

Supplement 1. Non-significant changes of developmental markers in HPRT-deficient MN9D cells

Gene	AG2	AG5	AG6	AG8	AG10	TG1	TG2	TG3	TG4	TG5	Overall Change	t-test
Catenin	73±5	91±3	94±28	45±0	33±5	27±19	18±0	38±27	36±8	17±9	47±9	p=0.05
Cdc42	77±11	56±6	83±5	76±8	-20±6	18±7	-8±3	9±5	48±2	28±2	37±12	p=0.03
Efnb2	-65±12	-70±1	25±3	-21±3	-73±13	-11±3	-37±1	-8±7	-3±1	-12±4	-28±10	p=0.26
Eno2	37±10	3±2	35±6	58±9	-48±3	89±11	-10±5	-29±1	20±3	-65±2	9±15	p=0.54
Frizzled	-65±0	-47±4	-36±0	-43±10	107±17	-61±4	-43±0	-48±4	-76±9	-36±2	-35±16	p=0.37
Groucho	47±11	75±6	100±9	56±3	51±5	45±0	28±4	23±5	188±68	36±2	63±16	p=0.15
Msx1	-9±7	-2±5	-17±2	-46±3	-29±11	217±33	333±42	325±27	-17±17	690±30	144±77	p=0.06
N-wasp	38±2	16±5	17±5	8±4	-6±1	-11±3	-27±1	-9±4	31±2	-15±3	4±7	p=0.62
Nkx6-1	-58±11	171±14	109±26	192±6	49±21	-67±4	-62±7	15±1	-43±4	-34±8	26±31	p=0.51
Ntrk3	-5±4	111±7	306±20	101±19	75±5	35±3	-35±5	38±4	-32±5	3±4	60±32	p=0.13
Nurr1	-39±4	77±11	3±1	-19±5	28±3	46±9	54±5	12±0	15±6	-33±5	13±12	p=0.29
Rac1	40±5	-27±1	-1±3	26±6	2±2	3±3	-18±1	16±4	28±4	-13±1	5±7	p=0.53
Tiam1	54±14	37±6	88±4	-9±4	9±4	21±2	12±1	-14±5	26±6	-19±3	19±11	p=0.12
Wnt1	234±31	-17±13	-82±1	-73±1	-77±4	-78±2	-62±8	7±12	-59±5	42±15	-16±31	p=0.60

The results for each mRNA in each cell line were determined in quadruplicate by qPCR and normalized to a simultaneously processed control mRNA, *My16* (myosin light polypeptide 6), where the raw data showed little variation among cell lines. Results from the HPRT lines are presented as percent changes relative to a simultaneously processed sample of the HPRT⁺ parent line. The overall change reflects the aggregate results of all the HPRT lines combined. The results for all 10 HPRT⁻ MN9D cell lines were compared as a group against the parent MN9D line via single-sample t-test test. A Bonferroni correction for the 29 simultaneous comparisons in this Table and Table 2 was used to define p<0.002 as a conservative estimate for statistical significance. Values of 0.002<p<0.05 were considered borderline.

