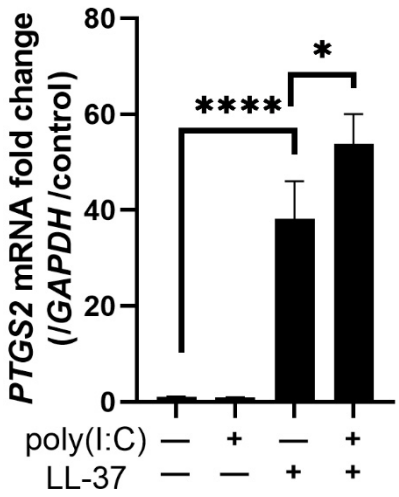
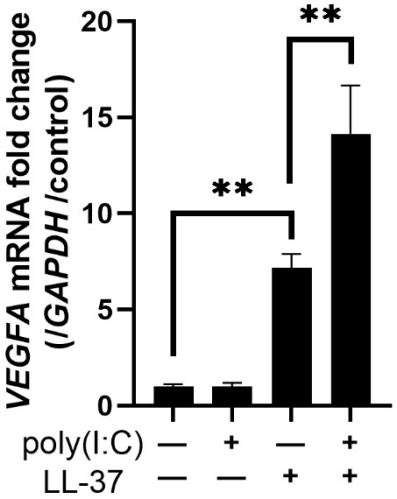
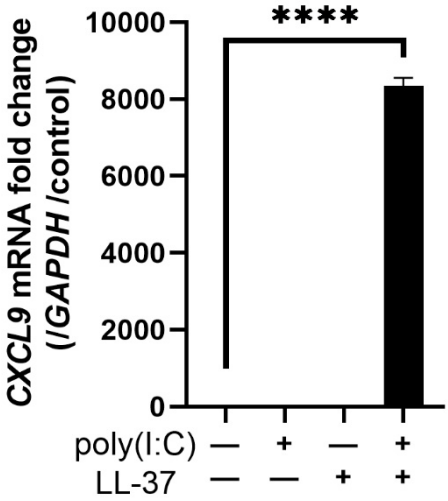

PTGS2 mRNA fold change
(/GAPDH /control)
80
60
40
20
0
****
*
poly(I:C) — + — +
LL-37 — — + +

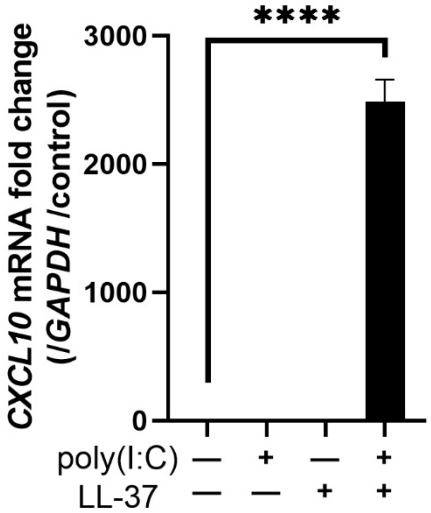
(a)


VEGFA mRNA fold change
(/GAPDH /control)
20
15
10
5
0
**
**
poly(I:C) — + — +
LL-37 — — + +

(b)


CXCL9 mRNA fold change
(/GAPDH /control)
10000
8000
6000
4000
2000
0
****
poly(I:C) — + — +
LL-37 — — + +

(c)


CXCL10 mRNA fold change
(/GAPDH /control)
3000
2000
1000
0
****
poly(I:C) — + — +
LL-37 — — + +

(d)

