Data S1. Supplementary materials and methods.

Measurement of skin thickness. The skin thickness was measured using a thickness gage three times.

Statistical analysis. Gene expression profiles from human skin disease tissues were retrieved from the Gene Expression Omnibus database. After carefully screening the content, discarding the datasets with incomplete information and those lacking control patients, the GDS2960 dataset (1) was obtained for Marfan syndrome, the GDS2200 dataset (2) for squamous cell carcinoma, and GDS1375 dataset (3) for malignant melanoma. R packages were used to annotate the raw data and make the expression matrix. The median of expression level was chosen for genes matched by several probes. The GDS2960 dataset comprised independent Marfan syndrome tissues and normal tissues. The GDS2200 dataset comprised independent squamous cell carcinoma, actinic keratosis and normal tissues, and the GDS1375 dataset comprised independent malignant melanoma, benign nevi and normal tissues.

Student's t-test was used for the analysis of statistical significance between two groups, and Bonferroni test was used for multiple comparisons after the analysis of variance. All statistical analyses were performed using SPSS 21.0 software (IBM Corp.). $P<0.05$ from a two-tailed test was considered to indicate a statistically significant difference.

Allele-specific amplification. The specificity and efficiency of RT-qPCR for *UPF1* insA were tested with allele-specific amplification on *UPF1* constructs (4). Allele-specific primers were designed based on wild-type or mutant sequences obtained from Sanger sequencing of the locus of interest. The 3-end terminated at the mutant base differentiated wild-type from mutant alleles (Fig. S4A). The allele-specific PCR primers were shown in Table SII. *UPF1* WT and *UPF1* insA vectors were tested at 55, 57, 59, 61, 63 and 65˚C gradient annealing temperatures to determine that the primer-specific effect was best at 65˚C. To analyze the proportion of *UPF1* mutants in the sample (Fig. S4B), qPCR was performed with allele-specific primers using QuantStudio™ 7 Flex Real-Time PCR system (Thermo Fisher Scientific, Inc.).

Analysis of cell area. All studied cells were adherent without fixation and the representative images (magnification, x20) of cell morphology were captured with an inverted microscope, and the area of cells was measured using ImageJ software (version 1.52a; Media Cybernetics, Inc.).

References

1. Yao Z, Jaeger JC, Ruzzo WL, Morale CZ, Emond M, Francke U, Milewicz DM, Schwartz SM and Mulvihill ER: A Marfan syndrome gene expression phenotype in cultured skin fibroblasts. BMC Genomics 8: 319, 2007.
2. Padilla RS, Sebastian S, Jiang Z, Nindl I and Larson R: Gene expression patterns of normal human skin, actinic keratosis, and squamous cell carcinoma: A spectrum of disease progression. Arch Dermatol 146: 288-293, 2010.
3. Talantov D, Mazumder A, Yu JX, Briggs T, Jiang Y, Backus J, Atkins D and Wang Y: Novel genes associated with malignant melanoma but not benign melanocytic lesions. Clin Cancer Res 11: 7234-7242, 2005.
4. Cheng C, Zhou Y, Yang C, Chen J, Wang J, Zhang J and Zhao G: Detection of rare point mutation via allele-specific amplification in emulsion PCR. BMB Rep 46: 270-275, 2013.

Figure S1. Epidermal thickening in IMQ-induced psoriasis-like skin. Mice received a daily topical IMQ cream for 7 days to induce psoriasis-like skin. Skin thickness was measured using a thickness gage. The epidermal thickness increased in all four psoriasis-like skin compared with their paired normal skin tissue. The results are presented as the mean ± SD. ***P<0.001. IMQ, imiquimod; PS, IMQ-treated psoriasis-like skin; PN, normal epidermal layer.

