

1 **Supplemental Table**

2 **Supplemental Table 1. Bone parameters measured by μ CT in *LepR-Cre;Slc7a5^{fl/fl}* mice.**

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	<i>Slc7a5^{fl/fl}</i>	<i>LepR-Cre;Slc7a5^{fl/fl}</i>
TV (mm³)	2.05 ± 0.06	2.17 ± 0.08
BV (mm³)	0.38 ± 0.02	0.49 ± 0.04 *
BS (mm²)	19.14 ± 0.74	23.11 ± 1.27 *
BS/BV (mm⁻¹)	51.41 ± 1.6	48.36 ± 1.44
Tb.Th (μm)	57.39 ± 1.88	60.97 ± 1.49
Tb.N (mm⁻¹)	2.29 ± 0.3	2.31 ± 0.09
Tb.Sp (μm)	142.24 ± 3.44	127.75 ± 3.39 **
Tb.Spac (μm)	199.63 ± 4.4	188.72 ± 3.56
Trabecular BMD (mg cm⁻³)	618.59 ± 11.56	624.38 ± 9.72
Trabecular BMC (mg)	0.24 ± 0.02	0.31 ± 0.02 *
Trabecular BMC/TV (mg cm⁻³)	114.57 ± 6.9	139.58 ± 8.39 *
Cortical BMD (mg cm⁻³)	974.66 ± 26.05	977.18 ± 21.43
Cortical BMC (mg)	1.15 ± 0.05	1.17 ± 0.03
Cortical BV (mm³)	1.18 ± 0.03	1.2 ± 0.03

4 Data are represented as mean ± SE.

5 * $P < 0.05$, ** $P < 0.01$ vs *Slc7a5^{fl/fl}*

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7 **Supplemental Table 2. Bone histomorphometric parameters in *LepR-Cre;Slc7a5^{fl/fl}* mice.**

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	<i>Slc7a5^{fl/fl}</i>	<i>LepR-Cre;Slc7a5^{fl/fl}</i>
N.Ob/B.Pm	25.71 ± 3.62	27.34 ± 0.99
Ob.S/B.S	18.65 ± 3.18	18.06 ± 1.43
N.Ob/Ob.Pm	126.84 ± 2.91	143.01 ± 6.47

9 Data are represented as mean ± SE.

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11 Supplemental Table 3. Bone parameters measured by μ CT in *LepR-Cre;Slc7a5^{fl/fl}* mice
 12 administrated with isoproterenol.

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	<i>Slc7a5^{fl/fl}</i>	<i>LepR-Cre;Slc7a5^{fl/fl}</i>	<i>LepR-Cre;Slc7a5^{fl/fl}</i>
	PBS	PBS	Isoproterenol
TV (mm³)	1.96 ± 0.10	2.08 ± 0.09	1.93 ± 0.10
BV (mm³)	0.3 ± 0.03	0.41 ± 0.03 *	0.28 ± 0.05 #
BS (mm²)	13.36 ± 1.20	19.18 ± 1.12 **	12.55 ± 1.69 ##
BS/BV (mm⁻¹)	45.03 ± 1.65	46.70 ± 1.55	47.27 ± 2.77
Tb.Th (μm)	44.92 ± 1.55	43.29 ± 1.55	43.46 ± 2.19
Tb.N (mm⁻¹)	3.37 ± 0.20	4.62 ± 0.18 ***	3.20 ± 0.33 ##
Tb.Sp (μm)	263.65 ± 21.93	176.54 ± 9.33 **	303.77 ± 41.31 #
Tb.Spac (μm)	308.57 ± 21.81	219.83 ± 9.40 **	347.23 ± 39.26 ##
Trabecular BMD (mg cm⁻³)	568.9 ± 17.2	524.59 ± 20.56	561.36 ± 19.39
Trabecular BMC (mg)	0.17 ± 0.02	0.22 ± 0.02	0.16 ± 0.03
Trabecular BMC/TV (mg cm⁻³)	85.28 ± 6.80	104.76 ± 7.83	82.82 ± 12.45
Cortical BMD (mg cm⁻³)	978.16 ± 14.74	955.37 ± 22.17	966.06 ± 15.92
Cortical BMC (mg)	1.15 ± 0.06	1.10 ± 0.06	1.11 ± 0.06
Cortical BV (mm³)	1.17 ± 0.06	1.15 ± 0.04	1.15 ± 0.05

