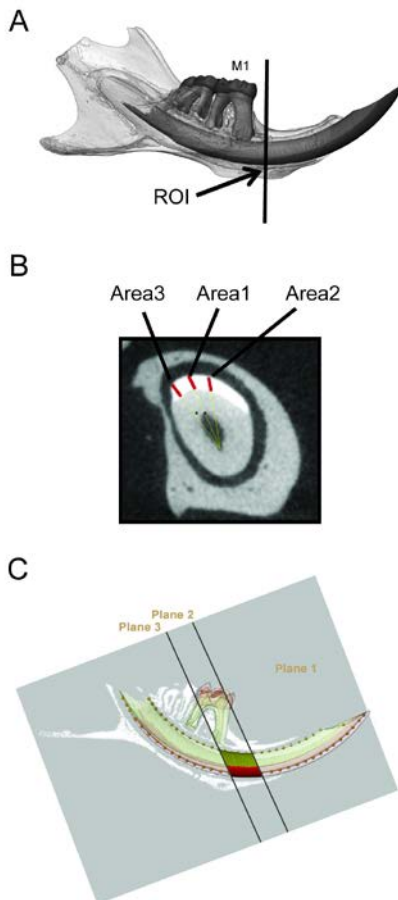


Title: Store-operated Ca^{2+} entry (SOCE) controls ameloblast cell function and enamel development

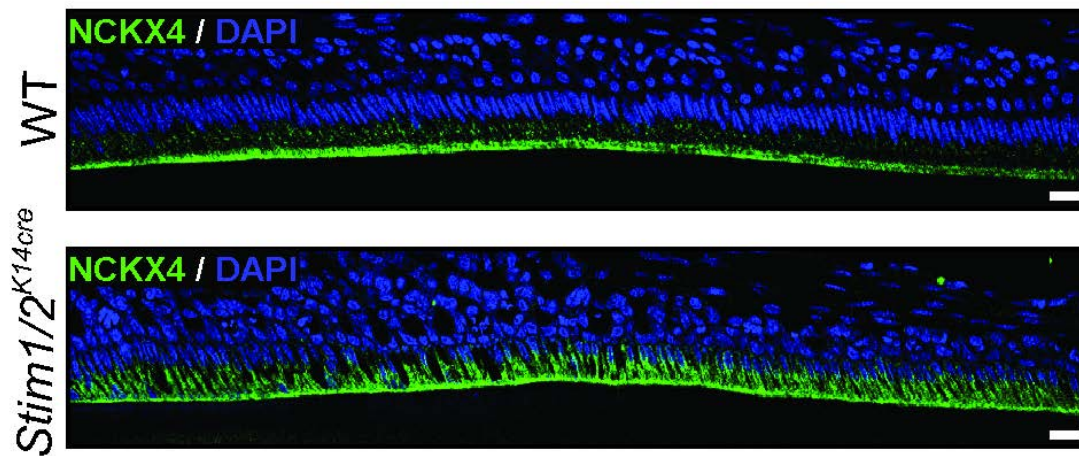
Miriam Eckstein, Martin Vaeth, Cinzia Fornai, Manikandan Vinu, Timothy G. Bromage, Meerim K. Nurbaeva, Jessica L. Sorge, Paulo G. Coelho, Youssef Idaghdour, Stefan Feske, and Rodrigo S. Lacruz

SUPPLEMENTAL FIGURES

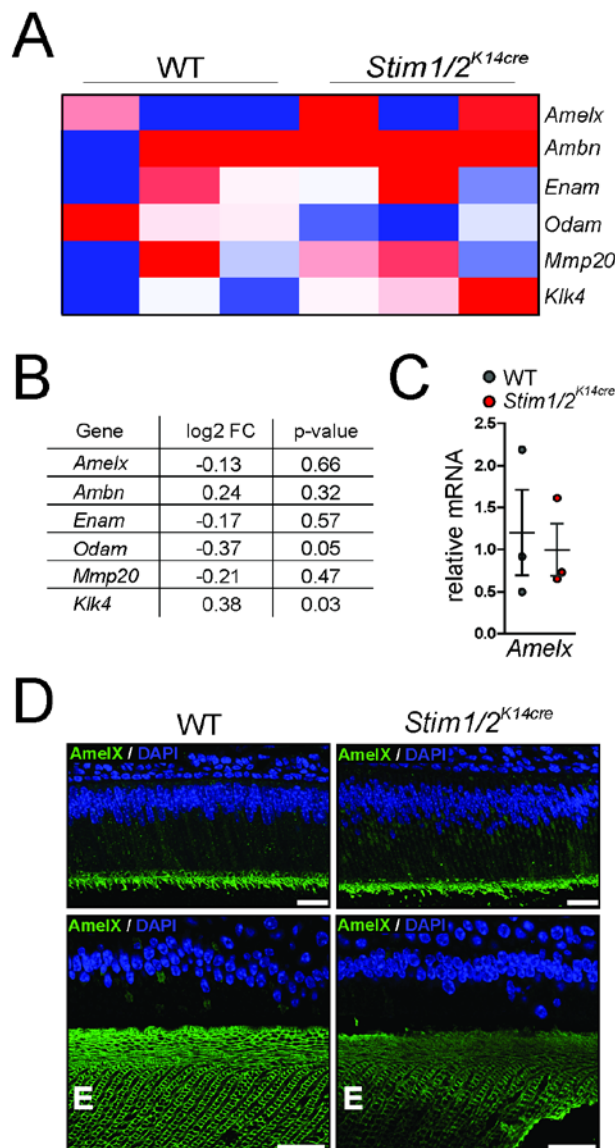
Supplemental Figure 1. Molar test sites for biophysical analysis. (A) Region of interest (ROI): Virtual reconstruction of a WT mandible showing the sampled area in the enamel of WT and *Stim1/2^{K14cre}* mice. This point is located just anterior of the lower Molar M1. Micro-hardness testing and SEM analysis were performed at this site. **(B) Linear enamel thickness:** X-ray of a virtual cross-section of an incisor showing the three regions of interest (Area 1-3) for linear enamel thickness-measurements in WT and *Stim1/2^{K14cre}* mice taken at the level shown in A. **(C) Enamel volume:** An interpolating plane (Plane 1) was set sagittally through a series of points tightly located on the superior and inferior keels of the incisor dentine, along its entire length. A plane perpendicular to Plane 1 and passing through the midpoint of the mesial cervical margin of the first molar crown (Plane 2) was calculated. Similarly, a third plane (Plane 3) was set at the most distal point of the first molar crown. The enamel volume was obtained for the portion of incisor included between Plane 2 and Plane 3. The average enamel thickness was calculated by dividing the enamel volume to the area of contact between enamel and dentine.