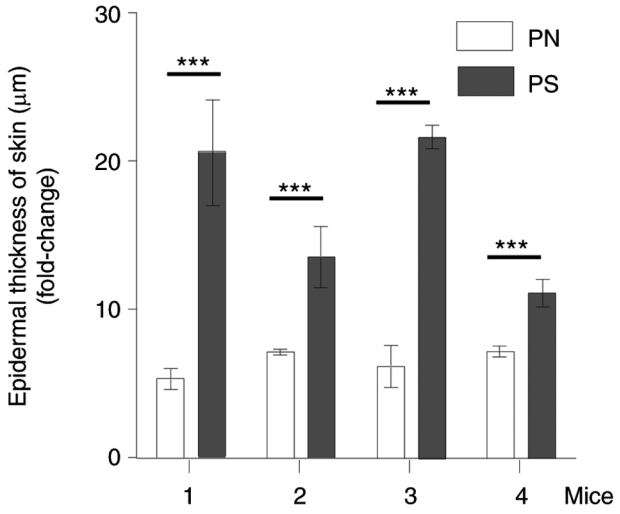

Figure S2. Analysis for skin disease databases from GEO. (A) Analysis of *UPF1* in Marfan Syndrome samples (n=60) and normal samples (n=41) from GEO dataset GDS2960. Independent samples test showed that *UPF1* expression increased significantly in lesions. (B) Multiple comparisons of *UPF1* expression in non-melanoma skin cancers (squamous cell carcinoma, n=5), actinic keratosis (n=4) and normal skin (n=6) from the GDS2200 dataset. *UPF1* expression increased significantly in squamous cell carcinoma compared with the normal group, there was no difference between actinic keratosis and normal group. (C) Multiple comparisons for *UPF1* expression in malignant melanoma (n=45), benign nevi (n=18) and normal skin (n=7) from the GDS1375 dataset. *UPF1* expression increased significantly in melanoma and benign nevi compared with normal skin, there was no difference between melanoma and benign nevi. **P<0.01 and ***P<0.001. *UPF1*, up-frameshift suppressor 1 homolog; ns, not significant; GEO, gene expression omnibus.

