Table 1. Expression levels of genes encoding RMT receptors in isolated human brain microvessels (BMV), brain and lung (RNAseq normalized read counts; average ± SD)

Receptors/proteins	**Human BMV**	**Human brain**	**Human lung**
TFRC	1645.22 ± 249.68	1560.20 ± 520.04	7856.40 ± 6648.12
INSR	3010.84 ± 1158.90*	854.14 ± 81.00	1260.72 ± 106.44
IGF1R	1304.87 ± 746.61	905.46 ± 229.11	800.57 ± 198.75
IGF2R	602.08 ± 550.37	613.27 ± 194.15	4162.89 ± 2237.01*
LRP1	6896.83 ± 2520.15	5797.91 ± 1220.33	12733.83 ± 4968.54
LDLR	1424.41 ± 2003.73*	294.13 ± 121.19	6952.95 ± 2791.13
LRP8 (ApoER2)	695.27 ± 650.56	734.55 ± 153.52	116.66 ± 69.72
CDC50A/TMEM30A	5578.82 ± 1174.14	7977.31 ± 2267.54	7621.38 ± 3189.82
SLC2A1/GLUT1	9579.89 ± 7741.88[#]	3110.70 ± 1033.78	472.20 ± 217.86
SLC3A2/CD98hc	6527.14 ± 3983.38	4619.39 ± 509.35	5088.29 ± 425.63
LEPR	1131.17 ± 617.91*	1932.75 ± 612.91	3549.49 ± 132.05

Comparison of gene expression (transcript abundance) across isolated human BMVs, brain and lung was performed using One-way ANOVA, followed by Tukey's multiple comparisons test. Significant difference was indicated by (*). For simplicity, statistical significance was shown only for comparisons of BMV against other tissues (but not among other tissues).

* INSR expression in BMV was significantly ($p<0.05$) higher compared to either brain or lung.

* IGF2R expression in lung tissue was significantly ($p<0.05$) higher compared to either brain vessels or brain.

*LDLR expression in BMV was significantly higher ($p<0.001$) compared to brain and significantly lower ($p<0.05$) compared to lung.

[#]SLC2A1/GLUT1: one sample out of 3 showed low transcript level, causing high SD. Therefore, despite overall high abundance, there was no significant difference compared to brain and lung.

*LEPR expression in BMV was significantly lower compared to lung ($p<0.001$).

Table 2. Expression levels of mouse genes encoding RMT receptors in isolated brain microvessels (BMV), whole brain, liver, spleen and lung vessels (RNAseq normalized read counts; average ± SD)

Receptors/proteins	BMV	Brain	Liver	Spleen	Lung vessels
TFRC	3690.57 ± 1577.32*	1366.54 ± 198.69	824.73 ± 70.64	3112.77 ± 1853.22	358.11 ± 79.98
INSR	3577.43 ± 889.85*	956.02 ± 215.79	1219.83 ± 877.37	561.32 ± 212.32	1475.28 ± 84.75
IGF1R	6876.68 ± 1430.93*	1102.77 ± 297.56	38.19 ± 27.33	386.79 ± 70.17	1920.06 ± 367.45
IGF2R	952.45 ± 129.07	705.28 ± 248.38	413.13 ± 188.02	926.11 ± 358.19	1531.46 ± 133.94*
LRP1	11506.40 ± 833.68*	8489.28 ± 1692.30	4448.88 ± 920.24	3403.74 ± 934.22	6397.87 ± 829.14
LDLR	1015.42 ± 223.35	584.67 ± 170.78	2210.82 ± 1160.86	850.94 ± 230.47	1062.21 ± 116.65
LRP8 (ApoER2)	3937.60 ± 777.50*	1318.88 ± 271.37	15.31 ± 20.31	310.13 ± 107.61	36.57 ± 12.07
CDC50A/TMEM30A	4159.55 ± 119.32*	8495.71 ± 1376.15	13191.59 ± 2020.86	2457.55 ± 424.88	3534.28 ± 715.38
SLC2A1/GLUT1	33418.54 ± 13876.59*#	2127.85 ± 246.70	216.14 ± 34.86	1164.86 ± 192.17	478.96 ± 48.42
SLC3A2/CD98hc	6369.22 ± 1046.86*	2665.44 ± 27.16	979.66 ± 147.88	7792.42 ± 1947.03	5596.12 ± 929.74
LEPR/leptin receptor	356.37 ± 14.03*	90.68 ± 1.77	107.97 ± 9.58	667.06 ± 116.16	1917.86 ± 469.42

Comparisons of gene expression (transcript abundance) across isolated mouse BMVs and peripheral tissues was performed using one-way ANOVA, followed by Tukey's multiple comparisons test. For simplicity, statistical significance was shown only for comparisons of BMVs against other tissues (but not among peripheral tissues).