Supplemental Figure 2: Overview of a long strip of maturation stage ameloblasts showing the cellular localization of the $\text{Na}^+/\text{Ca}^{2+}/\text{K}^+$ exchanger (NCKX4) in wild type (WT) and in Stim1-2 deficient cells by immunofluorescence. IN WT mice NCKX4 is expressed along the distal pole consistent with a localization in the ruffled-border. *Stim1/2*^{K14cre} ameloblasts showed a disruption of this pattern showing a more intracellular localization of NCKX4. Scale = 20 μm .

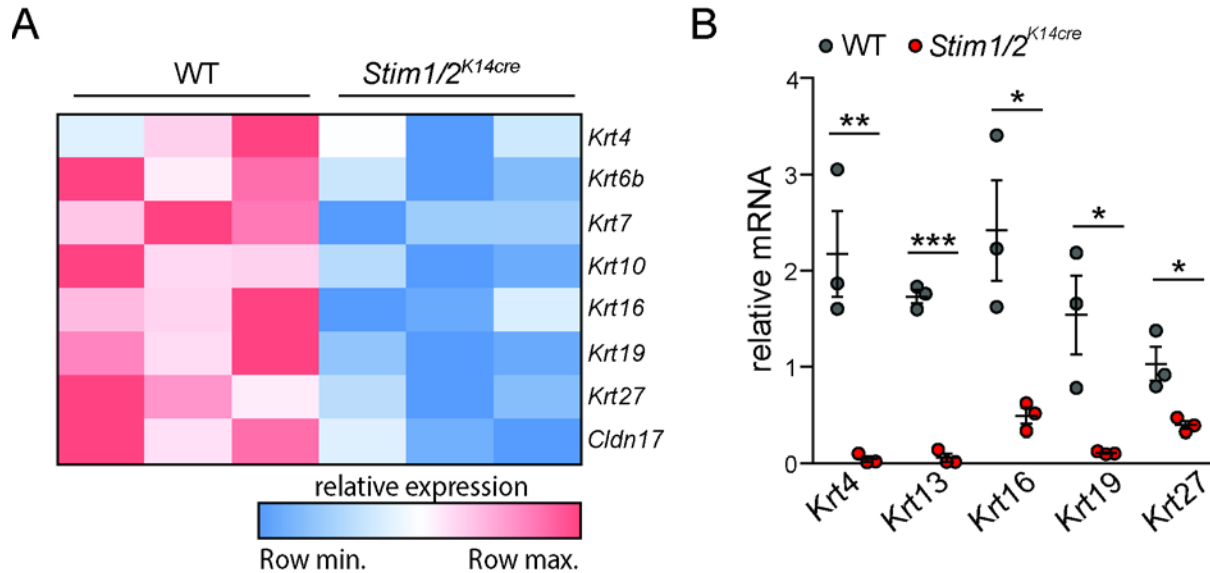


Supplemental Figure 3. Enamel gene expression is largely unaffected in enamel organ cells from *Stim1/2*^{K14cre} mice. **A)** Heatmap based on RNA sequence (RNAseq) data on the expression of enamel genes in WT and *Stim1/2*^{K14cre} mice. No clear differences in expression can be observed. **B)** Log2 of fold change from the same data shown in A. None of the *p* values are significant. **C)** qRT-PCR of enamel organ cells from WT and *Stim1/2*^{K14cre} mice indicating that average value of *Amelx* gene expression is lower but non-significant *Stim1/2*^{K14cre} animals compared with wild type (WT) mice (n=3 mice per group). **D)** Immunofluorescence analysis of *Amelx* protein expression in secretory (top panel) and maturation (bottom panel) ameloblast cells and in enamel. Samples are analyzed under the same conditions. These data indicate that ameloblasts synthesize and secrete *Amelx*. In some cases, particularly in maturation enamel, we have detected weaker fluorescence in the enamel (bottom panel). Collectively these data indicate minor or no changes in enamel genes and in particular in *Amelx* expression in *Stim1/2*^{K14cre} mice. Scale bar in D= 20μm.

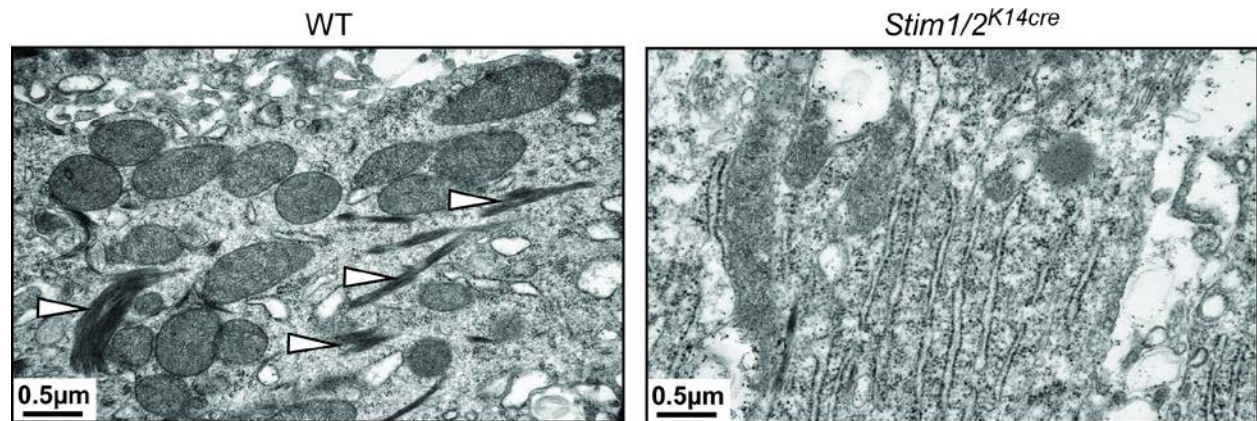


Supplemental Figure 4. Down-regulation of keratin genes in *Stim1/2*-deficient amelobalsts.