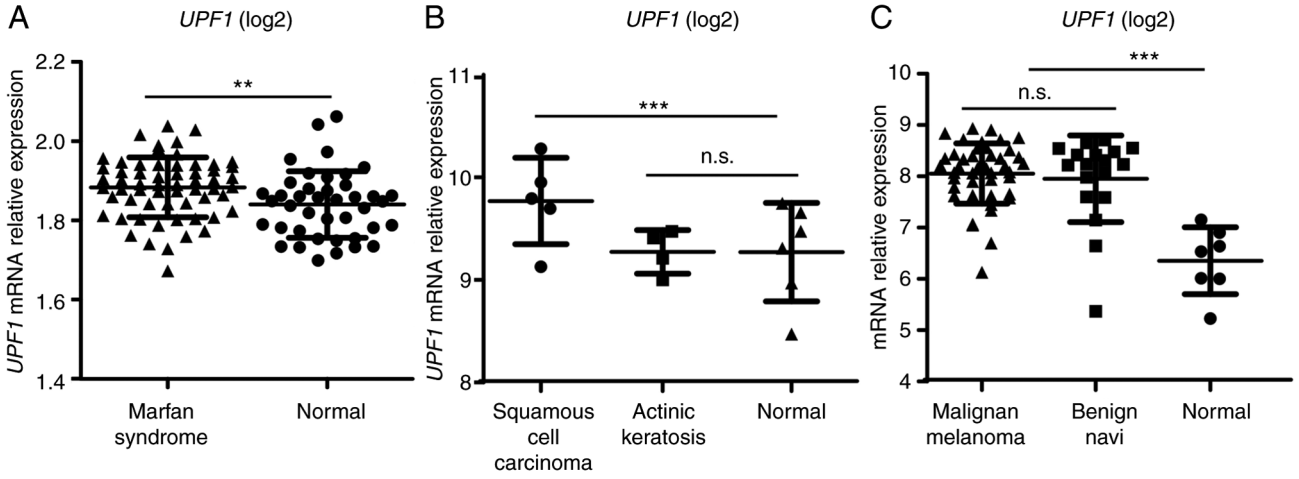

Figure S3. Test for availability of skin scale mRNAs from psoriasis patients. Cornified paired normal epidermal layer tissues were obtained for PA, PB, PC or PD patients as indicated with black frames, while the other six psoriasis scales were independent samples. PCR fragments of *UPF1* mRNA were amplified with *UPF1* F3-F4 primers, and *AREG* mRNA was amplified using its specific primers (Table SIII). The product length was indicated, and 5/10 samples were demonstrated to be available sources for RNA sequencing (P2, 4, A, B and 6). *UPF1*, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin; P, patient.

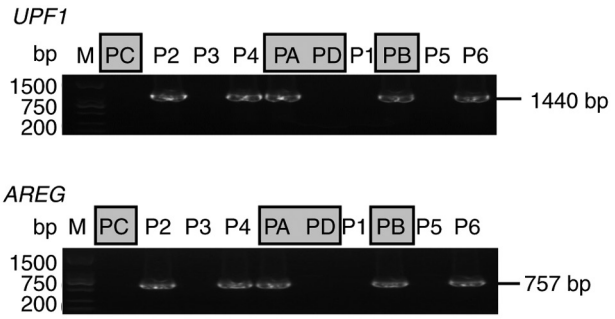

Figure S4. Allele-specific amplification of the *UPF1* insA transcript. (A) To determine the proportion of the heterozygous mutation *UPF1* c.2935_c.2936 insA in patient A, the universal forward primer F, and locus-specific reverse primers Rwt or Rmut were designed. (B) In the primers column, primer 1 indicated F/Rwt and primer 2 indicated F/Rmut. In the template column, the positive symbols referred to the *UPF1* WT vector presented in the upper panel, and the *UPF1* insA vector presented in the lower panel. The negative symbols in both panels referred to negative control, in which no DNA was added. The primer-specific effect was best at 65°C, as determined by setting the gradient annealing temperature with primers F/Rwt and F/Rmut, as indicated by the red frames. *UPF1*, up-frameshift suppressor 1 homolog.

