

Supplemental table 1. Differentially expressed genes at 4-weeks. Differentially expressed genes with an adjusted p value (padj) <0.05. Genes upregulated in OA are represented by a positive fold change (Log2FoldChange) and genes downregulated by a negative fold change.

Row.names	log2FoldChange	padj	external_gene_name
ENSRNOG00000016163	1.180428996	2.82E-08	Slc1a3
ENSRNOG00000004067	0.745566281	7.99E-06	Nrcam
ENSRNOG00000017693	0.902116131	0.000876432	Slc2a5
ENSRNOG00000054603	0.970000223	0.000876432	Pacsin1
ENSRNOG00000014851	0.661965165	0.001037881	Col4a4
ENSRNOG00000008182	0.70338452	0.001037881	Htra3
ENSRNOG00000038132	0.803639935	0.002615602	Vsig4
ENSRNOG00000033498	0.405260428	0.004188724	Cib1
ENSRNOG00000033261	-0.390366395	0.004494457	Fam107a
ENSRNOG00000008837	-0.577310749	0.005753927	Ass1
ENSRNOG00000005378	0.486977437	0.007076163	Gna15
ENSRNOG00000009919	-2.648723536	0.007585942	Acod1
ENSRNOG00000004494	0.355373947	0.008374958	Lta4h
ENSRNOG00000012779	0.632039589	0.01019025	Msr1
ENSRNOG00000030689	0.617601711	0.011195323	Ms4a6b1
ENSRNOG00000061524	0.490009107	0.014419012	AABR07068285.2
ENSRNOG000000051487	0.414310325	0.014419012	Kremen1
ENSRNOG00000017597	-2.737601371	0.014419012	Fbp1
ENSRNOG00000015948	-0.386477118	0.014419012	Slc1a5
ENSRNOG00000016164	0.925455677	0.014419012	Fcrl2
ENSRNOG00000018566	0.212444568	0.015166772	Ctsl
ENSRNOG00000047349	0.629392319	0.015166772	AABR07006269.1
ENSRNOG00000009982	0.19842526	0.015166772	Pnp
ENSRNOG00000018400	0.492888159	0.021751535	Golm1
ENSRNOG00000009341	-0.633612016	0.023346679	Hivep3
ENSRNOG00000017438	0.86350558	0.023346679	AABR07007068.1
ENSRNOG00000014475	0.40409469	0.023796129	Slc31a1
ENSRNOG00000019110	-1.745048249	0.027476515	Ocstamp
ENSRNOG00000013578	0.445099695	0.029400882	Trem2
ENSRNOG00000032133	-2.169371231	0.029400882	Rnase2
ENSRNOG00000005679	0.786819688	0.029400882	Fap
ENSRNOG00000026807	0.627138755	0.029400882	LOC362863
ENSRNOG00000056493	-0.691736731	0.029400882	Mybpc1
ENSRNOG00000037687	1.098177278	0.032049809	Rspo2
ENSRNOG00000018570	1.157760966	0.032214387	C1qtnf3
ENSRNOG00000012062	0.360866569	0.036526701	Npc2
ENSRNOG00000053332	-1.628415334	0.045540302	Cdh26
ENSRNOG00000049766	-1.747079821	0.045723635	Sctr
ENSRNOG00000005249	0.245673363	0.045723635	Snx6

ENSRNOG00000000142	0.317245961	0.045723635 Plxdc2
ENSRNOG00000000855	0.557795078	0.045843032 Lst1
ENSRNOG00000014603	0.80904359	0.04858025 Sgcg

Supplemental table 2. Differentially expressed genes at 12-weeks. Differentially expressed genes with an adjusted p value (padj) <0.05. Genes upregulated in OA are represented by a positive fold change (Log2FoldChange) and genes downregulated by a negative fold change.