Supplement 2. Primers and conditions for qPCR validation

ID	Gene	Product	Primer	Sequence	Tm (°C)	Amplicon length (bp)
NM_009630	Adora2a	A2a adenosine receptor	Fwd	GCCATCCCATTTCGCCATCA	71,5	122
			Rev	GCAATAGCCAAGAGGCTGAAGA	66,5	
NM_009633	Adra2b	Adrenergic receptor alpha2b	Fwd	TCTTCACCATTTTCGGCAATGC	69,8	121
			Rev	AGAGTAGCCACTAGGATGTCG	59,9	
NM_145429	Arrb2	Arrestin-beta2	Fwd	GGCAAGCGCGACTTTGTAG	65,8	107
			Rev	GTGAGGGTCACGAACACTTTC	63,5	
NM_009781	Cacna1c	Calcium channel, voltage dependent, L type, alpha 1C subunit	Fwd	GGATGCAAGACGCTATGGG	65,5	105
			Rev	CGCTCAAAACACCGAGAACC	66,8	
NM_007595	Camk2b	Calcium/calmodulin dependent protein kinase II beta	Fwd	CTACGGCAAACCTGTGGACAT	65,9	124
			Rev	ATACGCCCCAGCCTTGATCT	66,7	
NM_009793	Camk4	Calcium/calmodulin dependent protein kinase IV	Fwd	GAGAACCTCGTCCCGGATTAC	65,7	106
			Rev	ACACAATGGATGTAGCACCCC	65,7	
NM_021369	Chrna6	Cholinergic receptor, nicotinic, alpha polypeptide 6	Fwd	TCACGGTGCATTTTGAATTGGC	70,7	103
			Rev	TAGTCCTCCAGATGTGACGC	64,1	
NM_009602	Chrn2	Cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	Fwd	GAGGTGAAGCACTTCCCATT	64,1	104
			Rev	GCCACATCGCTTTTGAGCAC	68,0	
NM_016886	Gria3	Glutamate receptor ionotropic ampa3	Fwd	ATTTGAACTACCACGTAGACCAC	60,7	101
			Rev	TCCAAAGATAGCATAACCCCCT	63,3	
NM_008168	Grik5	Glutamate receptor ionotropic kainate 5	Fwd	CTGCCAAGGGGGTTGTATC	67,5	100
			Rev	TGATGTGGGGAATCTCCTTCT	64,6	
NM_013556	m-Hprt	mouse Hypoxanthine-guanine Phosphoribosyltransferase	Fwd	GTTAAGCAGTACAGCCCCAAA	62,8	131
			Rev	AGGGCATATCCAACAACAACACTT	64,3	
NM_000194	h-Hprt	human Hypoxanthine-guanine Phosphoribosyltransferase	Fwd	TGGACAGGACTGAACGTCTTG	65,3	111
			Rev	CCAGCAGGTCAGCAAAGAATTTA	66,1	
NM_008478	L1cam	L1 cell adhesion molecule	Fwd	AAAGGTGCAAGGGTGACATTC	65,0	104
			Rev	TCCCCACGTTCTGTAGGT	64,4	
NM_008712	Nos1	Nitric oxide synthase 1, neuronal	Fwd	AATGATCGGCCCTGGTAGA	67,6	170
			Rev	TGGGTCACACGGATGGTCT	66,7	
NM_007452	Prdx3	Peroxisome oxidoreductin 3	Fwd	TTAGCACCAAGTTCCTCTTTCCA	64,7	115
			Rev	CCCTTAAAGTCGTCGAGACTCAG	65,0	
NM_009217	Sstr2	Somatostatin receptor 2	Fwd	TACATCTTCAACGTCTTCCGT	63,7	196
			Rev	CGGATTGTGAATTGTCTGCCT	66,1	
NM_009377	Th	Tyrosine hydroxylase	Fwd	CTGTCTCGGGCTTTGAAAGTG	65,9	163
			Rev	GACGCACAGAAGTGGAGG	65,1	

Supplement 3. Neurodevelopmental markers quantification: Primers and conditions for qPCR

ID	Gene	Product	Primer	Sequence	Tm (°C)	Amplicon length (bp)
NM_007614	Catenin	Catenin (cadherin associated protein), beta 1	Fwd	CCCAGTCCTTCACGCAAGAG	67,1	102
			Rev	CATCTAGCGTCTCAGGGAACA	64,2	
NM_009861	Cdc42	Cell division cycle 42	Fwd	CCTTTCTTGCTTGTGGGACC	66,7	232
			Rev	GGCTCTTCTTCGGTTCTGGAG	66,3	
NM_010111	Efnb2	Ephrin B2	Fwd	AATCCAGGTTCTAGCACCGAT	63,6	159
			Rev	TCTCCTGCGGTACTTGAGCA	66,0	
NM_010133	m-En1	mouse Engrailed-1	Fwd	ACACAACCCTGCGATCCTACT	64,7	120
			Rev	GGACGGTCCGAATAGCGTG	67,7	
NM_010134	m-En2	mouse Engrailed-2	Fwd	AAGACGCTATCACTTCACGGT	62,6	188
			Rev	CGCGTGACAGTAGACCCAAG	66,9	
NM_001426	h-En1	human Engrailed-1	Fwd	GAGCGCAGGGCACCAAATA	68,3	138
			Rev	AATAACGTGTGCAGTACACCC	61,3	
NM_001427	h-En2	human Engrailed-2	Fwd	CCGGCGTGCGTCTACTGTA	66,0	101
			Rev	GGCCGCTTGTCTCTTTGTT	67,5	
NM_013509	Eno2	Enolase 2	Fwd	GTCCCTGGCCGTGTGTAAG	65,5	200
			Rev	CATCCCGAAAGCTCTCAGC	65,0	
NM_021457	Frizzled-1	Frizzled 1	Fwd	GTGGAGCGGGGAAAGTTCTC	67,1	115
			Rev	CGTAAACCTTGGTGGGTTTCG	66,2	
NM_011599	Groucho	Tle1 (transducin-like enhancer of split 1)	Fwd	TGCAAGCCCAACACACTCA	66,8	143
			Rev	TTTCATGCAGGCTCACTTCTTT	64,8	
NM_010592	Jund1	Jun proto-oncogene related gene d1	Fwd	GGCGGGATTGAAACCAGGG	70,7	147
			Rev	AGCCCGTTGGACTGGATGA	68,0	
NM_010453	Hoxa5	Homeo box A5	Fwd	CTCATTTTGCAGGTCGCTATCC	67,5	139
			Rev	ATCCATGCCATTGTAGCCGTA	66,1	
NM_010725	Lmx1b	LIM homeobox transcription factor 1 beta	Fwd	TTCCTGATGCGAGTCAACGAG	67,6	100
			Rev	TCCGATCCCGGAAGTAGCAG	68,4	
NM_010835	Msx1	Msh-like 1 homeo box	Fwd	CTCATGGCCGATCACAGGAAG	69,0	175
			Rev	GGAGTCCTCCGACTGAGAAATG	66,1	
NM_013601	Msx2	Msh-like 2 homeo box	Fwd	TTCACCACATCCCAGCTTCTA	64,5	159
			Rev	TTGCAGTCTTTTCGCCTTAGC	65,4	
NM_010860	Myf6	Myosin, light polypeptide 6, alkali, smooth muscle and non-muscle	Fwd	CCAGTGTGGGGATGTGATGC	68,9	226
			Rev	ATGACGGATTTTCAGCACCCAT	67,5	
NM_028459	N-wasp	Wiskott-Aldrich syndrome-like	Fwd	CCTGCCTTCTGATGGTGACC	67,0	145
			Rev	TAAAAGCGCATCCCTCCTGA	67,6	