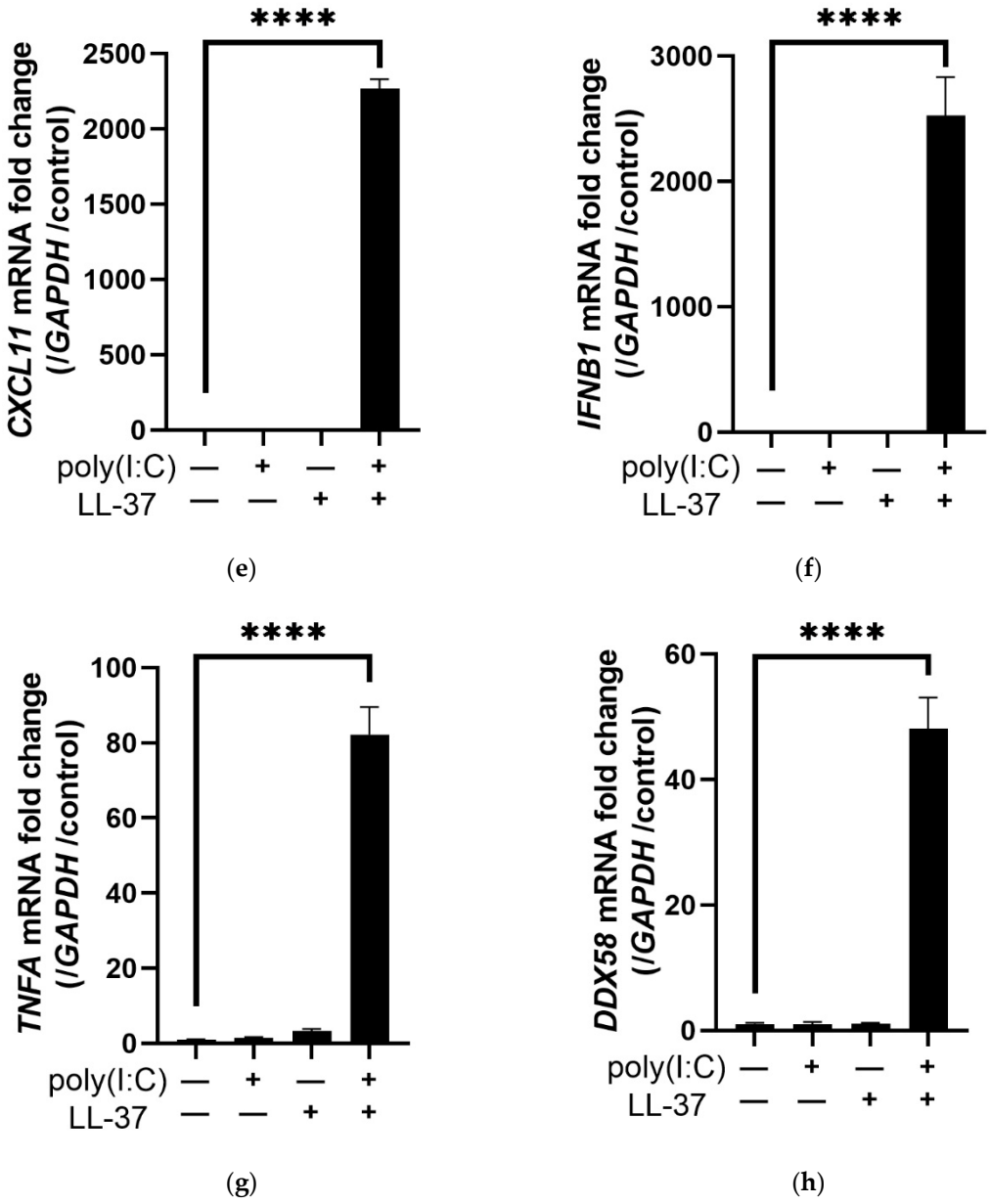
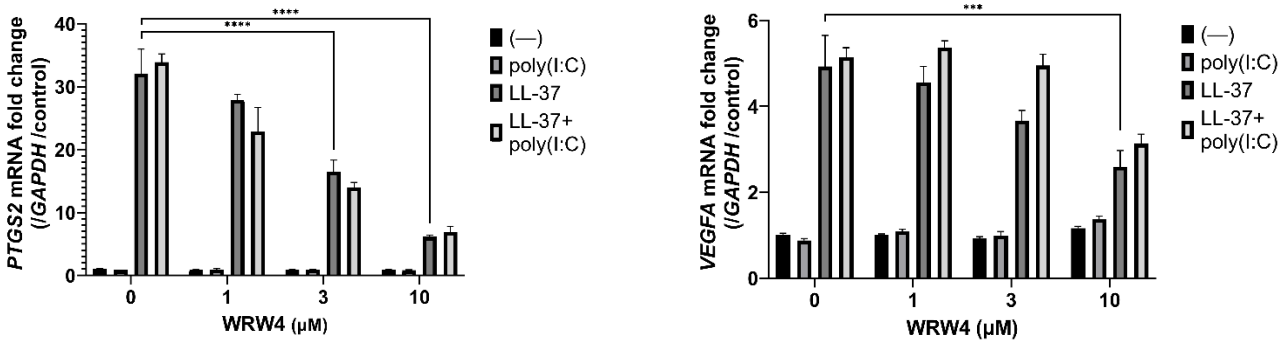


Figure S1. Various mRNAs were induced by stimulation with LL-37 alone or in combination with poly(I:C) in keratinocytes.