Row.names	log2FoldChange	padj	external_gene_name
ENSRNOG00000046261	0.890052296	1.11E-06	Acp5
ENSRNOG00000026302	0.621483643	3.72E-06	Lrrn4cl
ENSRNOG00000014603	0.999361928	1.30E-05	Sgcg
ENSRNOG00000008182	0.762441198	8.22E-05	Htra3
ENSRNOG00000012442	1.42799731	0.000306367	Cemip
ENSRNOG00000024998	0.451528157	0.000384099	Trps1
ENSRNOG00000006526	0.56583181	0.000384099	Sema3c
ENSRNOG00000010181	0.727980835	0.000384099	Clec4d
ENSRNOG00000016812	1.538124752	0.000814165	Adamts16
ENSRNOG00000017842	-0.961721711	0.001042466	Scnn1g
ENSRNOG00000054204	-0.566585949	0.001042466	Gria2
ENSRNOG00000000700	0.830366968	0.001042466	Tmem119
ENSRNOG00000000811	0.766698419	0.001464273	Pkib
ENSRNOG000000048924	0.73032045	0.001716486	Islr
ENSRNOG00000013269	-0.461252983	0.00235593	Tnfsf10
ENSRNOG00000018570	1.491432586	0.002378731	C1qtnf3
ENSRNOG00000004783	0.748665156	0.00255907	Fam171b
ENSRNOG00000023303	-0.493034271	0.002560881	Dpep2
ENSRNOG00000005931	0.505377634	0.002786547	Cpq
ENSRNOG00000007866	1.262693056	0.003122938	Clec2dl1
ENSRNOG00000005277	1.321259015	0.003122938	Ptprv
ENSRNOG00000009892	-0.580610529	0.00376258	Adamts15
ENSRNOG00000016372	-0.282071876	0.003915687	Slc12a7
ENSRNOG00000002372	0.874055931	0.004285156	Sgcd
ENSRNOG00000004067	0.630925222	0.004349213	Nrcam
ENSRNOG00000016968	-0.351973032	0.00457206	Gramd4
ENSRNOG00000010977	0.692385055	0.00457206	Igfbp6
ENSRNOG00000017786	0.834954167	0.004631346	Acta1
ENSRNOG00000007461	0.633547014	0.006052383	Klhl41
ENSRNOG00000027936	0.78188318	0.006141339	Ccdc8
ENSRNOG00000030210	0.730591683	0.006371413	Fndc1
ENSRNOG00000006548	0.692459913	0.006502247	Mrc2
ENSRNOG00000010918	0.401409229	0.007540242	Cebpa
ENSRNOG00000009972	-0.267587962	0.008098586	Rara
ENSRNOG00000002345	0.460519623	0.008098586	Rasgef1b
ENSRNOG00000005708	1.310923614	0.008974323	Mmp16
ENSRNOG00000008680	0.600455103	0.009054238	Lox11
ENSRNOG000000022710	0.722509356	0.009385557	Prrg4
ENSRNOG00000005679	0.824225794	0.009519663	Fap