14 Data are represented as mean ± SE.

15 * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ vs *Slc7a5^{fl/fl}/PBS*

16 # $P < 0.05$, ## $P < 0.01$ vs *LepR-Cre;Slc7a5^{fl/fl}/PBS*

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18 **Supplemental Table 4. Bone parameters measured by μ CT in *LepR-Cre* mice.**

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	WT	<i>LepR-Cre</i>
TV (mm³)	1.93 \pm 0.05	2.05 \pm 0.05
BV (mm³)	0.37 \pm 0.01	0.32 \pm 0.03
BS (mm²)	17.73 \pm 1.06	15.67 \pm 0.88
BS/BV (mm⁻¹)	47.28 \pm 2.15	49.35 \pm 2.53
BV/TV (%)	19.44 \pm 0.97	15.76 \pm 1.25
Tb.Th (μm)	42.59 \pm 2.10	41.06 \pm 2.11
Tb.N (mm⁻¹)	4.60 \pm 0.33	3.83 \pm 0.18
Tb.Sp (μm)	178.36 \pm 15.10	223.41 \pm 13.65
Tb.Spac (μm)	220.95 \pm 16.67	264.47 \pm 13.01
Trabecular BMD (mg cm⁻³)	529.60 \pm 30.12	645.38 \pm 67.34
Trabecular BMC (mg)	0.20 \pm 0.01	0.20 \pm 0.02
Trabecular BMC/TV (mg cm⁻³)	101.65 \pm 5.22	98.47 \pm 7.90
Cortical BMD (mg cm⁻³)	962.30 \pm 35.74	1132.00 \pm 103.07
Cortical BMC (mg)	1.18 \pm 0.14	1.21 \pm 0.10
Cortical BV (mm³)	1.22 \pm 0.10	1.08 \pm 0.06

20 Data are represented as mean \pm SE.

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22 Supplemental Table 5. Bone parameters measured by μ CT in *LepR-Cre;Slc7a5^{fl/fl}*
 23 /AAV-*Slc7a5* mice.

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	<i>LepR-Cre</i>	<i>LepR-Cre;</i> <i>Slc7a5^{fl/fl}</i>	<i>LepR-Cre</i>	<i>LepR-Cre;</i> <i>Slc7a5^{fl/fl}</i>
	AAV-Control	AAV-Control	AAV- <i>Slc7a5</i>	AAV- <i>Slc7a5</i>
TV (mm ³)	2.33 ± 0.07	2.28 ± 0.08	2.43 ± 0.08	2.1 ± 0.07 †
BV (mm ³)	0.38 ± 0.03	0.5 ± 0.02	0.36 ± 0.02	0.3 ± 0.05 ###
BS (mm ²)	20.44 ± 0.95	24.48 ± 0.79	19.73 ± 0.8	16.29 ± 1.69 ###
BS/BV (mm ⁻¹)	55.08 ± 1.94	49.35 ± 2.18	55.31 ± 0.79	56.63 ± 3.29
Tb.Th (μm)	36.84 ± 1.51	41.01 ± 1.81	36.19 ± 0.52	36.05 ± 2.12
Tb.N (mm ⁻¹)	4.38 ± 0.12	5.37 ± 0.13 **	4.06 ± 0.1	3.85 ± 0.34 ###
Tb.Sp (μm)	193.32 ± 6.85	145.77 ± 5.34	210.87 ± 6.85	238.57 ± 30.23 ##
Tb.Spac (μm)	230.15 ± 6.16	186.77 ± 4.17	247.06 ± 6.6	274.61 ± 28.47 ##
Trabecular BMD (mg cm ⁻³)	614.55 ± 11.65	631.91 ± 19.86	599.08 ± 6.44	592.1 ± 14.1
Trabecular BMC (mg)	0.24 ± 0.02	0.32 ± 0.02	0.22 ± 0.01	0.19 ± 0.03 ##
Trabecular BMC/TV (mg cm ⁻³)	100.57 ± 7.42	140.36 ± 12.62 *	88.77 ± 3.74	85.94 ± 13.35 ##
Cortical BMD (mg cm ⁻³)	1008.19 ± 11.4	1002.66 ± 11.86	1027.58 ± 5.92	1041.4 ± 12.86
Cortical BMC (mg)	1.11 ± 0.04	1.25 ± 0.05	1.11 ± 0.02	1.16 ± 0.04
Cortical BV (mm ³)	1.1 ± 0.03	1.25 ± 0.04 *	1.08 ± 0.02	1.12 ± 0.04