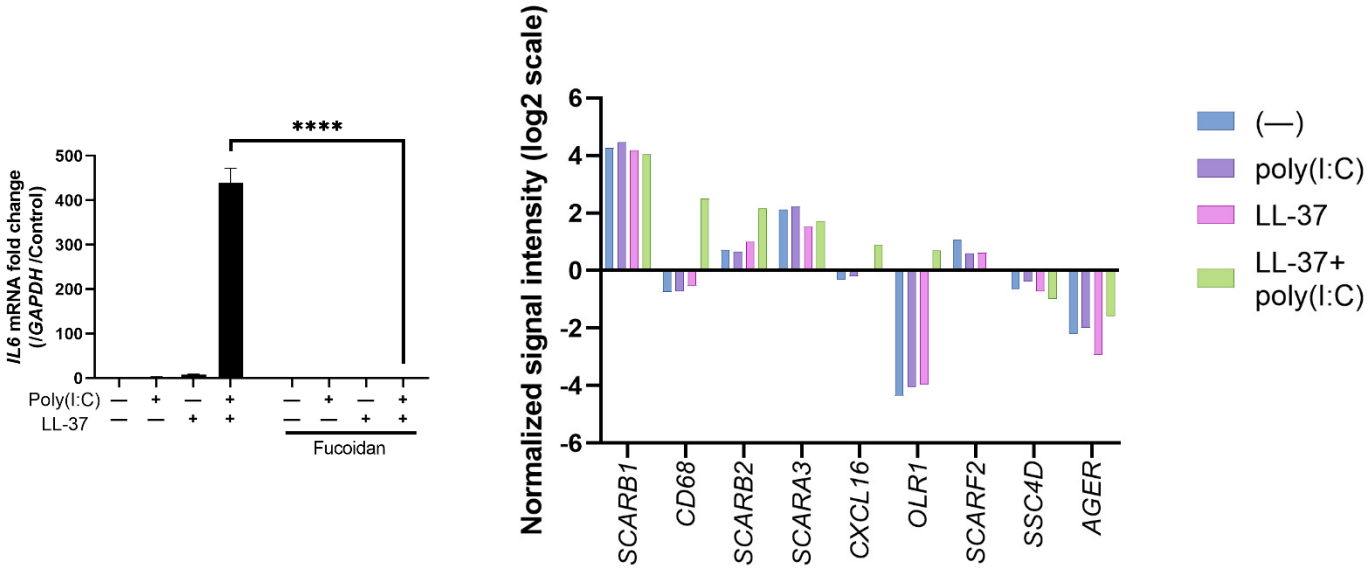
NHEKs were stimulated with LL-37 and poly(I:C) alone or in combination and incubated for 6 h. mRNA was extracted and relatively quantified by RT-PCR. (a) *PTGS2* and (b) *VEGFA* were mainly induced by LL-37 stimulation alone. (c) *CXCL9*, (d) *CXCL10*, (e) *CXCL11*, (f) *IFNB1*, (g) *TNFA*, and (h) *DDX58* were significantly induced by co-stimulation with LL-37 and poly(I:C). Data are means ± SEM of three biological replicates. * $p \leq 0.05$, ** $p \leq 0.01$, **** $p \leq 0.0001$ by two-way ANOVA with Bonferroni's post hoc test.



(**a**) (**b**)

Figure S2. Induction of *PTGS2* and *VEGFA* by LL-37 was decreased depending on the dose of WRW4 in NHEKs.

WRW4 (an FPR2 inhibitor) was applied to NHEKs at concentrations of 0–10 μM, and the cells were stimulated with LL-37 and poly(I:C) 1 h later. Cells were lysed and collected after 6 h of culture, and mRNA expressions of (a) *PTGS2* and (b) *VEGFA* were relatively quantified by RT-PCR. Data are means ± SEM of three biological replicates. ***p ≤ 0.001, ****p ≤ 0.0001 by two-way ANOVA with Bonferroni's post hoc test.



(**a**) (**b**)

Figure S3. Signal intensities of various scavenger receptors in DNA microarrays.

