Supplemental Materials

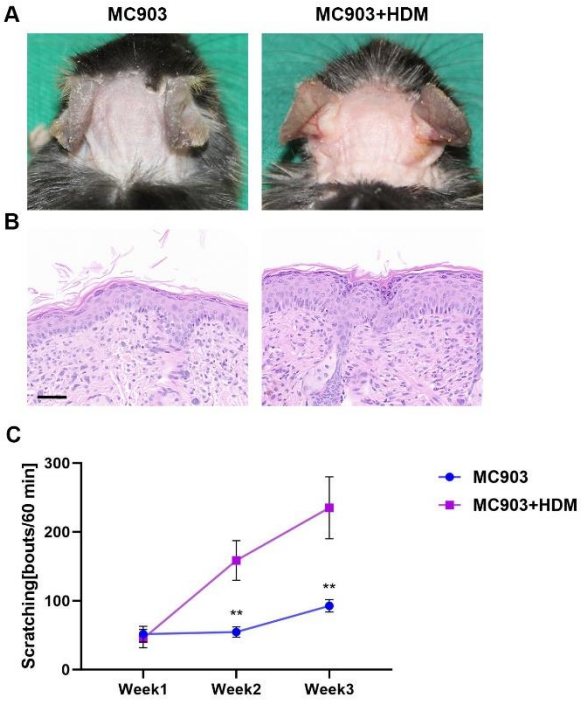

Figure S1. MC903+HDM treated mice exhibit severer AD symptoms compared to MC903 treated mice. (A) Skin appearance showed that MC903+HDM mice displayed more serious erythema, edema, and excoriation than MC903 mice. **(B)** H&E staining of skin sections showed that severer hyperkeratosis and inflammatory cell infiltration were found in MC903+HDM mice. Bar=50μm. **(C)** MC903+HDM mice had more scratching bouts in 60 minutes than MC903 mice. Unpaired *t* tests, **P < 0.01.