ENSRNOG00000004583	0.983260413	0.009647513 Mb
ENSRNOG000000051688	-0.502607515	0.010264192 Syt15
ENSRNOG000000030763	-0.638481422	0.011868307 Dpp4
ENSRNOG00000012681	-0.461006623	0.011868307 Lgals9
ENSRNOG00000018669	-0.450891881	0.011868307 Jak3
ENSRNOG00000014398	0.607866224	0.011868307 Scara5
ENSRNOG00000023812	0.965379606	0.011868307 Raver2
ENSRNOG00000010079	0.994431206	0.011868307 Ca3
ENSRNOG00000006052	0.507512071	0.011908438 Sulf2
ENSRNOG00000046494	1.488478451	0.012830497 LOC100361018
ENSRNOG00000009822	0.388653991	0.013189148 Tlr2
ENSRNOG00000021155	0.57562951	0.013189148 Ctsk
ENSRNOG00000030981	-0.521647457	0.014877556 Scnn1b
ENSRNOG000000053201	-0.398984485	0.014877556 Gpcpd1
ENSRNOG00000007545	-0.817073782	0.015648813 Angptl4
ENSRNOG00000013631	0.329871237	0.015648813 Slc31a2
ENSRNOG00000010666	0.884469294	0.015648813 Ccn5
ENSRNOG000000032297	0.323017785	0.016622334 Msmo1
ENSRNOG00000024620	0.562246532	0.016843063 Mamdc2
ENSRNOG00000018509	0.803547745	0.016843063 Cx3cr1
ENSRNOG000000033496	0.901376684	0.016843063 Igdcc4
ENSRNOG000000058329	0.911675704	0.016843063 Prrx2
ENSRNOG00000009079	-0.495296703	0.017365334 Prkar2b
ENSRNOG00000004400	-0.773219157	0.018797022 Avpr1a
ENSRNOG00000006787	0.350201837	0.018797022 Dhcr24
ENSRNOG00000000902	0.363357584	0.018797022 Hsph1
ENSRNOG000000049471	0.466777684	0.018797022 Steap3
ENSRNOG00000014166	0.758474523	0.018797022 Smoc2
ENSRNOG00000009343	1.191133669	0.018797022 Evpl
ENSRNOG00000043219	1.508025779	0.018871909 Fbn2
ENSRNOG000000047545	-0.570738111	0.019397831 Adra2a
ENSRNOG00000004672	-0.353325583	0.019397831 Sec14l2
ENSRNOG00000008749	0.5100935	0.019397831 Col5a1
ENSRNOG00000012196	0.740907822	0.019397831 Asah2
ENSRNOG00000020743	0.821799203	0.019397831 Cyp2s1
ENSRNOG00000049491	1.631670496	0.019566261 RT1-DMb
ENSRNOG000000057855	0.452330651	0.020988374 F5
ENSRNOG00000049994	-0.619010451	0.021769497 Ifi44l
ENSRNOG000000037838	0.563778448	0.023524739 RGD1560455
ENSRNOG000000039759	0.578150836	0.023524739 Gpr34
ENSRNOG00000000563	0.897097058	0.023524739 Adamts14
ENSRNOG00000016983	1.063372471	0.023524739 Myh7
ENSRNOG00000015972	1.292122146	0.024079731 Ano5
ENSRNOG00000008478	3.33248879	0.025744708 Mmp13

ENSRNOG00000050996	0.648347864	0.026128682 Kctd4
ENSRNOG00000034139	0.746484637	0.026128682 Lyc2
ENSRNOG00000014243	-0.349182886	0.02686541 Pear1
ENSRNOG00000013312	0.508594673	0.027085163 Kcnt2
ENSRNOG00000014505	-0.768625373	0.027244864 Pmfbp1
ENSRNOG00000004712	0.782565835	0.027250161 Angptl1
ENSRNOG00000004706	1.047587761	0.027821961 Vit
ENSRNOG000000061394	0.555255558	0.028158956 Clec4e
ENSRNOG00000017819	0.371624718	0.028312868 Cd14
ENSRNOG00000007036	0.517639602	0.028312868 Tgfbr1
ENSRNOG00000059507	-0.728965502	0.028512068 Lamc3
ENSRNOG00000008351	-0.476449962	0.029518787 RGD1308117
ENSRNOG00000019141	-0.452501871	0.030827837 Ch25h
ENSRNOG00000000653	-0.649222819	0.032074036 Nr5a2
ENSRNOG00000007918	0.587311781	0.032074036 Tbxas1
ENSRNOG00000015505	0.755290855	0.032074036 Mfap5
ENSRNOG00000007286	-0.441207605	0.033802817 Mdm1
ENSRNOG00000052880	-0.593995077	0.034327848 Prph
ENSRNOG00000034258	0.905499984	0.034327848 Xirp2
ENSRNOG00000007567	-0.429052156	0.034650884 Rem1
ENSRNOG00000003229	-0.366534807	0.034650884 Tspan7
ENSRNOG00000011659	0.662982576	0.035201619 Alpk3
ENSRNOG000000061845	-0.548642643	0.035251113 Ctnnbp2
ENSRNOG00000004273	-0.353401237	0.036880784 Ifitm1
ENSRNOG000000023148	0.839783456	0.037194877 Col11a1
ENSRNOG00000019757	-0.879158155	0.03860483 Dpep3
ENSRNOG00000039278	0.909031651	0.03860483 Mcart1
ENSRNOG00000043167	0.341170162	0.038812981 Itga9
ENSRNOG00000006867	0.37704266	0.038812981 Etv1
ENSRNOG00000054251	0.630452687	0.038907975 Clec7a
ENSRNOG00000009073	1.093680463	0.038907975 Tnni1
ENSRNOG00000025245	0.490228618	0.040783376 RGD1311946
ENSRNOG00000013663	0.689243577	0.042481784 Tmem86a
ENSRNOG00000014117	-0.341674826	0.042576729 Hmox1
ENSRNOG00000006859	0.365525243	0.042576729 Insig1
ENSRNOG00000017459	0.631539588	0.042576729 C1ql3
ENSRNOG00000002434	0.720128473	0.042576729 Tmem100
ENSRNOG00000032994	0.852028342	0.042576729 Myom3
ENSRNOG00000013179	-0.412391059	0.043321885 Tinagl1
ENSRNOG00000056118	-0.319453441	0.043321885 Cic
ENSRNOG00000038202	0.462908035	0.043515363 Calml4
ENSRNOG00000026604	0.522008395	0.043515363 Cercam
ENSRNOG00000022256	-0.537374547	0.043998835 Cxcl10
ENSRNOG00000013578	0.555124503	0.044615422 Trem2