*TFRC expression in BMV was significantly ($p<0.05$) higher compared to lung vessels

*INSR expression in BMV was significantly higher ($p<0.01$) compared to brain, liver, lung vessels or spleen.

*IGF1R expression in BMV was significantly ($p<0.0001$) higher compared to brain, liver, spleen or lung vessels.

*IGF2R expression in lung vessels was significantly higher compared to brain tissue ($p<0.01$) and liver ($p<0.001$).

*LRP1 expression in BMV was significantly ($p<0.01$) higher compared to liver, spleen, or lung vessels.

*LRP8 expression in BMV was significantly ($p<0.0001$) higher compared to brain, liver, spleen or lung vessels.

*CDC50A/TMEM30A expression in BMV was significantly ($p<0.01$) lower compared to brain or liver.

*SLC2A1/GLUT1 expression in brain vessels was significantly ($p<0.001$) higher compared to brain tissue, liver, spleen and lung vessels.

#SLC2A1/GLUT1 expression was significantly ($p<0.001$) higher in BMV compared to the expression off all other genes shown in Table 2.

*SLC3A2/CD98hc expression in BMV was significantly higher ($p<0.01$) compared to brain or liver.

*LEPR expression in BMV was significantly ($p<0.0001$) lower compared to lung vessels or spleen and significantly ($p<0.001$) higher compared to brain or liver

Table 3. Expression levels of genes encoding RMT receptors in isolated human and mouse brain microvessels (BMV) and whole brain tissues [RNAseq normalized for transcript per million (TPM); Mean ± SD]

Receptors/proteins	Human BMVs	Human brain	Mouse BMV	Mouse brain
TFRC	8.81 ± 4.43	11.25 ± 2.80	70.53 ± 32.21*	20.85 ± 4.41#
INSR	5.44 ± 3.70	4.75 ± 0.49	33.09 ± 8.63*	8.08 ± 3.31
IGF1R	2.38 ± 1.65	2.86 ± 0.69	61.06 ± 13.70*	7.36 ± 2.33#
IGF2R	3.09 ± 3.42	3.88 ± 2.06	9.88 ± 1.40*	5.86 ± 2.57
LRP1	21.18 ± 16.53	28.80 ± 6.61	179.85 ± 15.66*	69.87 ± 15.36#
LDLR	14.04 ± 19.25	5.19 ± 1.55	21.21 ± 5.00	9.67 ± 3.66
LRP8 (ApoER2)	6.09 ± 6.13	5.58 ± 1.75	20.66 ± 5.65	89.11 ± 20.41#
CDC50A/TMEM30A	28.62 ± 16.30	68.42 ± 15.01	98.36 ± 1.58*	158.57 ± 13.88#
SLC2A1/GLUT1	86.20 ± 88.50	41.64 ± 12.54	1314.53 ± 559.01*	64.62 ± 1.08#
SLC3A2/CD98hc	86.68 ± 75.46	89.37 ± 3.74	406.81 ± 66.31*	138.96 ± 14.72#
LEPR/leptin receptor	2.25 ± 1.96	1.19 ± 0.32	1.35 ± 1.35	2.10 ± 0.71
GAPDH	1563.77 ± 301.52	3924.81 ± 295.78	1571.31 ± 237.26	2824.45 ± 442.70[&]
S100B	520.09 ± 180.37	1005.79 ± 308.03	547.96 ± 5.82	231.91 ± 33.28[&]
TUBB4A	328.93 ± 126.15	363.04 ± 92.13	357.16 ± 110.37	552.25 ± 194.57

Statistical comparison of gene expression (transcript abundance) between human and mouse BMVs and human and mouse brain was performed using two-tailed student *t*-test. Significant difference between human and mouse BMVs was indicated by (*) and significant difference between human and mouse brain is indicated by (#),

*Receptor abundance is significantly higher (TFRC $p<0.01$; INSR $p<0.001$; IGF1R $p<0.01$; IGF2R $p<0.05$; LRP1 $p<0.001$; LRP8 $p<0.001$; CDC50A $p<0.01$; SLC3A2 $p<0.01$; SLC2A1 $p<0.01$) in mouse compared to human BMVs

[#]Receptor expression is significantly higher (TFRC $p<0.05$; IGF1R $p<0.05$; LRP1 $p<0.05$; LRP8 $p<0.005$; CDC50A $p<0.002$; SLC2A1 $p<0.05$; SLC3A2 $p<0.01$) in mouse compared to human brain.

[&]Genes encoding structural proteins: S100B is significantly ($p<0.001$) lower in mouse compared to human brain; GAPDH is significantly lower in mouse compared to human brain ($p<0.05$).