

## Disrupted Murine Gut to Human Liver Signaling Altered Bile Acid Homeostasis in Chimeric, Humanized Liver Mouse Model

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**Supplementary Table 1.** Mouse and human primer sequences for qPCR

	<b>Gene Bank Number</b>	<b>Forward (5' → 3' Sequence)</b>	<b>Reverse (5' → 3' Sequence)</b>
<i>hABCA1</i>	NM_005502.3	CACCCTATGAACAACATGAATGCCA	CAGGAGTCGGGTAACGGAAA
<i>hABCG5</i>	NM_022436.2	TGGACGCTGGGCTTACATC	GCCAAGAGAGCAGCAGAAAAAT
<i>hABCG8</i>	NM_022437.2	AGCAGCTGGGTCTAAGAGAG	CTGGAGGCCCGAGGTATC
<i>hAlbumin</i>	NM_000477.5	AGGGGTGTGTTTCGTCGAG	AAAGGCAATCAACACCAAGGCT
<i>hBCRP</i>	NM_004827.2	GCATCCTGAGATCCTGAGCC	TCTGGAGAGTTTTTATCTTTTCAGC
<i>hβ-KLTHO</i>	NM_175737.3	CTCAGTCTCCCAGTTCAAGCTAA	CCCCGTTGGACATTGTATTCTTA
<i>hBSEP</i>	NM_003742.2	AAAACCGAGGTTGGAAAAGGTT	CCAACGACCCTGTGAATATGAA
<i>hCAR</i>	NM_005122.4	CTTCTCTCCTGACCGACCTG	TCGCATACAGAAACCGATCC
<i>hCYP1A1</i>	NM_000499.3	CTACACTGATCATGCTTTTCCAATC	GCCCTGATTACCAGAATACCAGA
<i>hCYP2B6</i>	NM_000767.4	CCGGGGATATGGTGTGATCTT	AGTGGTCACAGAGAATCGCC
<i>hCYP2C9<sup>a</sup></i>	NM_000771.3	Hs04260376_m1 (Cat. # 4331182)	
<i>hCYP2C19</i>	NM_000769.1	TCAGGATTGTAAGCACCCCC	CCCGGAAATAATCAATGATAGTG
<i>hCYP2D6</i>	NM_001025161.2	GCTTCGACCAGTTGCGGC	AGCCATTGAGCACGACC
<i>hCYP2E1</i>	NM_000773.3	CTGTGTCATTCCCCGCTCAT	TGAGAAATCCTGACCTCAAACA

<i>hCYP27A1</i>	NM_000784.3	GAGGACCTATCCCGGTGTGG	CTTGGTCTGAACTCTGGGCG
<i>hCYP3A4</i>	NM_017460.5	CATTCCTCATCCCAATTCTTGAAGT	CCACTCGGTGCTTTTGTGTATCT
<i>hCYP7A1</i>	NM_000780.3	GAATGCTGGTCAAAAAGTC	TGAAATCCTCCTTAGCTGT
<i>hCYP7B1</i>	NM_004820.4	GGGAGACCACGGTGACATTC	TACTTCCACCAAGAAGAAGTGTG
<i>hCYP8B1</i>	NM_004391.2	GTGCCAGCTACTCCTTCCTG	AGTTCGGAGGCCATTTCTGG
<i>hFGF19</i>	NM_005117.2	TCCCTGAGCAGTGCCAAAC	GGAAATGAGAGAGTGAAGAAAGC
<i>hFGFR4</i>	NM_022963.2	TCAAGATGCTCAAAGACAACGC	CCACGATCACGTACAGGGG
<i>hFXR</i>	NM_001206993.1	TGGGGAAGTGAATGACTC	ACAGGCAAAGTGTTGAGGAT
<i>hGAPDH</i>	NM_002046.4	GAAGGTGAAGGTCGGAGTC	GAAGATGGTGATGGGATTC
<i>hGSTA4-4</i>	NM_001512.3	AAGAATGGGCAGGATCTCTTGTT	AAAATTAGGCAGAGACTGGAGGG
<i>hHMG CoA Reductase</i>	NM_000859.2	CTCCGAGCGTGCGTAAGG	CCTTGGATCCTCCAGATCTCACTA
<i>hHNF-1α</i>	NM_000545.5	CCTGTCCCAACACCTCAACAA	TTGAAACGGTTCCTCCGC
<i>hHNF-4α</i>	NM_001258355.1	AAGAGGAACCAGTGCCGCTA	CGCATTGATGGAGGGCAG
<i>hLRH-1</i>	NM_001276464.1	TACCGACAAGTGGTACATGGA	CGGCTTGTGATGCTATTATGGA
<i>hLXRα</i>	NM_001251935.1	GACCGACTGATGTTCCACG	CCATCCGGCCAAGAAAACAG
<i>hMDR1</i>	NM_000927.4	TGCTCAGACAGGATGTGAGTTG	AATTACAGCAAGCCTGGAACC
<i>hMRP2</i>	NM_000392.3	CAAACCTCTATCTTGCTAAGCAGG	TGAGTACAAGGGCCAGCTCTA
<i>hMRP3</i>	NM_003786.3	CTTAAGACTTCCCCTCAACATGC	GGTCAAGTTCCTCTTGCTC