ENSRNOG00000005592	0.581016282	0.044829054	Brinp2
ENSRNOG00000022597	-0.390437232	0.045006764	Cenpj
ENSRNOG00000019556	0.502988502	0.045006764	Cd9
ENSRNOG00000008622	0.542822201	0.045006764	Creb5
ENSRNOG00000013967	0.504059827	0.047724369	Blnk
ENSRNOG00000021521	-3.801777205	0.050067516	Chst5

Supplemental table 3. GSEA report for GO at 4-week. Gene sets positively enriched in PTOA from the Gene Ontology database at 4-weeks.

NAME	NES	NOM p-val	FDR q-val
GOBP_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDE_OR_POLYSACCHARIDE_ANTIGEN_VIA_MHC_CLASS_II	2.527666	0	0.006856685
GOBP_NUCLEOTIDE_SUGAR_METABOLIC_PROCESS	2.468147	0	0.005145371
GOBP_VESICLE_MEDIATED_TRANSPORT_BETWEEN_ENDOSOMAL_COMPARTMENTS	2.4302742	0	0.006869598
GOBP_PROTEIN_LOCALIZATION_TO_ENDOPLASMIC_RETICULUM	2.4022214	0	0.005152199
GOBP_ESTABLISHMENT_OF_PROTEIN_LOCALIZATION_TO_ENDOPLASMIC_RETICULUM	2.3398695	0	0.009028094
GOBP_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE	2.3228097	0	0.01155867
GOBP_POST_GOLGI_VESICLE_MEDIATED_TRANSPORT	2.304336	0	0.013865072
GOCC_MITOTIC_SPINDLE_POLE	2.2978964	0	0.012959702
GOBP_COLLAGEN_FIBRIL_ORGANIZATION	2.2952921	0	0.011519736
GOCC_COPI_COATED_VESICLE	2.2122838	0	0.02528621
GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT_CONFERRING_COMPRESSION_RESISTANCE	2.202142	0	0.025801998
GOBP_AUTOPHAGY_OF_MITOCHONDRION	2.1820586	0	0.029995421
GOBP_VACUOLE_ORGANIZATION	2.1803434	0	0.02768808
GOBP_REGULATION_OF_AUTOPHAGY_OF_MITOCHONDRION	2.1777034	0	0.02692886
GOBP_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_EXOGENOUS_PEPTIDE_ANTIGEN_VIA_MHC_CLASS_II	2.1706033	0	0.028117338
GOBP_CYTOSOLIC_TRANSPORT	2.1526976	0	0.031778224
GOBP_NUCLEOTIDE_SUGAR_BIOSYNTHETIC_PROCESS	2.1395595	0	0.03397925
GOBP_PROTEIN_QUALITY_CONTROL_FOR_MISFOLDED_OR_INCOMPLETELY_SYNTHESIZED_PROTEINS	2.1369963	0	0.032862827
GOCC_SITE_OF_DOUBLE_STRAND_BREAK	2.1286125	0	0.03311641
GOBP_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE	2.1202404	0	0.035254776
GOCC_CIS_GOLGI_NETWORK	2.1195056	0	0.034069378
GOCC_SPECIFIC_GRANULE_MEMBRANE	2.1105418	0	0.034882184
GOBP_LYTIC_VACUOLE_ORGANIZATION	2.1069336	0	0.035458162
GOCC_GOLGI_STACK	2.106341	0	0.034124304
GOBP_REGULATION_OF_EARLY_ENDOSOME_TO_LATE_ENDOSOME_TRANSPORT	2.1035776	0	0.03331029
GOBP_PROTEIN_LOCALIZATION_TO_CILIARY_MEMBRANE	2.098182	0	0.034179416
GOBP_GOLGI_TO_ENDOSOME_TRANSPORT	2.091858	0.005128205	0.03472157
GOMF_PRENYLTRANSFERASE_ACTIVITY	2.0665827	0	0.040544823