ID	Gene	Product	Primer	Sequence	Tm (°C)	Amplicon length (bp)
NM_009718	Ngn2	Neurogenin 2	Fwd	AACTCCACGTCCCCATACAG	63,7	103
			Rev	GAGGCGCATAACGATGCTTCT	67,4	
NM_144955	Nkx6-1	NK6 transcription factor related, locus 1	Fwd	CAGACCCACGTTCTCTGGAC	64,8	125
			Rev	TGACCTGACTCTCCGTCATCC	66,6	
NM_013613	Nr4a2	Nuclear receptor subfamily 4, group A, member 2	Fwd	AACACTGAAATTACTGCCACCA	63,2	138
			Rev	TTCTACCTTAATGGAGGACTGCT	61,8	
NM_008746	Ntrk3	Neurotrophic tyrosine kinase, receptor, type 3	Fwd	TCCACATCGCCAGTCAGATAG	65,1	135
			Rev	TGGACATGCCAAAATCTCCAAT	67,2	
NM_033620	Pard3	Par-3 (partitioning defective 3)	Fwd	TCAAGCCACAAGTCAAATTGAGG	67,1	103
			Rev	AGTGGAAAGGCCAGTTAAAGC	63,2	
NM_008782	Pax5	Paired box gene 5	Fwd	AAGGATAGTGGAACTTGCCCA	64,5	112
			Rev	TCCTGTCTCATAATACCTGCCA	63,2	
NM_008852	Pitx3	Paired-like homeodomain transcription factor 3	Fwd	CCTACGAGGAGGTGTACCCG	65,6	110
			Rev	CACGTTGACCGAGTTGAAGG	65,6	
NM_009007	Rac1	RAS-related C3 botulinum substrate 1	Fwd	TTTCCCTTGTGAGTCCTGCAT	65,7	103
			Rev	TTCGTCCCCACGAGGATGATA	68,6	
NM_133223	Rac3	RAS-related C3 botulinum substrate 3	Fwd	GCCAACGTGATGGTGGATG	67,6	89
			Rev	GAGAGTGGCCGAAGCCTAT	63,2	
NM_024457	Rap1b	RAS related protein 1b	Fwd	AAGGCTTCGCTCTGGTTTACT	63,0	181
			Rev	CTTGCTAGGTTCTGACCTTGTTT	62,9	
NM_016802	RhoA	Ras homolog gene family, member A	Fwd	GAGTTGGCTTTATGGGACACA	63,7	143
			Rev	GGAGTCCATTTTTCTGGGATGTT	65,9	
NM_009170	Shh	Sonic hedgehog	Fwd	AAAGCTGACCCCTTTAGCCTA	62,8	103
			Rev	TTCGGAGTTTCTTGTGATCTTCC	65,3	
NM_009384	Tiam1	T-cell lymphoma invasion and metastasis 1	Fwd	GAAGCACACTTCACGCTCC	63,7	154
			Rev	CTCCAGGCCATTTTCAGCCA	69,4	
NM_021279	Wnt1	Wingless-related MMTV integration site 1	Fwd	CGACTGATCCGACAGAACCC	67,0	149
			Rev	CGGTTGACGATCTTGCCGAA	70,4	
NM_009524	Wnt5	Wingless-related MMTV integration site 5	Fwd	AGCCTGTAAGTGTGATGGAGT	60,2	115
			Rev	CGCGGCGCTATCATACTTCT	66,2	