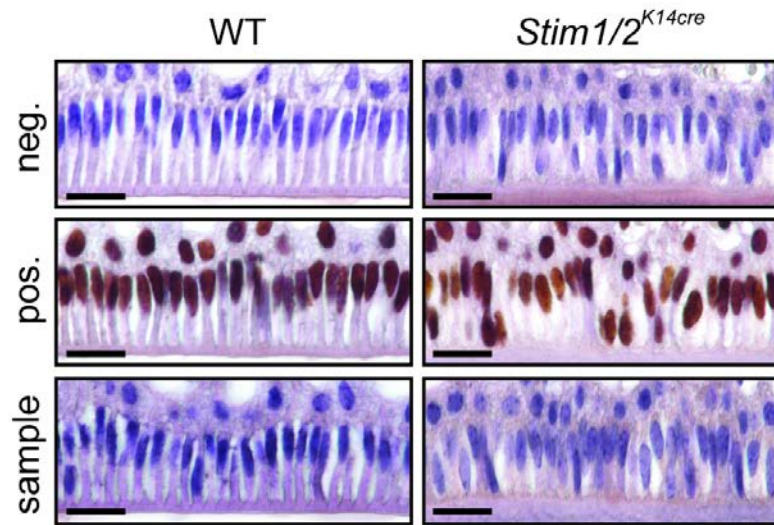
(A) RNA sequencing (RNAseq) revealed impaired expression of keratin (*Krt*) genes. Heatmap of selected keratin genes (*Krt4*, *Krt6b*, *Krt7*, *Krt10*, *Krt16* and *Krt27*) from RNAseq data as described in Figure 5B of the main text. **(B)** Analysis of relative mRNA abundance by qRT-PCR confirmed reduced expression of Keratins (*Krt*) 4, 13, 16, 19, 27 in *Stim1/2*^{K14cre} enamel cells; mean ($\pm$ SEM) of n=3 mice per group; (* P < 0.05 and ** P < 0.005, one way ANOVA). After Bonferroni correction for multiple comparisons, only *Krt4* and *Krt13* remain significant (** P < 0.01).



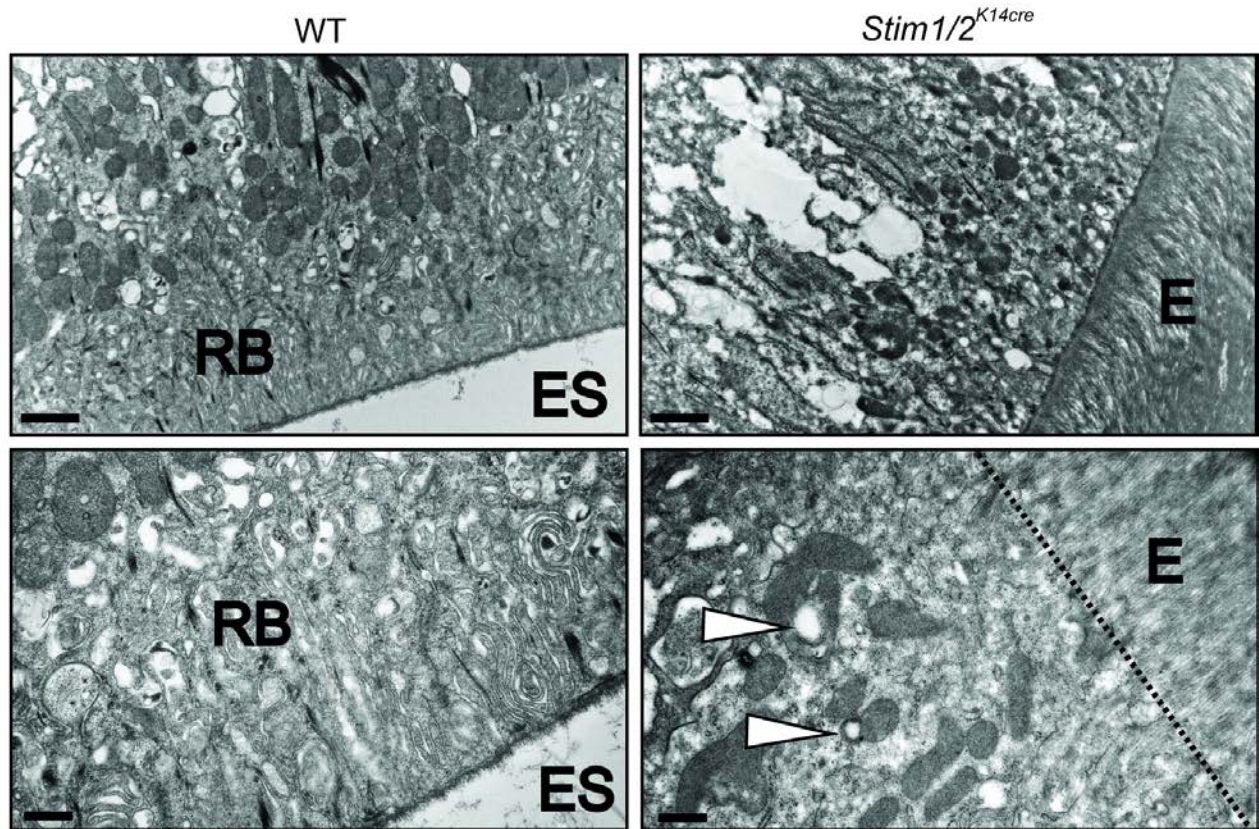
Supplemental Figure 5. Lack of tonofilaments in *Stim1/2*-deficient ameloblast cells. Representative TEM images showing a high abundance of tonofilaments (arrows) in wild type (WT) sections and a loss of these structures in *Stim1/2*^{K14cre} cells.