GOBP_PROTEIN_LOCALIZATION_TO_MICROTUBULE_ORGANIZING_CENTER	2.0622885	0	0.04121025
GOCC_DYSTROPHIN_ASSOCIATED_GLYCOPROTEIN_COMPLEX	2.054218	0.004854369	0.042858638
GOBP_REGULATION_OF_PHOSPHOLIPID_BIOSYNTHETIC_PROCESS	2.0388882	0	0.04750668
GOBP_ORGANELLE_DISASSEMBLY	2.0355656	0	0.046778537
GOBP_PROTEIN_EXIT_FROM_ENDOPLASMIC_RETICULUM	2.0342562	0	0.045675196
GOBP_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDE_ANTIGEN	2.032697	0	0.044633698
GOBP_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_EXOGENOUS_PEPTIDE_ANTIGEN	2.0310414	0	0.04376037
GOMF_PHOSPHATIDYLINOSITOL_MONOPHOSPHATE_PHOSPHATASE_ACTIVITY	2.0295067	0.004901961	0.043026023
GOBP_REGULATION_OF_ERYTHROCYTE_DIFFERENTIATION	2.0259774	0	0.0430956
GOBP_AMINO_SUGAR_METABOLIC_PROCESS	2.0242229	0	0.042323843
GOCC_COPI_COATED_VESICLE_MEMBRANE	2.0200748	0	0.04320737
GOCC_SPECIFIC_GRANULE	2.0038197	0	0.048485585
GOBP_PROTEIN_N_LINKED_GLYCOSYLATION	1.9997069	0	0.04856924
GOBP_ENDOPLASMIC_RETICULUM_TO_GOLGI_VESICLE_MEDIATED_TRANSPORT	1.9960654	0	0.048977233
GOBP_PROTEIN_LOCALIZATION_TO_CYTOSKELETON	1.9926087	0	0.049449492
GOBP_PROTEIN_DEGLYCOSYLATION	1.9904077	0.005780347	0.048943087
GOBP_MYELIN_ASSEMBLY	1.9891163	0.005291005	0.04833131
GOBP_POSITIVE_REGULATION_OF_GLYCOPROTEIN_METABOLIC_PROCESS	1.9876896	0	0.047952738

Supplemental table 4. GSEA report for GO at 12-week. Gene sets positively enriched in PTOA from the Gene Ontology database at 12-weeks.

Name	NES	NOM p-val	FDR q-val
GOBP_COLLAGEN_CATABOLIC_PROCESS	2.19	0	0.002
GOCC_COMPLEX_OF_COLLAGEN_TRIMERS	2.1	0	0.011
GOMF_ELECTRON_TRANSFER_ACTIVITY	2.03	0	0.034
GOMF_OXIDOREDUCTION_DRIVEN_ACTIVE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	2.02	0	0.028
GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT_CONFERRING_TENSILE_STRENGTH	2.02	0	0.022
GOMF_COLLAGEN_BINDING	1.98	0	0.036
GOBP TRABECULA FORMATION	1.98	0	0.036
GOCC_COLLAGEN_TRIMER	1.97	0	0.036
GOMF_FIBRONECTIN_BINDING	1.95	0	0.041
GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT	1.95	0	0.041
GOCC_A_BAND	1.94	0	0.044
GOMF_PROTON_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	1.92	0	0.05
GOCC_RESPIRASOME	1.92	0	0.047
GOBP_EXTERNAL_ENCAPSULATING_STRUCTURE_ORGANIZATION	1.92	0	0.045
GOBP_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDE_OR_POLYSACCHARIDE_ANTIGEN_VIA_MHC_CLASS_II	1.91	0	0.048

Supplemental table 5. GSEA report for Hallmark at 4-week. Gene sets positively enriched in PTOA from the Hallmark database at 4-weeks.

