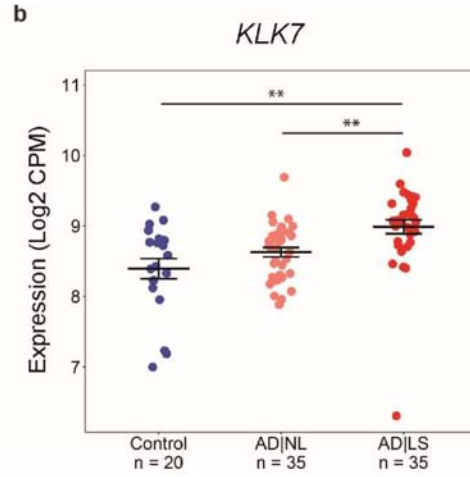
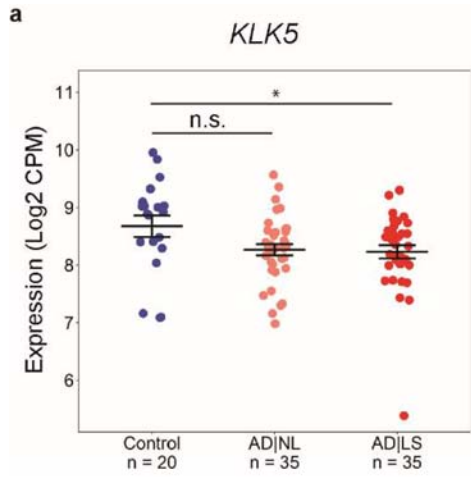


Table S1. Primers used for PCR

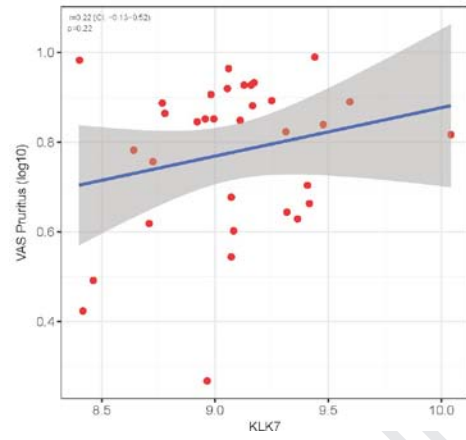
Gene	Forward Primer	Reverse Primer
<i>HS KLK5</i>	CACAAGGGTAATCTCCCCAG	AGATGACACCATGTTCTGCG
<i>HS KLK7</i>	GGGTACCTCTGCACACCAAC	GGATGTCAAGCTCATCTCCC
<i>HS ACTB</i>	ACCTTCTACAATGAGCTGCG	CCTGGATAGCAACGTACATGG
<i>MM Klk5</i>	GAACCACTTAGCCTCGACCTTTAT	GTTTCGGTTCCAGAGGGGTTG
<i>MM Klk7</i>	GTGCTGGCATTCTGACTCTA	CCATCACCCACCGTTTGTACT
<i>MM Gapdh</i>	CCCAGCAAGGACACTGAGCAA	TTATGGGGGTCTGGGATGGAAA
<i>MM Il4ra</i>	GTTACAGGAACAAGACCAGCA	TGGAGCCTGAACTCGCA
<i>MM Il4</i>	GAACGAGGTCACAGGAGAAG	ACCTTGGAAGCCCTACAGA
<i>MM Il13</i>	TGCCATCTACAGGACCCAGA	CTCATTAGAAGGGGCCGTGG