(a) NHEKs were stimulated with LL-37 alone or in combination with poly(I:C), with or without fucoidan, an inhibitor for multiple scavenger receptors, at a final concentration of 10 μg/ml for 6 h. mRNA was extracted and relatively quantified by RT-PCR. (b) NHEKs were stimulated with LL-37 and poly(I:C) alone or in combination and analyzed by DNA microarray. The signal intensities of scavenger receptors were examined, and the top 9 genes are shown. The expressions of *SCARB1* (SR-B1), *CD68* (SR-D1), *SCARB2* (SR-B2), *SCARA3* (SR-A3), *CXCL16* (SR-PSOX), *OLR1* (SR-E1), *SCARF2* (SR-F2), SSC4D, and AGER (SR-J1) are shown in order of signal intensity when stimulated with LL-37 and poly(I:C).

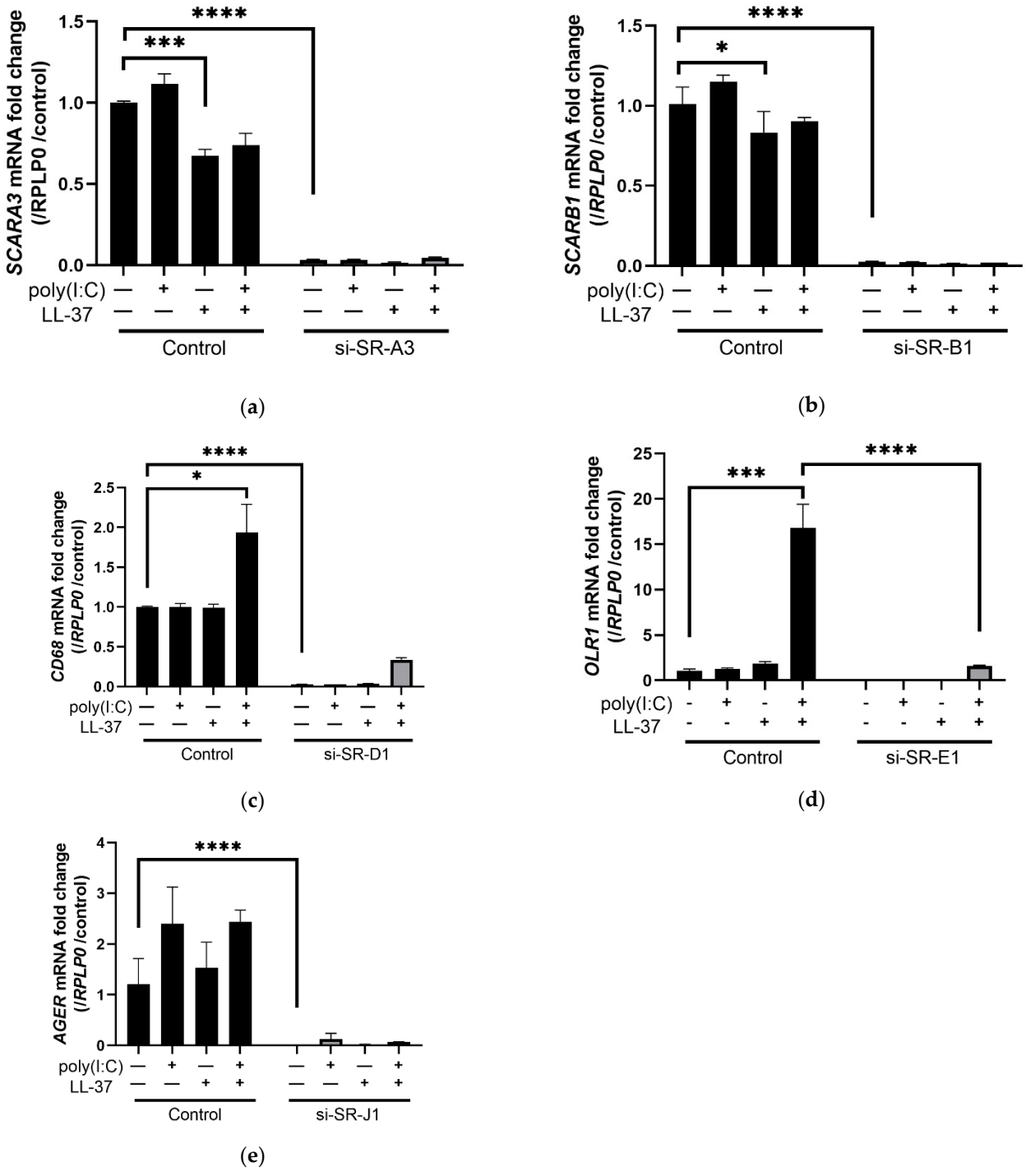
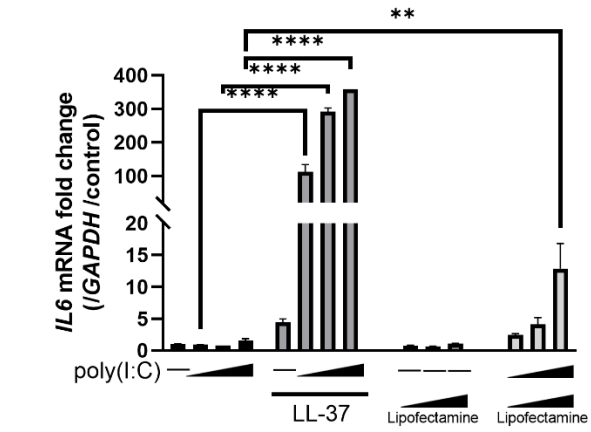
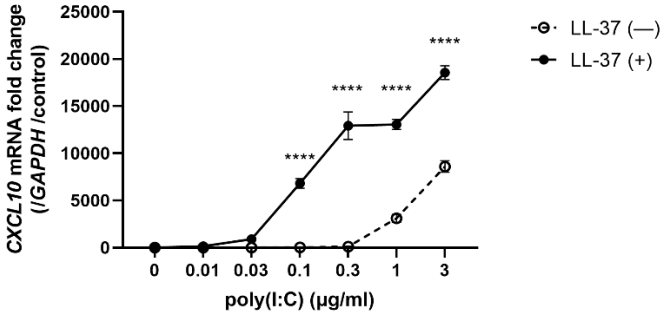