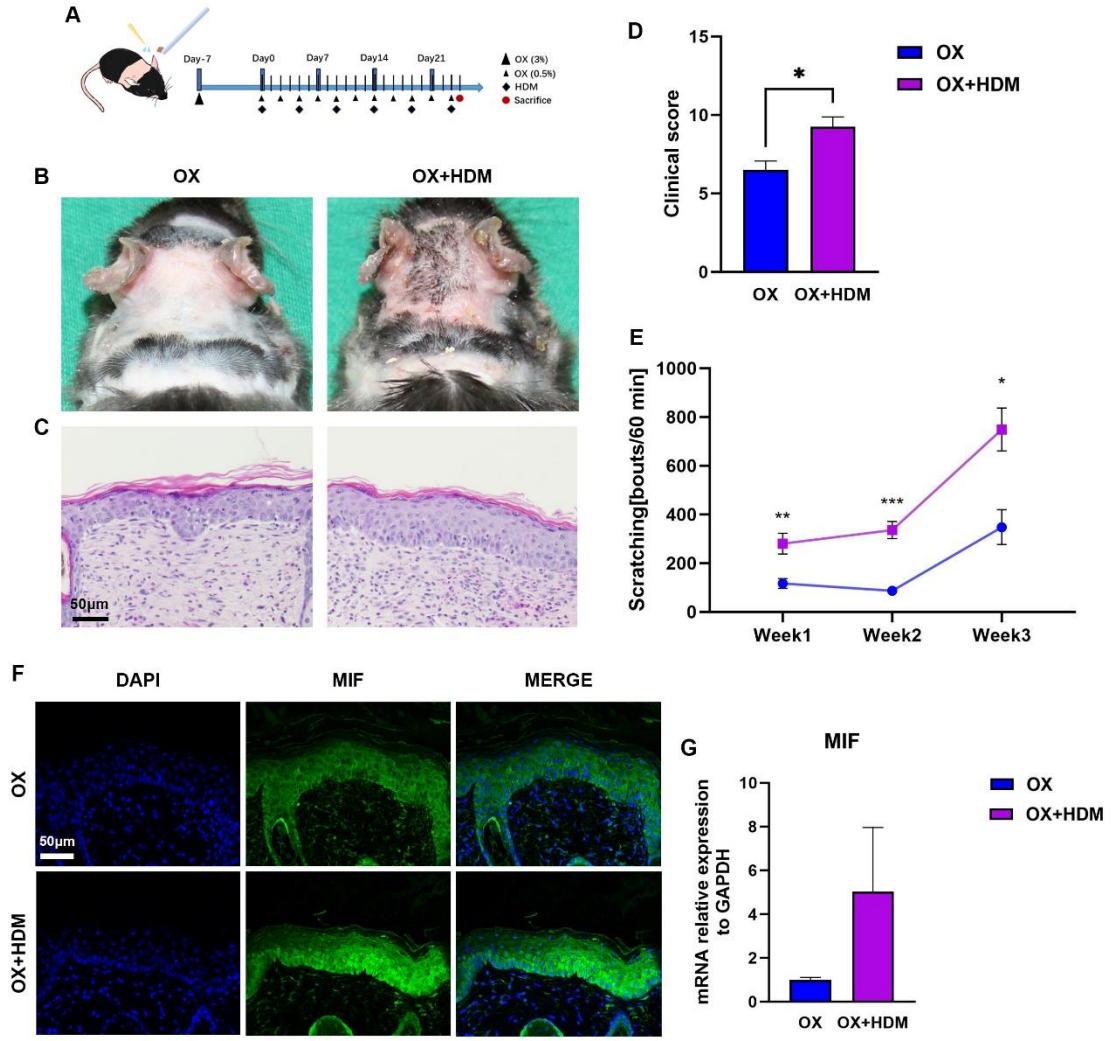

Figure S2. MIF expression is upregulated in the OX+HDM treated AD model compared to OX treated mice. ((A) Mice neck skin (2.5cm*2.5cm) was topically applied once with oxazolone (3% in 4 acetone: 1olive oil). After 7 days, 0.5% oxazolone was topically applied every other day for three weeks. HDM ointment was applied twice per week for 6 times. **(B)** Skin appearance showed that OX+HDM mice displayed more serious erythema, excoriation and desquamation than OX mice. **(C)** H&E staining of skin sections showed that severer hyperkeratosis and inflammatory cell infiltration were found in OX+HDM mice. Bar=50μm. **(D)** Higher clinical score (redness, bleeding, eruption and scaling scored 0-3 each) was found in OX+HDM mice than in OX mice. Unpaired *t* tests, *P < 0.05. **(E)** More scratching bouts in 60 minutes were found in OX+HDM mice than in OX mice. Unpaired *t* tests, *P < 0.05, **P < 0.01, ***P < 0.001. **(F)** Representative immunofluorescence images of MIF in skins showed that OX+HDM mice expressed more MIF than OX mice. Bar=50μm. **(G)** MIF mRNA expression in skin was higher in OX+HDM treated mice than in OX treated mice.
OX, oxazolone.