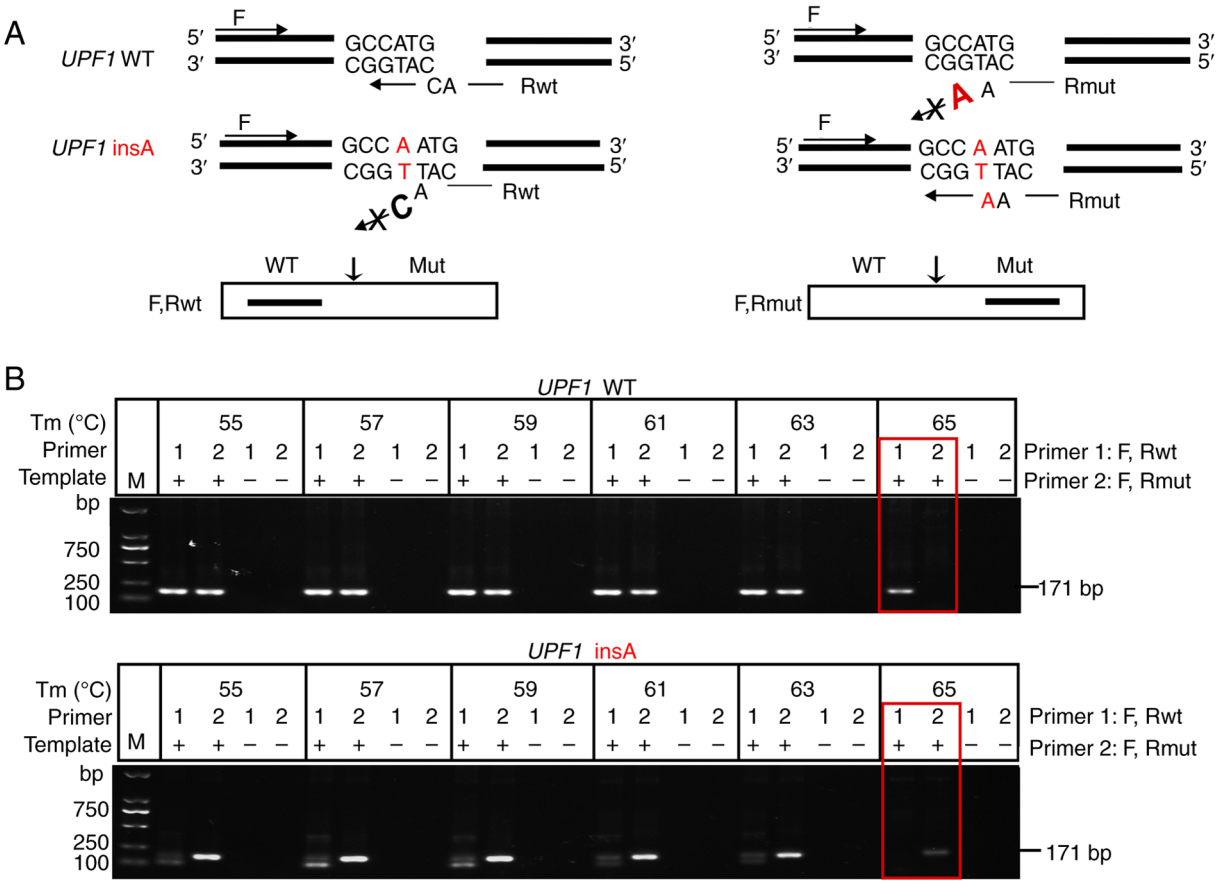

Figure S5. Reverse transcription-quantitative PCR for availability of constructs used in 293T cells. (A) The Phblv-U6-puro or Phblv-U6-puro-*UPF1* constructs were transfected into 293T cells in the left panel, the expression level of *UPF1* was decreased only in the Phblv-U6-puro-*UPF1* group. The pCMV-*MYC* or pCMV-*MYC-UPF1* vector was transfected into 293T cells in the right panel, only pCMV-*MYC-UPF1* upregulated the expression level of *UPF1* in cells. (B) The scrambled sequence or si*AREG* was transfected into 293T cells in the left panel, the si*AREG* decreased the *AREG* expression in cells, while the scrambled sequence had no effect on cells. The pEGFP-N1 or *AREG*-ORF-pEGFP vector was transfected into 293T cells in the right panel, only *AREG* construct increased the *AREG* expression. The results are presented as the mean ± SD from three independent experiments. ***P<0.001. *UPF1*, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin; n.s., not significant; NC, normal cells; si, small interfering RNA; scramble, scrambled control siRNA sequence.