Figure S4. Expressions of scavenger receptors were decreased by transfection with their siRNAs.

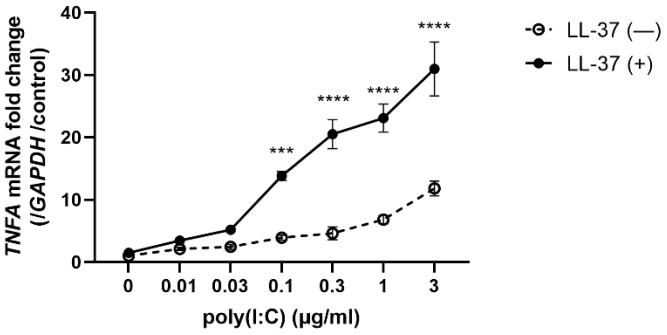
NHEKs were transfected with siRNAs of various scavenger receptors, stimulated with LL-37 and poly(I:C), and RT-PCR analysis was carried out. Samples were the same as in Figure 3a-e. The mRNA expressions of (a) *SCARA3* (SR-A3), (b) *SCARB1* (SR-B1), (c) *CD68* (SR-D1), (d) *OLR1* (SR-E1), and (e) *AGER* (SR-J1) are shown. Data are means ± SEM of three biological replicates. NS, $p > 0.05$, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$ by two-way ANOVA with Bonferroni's post hoc test.



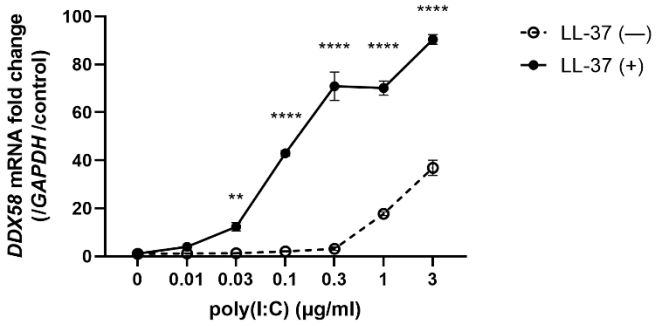
(a)



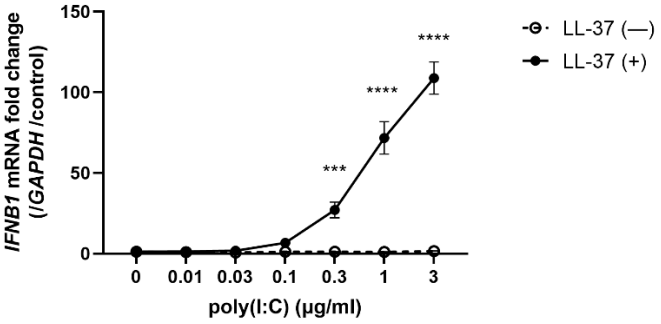
(b)



