

**Figure S1.** The evaluation of the CB1 receptor knockout efficiency. Electrophoresis of the *CB1* (*CNR1*) genomic DNA fragments obtained by PCR before (-) and after (+) *PvuII* restriction enzyme treatment; the disappearance of the *PvuII* cleavage would indicate the loss of the appropriate part of the gene, equaling to the successful gene modification.

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CNR1      CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 124
3.3       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 238
3.2       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 238
3.4       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 236
3.5       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 235
3.1       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 238
3.7       CAACAAGTCTCTCTCGTCCTTCAAGGAGAATGAGGAGAACATCCAGTGTGGGAGAACTT 236
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CNR1      CATGGACATAGAGTGTTCATGGTCCTGAACCCAGCCAGC-AGCTGGCCATTGCAGTCC 183
3.3       CGTGGACATAGAGTGTTCATGGTCCT----- 265
3.2       CATGGACATAGAGTGTTCATGGTCCTGAACCCAGCCAGCAAGCTGGCCATTGCAGTCC 298
3.4       CATGGACATAGAGTGTTCATGGTCCTGAACCCCA-----AGCTGGCCATTGCAGTCC 289
3.5       CATGGACATAGAGTGTTCATGGTCCTGAACCCAGCCA---AGCTGGCCATTGCAGTCC 292
3.1       CATGGACATAGAGTGTTCATGGTCCTGAACCCAGCCA---AGCTGGCCATTGCAGTCC 295
3.7       CATGGACATAGAGTGTTCATGGTCCTGAACCCAGCCA---AGCAGGCCATTGCAGTCC 293
* *****

CNR1      TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 243
3.3       -GTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 324
3.2       TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 358
3.4       TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 349
3.5       TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 352
3.1       TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 355
3.7       TGTCCCTCACGCTGGGCACCTTCACGGTCCTGGAGAACCCTCCTGGTGCTGTGCGTCATCC 353
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**Figure S2.** The evaluation of the CB1 receptor knockout efficiency. Sequencing results alignment with the native *CNR1* mRNA. *PvuII* cleavage site is shown in bold.

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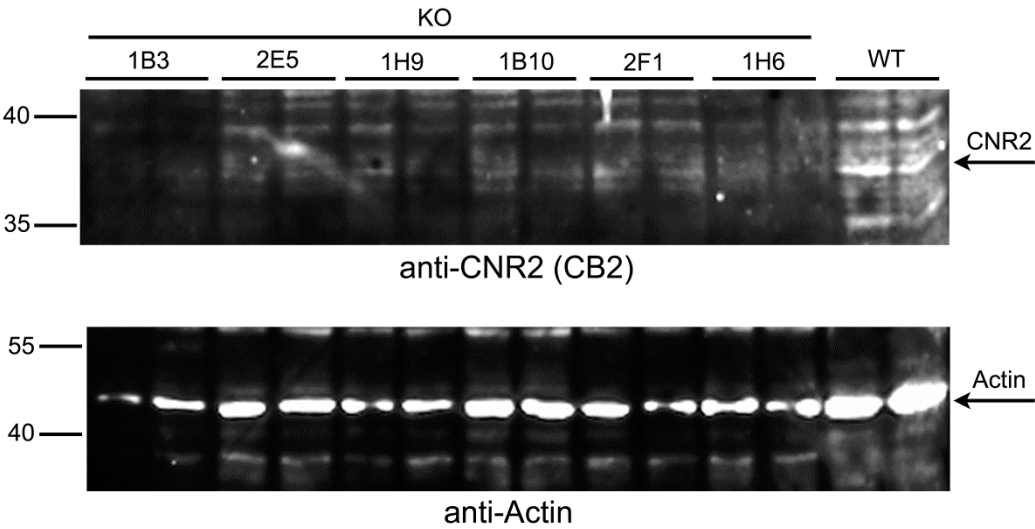
cnr2      TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 65
2e5       TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 179
1h9       TCCT - CTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 176
1h6       TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 176
2f1       TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 178
1b10      TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 179
1b3       TCCTGCTGAAGATTGGCAGCGTGAATGACCTTCACAGCCTCTGTGGGTAGCCTCCTGC 179
**** *****

