

Supplementary tables

Supplementary Table S1

Genotyping primer

Name	Sequence	Allele	Length
LacZ_2_small_F	ATCACGACGCGCTGTATC L	LacZ	108
LacZ_2_small_R	ACATCGGGCAAATAATATCG	LacZ	108
CRE Forward	GAAAGCAGCCATGTCCAATTTACTGACCGTAC	Cre	
CRE Reverse	GCGCGCCTGAAGATATAGAAGA	Cre	

Supplementary Table S2

RT-PCR primer

Primer name	Sequence	Source
MRGPRA3 fwd	5'CTCAAGTTTACCCTACCCAAAGG 3'	Harvard PrimerBank
MRGPRA3 rev	5' CCGCAGAAATAACCATCCAGAA 3'	Harvard PrimerBank
MRGPC11 fwd	5' TCTCATCCCACGACACAGAAT 3'	Harvard PrimerBank
MRGPC11 rev	5' AGCCAGAGTACAATGGTGTTC 3'	Harvard PrimerBank
LPAR2 fwd	5' GGCCGTGTGGTCACACTC 3'	(Contos et al. 2002)
LPAR2 rev	5' CCCAGAATGATGACAACCGTCTT 3'	(Contos et al. 2002)
LPAR5 fwd	5' CAAGAAGGTCTCCACTGCTGA 3'	
LPAR5 rev	5' GTGGTAGCCTGGTGGCAATA 3'	

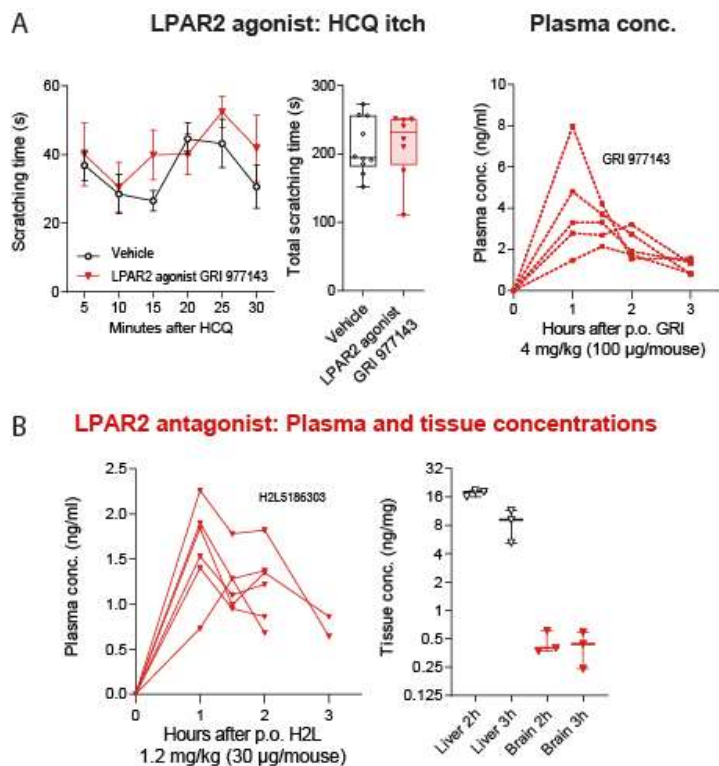
Supplementary Table S3

Primary antibodies and fluorophore conjugates

Antibody	Manufacturer	Product #	Dilution	Host	Type	Use
Beta Gal	Abcam	Ab116	1:500	mouse	mab	IFL
Beta Gal	Abcam	Ab9361	1:200	chicken	pab	IFL
GAD65 and GAD67	Abcam	Ab49832	1:200	rabbit	pab	IFL
Homer	SCBT	Sc-15321	1:200	rabbit	pab	IFL
IB4 Alexa 488	Invitrogen	I 21411	1:200			IF
IB4 Alexa 594	Invitrogen	I21413	1:200			IF
MrgprX1	Abcam	Ab77519	1:200	Rabbit	pab	IFL
NeuN	Abcam	Ab177487	1:500	rabbit	mab	IFL
Peripherin	Chemicon	Ab1530	1:50	Rabbit	pab	IFL
Tuj-1	Promega	G7121	1:500	Mouse	mab	IFL