<i>hMRP4</i>	NM_005845.3	AATGTGACCGTCCATCCTCC	AGGTTTGGCCTTCTTGGA
<i>hNTCP</i>	NM_003049.3	GGATGCCAAAATGTCCAAC	TGAGGTGCCATTTCCAGA
<i>hOATP1B3</i>	NM_019844.3	GGGTGAATGCCCAAGAGATA	ATTGACTGGAAACCCATTGC
<i>hOATP2B1</i>	NM_001145211.2	TGATTGGCTATGGGGCTATC	CATATCCTCAGGGCTGGTGT
<i>hOATP1B1</i>	NM_006446.4	GCCCAAGAGATGATGCTTGT	ATTGAGTGGAAACCCAGTGC
<i>hOST-<math>\alpha</math></i>	NM_152672.5	TGTTGGGCCCTTTCCAATAC	GGCTCCCATGTTCTGCTCAC
<i>hOST-<math>\beta</math></i>	NM_178859.3	CAGGCAAGCAGAAAAGAAAAG	CCGGAAGGAAAACCTGACA
<i>hPPAR<math>\gamma</math></i>	NM_138711.3	AAGACCACTCCCACTCCTTG	TTTGATTGCACTTTGGTACTCTGA
<i>hPXR</i>	NM_022002.2	CAAGCGGAAGAAAAGTGAACG	CACAGATCTTCCGGACCTG
<i>hSHP</i>	NM_021969.2	GGCTTCAATGCTGTCTGGAGT	CCCTTTCAGGCAGGCATATT
<i>hSULT1A1</i>	NM_177530.2	AACCCTATGACCAACTACACCA	CACAGCTCAGAGCGGAAG
<i>hSULT1A2</i>	NM_177528.2	CATGGCCAAAGTGTACCCTCA	GGACCCATAGGACACTTCTCCA
<i>hSULT1E1</i>	NM_005420.2	GGTGATGTGGAAAAGTGCAAAGA	G TTCAGGTGGCAAATGAGTCTTC
<i>hSULT2A1</i>	NM_003167.3	TCGTGATAAGGGATGAAGATGTAATAA	TGCATCAGGCAGAGAATCTCA
<i>hTGFB<math>\beta</math>2</i>	NM_11024847.2	GTCTGTGTGGCTGTATGGAGA	TTGGGGTCATGGCAAACCTGT
<i>hUGT1A1</i>	NM_000463.2	CCCATGCTGGGAAGATACTGTT	GCGTCAGGTGCTAGGACAAC
<i>m<math>\beta</math>-actin</i>	NM_007393.3	TGGAATCCTGTGGCATCCATGAAAC	TAAAACGCAGCTCAGTAACAGTCCG
<i>mAsb<sup>f</sup> (for intestine)</i>	NM_011388.2	GATAGATGGCGACATGGACCTC	CAATCGTTCCCGAGTCAACC

