



Figure	Protein	Normalized to WT				Protein	Raw Data									
6	CatD pro	WT	TM -/-	GRN -/-	GRN & TM -/-	CatD pro	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	107	163	156	435	A	4.806.452	7.329.632	7.031.741	19.594.508	wild type vs. Tmem106b -/-	-63.95	-140.8 to 12.94	No	ns	0.1069
	B	104	126	120	386	B	4.698.608	5.657.605	5.409.668	17.379.535	wild type vs. Grn -/-	-22.9	-99.78 to 53.99	No	ns	0.7782
	C	89	204	93	436	C	4.012.822	9.175.207	4.171.659	19.654.629	wild type vs. Grn -/- & Tmem106b -/-	-318.9	-395.8 to -242.0	Yes	****	<0.0001
											Tmem106b -/- vs. Grn -/-	41.05	-35.83 to 117.9	No	ns	0.3786
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-255	-331.9 to -178.1	Yes	****	<0.0001
											Grn -/- vs. Grn -/- & Tmem106b -/-	-296	-372.9 to -219.1	Yes	****	<0.0001
6	CatD hc	WT	TM -/-	GRN -/-	GRN & TM -/-	CatD mat	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	176	122	343	1,014	A	1.160.322	803.631	2.264.175	6.698.632	wild type vs. Tmem106b -/-	-39.46	-166.1 to 87.21	No	ns	0.7551
	B	100	142	310	1,000	B	663.748	935.485	2.048.410	6.608.073	wild type vs. Grn -/-	-196.1	-322.8 to -69.44	Yes	**	0.0049
	C	24	155	236	977	C	158.702	1.026.073	1.558.487	6.460.434	wild type vs. Grn -/- & Tmem106b -/-	-896.9	-1024 to -770.3	Yes	****	<0.0001
											Tmem106b -/- vs. Grn -/-	-156.6	-283.3 to -29.98	Yes	*	0.0176
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-857.5	-984.2 to -730.8	Yes	****	<0.0001
											Grn -/- vs. Grn -/- & Tmem106b -/-	-700.8	-827.5 to -574.2	Yes	****	<0.0001
6	CatB pro	WT	TM -/-	GRN -/-	GRN & TM -/-	CatB upper	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	98	108	152	625	A	2.255.681	2.494.929	3.489.328	18.372.499	wild type vs. Tmem106b -/-	-11.44	-148.4 to 125.5	No	ns	0.9928
	B	104	126	89	430	B	2.387.394	2.898.404	2.647.617	9.887.929	wild type vs. Grn -/-	-10.19	-147.2 to 126.8	No	ns	0.9949
	C	98	100	90	531	C	2.260.340	2.299.595	2.069.770	12.219.868	wild type vs. Grn -/- & Tmem106b -/-	-428.4	-565.4 to -291.5	Yes	****	<0.0001
											Tmem106b -/- vs. Grn -/-	1.25	-135.7 to 138.2	No	ns	>0.9999
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-417	-554.0 to -280.0	Yes	****	<0.0001
											Grn -/- vs. Grn -/- & Tmem106b -/-	-418.3	-555.2 to -281.3	Yes	****	<0.0001
6	CatB sc	WT	TM -/-	GRN -/-	GRN & TM -/-	CatB lower	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	155	84	97	249	A	13.525.188	7.346.178	8.478.516	21.661.937	wild type vs. Tmem106b -/-	6.023	-86.20 to 98.25	No	ns	0.9965
	B	88	99	129	212	B	7.658.238	8.583.749	11.269.000	18.487.892	wild type vs. Grn -/-	1.42	-90.81 to 93.65	No	ns	>0.9999
	C	57	99	69	289	C	4.951.532	8.630.426	6.015.899	25.204.912	wild type vs. Grn -/- & Tmem106b -/-	-150.1	-242.3 to -57.84	Yes	**	0.0036
											Tmem106b -/- vs. Grn -/-	-4.603	-96.83 to 87.62	No	ns	0.9984
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-156.1	-248.3 to -63.86	Yes	**	0.0028
											Grn -/- vs. Grn -/- & Tmem106b -/-	-151.5	-243.7 to -59.26	Yes	**	0.0034
6	CatL pro	WT	TM -/-	GRN -/-	GRN & TM -/-	CatL upper	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	100	93	109	120	A	7.062.509	6.554.945	7.702.314	8.439.082	wild type vs. Tmem106b -/-	-6	-53.46 to 41.46	No	ns	0.9761
	B	92	121	93	142	B	6.480.134	8.545.450	6.576.124	9.993.737	wild type vs. Grn -/-	-17.67	-65.13 to 29.80	No	ns	0.6481
	C	107	103	150	116	C	7.561.338	7.252.167	10.549.781	8.138.586	wild type vs. Grn -/- & Tmem106b -/-	-26.33	-73.80 to 21.13	No	ns	0.3494
											Tmem106b -/- vs. Grn -/-	-11.67	-59.13 to 35.80	No	ns	0.8583
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-20.33	-87.80 to 27.13	No	ns	0.5481
											Grn -/- vs. Grn -/- & Tmem106b -/-	-8.667	-56.13 to 38.80	No	ns	0.9339
6	CatL sc	WT	TM -/-	GRN -/-	GRN & TM -/-	CatL lower	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	165	64	68	191	A	2.162.050	841.573	888.674	2.510.866	wild type vs. Tmem106b -/-	35.25	-55.04 to 125.5	No	ns	0.6155
	B	91	69	67	232	B	1.198.243	906.844	881.206	3.044.978	wild type vs. Grn -/-	19.67	-70.62 to 110.0	No	ns	0.8952
	C	44	61	106	193	C	577.557	801.386	1.393.457	2.530.811	wild type vs. Grn -/- & Tmem106b -/-	-105.4	-195.7 to -15.07	Yes	*	0.0238
											Tmem106b -/- vs. Grn -/-	-15.58	-105.9 to 74.71	No	ns	0.9433
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-140.6	-230.9 to -50.32	Yes	**	0.0047
											Grn -/- vs. Grn -/- & Tmem106b -/-	-125	-215.3 to -34.74	Yes	**	0.0094
6	CatL hc	WT	TM -/-	GRN -/-	GRN & TM -/-	CatL middle	WT	TM -/-	GRN -/-	GRN & TM -/-	Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
	A	130	81	122	137	A	28.383.367	17.637.561	26.581.915	29.971.904	wild type vs. Tmem106b -/-	9.933	-47.63 to 67.49	No	ns	0.9432
	B	81	96	123	185	B	17.686.467	20.913.573	26.912.033	40.246.158	wild type vs. Grn -/-	-34.5	-92.06 to 23.06	No	ns	0.2927
	C	89	93	158	136	C	19.346.553	20.365.816	34.494.488	29.685.360	wild type vs. Grn -/- & Tmem106b -/-	-52.72	-110.3 to 4.839	No	ns	0.0731
											Tmem106b -/- vs. Grn -/-	-44.44	-102.0 to 13.12	No	ns	0.1397
											Tmem106b -/- vs. Grn -/- & Tmem106b -/-	-62.65	-120.2 to -5.095	Yes	*	0.0336
											Grn -/- vs. Grn -/- & Tmem106b -/-	-18.22	-75.78 to 39.34	No	ns	0.7466