(c)



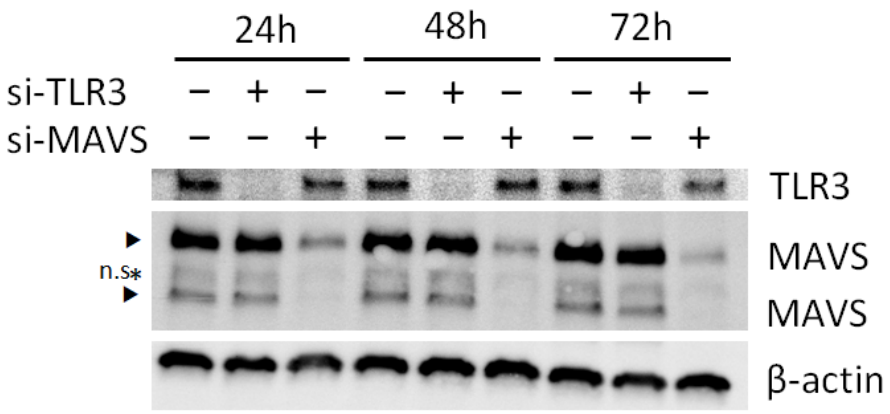
(d)



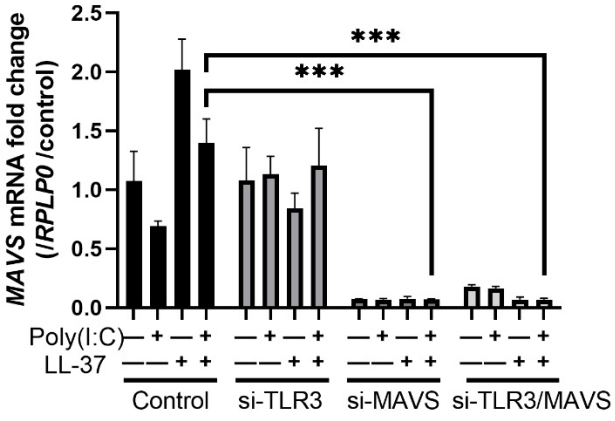
(e)

Figure S5. Poly(I:C) induced cytokines in combination with a transfection reagent or at high concentration, but to a weaker extent than with LL-37.

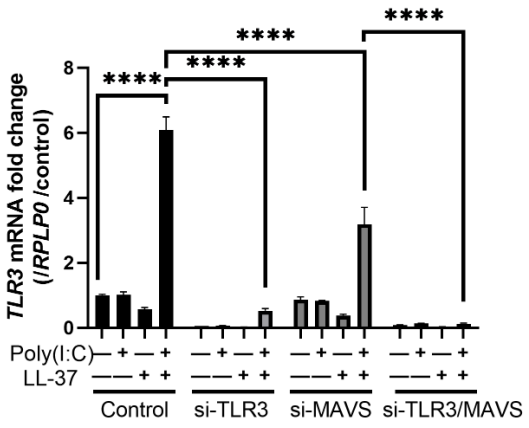
(a) NHEKs were stimulated with poly(I:C) and LL-37 or Lipofectamine 3000 reagent alone or in combination. Poly(I:C) was used at 0.1, 0.3, and 1 μg/ml, and Lipofectamine 3000 reagent was premixed and administered according to the amount of poly(I:C) used. The induction of *IL6* mRNA after 6 hours of stimulation was shown. Data are means ± SEM of two biological replicates. NHEKs were stimulated with poly(I:C) at different concentrations (0.01–3 μg/ml) alone or in combination with LL-37. RT-PCR was performed to quantify the mRNA expressions of (b) *CXCL10*, (c) *TNFA*, (d) *DDX58*, and (e) *IFNB1*. Data are means ± SEM of three biological replicates. **p ≤ 0.01, ***p ≤ 0.001, ****p ≤ 0.0001 by two-way ANOVA with Bonferroni's post hoc test.



(**a**)



(**b**)



(**c**)

Figure S6. siRNAs of TLR3 and MAVS were transfected into NHEKs.