NAME	NES	NOM p-val	FDR q-val
HALLMARK_PROTEIN_SECRETION	2.7417886	0	0
HALLMARK_TGF_BETA_SIGNALING	2.3160634	0	0
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	2.2345629	0	0
HALLMARK_MITOTIC_SPINDLE	2.1072602	0	0
HALLMARK_OXIDATIVE_PHOSPHORYLATION	1.9979291	0	0.001599587
HALLMARK_MTORC1_SIGNALING	1.9896821	0	0.001332989
HALLMARK_G2M_CHECKPOINT	1.8814024	0	0.00647452
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	1.7856348	0	0.00866443
HALLMARK_ANGIOGENESIS	1.6482159	0.016129032	0.014726359
HALLMARK_DNA_REPAIR	1.6304616	0	0.013786918
HALLMARK_MYC_TARGETS_V1	1.6286215	0	0.012533561
HALLMARK_GLYCOLYSIS	1.5741733	0	0.018020747
HALLMARK_ANDROGEN_RESPONSE	1.5708091	0	0.01786499
HALLMARK_UV_RESPONSE_DN	1.5558542	0	0.0171602
HALLMARK_INFLAMMATORY_RESPONSE	1.4775454	0	0.026116434
HALLMARK_E2F_TARGETS	1.4163634	0	0.038666215

Supplemental table 6. Individual linear mixed effects models, PAM. Individual linear mixed effects modelling of pressure pain threshold in Veh-lip (A), Clod-lip (B), STAT1i-lip (C), and STAT6i-lip (D).

A
Model 1 PAM Veh-lip

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	-70.57	16.23	-102.37 to -38.77
8	36.42	16.23	4.62 to 68.22
12	0.37	16.23	-31.43 to 32.17
Intercept	434.52	11.47	412.03 to 457.01
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	1316.24	310.24	829.29 to 2089.13

B
Model 2 PAM Clod-lip

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	42.18	23.19	-3.27 to 87.63
8	36.81	23.19	-8.64 to 82.26
12	123.32	23.19	77.87 to 168.77
Intercept	406.92	16.40	374.78 to 439.06
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	2688.65	633.72	1693.96 to 4267.42

C
Model 3 PAM STAT1i-lip

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	-96.64	25.28	-146.19 to -47.09
8	-32.44	25.28	-81.99 to 17.11
12	-22.84	25.28	-72.39 to 26.71
Intercept	480.18	17.88	445.14 to 515.22
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	3196.11	753.33	2013.68 to 5072.85

D
Model 4 PAM STAT6i-lip

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	67.86	21.17	26.38 to 109.34
8	153.85	21.17	112.37 to 195.33
12	73.97	21.17	32.49 to 115.45
Intercept	380.6	14.97	351.27 to 409.93
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	2239.98	527.97	1411.28 to 3555.28

Supplemental table 7. Linear mixed effects model with pairwise comparisons, PAM.

Model 5: PAM

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Treatment			
Veh-Lip	Reference	Reference	Reference
Clod-Lip	-27.60	21.72	-70.18 to 14.98
Stat1i-Lip	45.66	21.72	3.08 to 88.24
Stat6i-Lip	-53.92	21.72	-96.50 to -11.34
Time (weeks)			
0	Reference	Reference	Reference
4	-70.57	22.42	-114.52 to -26.62
8	36.42	22.42	-7.53 to 80.37
12	0.37	22.42	-43.58 to 44.32
Treatment x Time			
Clod-Lip (4wk)	112.75	31.71	50.60 to 174.90
Clod-Lip (8wk)	0.39	31.71	-61.76 to 62.54
Clod-Lip (12wk)	122.95	31.71	60.80 to 185.10
Stat1i-Lip (4wk)	-26.07	31.71	-88.22 to 36.08
Stat1i-Lip (8wk)	-68.86	31.71	-131.01 to -6.71
Stat1i-Lip (12wk)	-23.21	31.71	-85.36 to 38.94
Stat6i-Lip (4wk)	138.43	31.71	76.28 to 200.58
Stat6i-Lip (8wk)	117.43	31.71	55.28 to 179.58
Stat6i-Lip (12wk)	73.60	31.71	11.45 to 135.75
Intercept	434.52	15.36	404.41 to 464.63
<i>Random Effects</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept (all)	2360.24	279.92	1870.71 to 2977.88
Intercept (by group)	-153.50	140.87	-429.61 to 122.60
Exchangeable covariance matrix used to control for repeated measures			