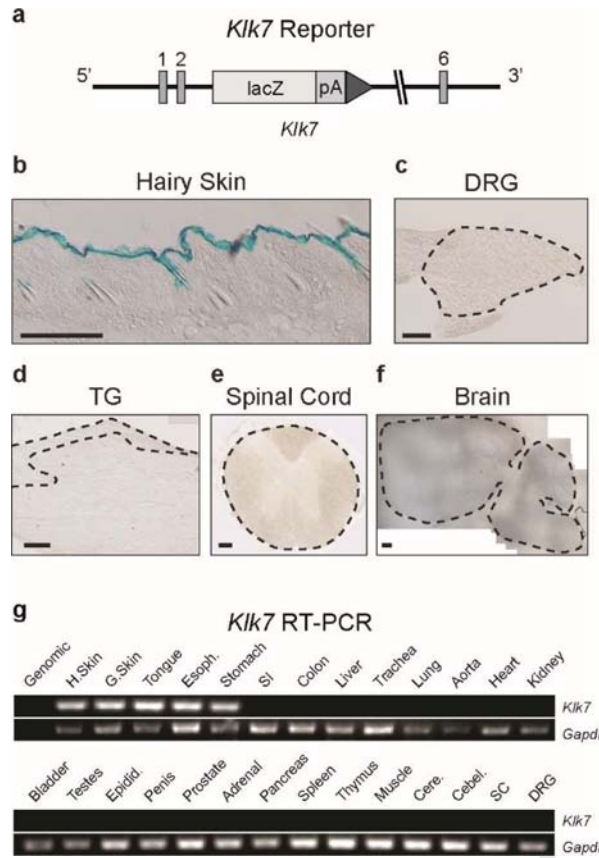
Table S2. Primary antibodies for flow cytometry

Antibody	Vendor	Catalog #	Antibody	Vendor	Catalog #
CD49b APC	Biolegend	17-5971-82	Siglec-F BV421	BD	562681
CD11b BV510	Biolegend	101245	CD117 BV605	Biolegend	135122
CD3ε PerCP/Cy5.5	eBioscience	45-0031-82	CD5 PerCP/Cy5.5	eBioscience	45-0051-82
CD11c PerCP/Cy5.5	eBioscience	45-0114-82	CD19 PerCP/Cy5.5	eBioscience	45-0193-82
NK1.1 PerCP/Cy5.5	eBioscience	45-5941-82	ST2-Biotin	Biolegend	145307
KLRG1 PE/Dazzle	Biolegend	138424	CD25 BV605	Biolegend	102035
FcεRIα FITC	eBioscience	11-5898-85	IgE FITC	eBioscience	11-5992-81
CD90.2 PE/Cy7	Biolegend	140309	CD45 APC	Biolegend	103111
CD45.2 PE	Biolegend	109808	CD3ε PE	Biolegend	100307