(a)NHEKs were transfected with control, TLR3 or MAVS siRNA for 24-72 hours, medium was exchanged, and samples were collected after 24 hours. Immunoblotting of TLR3 and MAVS were shown. β-actin was used as a loading control. NHEKs were transfected with TLR3 and MAVS siRNAs alone or in combination for 24 hours and stimulated with LL-37 and poly(I:C). Samples were the same as in Figures 4i-k. Expression of (b) *MAVS* and (c) *TLR3* mRNA was analyzed by RT-PCR. Data are means ± SEM of three biological replicates. NS, $p > 0.05$, * $p \leq 0.05$, ***$p \leq 0.001$, by two-way ANOVA with Bonferroni's post hoc test.

Table S1. List of antibodies.

Antibodies	Origin	Source	Identifier	Dilution
CD68 (SR-D1)	Rabbit	Abcam	Cat#ab125212	1:500
LL-37	Mouse	Santa Cruz	Cat#sc-166770	1:200
LOX1 (SR-E1)	Rabbit	Abcam	Cat#ab60178	1:100
RAGE (SR-J1)	Rabbit	Abcam	Cat#ab3611	1:100
SCARA3 (SR-A3)	Rabbit	Sigma	Cat#HPA047386	1:200
SR-B1	Rabbit	Novus Biologicals	Cat#NB400-104	1:200
β-actin HRP conjugate	Rabbit	Cell signaling	Cat#5125	1:1000
IRF-3	Rabbit	Cell signaling	Cat#4302	1:1000
MAVS	Rabbit	Cell signaling	Cat#3993	1:1000
p38	Rabbit	Cell signaling	Cat#9212	1:500
Phospho-IRF-3	Rabbit	Cell signaling	Cat#4947	1:1000
Phospho-p38	Rabbit	Cell signaling	Cat#9211	1:1000
Phospho-TBK1	Rabbit	Cell signaling	Cat#5483	1:1000
TLR3	Rabbit	Cell signaling	Cat#6961	1:1000
TBK1	Rabbit	Cell signaling	Cat#3504	1:1000
Rabbit IgG, HRP-linked	Goat	Cell signaling	Cat#7074	1:1000
Biotin, HRP-Linked	Goat	Cell signaling	Cat#7075	1:1000-3000
IRDye® 800CW anti-Rabbit IgG	Donkey	LI-COR	Cat#926-32213	1:3000
Duolink® In Situ PLA® Probe Anti-Mouse MINUS	Donkey	Sigma	Cat#DUO92004	N/A
Duolink® In Situ PLA® Probe Anti-Rabbit PLUS	Donkey	Sigma	Cat#DUO92002	N/A

Table S2. Assay ID of quantitative PCR primers and probes.

Gene	Reference sequence	Taqman® Gene Expression Assay ID
CD68	NM_001040059.1 NM_001251.2	Hs02836816_g1
CXCL9	NM_002416.2	Hs00171065_m1
CXCL10	NM_001565.3	Hs00171042_m1
CXCL11	NM_001302123.1 NM_005409.4	Hs00171138_m1
DDX58	NM_014314.3	Hs01061436_m1
IFNB1	NM_002176.3	Hs01077958_s1
IL6	NM_000600.4	Hs00985639_m1

IL36G	NM_001278568.1 NM_019618.3	Hs00219742_m1
MAVS	NM_001206491.1 NM_020746.4	Hs00920075_m1
OLR1	NM_001172632.1 NM_001172633.1 NM_002543.3	Hs01552593_m1
PTGS2	NM_000963.3	Hs00153133_m1
AGER	NM_001136.4 Other 8 sequences	Hs00542584_g1
RPLP0	NM_001002.3 NM_053275.3	Hs99999902_m1
SCARA3	NM_016240.2 NM_182826.1	Hs00939871_m1
SCARB1	NM_001082959.1 NM_005505.4	Hs00969821_m1
TLR3	NM_003265.2	Hs01551078_m1
TNFA	NM_000594.3	Hs00174128_m1
VEGFA	NM_001025366.2 Other 19 sequences	Hs00900055_m1

Gene	**Reference sequence**	**Primer sequence (5′-3′)**	**Probe sequence (5′-3′)**
GAPDH	NM_002046	GAAGGTGAAGGTCGGAGTC GAAGATGGTGATGGGATTTC	TGGCAAATTCCATGGCAC- CGTCA