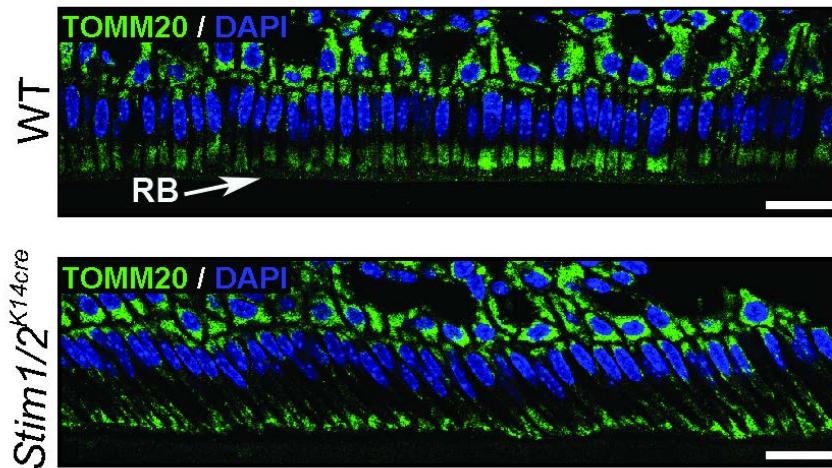
Supplemental Figure 6. SOCE-deficient ameloblasts do not show elevated apoptosis.
Tissue sections of wild type (WT) and *Stim1/2*^{K14cre} ameloblast cells were analyzed for apoptotic cells by TUNEL assay. Controls included DNase-treated sections (positive control; brown nuclei) and unstained cells (negative control; blue nuclei). Scale bars represent 20 μ m.



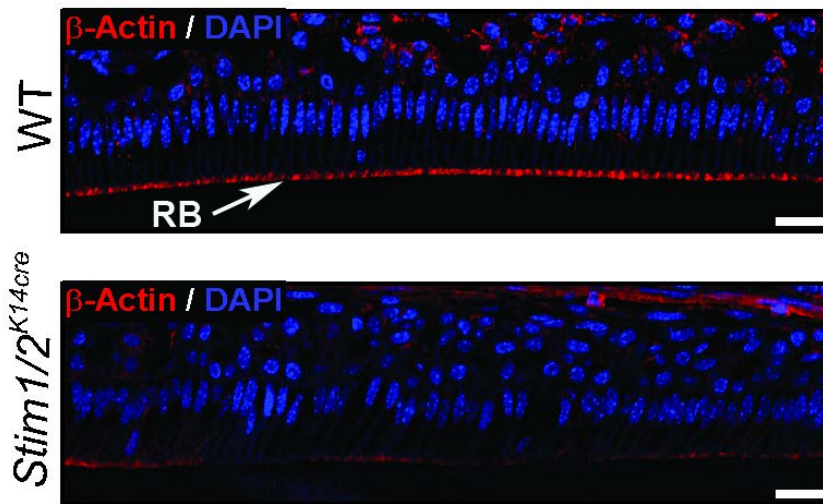
Supplemental Figure 7. *Stim1/2*^{K14cre} ameloblasts lose the ability to form an apical ruffled-border. Representative transmission electron microscopy (TEM) analyses of wild type (WT) and *Stim1/2*^{K14cre} ameloblast cells showing absence of the distal ruffled-border in *Stim1/2*-deficient ameloblasts. Enamel space (ES), enamel (E), ruffled-border (RB) and abnormal mitochondria (arrows) are indicated. Scale bars indicate 1 μ m for upper panel and 0.5 μ m for lower panel.



Supplemental Figure 8: Overview of a long strip of maturation stage ameloblasts showing immunofluorescence staining using the mitochondrial import receptor TOMM20 as a marker. Mitochondria adopt a uniform clustering of mitochondria outside the ruffled-border (RB) in the distal pole in wild type (WT) but not *Stim1/2*^{K14cre} ameloblasts, in which mitochondria were located close to the distal pole. Scale = 20 μ m.



Supplemental Figure 9: Overview of a long strip of maturation stage ameloblasts showing the localization of actin by immunofluorescence. We found strong actin expression at the distal pole and the ruffled-border (RB) of wild type (WT) ameloblasts but a very diffuse and weak signal in *Stim1/2*-deficient ameloblasts consistent with abnormal development of the RB when disrupting SOCE. Scale = 20 μ m.



Supplemental Tables

Supplemental Table 1

Representative average measurements taken by EDAX of elemental composition of the enamel of wild type and Stim1/2 deficient mice. Ca²⁺ has been highlighted.

Wild type	
Element	Weight%
C K	10.28
O K	35.29
Na K	0.46
Mg K	0.31
P K	17.21
Cl K	0.2
Ca K	39.33
Ir M	-3.08
Totals	100

<i>Stim1/2</i> ^{K14cre}	
Element	Weight%
C K	14.62
O K	50.36
Na K	0.81
Mg K	0.37
P K	13.18
S K	0.15
Cl K	0.13
Ca K	20.38
Totals	100

Supplemental Table 2

Up- and downregulated Genes from RNA_Seq Analysis: Genes shown in **bold** are related to cell/ER stress.

A) upregulated Genes

Gene	Log2 Fold Change	p_value
<i>Qrfp</i>	5.14597	0.00015
<i>Tmem179</i>	5.11802	0.00005
<i>Has1</i>	4.2502	0.00005
<i>Tph1</i>	3.90422	0.00005
<i>Bsnd</i>	3.57223	0.0007
<i>Nrxn2</i>	3.40495	0.00005
<i>Chst13</i>	3.30167	0.00365
<i>Ccdc80</i>	2.95406	0.00005
<i>Abca13</i>	2.95287	0.00005
<i>Gm8976</i>	2.94608	0.00215
<i>Htra4</i>	2.90145	0.0017
<i>Ptprr</i>	2.89411	0.00005
<i>Gucy2c</i>	2.79869	0.00005
<i>Defb42</i>	2.7669	0.00075
<i>Acvr1c</i>	2.75042	0.00125
<i>D7Erttd443e</i>	2.74442	0.00015
<i>Gm8890</i>	2.72082	0.00045
<i>Cd3g</i>	2.64064	0.00825
<i>Csn3</i>	2.61643	0.00005
<i>Gm8857,Gm8871</i>	2.57501	0.00005
<i>Gm23925,Gm26003,Snhg17</i>	2.57055	0.00005
<i>RP23-111G16.8</i>	2.39654	0.00665
<i>Phactr1</i>	2.36472	0.00005
<i>Hrh1</i>	2.35648	0.00005
<i>1810011O10Rik</i>	2.3079	0.00005
<i>Gm12349</i>	2.30753	0.00005
<i>4732456N10Rik</i>	2.30222	0.00125
<i>Mgam</i>	2.2718	0.0008
<i>Lgr5</i>	2.26347	0.0031
<i>Gm8906</i>	2.24706	0.00005
<i>Gm29483</i>	2.22569	0.00005
<i>Igha</i>	2.18017	0.00005
<i>Gm5152</i>	2.1083	0.0034
<i>Cd40</i>	2.04291	0.00005