25 Data are represented as mean ± SE.

26 **P* < 0.05, ***P* < 0.01 vs *LepR-Cre/AAV-Control*

27 †*P* < 0.05 vs *LepR-Cre/AAV-Slc7a5*

28 ###*P* < 0.01, ####*P* < 0.001 vs *LepR-Cre;Slc7a5^{fl/fl}/AAV-Control*

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30 Supplemental Table 6. Bone parameters measured by μ CT in *LepR-Cre;Slc7a5^{fl/fl};Tsc1^{fl/+}*
 31 mice.

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	<i>Slc7a5^{fl/fl}</i>	<i>LepR-Cre;Slc7a5^{fl/fl}</i>	<i>LepR-Cre; Slc7a5^{fl/fl};Tsc1^{fl/+}</i>
TV (mm³)	2.01 \pm 0.04	2.35 \pm 0.08 **	1.98 \pm 0.12 #
BV (mm³)	0.36 \pm 0.02	0.58 \pm 0.04 ***	0.37 \pm 0.04 ##
BS (mm²)	18.93 \pm 0.72	26.58 \pm 1.54 ***	19.31 \pm 2.23 ##
BS/BV (mm⁻¹)	52.79 \pm 1.4	46.37 \pm 1.1 *	52.78 \pm 0.69
Tb.Th (μm)	18.04 \pm 0.88	24.36 \pm 1 ***	18.41 \pm 1.21 #
Tb.N (mm⁻¹)	57.35 \pm 0.95	61.05 \pm 0.95	57.4 \pm 1.92
Tb.Sp (μm)	2.01 \pm 0.06	2.51 \pm 0.09 ***	2.01 \pm 0.13 ##
Tb.Spac (μm)	139.03 \pm 2.52	123.01 \pm 3.84 **	134.31 \pm 6.31
Trabecular BMD (mg cm⁻³)	196.38 \pm 2.49	184.06 \pm 4.26	191.71 \pm 8.17
Trabecular BMC (mg)	599.56 \pm 6.83	633.75 \pm 10.42 *	596.3 \pm 8.37
Trabecular BMC/TV (mg cm⁻³)	0.22 \pm 0.01	0.37 \pm 0.03 ***	0.22 \pm 0.02 ##
Cortical BMD (mg cm⁻³)	108.61 \pm 5.97	153.9 \pm 8.1 ***	109.5 \pm 6.11 #
Cortical BMC (mg)	981.61 \pm 22.62	977.88 \pm 25.29	1023.77 \pm 17.98
Cortical BV (mm³)	1.1 \pm 0.04	1.22 \pm 0.06	1.11 \pm 0.07
Cortical BV (mm³)	1.12 \pm 0.03	1.24 \pm 0.03 *	1.08 \pm 0.06

33 Data are represented as mean \pm SE.

34 * P < 0.05, ** P < 0.01, *** P < 0.001 vs *Slc7a5^{fl/fl}*

35 # P < 0.05, ## P < 0.01 vs *LepR-Cre;Slc7a5^{fl/fl}*

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37 **Supplemental Table 7. Bone parameters measured by μ CT in *LepR-Cre;Tsc1^{fl/+}* mice.**

