

TABLE 1

Expression of Huntington's Disease Mutation in Mice

Model design

Behavioral disorder

Neuropathology

LAB	Background	Promoter/ gene size/ CAG repeats	Protein expression level	Clasping Phenotype	Rotarod	Other symptoms	NII Cell Pathology	Cell Loss	Brain Atrophy
Transgenic HD models									
Bates ₁	CBA/ C57B16	HD promoter exon 1 R6/2 144Q (expanded to 170 - 190 Q), R6/1 115 Q	RNA levels < 1x	Onset 2 mo. (R6/1 onset 5 mo.)	Abnormal by 5 weeks	Tremors & abnormal gait, learning deficit, hypokinesia, diabetes	NII and neuropil aggregates throughout brain, fewer dendritic spines, depol. Str. Cells	Frontal cortex, dorsal striatum and cerebellar Purkinje cells at late stage	Overall brain atrophy
Hayden ₁₀	FVB/N	HD YAC Full-length 72Q, 46Q, 18Q	2X	72Q (#2498) onset by 3 mo.	not reported	Hyperactive & circling	Inclusions in striatum	Cell loss in striatum	not reported
Ross/Borchelt ₂	C3H/B16	PrP prom. N171 82Q, 44Q, 18Q	1/5X to 1/10X	82Q onset 5 mo.	Abnormal by 3 mo.	Tremors & abnormal gait, hypokinesia, weight loss, early death	Inclusions: striatum, ctx, hippocampus, amygdala, cb. Diffuse nuclear accumu. of htt protein	toluidine blue reveals cells w/a degenerative morphology in the lateral striatum	Overall brain atrophy
Tagle _{3, 4, 5}	FVB/N	CMV prom. Full-length 89Q, 48Q, 16Q	5X	89Q&48Q onset 4 mo.	not reported	Circling, hyperactivity, end-stage hypoactivity & urinary incontinence	Fewer inclusions throughout brain	20% cell loss in striatum of some animals	not reported
	FVB/N	CMV prom Ex1-3, 89Q	Endogenous to 2x	ex1-3:89Q onset 4 mon.	not measured	Prolonged Hyperactivity	Fewer inclusions throughout the brain	not reported	not reported
Aronin/ DiFiglia ₆	SJL/ C57B16	rat NSE 3 kb fragment 100Q, 48Q, 18Q	>endogenous about 1/5X	100Q onset 3-4 mo.	Abnormal about 4 mo.	Hyperactivity to endstage hypoactivity	Inclusions in Q100 (few in Q46), DN's observed	20% cell loss ~ 8mo. in some animals	Brain atrophy in some animals
Hen/Yamamoto ₇	CBA/ C57B16	tet-off (CamKII α -tTA) TetO Exon1 94Q	>endogenous	94Q onset in 50% by 2.5 mo.	Onset about 2.5 mo.	Late onset tremor & abnormal gait	Inclusions in striatum, septum, ctx, hippo., & reactive astrocytes	not reported	Brain atrophy & progressive striatal atrophy
Targeted <i>Hdh</i> models									
MacDonald/ Joyner _{11, 12, 13}	129/CD1	<i>Hdh</i> promoter Knock-in 111Q, 92Q, 50Q	endogenous	no movement Sx.	no difficulties found	cellular phenotype see neuropath	CAG- & age- depend.HTT nuclear relocalization at 1.5 mo, inclusion >6 mo.	none observed	not reported
	SW	<i>neo</i> & <i>Hdh</i> prom., Knock-in 111Q,20Q	<50% of endog.	<i>Hdh</i> ^{nQ20/nQ111} have onset ~ 2 mo.	not measured	nQ20/nQ111 show disorders similar to Exon1-Q144 mouse	age- dependent HTT nuclear re-localization and inclusions	none observed	preliminary result: brain atrophy
Myers ₁₄	FVB- N/B16	<i>Hdh</i> prom., Knock-in 80Q,72Q	2X	no movement Sx.	none reported	Early onset aggressive behavior	Late inclusions, hipp. LTP impaired, repeat instability in striatum	none observed	not reported
Zeitlin ₁₅	C57B16	<i>Hdh</i> prom., Knock-in 94Q, 71Q	~2X	no movement Sx.	none reported	No movement Sx.; NMDA sensitivity	No inclusions	Striatal cell swelling in response to NMDA	smaller striatal cells
Targeted Non-<i>Hdh</i> polyQ									
Detloff ₈	129/ C57B16	x-link <i>Hprt</i> locus 146Q insert	endogenous	Onset ~5 mo.	none reported	Handling-induced seizures & early death	Inclusions throughout brain	None	not reported

Transgenic DRPLA model

Ross/Borchelt ₉	C3H/B16	PrP Promotor, full length atrophin-1 cDNA(1184aa), 65Q and 26Q	about 1-3x (two lines)	less than HD	abnormal by two months	tremors, ataxia, twitchy movements, loss of coordination, seizures, early death	Widespread Inclusions, also accumulation of truncated N-terminal fragment of atrophin, similar to a fragment seen in DRPLA brains	approx. 30% loss in cerebellar Dentate nucleus(site of DRPLA path)	Overall brain atrophy
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Table Created by Marina Chicurel, Ph.D., Marc S. Hurlbert, Ph.D., Erik Schweitzer, and Ai Yamamoto March 2000

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