageJ software and represented as mean fold ± SEM. $^{\#}p < 0.05$; lesional skin vs. nonlesional skin of the same patients with NE (Wilcoxon signed-rank test); $^{*}p < 0.05$, lesional or nonlesional skin vs. the healthy skin (Mann-Whitney U test). $^{\dagger}p < 0.05$; aprotinin 0 μg/ml vs. aprotinin 20 μg/ml-treated skin of the same patients with NE or healthy skin (Wilcoxon signed-rank test). In this result, lesional SC samples showed much higher caseinolytic activity than heathly or nonlesional SC samples, but those activity was not inhibited by treatment with 20 μg/ml of aprotinin, suggesting that those caseinolytic activity is not from serine proteases. Therefore, no serine protease activity was observed in NE lesional SC, while healthy and NE nonlesional SC samples showed some extent of serine protease activity. This experiment could not directly specify the net activity of KLK5 and KLK7. Nonetheless, this result can indirectly suggest that activities of KLKs in lesional SC of patients with NE are probably inhibited by increased expression of LEKTI-1.


(a)
Aprotinin
0 μg/ml
Aprotinin
20 μg/ml
Healthy
Nonlesional
Lesional


(b)
In situ caseinolytic activity
Relative signal intensity (%)
600
500
400
300
200
100
0
**
#
†
†
Aprotinin 0
Aprotinin 20
Aprotinin 0
Aprotinin 20
Aprotinin 0
Aprotinin 20
(μg/ml)
Healthy
Non-lesional
Lesional