Supplemental table 8. Individual linear mixed effects models, eVF. Individual linear mixed effects modelling of hind paw withdrawal threshold in Veh-lip (A), Clod-lip (B), STAT1i-lip (C), and STAT6i-lip (D).

A			
Model 6 eVF Veh-lip			
<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	-9.18	4.08	-17.18 to -1.18
8	-8.23	4.08	-16.23 to -0.22
12	-12.93	4.08	-20.93 to -4.93
Intercept	79.91	3.12	73.80 to 86.02
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	83.32	22.68	48.88 to 142.04
B			
Model 7 eVF Clod-lip			
<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	-3.28	4.08	-11.28 to 4.73
8	2.6	4.08	-5.40 to 10.60
12	0.83	4.08	-7.18 to 8.83
Intercept	68.77	2.89	63.11 to 74.43
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	83.34	19.64	52.51 to 132.27
C			
Model 8 eVF STAT1i-lip			
<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	0.40	2.13	-3.78 to 4.58
8	5.89	2.13	1.71 to 10.07
12	-10.16	2.13	-14.34 to -5.98
Intercept	73.12	1.55	70.06 to 76.15
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	22.72	6.18	13.33 to 38.73
D			
Model 9 eVF STAT6i-lip			
<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Time (weeks)			
0	Reference	Reference	Reference
4	1.27	3.45	-5.49 to 8.01
8	6.20	3.45	-0.55 to 12.96
12	-0.68	3.45	-7.43 to 6.07
Intercept	67.34	2.63	62.18 to 72.50
<i>Random Effect</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept	59.35	16.15	34.82 to 101.19

Supplemental table 9. Linear mixed effects model with pairwise comparisons, eVF.

Model 10 eVF

<i>Fixed Effects</i>			
Variable	β coefficient	Standard Error	95% Confidence Intervals
Treatment			
Veh-Lip	Reference	Reference	Reference
Clod-Lip	-11.14	3.70	-18.40 to -3.89
Stat1i-Lip	-6.81	3.70	-14.06 to 0.45
Stat6i-Lip	-12.58	3.70	-19.83 to -5.32
Time (weeks)			
0	Reference	Reference	Reference
4	-9.18	3.62	-16.27 to -2.09
8	-8.23	3.62	-15.32 to -1.14
12	-12.93	3.62	-20.02 to -5.84
Treatment x Time			
Clod-Lip (4wk)	5.90	5.12	-4.13 to 15.93
Clod-Lip (8wk)	10.83	5.12	0.80 to 20.85
Clod-Lip (12wk)	13.75	5.12	3.73 to 23.79
Stat1i-Lip (4wk)	9.58	5.12	-0.45 to 19.61
Stat1i-Lip (8wk)	14.12	5.12	4.09 to 24.14
Stat1i-Lip (12wk)	2.77	5.12	-7.26 to 12.80
Stat6i-Lip (4wk)	10.45	5.12	0.42 to 20.47
Stat6i-Lip (8wk)	14.43	5.12	4.40 to 24.46
Stat6i-Lip (12wk)	12.26	5.12	2.23 to 22.28
Intercept	79.91	2.62	74.78 to 85.04
<i>Random Effects</i>			
Variable	Variance	Standard Error	95% Confidence Intervals
Intercept (all)	68.53	8.10	54.36 to 86.40
Intercept (by group)	3.10	5.10	-6.89 to 13.09
Exchangeable covariance matrix used to control for repeated measures			