<i>mAsbt (for liver)</i>	NM_011388.3	TTGCCCTTGGAAATGATGCCT	GCAACCAGAGAAATACCAATGC
<i>mBaat</i>	NM_007519.3	AGTGTTGTCAGAGCCTTGGTT	CACCAAAACAGTAGTTTTACAGCA
<i>mBcrp</i>	NM_011920.3	AAATGGAGCACCTCAACCTG	CCCATCACAACGTCATCTTG
<i>mCar</i>	NM_001243063.1	TCAACACGTTTATGGTGCAA	CTGCGTCCTCCATCTTGTAG
<i>mCK19</i>	NM_008471.3	GGACCCTCCCGAGATTACAAC	AGGCGTGTTCTGTCTCAAAC
<i>mCxcl16</i>	NM_023158.6	TTCTTGTTGGCGCTGCTGAC	TGCGCTCAAAACAGTCCACTAG
<i>mCyclophilin<sup>b</sup></i>	NM_011149.2	GGAGATGGCACAGGAGGAA	GCCCGTAGTGCTTCAGCTT
<i>mCyp1a1</i>	NM_001136059.2	GGAGACCTTCCGGCATTCA	GCCATTCAGACTTGTATCTCTTGTG
<i>mCyp1a2</i>	NM_009993.3	GAGAGATACAATTCTTTCCCCATTT	TTATGGGGTGAACATGATAGACACT
<i>mCyp2e1</i>	NM_021282.2	CTTGAAAAGCCAAGGAACACC	TCCTGCAAAGAACAGGTCGG
<i>mCyp27a1</i>	NM_024264.4	CTGCGTCAGGCTTTGAAACA	TCGTTTAAGGCATCCGTGTAGA
<i>mCyp3a11</i>	NM_007818.3	AGAACTTCTCCTTCCAGCCTTGT	GAGGGAGACTCATGCTCCAGTTA
<i>mCyp7b1</i>	NM_007825.4	CTTGGTCTGCCTGGAAAGCA	AAAGGAGACGGCAGAATCGG
<i>mFxr</i>	NM_001163700.1	CGGAACAGAAACCTTGTTTCG	TTGCCACATAAATATTCATTGAGATT
<i>mGsta3-3</i>	NM_001077353.1	CCCAAGCAACTGCTGCCAT	CCACCGGATAGGCTCCATTC
<i>mGsta4-4</i>	NM_010357.3	AGAGGCTTTTCTCGTTGGCA	AAGCACGCTGCACTAGAAC
<i>mHnf-4a</i>	NM_008261.2	CCAAGAGGTCCATGGTGTTTAAG	GTGCCGAGGGACGATGTAGT
<i>mIbabp<sup>c</sup></i>	NM_008375.2	CAAGGCTACCGTGAAGATGGA	CCCACGACCTCCGAAGTCT

<i>mLrh-1</i>	NM_001159769.2	CCCTGCTGGACTACACGGTTT	CGGGTAGCCGAAGAAGTAGCT
<i>mLxra</i>	NM_001177730.1	GGATAGGGTTGGAGTCAGCA	GGAGCGCCTGTTACACTGTT
<i>mMdr1a</i>	NM_011076.2	ATGGTGTTTAATCCAAGTCAAAAGGA	CAAAGCCTCTGAAGACTCTAAACC
<i>mMrp1<sup>c</sup></i>	NM_008576.3	AGGTCGTACGGGAGCTGGGAAATCAT	CCAGGGCCATCCAGACTTCTTCATCA
<i>mMrp2</i>	NM_013806.2	GCTTCCCATGGTGATCTCTT	CTTGGATTGTGGCTTCCAAG
<i>mMrp3</i>	NM_029600.3	TATGGGATGGCCAAGGATGC	GGCCATCGAGTCCATCTGAC
<i>mMrp4</i>	NM_001163676.1	CACACCGAGGTGAAACCCAA	AGTCTCCGCTTATGACCAGTTTT
<i>mOat1<sup>c</sup></i>	NM_008766.3	ATCAACTGCATGACACTAAACATGG	ACATAGCCAATCAAGGTGCC
<i>mOat3<sup>c</sup></i>	NM_031194.5	ATCCAGCTCCAACCACCAGTTTT	TGCTTCCAACACGGTCCAGAA
<i>mOatp1a1</i>	NM_013797.5	TGAGAAAGACAGCAGTAGGACT	AAGAATCTGCCTTCTGTGTTGC
<i>mOatp1a4</i>	NM_030687.1	GGCTCCTTCATGTGTGGACTT	TCGCCACCTGAAGATTCCTTT
<i>mOatp2b1</i>	NM_001252531.1	GCTGCTTTCAATGAGGTAGGGAA	CGATCATCCGGGGTCTGTG
<i>mOst-<math>\alpha</math></i>	NM_145932.3	TTGGAAGGAAGGGTTGGGTAG	GGTCCCTTCCACCTCTTTCAG
<i>mOst-<math>\beta</math></i>	NM_178933.2	CAATCAGGAGCAGAAACATGGAC	GAATAATTCCAAGGAGCCGCATC
<i>mPepT1<sup>c</sup></i>	NM_053079.2	CCACAATGGGGATGTCCAAGTCT	CATTGACCACGATGAAGAAGATGC
<i>mPepT2<sup>c</sup></i>	NM_021301.3	ATGAGTCCAAGGAAACGCTCTT	AGAGCTTCGGAGTTGACTTCTTT
<i>mPxr</i>	NM_010936.3	GCCGATGTGTCAACCTACAT	CTCAGGATGCACATCTCAAA
<i>mShp</i>	NM_011850.2	CAGCGCTGCCTGGAGTCT	AGGATCGTGCCCTTCAGGTA