cnr2      TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 125
2e5       TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 239
1h9       TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 236
1h6       TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 236
2f1       TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 238
1b10      TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 239
1b3       TGACCGCCATTGACCGATACCTCTGCCTGCGCTATCCACCTTCCTACAAAGCTCTGCTCA 239
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cnr2      CCCGTGGAAGGGCACTGGTGACCCCTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 185
2e5       CCCGTGGAAGGGCACTGGTGAC-CTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 298
1h9       CCCGTGGAAGGGCACTGG- --CCCTGGGTATCATGTGGGTCCTCTCAGCACTAGTCTCCT 293
1h6       CCCGTGGAAGGGCACTGGTGAC-CTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 295
2f1       CCCGTGGAAGGGCACTGGTGAC-CTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 297
1b10      CCCGTGGAAGGGCACTGGTGAC-CTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 298
1b3       CCCGTGGAAGGGCACTGGTGAC-CTGGGCATCATGTGGGTCCTCTCAGCACTAGTCTCCT 298
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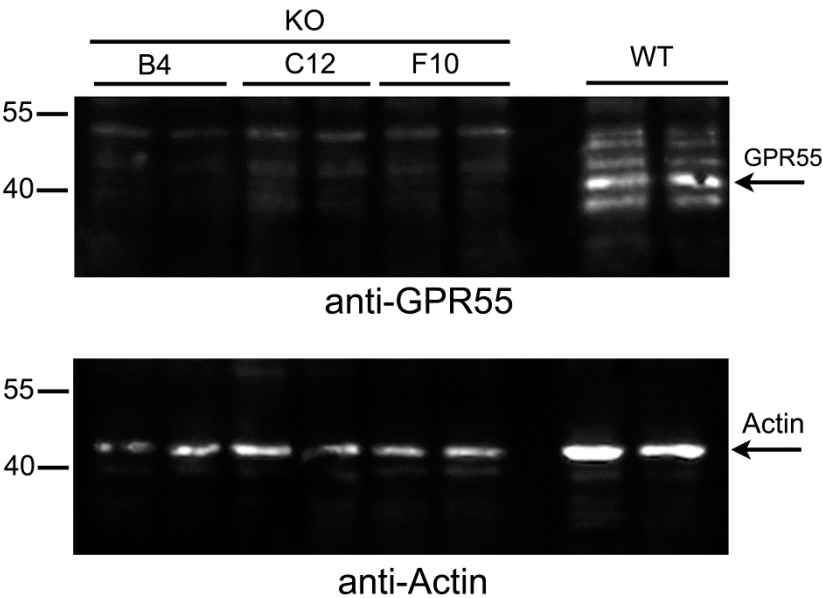
**Figure S3A.** The evaluation of the CB2 receptor knockout efficiency. Sequencing results alignment with the native *CNR2* mRNA. *PasI* cleavage site is shown in bold.



**Figure S3B.** The evaluation of the CB2 receptor knockout efficiency. Western blot data.

GPR55	GCATCCCTATCTACAGTTT <b>CCATGGG</b> AAAGTGGAAAAATACATGTGCTTCCACAACATGT	231
1B4	GCATCCCTATCTACAGTTTC---GGGAAAGTGGAAAAATACATGTGCTTCCACAACATGT	295
C12	GCATCCCTATCTACAGTTTC--TGGGAAAGTGGAAAAATACATGTGCTTCCACAACATGT	298
F10	GCATCCCTATCTA-----AGTGGAAAAATACATGTGCTTCCACAACATGT	296
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**Figure S4A.** The evaluation of the GPR55 receptor knockout efficiency. Sequencing results alignment with the native *GPR55* mRNA. *NcoI* cleavage site is shown in bold.



**Figure S4B.** The evaluation of the GPR55 receptor knockout efficiency. Western blot data.

GPR18	CATTGCTTTATGGCTTCTTGCCTTTATTAGTGTGCTGACAGATACATGGCCATT <b>TGTACAGCC</b>	189
1f2	CATTGCTTTATGGCTTCTTGCCTTTATTAGTGTGCTGACAGATACATGGCCATT-TACTGCC	299
2d9	CATTGCTTTATGGCTTCTTGCCTTTGTTAGTGTGCTGACAGATACATGGCCATT-TACAGCC	299
1h7	CATTGCTTTATGGCTTCTTGCCTTTATTAGTGTGCTGACAGATACATGGCCATT-TACAGCC	298
2b9	CATTGCTTTATGGCTTCTTGCCTTTATTAGTGTGCTGACAGATACATGGCCATT-TACAGCC	298
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**Figure S5.** The evaluation of the GPR18 receptor knockout efficiency. Sequencing results alignment with the native *GPR18* mRNA. *BstAUI* cleavage site is shown in bold.