IFL, Immunofluorescence; FL, fluorescence; mab, monoclonal antibody; pab, polyclonal antibody

Supplementary figures



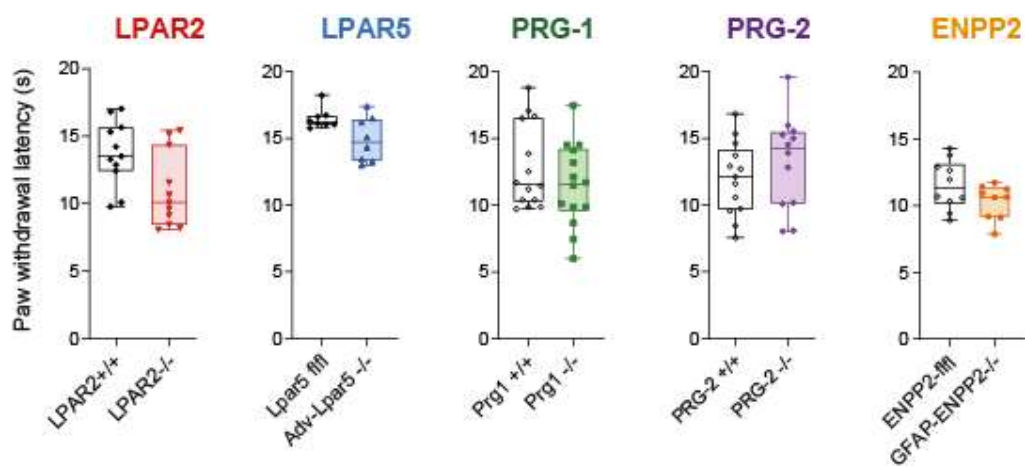
Supplementary Figure S1

Itch behavior and drug concentrations in plasma and tissue

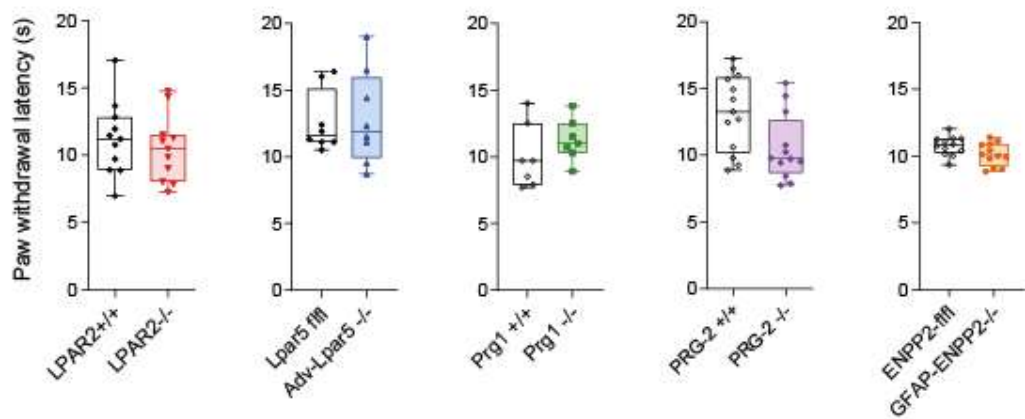
A: Scratching behavior in mice treated with the LPAR2 agonist GRI 977143 (100 µg/mouse; ≈ 4 µg/g) and plasma concentrations after oral administration of the drug. Scratching behavior was evoked by intradermal injection hydroxychloroquine (HCQ) ($n = 8$ per group). Plasma concentration time courses were measured by HPLC-MS-MS analysis of $n = 5$ per group.

B: Plasma and tissue concentrations of the LPAR2 antagonist H2L5186303 upon oral administration of 30 µg/mouse (≈ 1.2 µg/g) in $n = 6$ mice per group. The group was split to assess liver and brain concentrations at 2 and 3 hours.