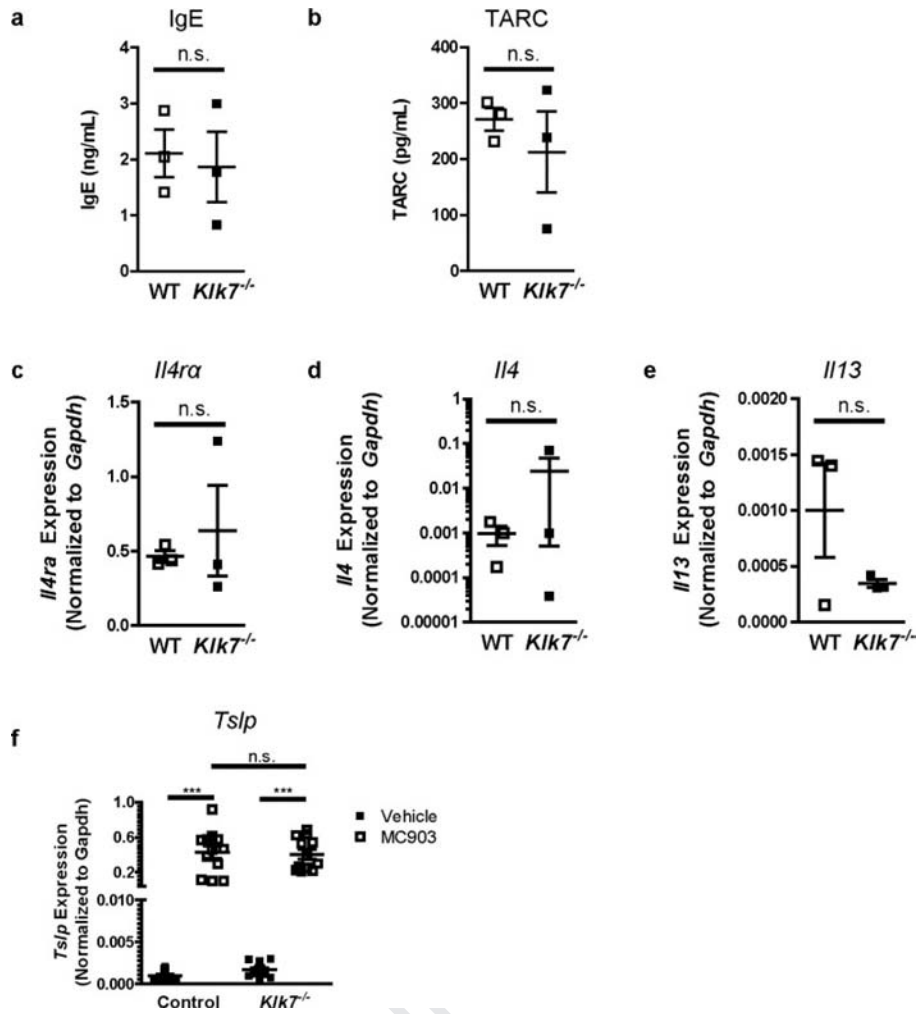


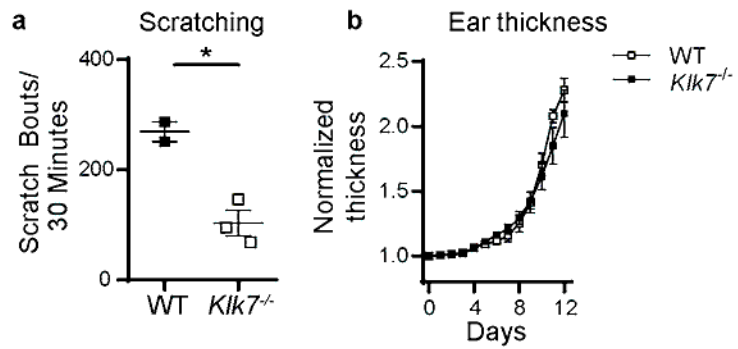
c Pearson correlation



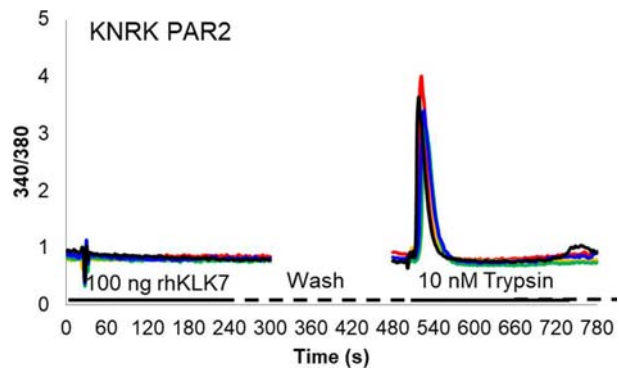


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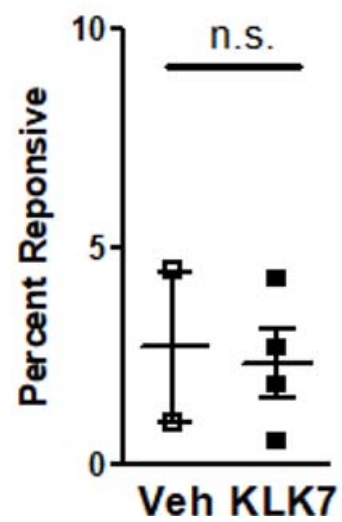
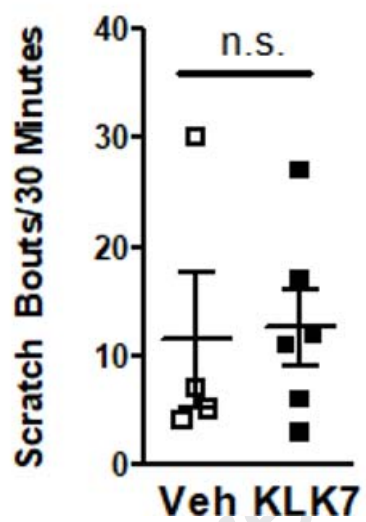
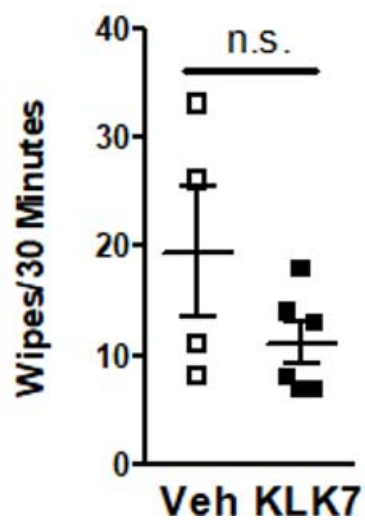
a.