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	<i>Tsc1^{fl/+}</i>	<i>LepR-Cre;Tsc1^{fl/+}</i>
TV (mm³)	1.98 ± 0.13	2.13 ± 0.09
BV (mm³)	0.27 ± 0.08	0.28 ± 0.03
BS (mm²)	15.61 ± 2.92	16.93 ± 1.88
BS/BV (mm⁻¹)	62.90 ± 4.97	60.45 ± 2.04
Tb.Th (μm)	13.05 ± 2.86	13.13 ± 1.28
Tb.N (mm⁻¹)	32.78 ± 3.12	33.23 ± 1.08
Tb.Sp (μm)	3.83 ± 0.47	3.94 ± 0.33
Tb.Spac (μm)	242.90 ± 32.84	229.93 ± 28.18
Trabecular BMD (mg cm⁻³)	275.68 ± 30.38	263.16 ± 27.87
Trabecular BMC (mg)	739.28 ± 40.88	758.48 ± 32.21
Trabecular BMC/TV (mg cm⁻³)	0.21 ± 0.07	0.22 ± 0.03
Cortical BMD (mg cm⁻³)	100.36 ± 27.98	100.2 ± 11.73
Cortical BMC (mg)	1490.18 ± 66.79	1479.64 ± 48.71
Cortical BV (mm³)	1.44 ± 0.14	1.43 ± 0.07
Cortical BV (mm³)	0.97 ± 0.10	0.96 ± 0.02

39 Data are represented as mean ± SE.

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41 **Supplemental Table 8. List of primers used for genotyping.**

Gene	Forward (5'-3')	Reverse (5'-3')
<i>Slc7a5 flox</i>	GGCTCCTGGACTTATCTTGACCAAT	AGATAATGTGGTCACACATCTGGAAG
<i>Tsc1 flox</i>	AGGAGGCCTCTTCTGCTACCACTTTT GATG	GAAGGCAGCTCCGACCATGAAGTGCT GTGT
<i>LepR-Cre</i>	ATGTCCAATTTACTGACCGTACA	CGCATAACCAGTGAAACAGCATT
<i>Rosa26-tdTomato</i>	GGCATTAAAGCAGCGTATCC	CTGTTCTGTACGGCATGG

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43 **Supplemental Table 9. List of primers used for deletion PCR.**

Gene	Forward (5'-3')	Reverse (5'-3')
<i>Slc7a5</i>	GGCTCCTGGACTTATCTTGACCAATG	GTGGTGCTTTGCTGAAGGCAGGG

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45 **Supplemental Table 10. List of primers used for real-time PCR.**

Gene	Forward (5'-3')	Reverse (5'-3')
<i>Adrb3</i>	TGCGCACCTTAGGTCTCATTATGG	AAACTCCGCTGGGAACTAGAGAGG
<i>Cidea</i>	ATCACAACCTGGCCTGGTTACG	TACTACCCGGTGTCCATTTCT
<i>Cox5b</i>	GCTGCATCTGTGAAGAGGACAAC	CAGCTTGTAATGGGTCCACAGT
<i>Cox7a1</i>	CAGCGTCATGGTCAGTCTGT	AGAAAACCGTGTGGCAGAGA
<i>Cox8b</i>	GAACCATGAAGCCAACGACT	GCGAAGTTCACAGTGGTTCC
<i>Cycl</i>	GCTACCCATGGTCTCATCGT	CATCATCATTAGGGCCATCC
<i>Dio2</i>	GGTGGTCAACTTTGGTTCAGCC	AAGTCAGCCACCGAGGAGAACT
<i>Gapdh</i>	AGGTCGGTGTGAACGGATTG	TGTAGACCATGTAGTTGAGGTCA
<i>Il6</i>	CACCAAGAACGATAGTCAATTCCA	TCACCAGCATCAGTCCCAAG
<i>Nrf1</i>	CAACAGGGAAGAAACGGAAA	GCACCACATTCTCCAAAGGT
<i>Nrf2</i>	AGGTTGCCACATTCCCAAACAAG	TTGCTCCATGTCCTGCTCTATGCT
<i>Pgc1a</i>	GAATCAAGCCACTACAGACACCG	CATCCCTCTTGAGCCTTTCGTG
<i>Tfam</i>	GTCCATAGGCACCGTATTGC	CCCATGCTGGAAAAACACTT
<i>Ucp1</i>	TACCAAGCTGTGCGATGTCC	GCACACAAACATGATGACGTTCC

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47 **Supplemental Table 11. List of primers used for real-time PCR to quantify mtDNA.**

Gene	Forward (5'-3')	Reverse (5'-3')
<i>mtDNA</i>	CCGCAAGGGAAGATGAAAGAC	TCGTTTGGTTTCGGGGTTTC
<i>Nuclear DNA</i>	GCCAGCCTCTCCTGATTTAGTGT	GGGAACACAAAAGACCTCTTCTGG

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