FIGURE 6 C

CTSB assay

	delta 60-1	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			7,24	5,91	7,47	7,49
B			5,66	5,34	6,30	8,30
C			6,14	4,69	6,19	10,04
	normalized on wt	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			114,02	93,07	117,61	118,05
B			89,20	84,13	99,28	130,69
C			96,77	73,86	97,48	158,21
Tukey's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value	
<i>wild type vs. Tmem106b -/-</i>	16,31	-20,66 to 53,29	No	ns	0,5261	A-B
<i>wild type vs. Grn -/-</i>	-4,79	-41,77 to 32,19	No	ns	0,9744	A-C
<i>wild type vs. Grn -/- & Tmem106b -/-</i>	-35,65	-72,63 to 1,321	No	ns	0,0587	A-D
<i>Tmem106b -/- vs. Grn -/-</i>	-21,1	-58,08 to 15,88	No	ns	0,3284	B-C
<i>Tmem106b -/- vs. Grn -/- & Tmem106b -/-</i>	-51,96	-88,94 to -14,99	Yes	**	0,0086	B-D
<i>Grn -/- vs. Grn -/- & Tmem106b -/-</i>	-30,86	-67,84 to 6,111	No	ns	0,1055	C-D

CTSD assay

	delta 60-1	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			15,46	16,60	18,33	22,73
B			15,34	16,32	17,18	25,71
C			16,19	17,46	17,42	26,82
	normalized on wt	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			98,70	105,96	117,01	145,11
B			97,95	104,19	109,70	164,15
C			103,35	111,49	111,21	171,24
Tukey's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value	
<i>wild type vs. Tmem106b -/-</i>	-7,215	-26,63 to 12,20	No	ns	0,6493	A-B
<i>wild type vs. Grn -/-</i>	-12,64	-32,06 to 6,779	No	ns	0,2365	A-C
<i>wild type vs. Grn -/- & Tmem106b -/-</i>	-60,17	-79,59 to -40,75	Yes	****	<0,0001	A-D
<i>Tmem106b -/- vs. Grn -/-</i>	-5,425	-24,84 to 13,99	No	ns	0,8081	B-C
<i>Tmem106b -/- vs. Grn -/- & Tmem106b -/-</i>	-52,95	-72,37 to -33,53	Yes	***	0,0001	B-D
<i>Grn -/- vs. Grn -/- & Tmem106b -/-</i>	-47,53	-66,95 to -28,11	Yes	***	0,0002	C-D

CTSL assay

	delta 60-1	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			62,71	60,92	66,57	88,97
B			58,94	55,43	66,85	87,63
C			64,53	53,91	72,03	91,09
	normalized on wt	WT	TMEM106B KO	GRN KO	GRN KO x TMEM106B KO	
A			101,04	98,16	107,27	143,35
B			94,97	89,31	107,71	141,20
C			103,98	86,86	116,07	146,78
Tukey's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value	
<i>wild type vs. Tmem106b -/-</i>	8,558	-3,769 to 20,89	No	ns	0,1965	A-B
<i>wild type vs. Grn -/-</i>	-10,35	-22,68 to 1,979	No	ns	0,1033	A-C
<i>wild type vs. Grn -/- & Tmem106b -/-</i>	-43,78	-56,11 to -31,45	Yes	****	<0,0001	A-D
<i>Tmem106b -/- vs. Grn -/-</i>	-18,91	-31,23 to -6,579	Yes	**	0,0052	B-C
<i>Tmem106b -/- vs. Grn -/- & Tmem106b -/-</i>	-52,34	-64,66 to -40,01	Yes	****	<0,0001	B-D
<i>Grn -/- vs. Grn -/- & Tmem106b -/-</i>	-33,43	-45,76 to -21,10	Yes	***	0,0001	C-D

Source data Figure 6