b.

c.

Behavior

Cultured DRGs



Journal Pre

SUPPLEMENTAL TEXT

Figure S1. *KLK7*, but not *KLK5*, is upregulated in human lesional AD skin. **a.** Log₂ read counts per million (CPM) of *KLK5* in control skin from donors without AD (N=20, age = 36.8 ± 2.4 years, 42.9% female), and matched pairs of non-lesional (NL) skin and lesional (LS) skin from donors with AD (N=35, age = 34.3 ± 2.5 years, 50% female). **b.** Log₂ CPM of *KLK7* in the same RNA-seq data set. Note that *KLK7* is overexpressed only in lesional AD skin. n.s. no significance. * $p < 0.05$. ** $p < 0.01$. **c.** Pearson correlation between *KLK7* transcript abundance in lesional skin and the Visual Analog Scale (VAS) itch scores from AD patients. $R = 0.22$ (CI -0.13 – 0.52), $p = 0.22$.

Figure S2. *Klk7* expression is restricted to the epidermis in mouse skin. **a.** Genomic construct of the *Klk7*^{tm1(KOMP)Vlcg} allele. Exons 3-5 within the coding region of *Klk7* is replaced with a *LacZ-β-galactosidase* reporter. **b.** X-gal staining (blue) of hair-bearing skin from a *Klk7*^{LacZ} mouse, in which LacZ expression is controlled under the *Klk7* promoter. **c-f.** X-gal staining of **c.** dorsal root ganglia (DRG), **d.** trigeminal ganglia (TG), **e.** spinal cord, **f.** and brain. **g.** RT-PCR screening of *Klk7* expression in tissues from a WT control mouse. n = 3 biological replicates for panels **b-g**.
H. Skin = hairy skin. G. Skin = glabrous skin. SI = Small intestine.

Figure S3. *Klk7*^{-/-} mice do not show lowered Th2 and inflammatory markers after MC903 Treatment. **a-b.**

ELISA based quantification of serum **a.** IgE and **b.** TARC levels in MC903 treated control and *Klk7*^{-/-}

mice. **c-e.** RT-qPCR quantification of **c.** *Il4ra*, **d.** *Il4*, and **e.** *Il13* expression in MC903 treated skin of

control and *Klk7*^{-/-} mice. **f.** RT-qPCR quantification of *Tslp* expression in vehicle or MC903 treated skin

of control and *Klk7*^{-/-} mice. n.s. no significance. *** $p < 0.001$

Figure S4. rhKLK7 does not activate PAR2 receptors. Representative calcium transients of KRNK cells

stably transduced with PAR2 expression after treatment with rhKLK7 and Trypsin.

Figure S5. Acute *in vivo* and *in vitro* effects of rhKLK7. a.-b. Acute pain (wiping) and itch (scratching)

behavioral responses of C57BL/6J mice to v n.s. or 1 μ g rhKLK7 injections. c. Quantification of

calcium responses of culture DRG neurons from *Pirt*^{GCaMP/+} mice to acute application of vehicle or 20

ng/ μ l rhKLK7. Percent responsive represents fraction of all DRG neurons in field. Data is presented as

mean \pm SEM. Statistical significance was determined using two tailed Student's *t* test. n.s. denotes no

significance.