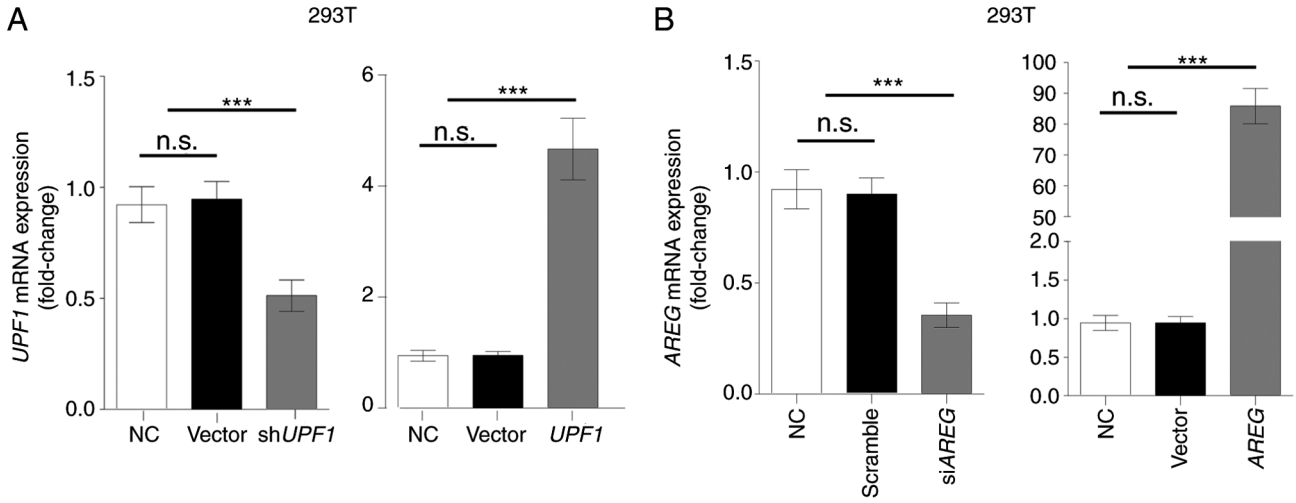

Figure S6. RT-qPCR for availability of constructs used in keratinocyte cells. (A) The Phblv-U6-puro or Phblv-U6-puro-*UPF1* was transfected into HaCaT cells in the upper panel, and Hekα cells in the below panel. Western blotting was used to measure the protein expression level. The expression level of *UPF1* was decreased only in the Phblv-U6-puro-*UPF1* group. (B) The pCMV-*MYC* or pCMV-*MYC-UPF1* vector was transfected into HaCaT cells in the upper panel, and Hekα cells in the below panel. Western blotting was used to measure the protein expression level. Only pCMV-*MYC-UPF1* upregulated the expression level of *UPF1* in cells. (C) The scrambled sequence or si*AREG* was transfected into HaCaT cells in the upper panel, and Hekα cells in the below panel. Western blotting was used to measure the protein expression level. The si*AREG* decreased the *AREG* expression in cells, while the scrambled sequence had no effect on cells. The results are presented as the mean ± SD from three independent experiments. ***P<0.001. *UPF1*, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin; n.s., not significant; NC, normal cells.