<i>Fgf16</i>	1.97861	0.00205
<i>Acsbg1</i>	1.96133	0.00005
<i>Islr2</i>	1.94134	0.00005
<i>Smoc1</i>	1.92604	0.00005
<i>Olfm2</i>	1.9224	0.00005
<i>Gm8879</i>	1.91267	0.00005
<i>Lrat</i>	1.91046	0.00005
<i>Crygn</i>	1.90149	0.0038
<i>4930438A08Rik</i>	1.86642	0.00005
<i>Hoxc13</i>	1.86523	0.00115
<i>Col9a1</i>	1.86083	0.00055
<i>Ptchd2</i>	1.85906	0.0016
<i>lbsp</i>	1.84337	0.00005
<i>Apoc2,Apoc4</i>	1.83854	0.00365
<i>Sct</i>	1.82903	0.00135
<i>Gm8897</i>	1.82318	0.00285
<i>Itgae</i>	1.81311	0.00515
<i>Gm5861</i>	1.80426	0.00025
<i>Creg2</i>	1.80121	0.00005
<i>Zfand4</i>	1.79822	0.00085
<i>Fam196b</i>	1.78016	0.00175
<i>Dtna</i>	1.74969	0.00005
<i>Gm6465</i>	1.74194	0.00175
<i>Serpinb11</i>	1.71247	0.0087
<i>Plbd1</i>	1.705	0.00005
<i>Jam2</i>	1.69541	0.00005
<i>Mmp12</i>	1.6838	0.00005
<i>Stc1</i>	1.67132	0.00005
<i>Dusp2</i>	1.66543	0.00005
<i>Gjb2</i>	1.65941	0.00005
<i>Glrh</i>	1.64229	0.00185
<i>Sid1</i>	1.63988	0.00005
<i>Mmp13</i>	1.59828	0.00005
<i>Col5a3</i>	1.59024	0.00005
<i>Mgarp</i>	1.56472	0.00005
<i>Ppbp</i>	1.53559	0.0029
<i>Mdga2</i>	1.52604	0.0008
<i>Nrxn1</i>	1.49966	0.0041
<i>Bik</i>	1.49289	0.0042
<i>Lypd3</i>	1.47576	0.00005
<i>Calcb</i>	1.4692	0.00225

Derl3	1.4581	0.00005
<i>Tnmd</i>	1.44371	0.00005
<i>Bpifb4</i>	1.4362	0.00105
<i>Insc</i>	1.43345	0.00005
<i>Tmem215</i>	1.43333	0.00005
<i>Sytl2</i>	1.42786	0.00005
<i>Gap43</i>	1.42487	0.00055
<i>Hal</i>	1.41793	0.0075
Dusp6	1.39934	0.00005
<i>Krtap24-1</i>	1.38703	0.0056
<i>Atp4a</i>	1.37255	0.00065
<i>Endou</i>	1.36141	0.0005
<i>Chrna5</i>	1.35143	0.0001
<i>Prg2</i>	1.34489	0.00225
<i>Ighm</i>	1.33075	0.00005
<i>Egr3</i>	1.32959	0.00025
<i>Mettl17,Slc39a2</i>	1.32881	0.00005
<i>Prrg1</i>	1.31121	0.00335
<i>Igkc</i>	1.30028	0.00005
<i>Krt25</i>	1.282	0.0005
<i>Gfra3</i>	1.27131	0.00035
<i>Spink8</i>	1.26854	0.0013
<i>Gpr153</i>	1.26098	0.00005
<i>RP24-299A7.2,Spp1</i>	1.25959	0.00005
<i>Cela1</i>	1.25703	0.00665
<i>Sel1l3</i>	1.25539	0.00005
<i>Drp2</i>	1.25461	0.00005
<i>Grhl1</i>	1.25201	0.00005
<i>Usp18</i>	1.24646	0.0004
<i>Actg2</i>	1.23987	0.0068
<i>Serp2</i>	1.23674	0.0091
<i>Pf4</i>	1.23496	0.0022
<i>Gm19569</i>	1.23154	0.00295
<i>Gm1045</i>	1.22974	0.00005
<i>Ubxn10</i>	1.22836	0.0065
<i>Gm3512</i>	1.21707	0.00515
<i>Gfra2</i>	1.21313	0.0002
<i>Spsb4</i>	1.21134	0.00005
<i>Slc52a3</i>	1.20744	0.00005
<i>Cdca5</i>	1.20404	0.0045
<i>Fam72a</i>	1.20139	0.0008

<i>Ctgf</i>	1.20085	0.00005
<i>Plb1</i>	1.19711	0.00005
<i>Gpnmb</i>	1.18935	0.00005
<i>Oasl2</i>	1.187	0.00005
<i>Htatip2</i>	1.187	0.00005
<i>Gm13010</i>	1.18302	0.00005
<i>Shcbp1</i>	1.17179	0.0066
<i>Egflam</i>	1.17127	0.00125
<i>Ube2ql1</i>	1.171	0.00005
<i>Sdc3</i>	1.16975	0.00005
<i>C1ql2</i>	1.16888	0.00005
<i>Inhba</i>	1.16857	0.00005
<i>Gm17501</i>	1.15368	0.00305
<i>Bean1</i>	1.1528	0.00005
<i>Krt71</i>	1.15052	0.0001
<i>Mfsd2a</i>	1.14836	0.00005
<i>Best1</i>	1.1458	0.00005
<i>Phactr3</i>	1.14575	0.00105
<i>Csdc2</i>	1.14489	0.00005
<i>Shd</i>	1.13794	0.00465
<i>Rassf6</i>	1.13708	0.0024
<i>Pcdh1</i>	1.1358	0.00005
<i>Wscd2</i>	1.13532	0.00435
<i>Hmmr</i>	1.13492	0.0016
<i>Stab1</i>	1.12926	0.00005
<i>Padi3</i>	1.11973	0.00095
<i>Ccdc74a</i>	1.11551	0.00565
<i>Sdcbp2</i>	1.11234	0.0001
<i>Batf3</i>	1.10995	0.0076
<i>Ret</i>	1.10873	0.00005
<i>Stmn4</i>	1.1049	0.0078
<i>Krt24</i>	1.10407	0.0001
<i>Mall</i>	1.10196	0.00005
<i>Acot7</i>	1.0949	0.00005
<i>Trem2</i>	1.09428	0.0017
<i>Cbln1</i>	1.09345	0.00005
<i>AF251705</i>	1.09244	0.0042
<i>Rgs16</i>	1.09232	0.0003
<i>Lypd8</i>	1.09074	0.00025
<i>Gsg2</i>	1.08708	0.00005
<i>Trp53i11</i>	1.08003	0.00005