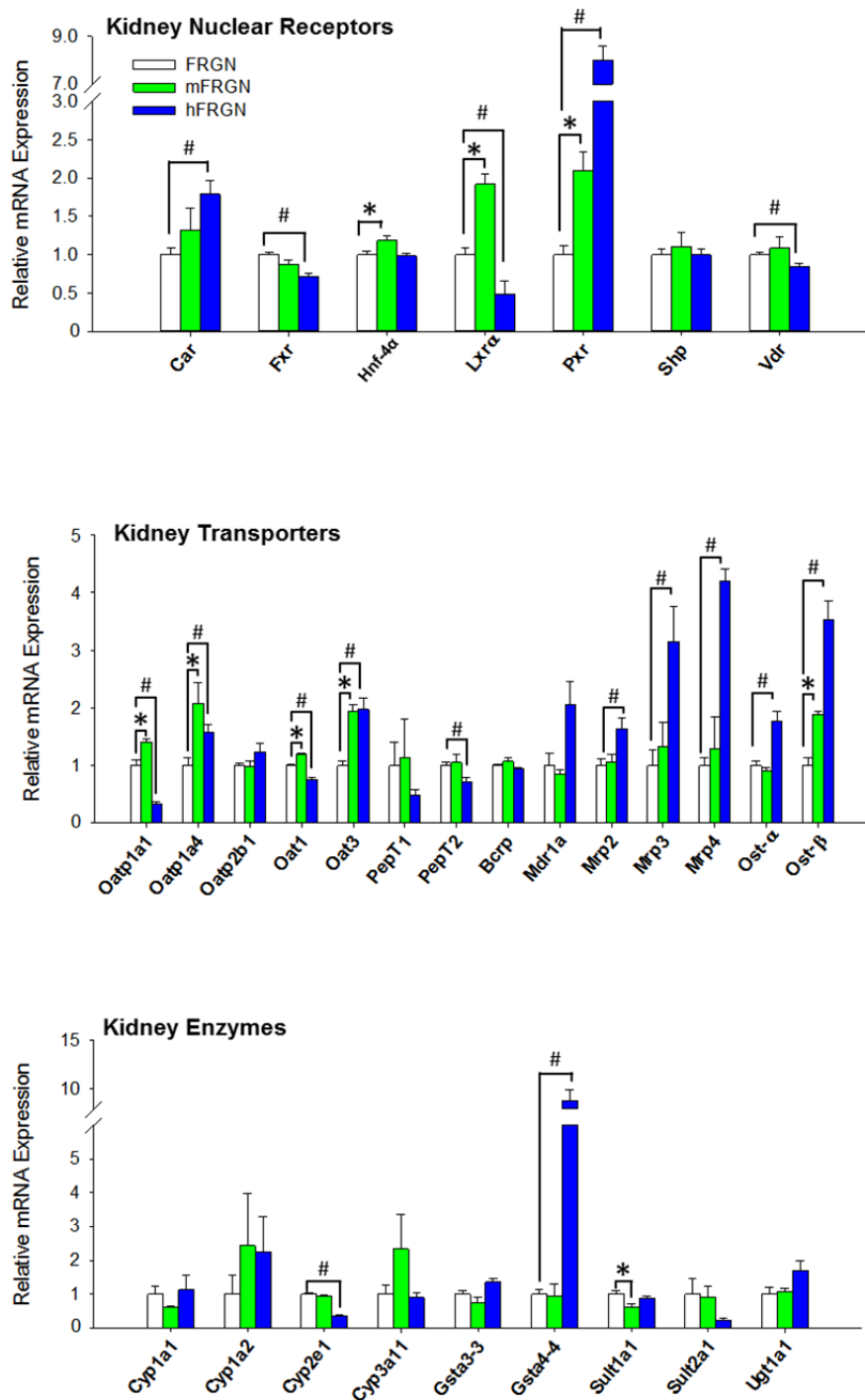
<i>mSult1a1</i>	NM_133670.1	TCCCCCAGGTCTTGAAACT	TAAGGACAAGGGCAGATGTGTCT
<i>mTgr5</i>	NM_174985.1	GCGATGTACCCTCAACCCTG	CGCTCATAGGCCAAGACTGA
<i>mTgf-<math>\beta</math>1</i>	NM_011577.2	GTCACTGGAGTTGTACGGCA	GGGCTGATCCCGTTGATTC
<i>mUgt1a1</i>	NM_201645.2	GGCTGTTAGTGTTCCCTATGGATG	GATTAAAGGCAGTCCGTCCAAGT
<i>mVdr<sup>e</sup></i>	NM_009504.4	GAGGTGTCTGAAGCCTGGAG	ACCTGCTTTCCTGGGTAGGT
<i>mVegf-a</i>	NM_001025257.3	CCACGTCAGAGAGCAACATC	TTGTTCTGTCTTCTTTGGTCTGC
<i>mVegf-c</i>	NM_009506.2	TGCACTTGCTGTGCTTCTTGT	TCTTTGCCTTCAAAAGCCTTGAC
<i>mVillin<sup>c</sup></i>	NM_009509.2	TCCTGGCTATCCACAAGACC	CTCTCGTTGCCTGAACCTC