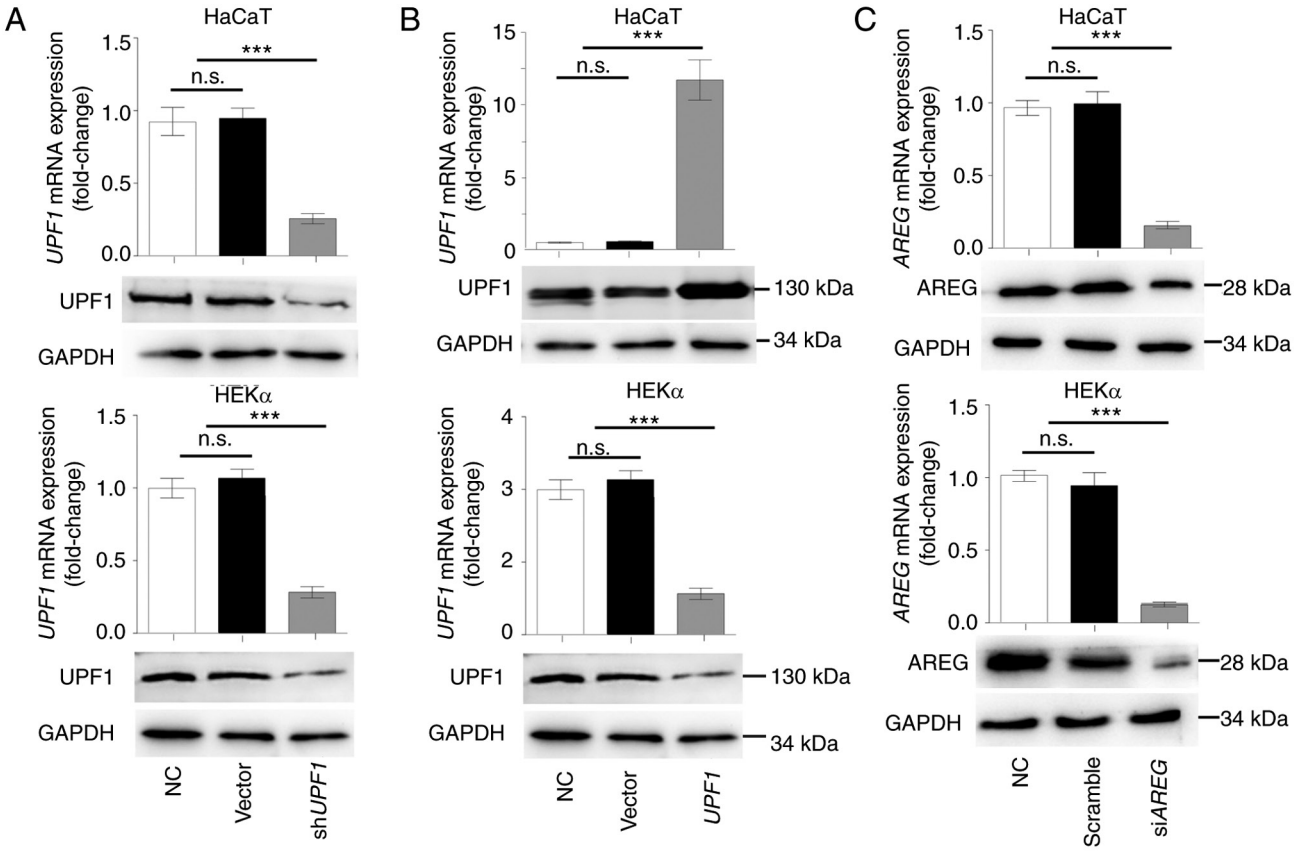

Figure S7. Cell morphology and area of transfected keratinocyte cells. (A) Cell morphology of cultured and transfected keratinocyte cells. (B) The area of keratinocyte cells was measured using the ImageJ software, and there was no significant difference between groups. The results are presented as the mean ± SD from ~50 measurements. *UPF1*, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin; n.s., not significant; NC, normal cells.

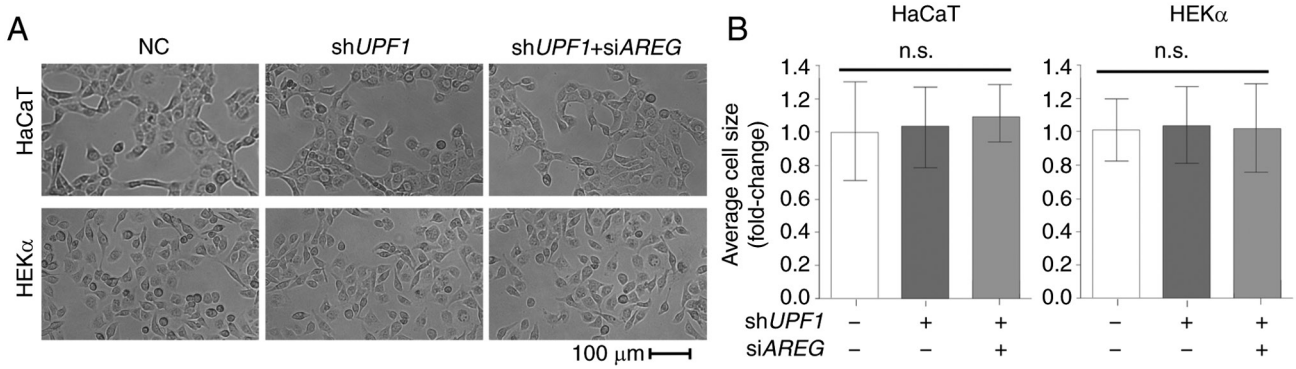

Table SI. Characteristics of patients with psoriasis vulgaris.