<i>Col13a1</i>	1.0793	0.00005
<i>Ackr2</i>	1.07258	0.0031
<i>Fcrls</i>	1.07035	0.00005
<i>Mgmt</i>	1.06777	0.0003
<i>Gm5532</i>	1.06514	0.00005
<i>Ano2</i>	1.05881	0.0051
<i>Plk1</i>	1.05436	0.0034
<i>Otos</i>	1.05283	0.0023
<i>Slc16a7</i>	1.04952	0.00005
<i>Spon2</i>	1.0479	0.00335
<i>Uhrf1</i>	1.04647	0.0055
<i>Rgs4</i>	1.04498	0.0024
<i>Lyz2</i>	1.0412	0.00005
<i>Ccdc64b</i>	1.04079	0.00645
<i>Plekha2</i>	1.03473	0.00005
<i>Aurkb</i>	1.03373	0.0038
<i>Iqj, Schip1</i>	1.03036	0.00005
<i>Sulf2</i>	1.01669	0.00005
<i>Pdgfrl</i>	1.00975	0.00005
<i>Gfra4, Mir6973b</i>	1.00704	0.00855
<i>Iglon5</i>	1.00604	0.00965
<i>Plau</i>	1.00588	0.00005
<i>Fxyd4</i>	1.00306	0.00005
<i>Errfi1</i>	1.00169	0.00005
<i>Slc7a8</i>	1.00025	0.00005

B) downregulated Genes: Genes shown in **bold** are related to cell/ER stress.

Gene	Log2 Fold Change	p_value
Eno1b	-8.70946	0.0026
<i>Gm20257</i>	-7.71893	0.00005
<i>Slc40a1</i>	-6.01064	0.00005
Tgm3	-5.15786	0.00005
<i>Dynap</i>	-5.10094	0.00005
Calm4	-5.03798	0.0001
<i>RP23-57A17.2</i>	-4.76243	0.0001
<i>Slc5a8</i>	-4.68526	0.00005
<i>Bpifa5</i>	-4.5834	0.0026

<i>Cdo1</i>	-4.11389	0.00005
<i>Ly6g6c</i>	-3.71803	0.00075
<i>Ano4</i>	-3.64579	0.00005
<i>Slc26a4</i>	-3.59931	0.00005
<i>Cela3b</i>	-3.57278	0.0007
<i>AC159477.1,Pcdh15</i>	-3.54334	0.00005
<i>2610305D13Rik</i>	-3.5391	0.00005
<i>Nccrp1</i>	-3.46659	0.00515
<i>Krt4</i>	-3.41536	0.00005
<i>Drd2</i>	-3.38726	0.0031
<i>Gfpt2</i>	-3.15444	0.00005
<i>Ptpn22</i>	-3.02544	0.00005
<i>Spr3</i>	-2.89599	0.00005
<i>Bglap2</i>	-2.76788	0.00005
<i>Cnfn</i>	-2.74372	0.0005
<i>Spr1a</i>	-2.74078	0.00045
<i>Gm4208</i>	-2.73184	0.0038
<i>Col6a5</i>	-2.72996	0.00005
<i>Tmprss11b</i>	-2.72854	0.00005
<i>Krt13</i>	-2.66435	0.00005
<i>Gm13212</i>	-2.66416	0.00005
<i>Ccdc180</i>	-2.66248	0.0006
<i>Tmprss11g</i>	-2.65299	0.00005
<i>Igkv10-96</i>	-2.65141	0.00455
<i>Cdhr1</i>	-2.64299	0.00005
<i>Vnn1</i>	-2.61672	0.00005
<i>Hrc</i>	-2.59251	0.00145
<i>Mybpc2</i>	-2.58525	0.00005
<i>Tmem252</i>	-2.50765	0.00005
<i>Kcnmb2</i>	-2.46743	0.0088
<i>Krt27</i>	-2.46718	0.00005
<i>Gm11375</i>	-2.41764	0.0017
<i>Mss51</i>	-2.40256	0.00025
<i>Pgm5</i>	-2.29559	0.00005
Gsta3	-2.27447	0.00005
<i>Serpinb6c</i>	-2.27179	0.0037
<i>Krt6b</i>	-2.21927	0.00005
<i>Gm17660,RP23-102H7.9</i>	-2.20977	0.00005
<i>Il1f9</i>	-2.14274	0.00335
<i>Clgn</i>	-2.13813	0.00005
<i>Ifitm6</i>	-2.13563	0.0059

<i>Ifi202b</i>	-2.13303	0.00005
<i>RP23-307l19.5</i>	-2.12671	0.0061
<i>Gsta4</i>	-2.1215	0.00005
<i>Vit</i>	-2.11863	0.00005
<i>Mboat1</i>	-2.08307	0.00005
<i>Crct1</i>	-2.06703	0.00225
<i>Lcn2</i>	-2.06548	0.00005
<i>Rbm20</i>	-2.06128	0.00285
<i>Trim63</i>	-2.05827	0.0034
<i>Rgma</i>	-2.04735	0.00005
<i>Actn3</i>	-2.04216	0.0002
<i>Gm6472,Rpl7a-ps12</i>	-2.03939	0.00005
<i>Prdm1</i>	-2.02205	0.00005
<i>Chl1</i>	-1.99152	0.00005
<i>Krt6a</i>	-1.96177	0.00005
<i>Krtdap</i>	-1.95044	0.00165
<i>Gm37857,Rptn</i>	-1.93449	0.0073
<i>Neb</i>	-1.93374	0.0019
<i>Fam25c</i>	-1.91358	0.00005
<i>B230216N24Rik,Pam</i>	-1.90112	0.00005
<i>Krt42</i>	-1.88569	0.00005
<i>Sox6</i>	-1.87805	0.00005
<i>Slc39a8</i>	-1.86829	0.00005
<i>Kif19a</i>	-1.81947	0.00005
<i>Vat1l</i>	-1.81736	0.00005
<i>Stim1</i>	-1.79284	0.00005
<i>Pvalb</i>	-1.78984	0.00005
<i>Bglap3</i>	-1.77568	0.00285
<i>Fosb</i>	-1.7689	0.00005
<i>Obscn</i>	-1.75048	0.0056
<i>Gldc</i>	-1.72952	0.00005
<i>Tmem63c</i>	-1.7203	0.00005
<i>Slc15a2</i>	-1.71408	0.00005
<i>Adora2b</i>	-1.69842	0.00005
<i>Itgb7</i>	-1.68364	0.00005
<i>Bglap</i>	-1.67548	0.00005
<i>AI593442</i>	-1.65645	0.0001
<i>Cldn17</i>	-1.65202	0.00015
<i>2010107G12Rik</i>	-1.64185	0.00755
<i>Casp14</i>	-1.63576	0.0011
<i>Abcc3</i>	-1.62968	0.0019