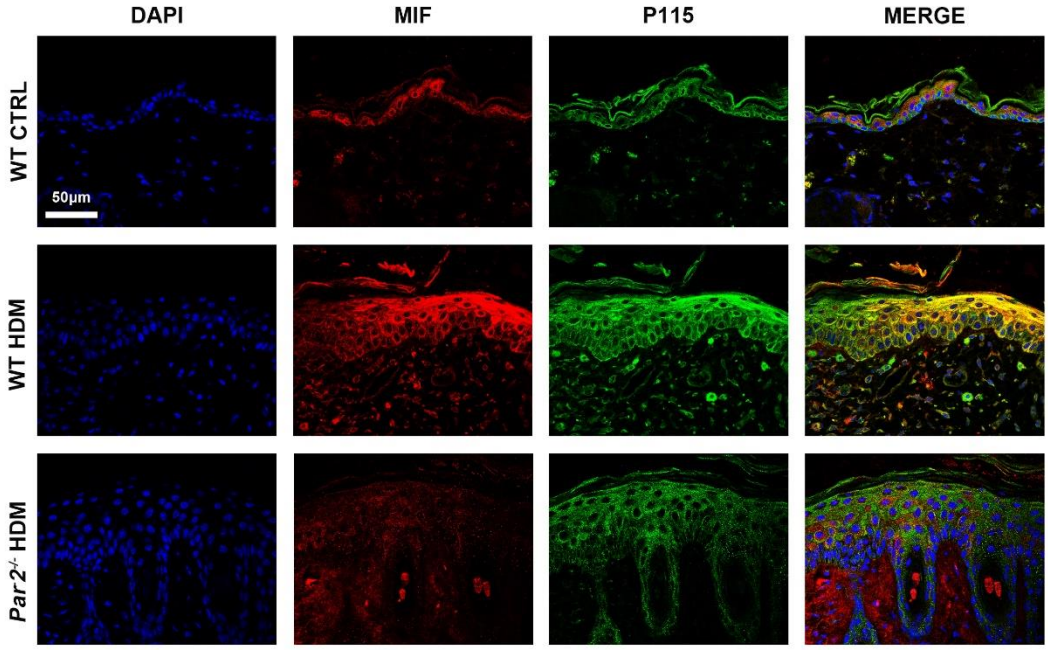

Figure S3. Representative images of MIF and P115 expression in the skin of AD mice and control group. Stronger MIF and P115 expressions and co-localization in skin were found in HDM-WT mice than in HDM-*Par2*$^{-/-}$ mice. Bar=50μm. WT, wild type. CTRL, control.

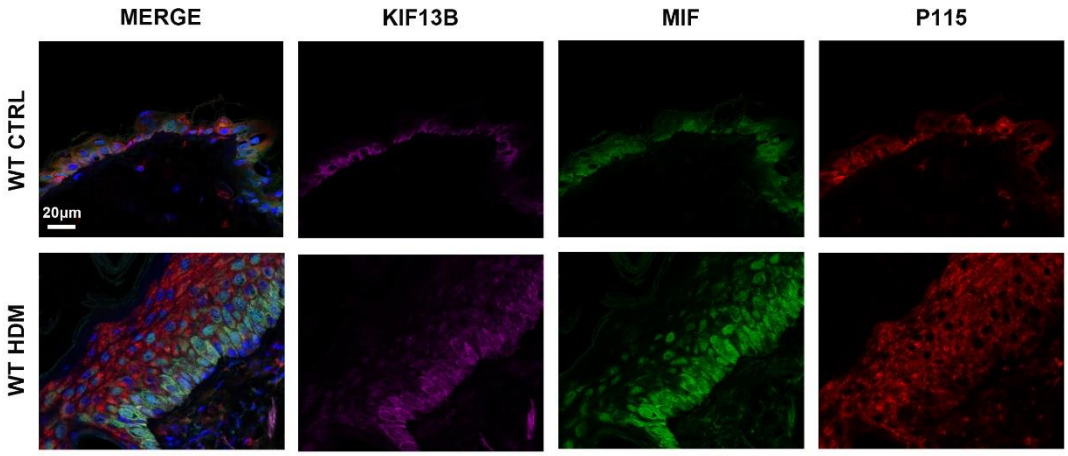

Figure S4. Representative images of of KIF13B, MIF and P115 expression in the skin of AD mice and control group. Stronger MIF expression and co-localization of KIF13B, MIF and P115 in skin were found in HDM-WT mice than in control group. . Bar=20μm.WT, wild type. CTRL, control.