Patient number	Sex	Age	Lesion location	Course	Sample location	Sample type
P1	Male	22	Head, double upper extremity	1 month	Double upper extremity (PS)	Independent
P2	Female	35	Extremities	2 years	Right lower extremity (PS)	Independent
P3	Male	59	Back	>20 years	Back (PS)	Independent
P4	Male	43	Right lower extremity	-	Right lower extremity (PS)	Independent
P5	Male	85	Right lower extremity	>10 years	Right lower extremity (PS)	Independent
P6	Male	51	Right lower extremity	>10 years	Right lower extremity (PS)	Independent
PA	Male	36	Buttock	-	Buttock (PS and PN)	Paired
PB	Female	48	Arms	2 months	Arms (PS and PN)	Paired
PC	Male	72	Double lower extremity	-	Double lower extremity (PS and PN)	Paired
PD	Female	41	Right lower extremity	-	Right lower extremity (PS and PN)	Paired

P, patient; -, not available; PS, psoriasis scales; PN, normal cornified epidermal layer.

Table SII. Primers used for reverse transcription-quantitative PCR.

Primer name	Primer sequence (5' → 3')	
	Forward	Reverse
18S	GTAACCCGTTGAACCCCATT	CCATCCAATCGGTAGTAGCG
UPF1	GAAGCGCACCGCAGAGA	CGGCGCCCACACATGT
GAPDH mouse	CATCCTTGTGCCTTCCGGT	ACGCTGAAGTTGTCGTTTGAG
UPF1 mouse	GCCACGTCATCAAGGTTCCTG	CCCTGACACAGAGGTCTCGTC
AREG mouse	GCCATCATCCTCGCAGCTAT	ATGTCATTTCCGGTGTGGCT
IL-17 mouse	TACCTCAACCGTTCCACGTC	TTTCCCTCCGCATTGACACA
IL-6 mouse	TGATGGATGCTACCAAACTGGA	TGTGACTCCAGCTTATCTCTTGG
*TNF*α mouse	CATGTTCTCTGGGAAATCGTGG	TGGTACTCCAGAAGACCAGAGG
CXCL2 mouse	GAAGTCATAGCCACTCTCAAGG	TTTCTCTTTGGTTCTTCCGTTG
NIK	TTCATCGCTGGGTCCAAACA	CAACACACACGGGCCATTTT
NAT9	AGGAAGATGCAGACAAGTGT	TGCAATCATGACCTCGATCT
TBL2	CAGAGGACTTCCCTAAAAAG	AGCAGCGTGTGTGTTGTTCA
UPF1 insA	CGCTTCATGACCACAGCCATGT	AGGGGATGGGAATGTTCATG
		AGGGGATGG GAATGTTCATT
UPF1 del	CACCGAGCCGGAGTGCATGG	GGCGCTCGAAGAGCGACTGT
		AGGCGGATGGGCCTTGGCC
AREG	CGCTCTTGATACTCGGCTCA	ATCCATCAGCACTGTGGTCC
Ki67	TGGTGCTTCGGAAGCAAATCTG	ATTGACTGTGAACTTCGCCCAC
BAD	AGGCTCCGGCAAGCATCAT C	CCTTCGTCGTCCTCCGTCCC
FLG	GAATTTCGGCAAATCCTGAAG	AGCCAACTTGAATACCATCAG
K10	CCTCGTGACTACAGCAAATAC	CAGAGCTACCTCATTCTCATAC
K5	AGGAGCTCATGAACACCAAG	CCATATCCAGAGGAAACACTGCT
COX2	CCAGTATAAG TGCGATTGTA	ACAACGTTCC AAAATCCCTT
MMP1	TGGCTCAGTT TGTCCTCACT	AGAGACCTTG GTGAATGTCA
CCL20	CTGCTACTCCACCTCTGCG	CGCAGAGGTGGAGTAGCAG
CXCL1	CTTGCCTCAATCCTGCATCCC	GGGATGCAGGATTGAGGCAAG

Table SIII. Amplification primers for mRNA sequencing.