<i>Asprv1</i>	-1.62676	0.0023
<i>Mal</i>	-1.6141	0.0049
<i>Nr4a3</i>	-1.59082	0.00005
<i>Tgfa</i>	-1.57411	0.00005
<i>Fxyd2</i>	-1.57189	0.0006
<i>Cpeb1</i>	-1.56798	0.0022
<i>Tspan8</i>	-1.55979	0.0001
<i>Krt19</i>	-1.55216	0.0001
<i>Krt10</i>	-1.54723	0.00005
<i>Il1rl1</i>	-1.547	0.00005
<i>Camp</i>	-1.54219	0.0011
<i>Krt16</i>	-1.53763	0.00005
<i>Ngp</i>	-1.521	0.00005
<i>Klrb1b,Klrb1c,RP24-127M20.8</i>	-1.51462	0.001
<i>Ly6g6e</i>	-1.5061	0.00005
<i>Tbc1d4</i>	-1.50018	0.00005
<i>Pamr1</i>	-1.4986	0.0008
<i>S100a8</i>	-1.49056	0.00005
<i>Gpr88</i>	-1.48076	0.0003
<i>Dpt</i>	-1.46942	0.00295
<i>Ncoa4</i>	-1.46436	0.00005
<i>Gm21897</i>	-1.46235	0.00005
<i>Fbxo27</i>	-1.45816	0.00195
<i>Nat8l</i>	-1.45044	0.00005
<i>Hist2h4</i>	-1.44593	0.00645
<i>Il13ra2</i>	-1.43863	0.0055
<i>4632428C04Rik</i>	-1.43442	0.0004
<i>Srgap3</i>	-1.38629	0.00005
<i>Gm6768</i>	-1.33925	0.00045
<i>Stim2</i>	-1.32058	0.00005
<i>S100a9</i>	-1.31417	0.00005
<i>Ada</i>	-1.29838	0.00095
<i>Klf12</i>	-1.29661	0.0021
<i>D930020B18Rik</i>	-1.29484	0.00005
<i>Slc22a4</i>	-1.28252	0.00005
<i>Fry</i>	-1.28171	0.00005
<i>Hs6st2</i>	-1.27198	0.0012
<i>Kcng2</i>	-1.2633	0.00015
<i>Gm5900</i>	-1.25405	0.00725
<i>Gpr87</i>	-1.25315	0.00075
<i>Malat1</i>	-1.25292	0.00005

<i>S100a14</i>	-1.24845	0.00005
<i>Foxq1</i>	-1.24553	0.00005
<i>Wfdc2</i>	-1.22604	0.00005
<i>Mgat3</i>	-1.22406	0.00005
<i>Stmn2</i>	-1.22292	0.0003
<i>2610037D02Rik</i>	-1.22098	0.0052
Gstp2	-1.21969	0.00565
<i>Sh2d4a</i>	-1.21137	0.00005
Casp1	-1.19692	0.00005
<i>Wbscr17</i>	-1.19628	0.0001
<i>Foxn1</i>	-1.19436	0.00135
<i>Selenbp1</i>	-1.19365	0.00005
<i>Gm16344</i>	-1.19288	0.0007
Atg9b	-1.1843	0.0001
<i>Dnaic2</i>	-1.18075	0.0008
<i>Nr2f2</i>	-1.17349	0.00005
<i>Cyp4f39</i>	-1.1718	0.0003
<i>Foxj1</i>	-1.17003	0.00005
<i>Fam111a</i>	-1.16317	0.00005
<i>Bcat1</i>	-1.16062	0.00005
<i>Abca8b</i>	-1.15705	0.00035
<i>Dgat2</i>	-1.14341	0.00005
<i>Zfat</i>	-1.14015	0.00005
<i>Cer1</i>	-1.1377	0.00005
<i>Anxa8</i>	-1.13356	0.00005
<i>Pof1b</i>	-1.13049	0.00005
<i>Adam8</i>	-1.13009	0.00395
<i>Myc</i>	-1.125	0.00005
<i>Gjb6</i>	-1.12089	0.00005
<i>Slc25a27</i>	-1.11885	0.0016
<i>Slc25a48</i>	-1.11795	0.00165
<i>Pkp2</i>	-1.1103	0.0004
<i>Plet1</i>	-1.10185	0.00085
<i>Hp</i>	-1.09547	0.0044
<i>Fam227a</i>	-1.09432	0.00475
<i>Slc6a14</i>	-1.09196	0.00005
<i>Sema3d</i>	-1.08971	0.00005
<i>Oxtr</i>	-1.08709	0.0027
<i>Nckap5</i>	-1.08588	0.005
<i>Krt7</i>	-1.0843	0.0081
<i>Cryga,D630023F18Rik,Gm28845</i>	-1.07419	0.00005

Mapkapk3	-1.07037	0.00005
Ahnak2	-1.05755	0.00005
Sec14l4	-1.05634	0.0008
Gm38399,Nav1	-1.05469	0.00055
Susd1	-1.05102	0.0056
Rgs2	-1.04223	0.00005
Ankrd35	-1.04081	0.0082
Fat3	-1.03373	0.00005
Casz1	-1.02555	0.00005
Cilp	-1.02095	0.00015
Gm27702,Neat1	-1.01632	0.00005
Serpinb12	-1.0103	0.00015
Gsta1	-1.01002	0.003
Egfl6	-1.00931	0.00795
Calml3	-1.00073	0.00005