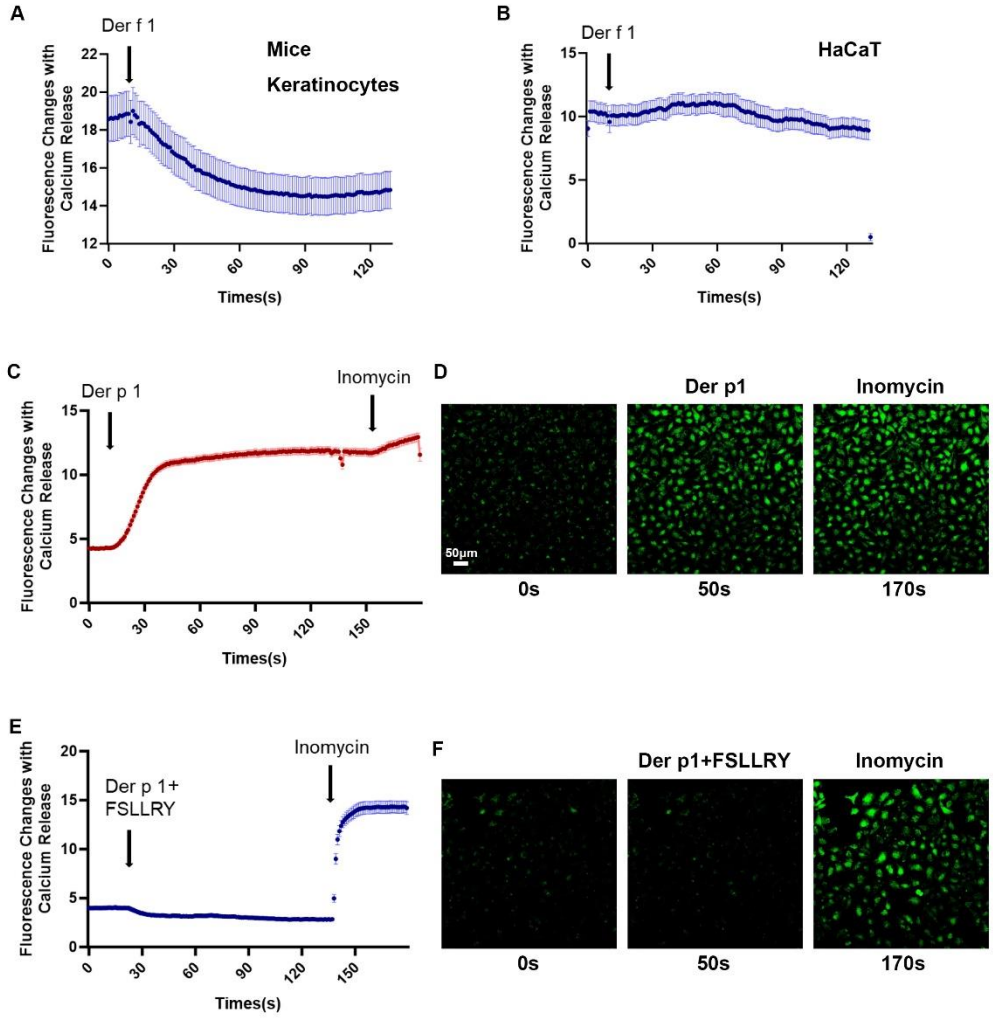

Figure S5. Neither mice keratinocytes nor HaCaT cells exhibit Ca^{2+} mobilization in response to *Der f1*. In contrast, Der p1 successfully triggers Ca^{2+} mobilization in HaCaT cells, which can be inhibited by the PAR2 antagonist FSLLRY. (A) Representative traces showed that there were no intracellular Ca^{2+} responses elicited by *Der f1* (20μg/μl) in mouse keratinocytes. **(B)** Representative traces showed that there were no intracellular Ca^{2+} responses elicited by *Der f1* (20μg/μl) in HaCaT cells. **(C)** Representative traces showed that Ca^{2+} mobilization was elicited by *Der p1* (25μg/μl) in HaCaT cells. Inomycin served as a positive control. **(D)** Representative fluorescence images of Fluo 4 (5 μM) loaded HaCaT cells showed the Ca^{2+} responses stimulated by *Der p1* at 0s, 50s and 170s. Bar=50μm. **(E)** Representative traces showed that the Ca^{2+} mobilization induced by *Der p1* (25μg/μl) in HaCaT cells was inhibited by pretreatment of FSLLRY (100μM). Inomycin served as a positive control. **(F)** Representative fluorescence images of Fluo 4 (5 μM) loaded HaCaT cells showed that the Ca^{2+} responses induced by *Der p1* was inhibited by *Der p1*+FSLLRY treatment at 0s, 50s and 170s. N = 3 mice per group.