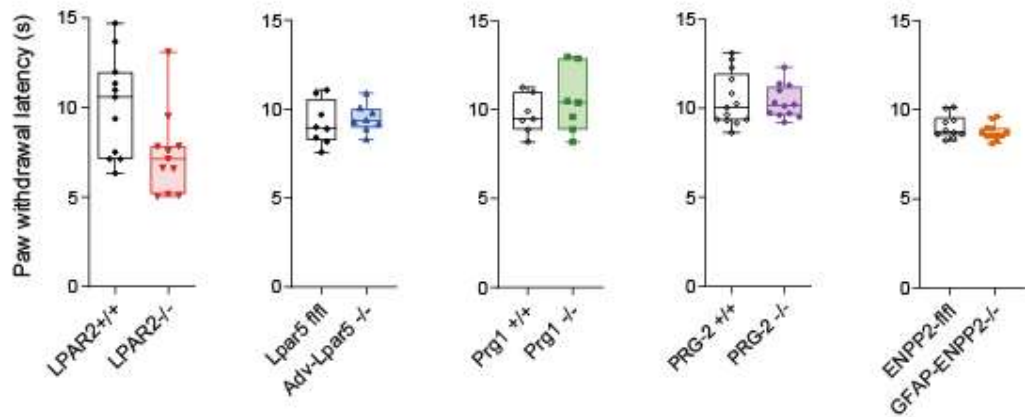
Hotplate 52°C



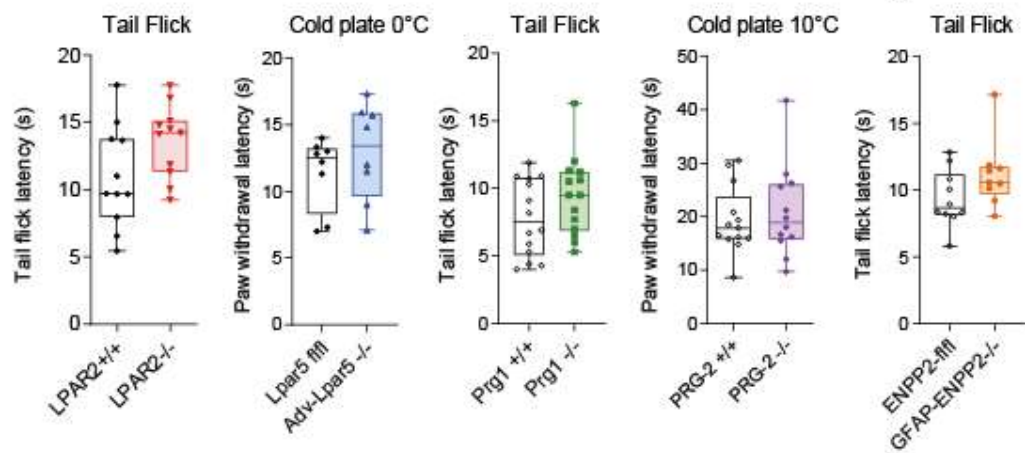
Hargreaves



Dynamic Plantar



Tail flick or Cold plate



Supplementary Figure S2

Basic nociceptive behavior upon thermal or mechanical stimulation

Paw withdrawal latencies were measured upon heat stimulation on a 52°C Hotplate, upon mechanical stimulation with a dynamic von Frey aesthesiometer, upon thermal stimulation with the Hargreaves test, upon heat stimulation of the tail (tail flick) or cold stimulation on a cold plate. The genotypes were LPAR2^{-/-} versus wildtype, Advillin-LPAR5^{-/-} versus floxed controls (LPAR5-fl/fl), Prg1/LPPR4^{-/-} versus wildtype, Prg2/LPPR5^{-/-} versus wildtype and GFAP-ENPP2^{-/-} versus ENPP2-fl/fl controls (ENPP2 = autotaxin). The boxes show the interquartile range, the line is the median, whiskers show minimum to maximum and the scatters represent individual mice. Unpaired 2-tailed Student's t-tests did not show significant differences between the respective genotypes.