A, First primer set

Primer name	Primer sequence (5' → 3')	
	Forward	Reverse
UPF1 f1-r1	CCAGTTGTTGGCTGAGTTGAA	AGGTGGTAGACGATGGTGGC
UPF1 f2-r2	AGGTGGATTTTGTGTGGAAGT	GCTCGAAGAGCGACTGTGAC
UPF1 f3-r3	AGGTGGATTTTGTGTGGAAGT	TGTTCATGGCAGCCACGTGG
UPF1 f4-r4	CTGGAACCACCTGCTGAAC	CTGGTACGTGGAGTCCTGTG
UPF1 f5-r5	TCACAGCCCTTCTCTCAGGG	CCAGAATAAGATGCTGATGG
AREG F-R	CAATGAGAGCCCCGCTGCTA	TGCTATAGCATGTACATTTC

B, Second primer set

Primer name	Primer sequence (5' → 3')	
	Forward	Reverse
F1-R1 specific to f1-r1	TATTACACGAAGGACCTCCC	CTGGATCAGGCTCAGTGGTC
F2-R2 specific to f2-r2	TCAAGTGCCAGCTGCCCAAG	GAGGACCACGGGAACCAT
F3-R3 specific to f3-r3	TGAAAGACGAGACTGGGGAG	GTTGCCCACAATGATGACG
F4-R4 specific to f4-r4	TGCGTGAGAGCCTCATGCAG	TGGAGATGTAGCCCTGCGTC
F5-R5 specific to f5-r5	CGCAGGGCTACATCTCCATG	CGTTGCTTAGCTCTTCCGCC

UPF1, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin.

Table SIV. Primers for plasmid construction.

Primer name	Primer sequence (5' → 3')	
	Forward	Reverse
sh-*UPF1* top and bottom strand	GATCCGGAACCACCTGCTGAACTAC TTTCAAGAGAAGTAGTTCAGCAGGT GGTTCCTTTTTTG	AATTCAAAAAAGCCAACACCAGA AGAACATGTCTCTTGAACATGTTC TTCTGGTGTTGGCG
pCMV-*MYC-UPF1*(insA)	GCCACGTGGCTGCCAATGAACATT CCCATC	GATGGGAATGTTCATTGGCAGCCA CGTGGC
pCMV-*MYC-UPF1*(del)	AGGCGGCCAAGGCCCATCCG	GCAAGCGGATGGGCCTTGGC
AREG-ORF-pEGFP	CCCAAGCTTACAATGAGAGCCCCG CTGCTA	CGGGATCCCGTGCTATAGCATGTA CATTTC
AREG-3'UTR-pEGFP	CCCAAGCTTACAATGAGAGCCCCG CTGCTA	CGGGATCCCGTTTTTTTTTTTTTT CTGTTTGG
pEZX-*AREG*-3'UTR	CCGGAATTCCTGAAGATAAA ATT ACAGGA	GGACTAGTCCTTTTTTTTTTTTTT CTGTTTGG

UPF1, up-frameshift suppressor 1 homolog; *AREG*, amphiregulin.

Table SV. Examples of 3'UTR exon-exon junction-induced NMD substrates.

Author, year	Inducing feature	Gene	Relative increase (fold change)	(Refs.)
Mendell *et al*, 2004	3'UTR exon-exon junction	Growth arrest and DNA-damage-inducible β	6.2	(8)
		Hypothetical protein DJ167A19.1	3.4	
		Mitochondrial ribosomal protein L49	2.1	
		Dexamethasone-induced transcript	2.1	
		DNAJ homolog B2	3.6	

3'UTR, 3' untranslated region; NMD, nonsense-mediated RNA decay.