h, human; m, mouse;

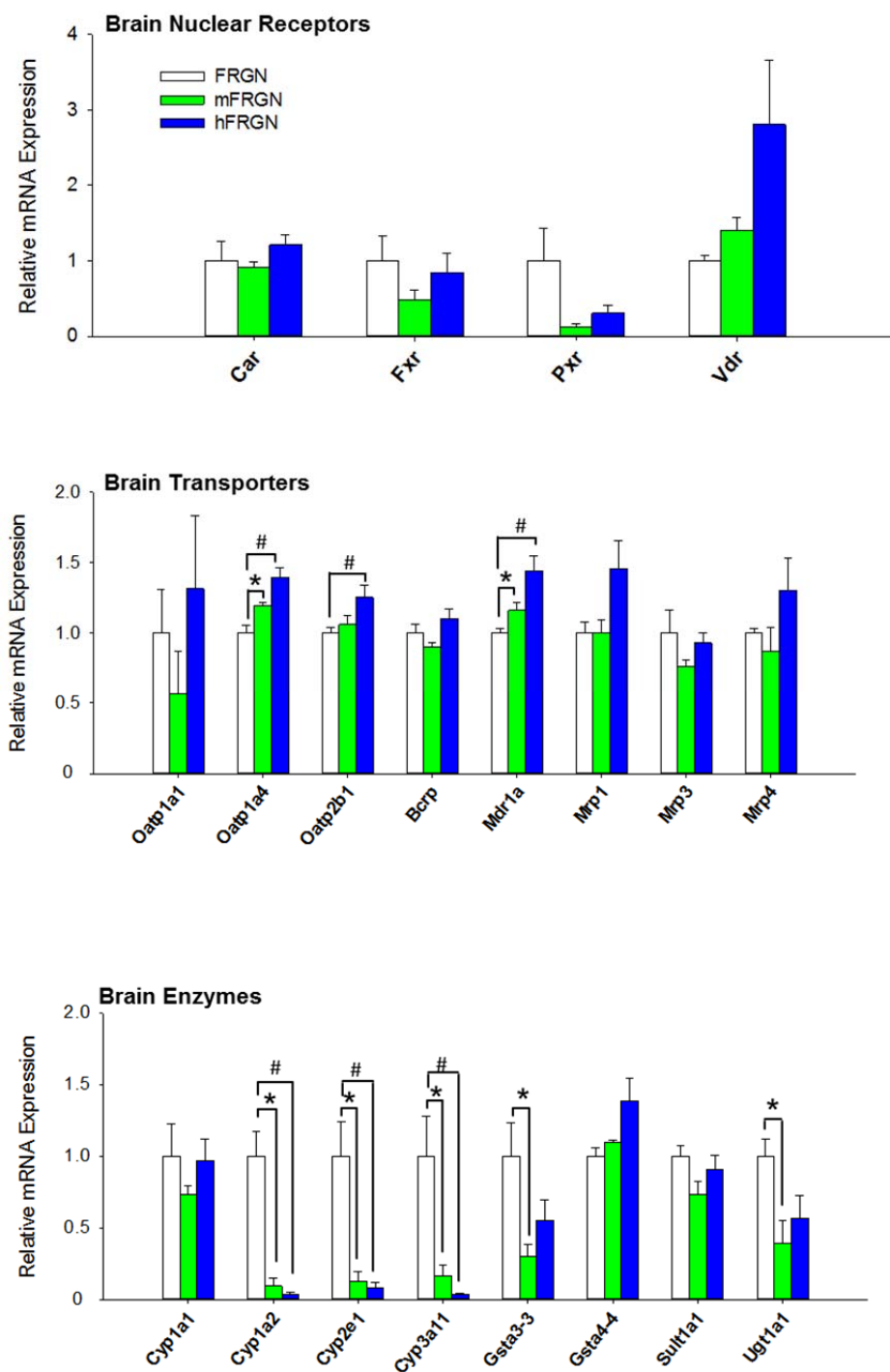
<sup>a</sup> denotes that primer set is for Taqman probe detection;

<sup>b</sup> denotes that the gene cross-react between human and mouse;

<sup>c</sup> denotes primers that were not tested for specificity for human and mouse



**Supplemental Figure 1. In kidney, mRNA expression of mouse nuclear receptors, transporters, and enzymes in FRGN, mFRGN, and hFRGN mice (n=4-8).** In mFRGN kidneys, renal gene expression was generally similar to those of FRGN kidneys, except the slightly higher expression in *Lxr $\alpha$* , *Pxr*, *Oatp1a1*, *Oatp1a4*, *Ost- $\beta$* , *Oat1*, and *Oat3* and lower expression of *Sult1a1*. Renal mRNA expression levels of *Car*, *Pxr*, *Ost $\alpha$* , *Ost $\beta$* , *Oat3*, *Mrp2*, *Mrp3*, and *Mrp4* and *Gsta4-4* in hFRGN kidneys were, however, significantly higher compared to those of FRGN kidneys; *Oatp1a4* expression was slightly higher whereas *Fxr*, *Lxr $\alpha$* , *Vdr*, *Oatp1a1*, *Oat1*, *PepT2*, and *Cyp2e1* expression was lower. \*  $P < 0.05$  denotes comparison between FRGN and mFRGN kidneys using 2-tailed Student's *t*-test. #  $P < 0.05$  denotes comparison between FRGN and hFRGN kidneys using 2-tailed Student's *t*-test.



**Supplementary Figure 2.** In brain, mRNA expression of mouse nuclear receptors, transporters, and enzymes in FRGN, mFRGN, and hFRGN mice (n=4-8). In mFRGN brains, mRNA expression of Cyp1a2, Cyp2e1, Cyp3a11, Gsta3-3, and Ugt1a1 were significantly lower compared to those of FRGN brains, although those for Oatp1a4 and Mdr1a expression were higher. In hFRGN brains, mRNA expression of Cyp1a2, Cyp2e1, and Cyp3a11 were significantly lower compared to those of FRGN brains. \*,  $P < 0.05$  between FRGN and mFRGN brains and #,  $P < 0.05$  between FRGN and hFRGN brains, using the 2-tailed Student's *t*-test.