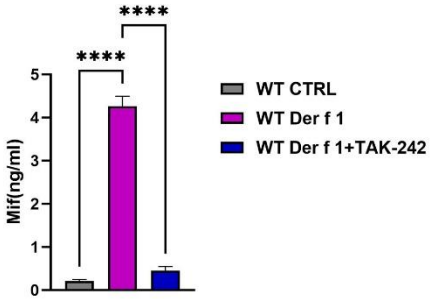

Figure S6. MIF release in the supernatant of mouse primary keratinocytes treated with Der f1 or the TLR4 antagonist TAK-242. ELISA of MIF showed that mouse primary keratinocytes ($1.5*10^5$ cells) treated with *Der f1* (10μg/μl)+TAK-242 (10μM) for 12 hours inhibited the MIF release induced by *Der f1* stimulation. (1.5×10^5 cells per group). One-way ANOVA. ****$p < 0.0001$. WT, wild type.

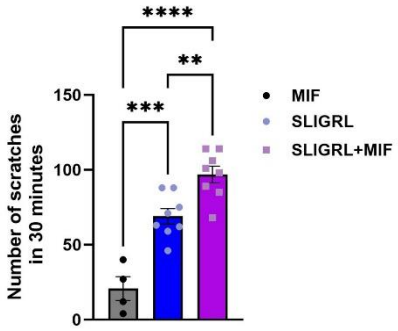

Figure S7. MIF synergized with PAR2 agonist SLIGRL to promote mice acute itch. Mice scratching bouts increased obviously induced by intradermal injection of SLIGRL (50μg) +MIF (0.5μg) than injecting SLIGRL only group. One-way ANOVA, n=4-8, ** $p < 0.01$, *** $p < 0.001$, ****$p < 0.0001$.

Table S1. Primers for quantitative PCR.

mMif Gene ID:17319	Up	5′-TTAGCGGCACGAACGATCC -3′
	Down	5′-ACAGCAGCTTACTGTAGTTGC -3′
mKif13b Gene ID:16554	Up	5′-GCTCTGTAGTGGACTCTTTGAAC -3’
	Down	5′-TTTGGGGTCAAGAAGGTCTCG -3’
mIL-4 Gene ID:16189	Up	5′-GGTCTCAACCCCCAGCTAGT -3’
	Down	5′-GCCGATGATCTCTCTCAAGTGAT -3’
mIL-13 Gene ID:16163	Up	5′-CCTGGCTCTTGCTTGCCTT -3’
	Down	5′-GGTCTTGTGTGATGTTGCTCA -3’
mTslp Gene ID:53603	Up	5′-ACGGATGGGGCTAACTTACAA -3’
	Down	5′-AGTCCTCGATTTGCTCGAACT -3’
mArg1 Gene ID:11846	Up	5′-CTCCAAGCCAAAGTCCTTAGAG-3’
	Down	5′-AGGAGCTGTCATTAGGGACATC-3’
mIl1b Gene ID:16176	Up	5′-TTCAGGCAGGCAGTATCACTC-3’
	Down	5′-GAAGGTCCACGGGAAAGACAC-3’
mIl6 Gene ID:16193	Up	5′-TAGTCCTTCCTACCCCAATTTCC-3’
	Down	5′-TTGGTCCTTAGCCACTCCTTC-3’
mIl10 Gene ID:16153	Up	5′-CTTACTGACTGGCATGAGGATCA-3’
	Down	5′-GCAGCTCTAGGAGCATGTGG-3’
mGapdh Gene ID:14433	Up	5′- AGGTCGGTGTGAACGGATTTG -3′
	Down	5′- TGTAGACCATGTAGTTGAGGTCA -3′

Table S2. KC_cluster identity

Cell type	**Genes**
Undifferentiated KC	*KRT5, KRT14, CCL27A, CXCL14, KRT15*
Basal_1	*TSLP, IGFBP3*
Basal_2	*COL23A1, FST*
Basal_3	*IL31RA, POSTN*
Differentiated KC	*KRT1, KRT10, KRTDAP*
Spinous_1	*S100A9, S100A8*
Spinous_2	*SKINT6, KRT6A*
Inner root sheath cell	*KRT71, KRT73, TCHH*
Proliferating KC	*MKI67, TOP2A, HIST1H2AP, HIST1H2AE*

KC：Keratinocytes.