Supplemental Table 3

Pathway analysis of RNA_Seq data

PANTHER	P-value	%
<i>Oxidative stress response*</i>	1.0 ⁻⁰¹	0.1
KEGG	P-value	%
Cell adhesion molecules (CAMs)	1.8 ⁻⁰²	0.3
ECM-receptor interaction	2.6 ⁻⁰²	0.2
<i>Glutathione metabolism*</i>	3.3 ⁻⁰²	0.1
Thyroid cancer	5.8 ⁻⁰²	0.1
Metabol. of xenob. by cyt. P450	6.0 ⁻⁰²	0.1
MAPK signaling pathway	6.7 ⁻⁰²	0.3
Vascular smooth muscle contraction	8.0 ⁻⁰²	0.2
Drug metabolism	8.1 ⁻⁰²	0.1
IPA	P-value	%
<i>Glutathione-mediated Detoxification*</i>	5.67 ⁻⁰⁴	16.7
Hepatic Fibrosis/Hep. Stellate Cell Act.	6.37 ⁻⁰⁴	5.7
Granulocyte Adhesion and Diapedesis	9.23 ⁻⁰³	5.9
Agranulocyte Adhesion and Diapedesis	1.44 ⁻⁰³	5.5
LPS/IL-1 Med. Inhibition of RXR Funct.	1.74 ⁻⁰³	5.0

Supplemental Table 4

Summary of Ingenuity Pathway Analysis

Top Upstream Regulators

Upstream Regulator	P-value of overlap
<i>Alpha catenin</i>	1.67^{-07}
<i>KCNE3</i>	1.32^{-06}
<i>TAF4B</i>	2.48^{-06}
<i>IL1B</i>	1.21^{-05}
<i>DLX3</i>	1.83^{-05}

Top Diseases and Disorders

Name	P-value of overlap	#Molecules
Cancer	1.84^{-02} - 5.32^{-07}	47
Organismal Injury and Abnormalities	1.84^{-02} - 5.32^{-07}	79
Dermatological Diseases and Conditions	1.63^{-02} - 1.58^{-06}	27
Inflammatory Response	1.89^{-02} - 4.28^{-06}	58
Infectious Diseases	1.63^{-02} - 4.20^{-05}	22

Molecular and Cellular Functions

Name	P-value of overlap	#Molecules
Drug Metabolism	1.63^{-02} - 1.01^{-06}	7
Cellular Movement	1.89^{-02} - 1.67^{-05}	54
Cell-To-Cell Signaling and Interaction	1.83^{-02} - 1.81^{-04}	30
Cellular Function and Maintenance	1.87^{-02} - 1.81^{-04}	38
Molecular Transport	1.83^{-02} - 3.69^{-04}	54

Physiological System Development and Function

Name	P-value of overlap	#Molecules
Embryonic Development	1.63^{-02} - 2.35^{-08}	36
Hair and Skin Development and Function	1.63^{-02} - 2.35^{-08}	21
Organ Development	1.63^{-02} - 2.35^{-08}	33
Organismal Development	1.63^{-02} - 2.35^{-08}	66
Tissue Development	1.63^{-02} - 2.35^{-08}	61

Supplemental Table 5

Specific mouse Primers designed for Genotyping

Primer	Forward sequence	Reverse sequence
<i>Cre</i>	ACGACCAAGTGACAGCAATG	CTCGACCAGTTTAGTTACCC
<i>Stim1_KO</i>	5'-AACGTCTTGCAGTTGCTGTAGGC-3'	
<i>Stim1_WT</i>	5'-CGATGGTCTCACGGTCTCTAGTTTC-3'	
<i>Stim1_AS</i>	5'-GGCTCTGCTGACCTGGAAGTATAGTG-3'	
<i>Stim2_KO</i>	5'-GCTGAACTGTTGTGCTTGACTGTGC-3'	
<i>Stim2_WT</i>	5-CATCAGAAGGTAAAGTGTGCAGTGCTC-3'	
<i>Stim2_AS</i>	5'-GGATGTGTGCTTGACTGTAGC-3'	

Specific mouse Primers designed for qRT-PCR

Primer	Forward sequence	Reverse sequence
<i>Hprt1</i>	GCTGACCTGCTGGATTACAT	TTGGGGCTGTACTGCTTAAC
<i>Stim1</i>	ATTCGGCAAACTCTGCTTC	GGCCAGAGTCTCAGCCATAG
<i>Stim2</i>	TCGAAGTGGACGAGAGTGATG	TTTCCACTGTTTCCACAAATCC
<i>Htra4</i>	AGCCACCGTCAAAGACATCG	TGTGGTGCTGACAATCCCTG
<i>Rcan1</i>	ACGACACTCGGTGAACATTT	GAACATCAACCCATTTGCTC
<i>CHOP</i>	GACCAGGTTCTGCTTTCAGG	CAGCGACAGAGCCAGAATAA
<i>BiP/Grp78</i>	AGTCCAGCAATAGTGCCAGC	AAGGAGACTGCTGAGGCGTA
<i>Rcan1</i>	ACGACACTCGGTGAACATTT	GAACATCAACCCATTTGCTC
<i>Gsta1</i>	CATTGAAGTGGTGAAGCACG	CTGGACTGTGAGCTGAGTGG
<i>Gsta4</i>	CGTCCCCTGCCATTAAAGTA	GCTTCTTTCTCGAGTGCCTG
<i>Krt4</i>	TCGGCAGCAGAAGTCTTTACA	CAGCACCGTATCCTCCAACG
<i>Krt13</i>	TCATCTCGGTTTGTCACTGGA	TGATCTTCTCGGTGCCAGAGAG
<i>Krt16</i>	GGTGGCCTCTAACAGTGATCT	TGCATACAGTATCTGCCTTTGG
<i>Krt19</i>	GGGGGTTCAGTACGCATTGG	GAGGACGAGGTCACGAAGC
<i>Krt27</i>	TATGGGCGGTGCTTCTTG TG	TCCAGTGCTTGACGTTCTC
<i>AmelX</i>	GCCGTATCCTTCCTATGGTT	GATGTTTGGCTGATGGTGTT