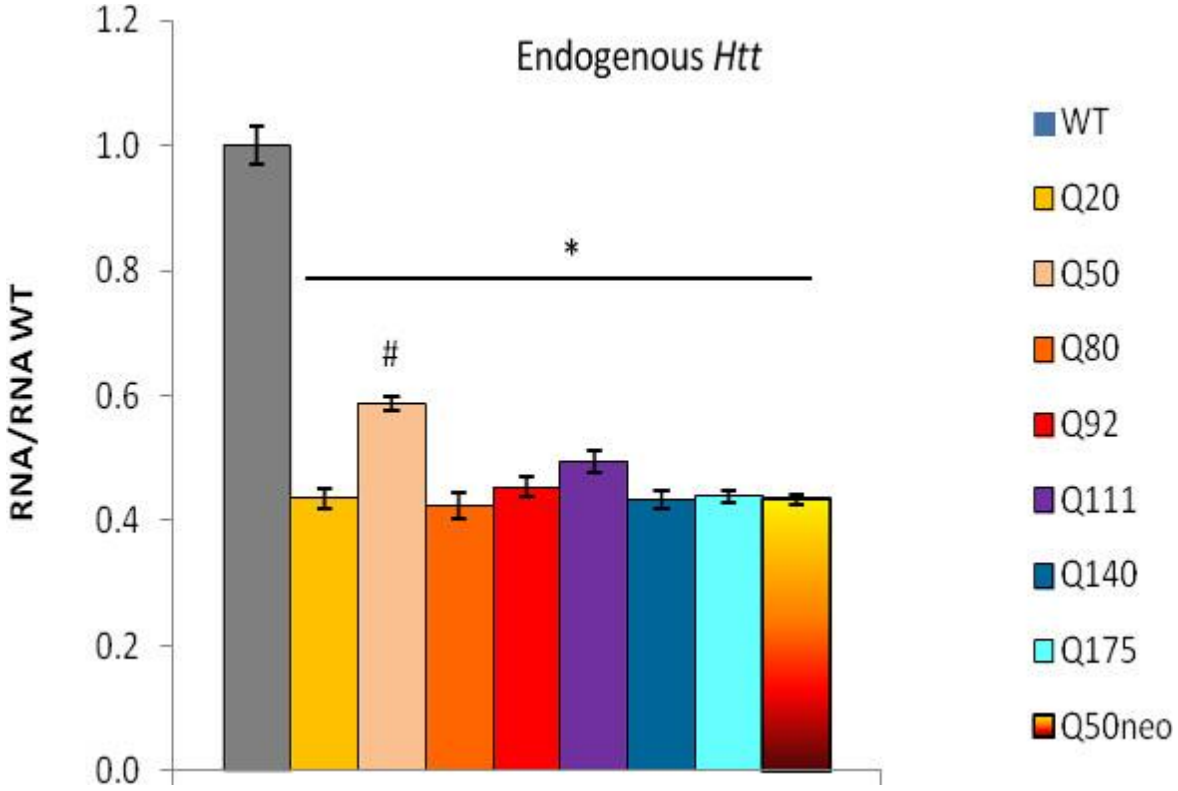
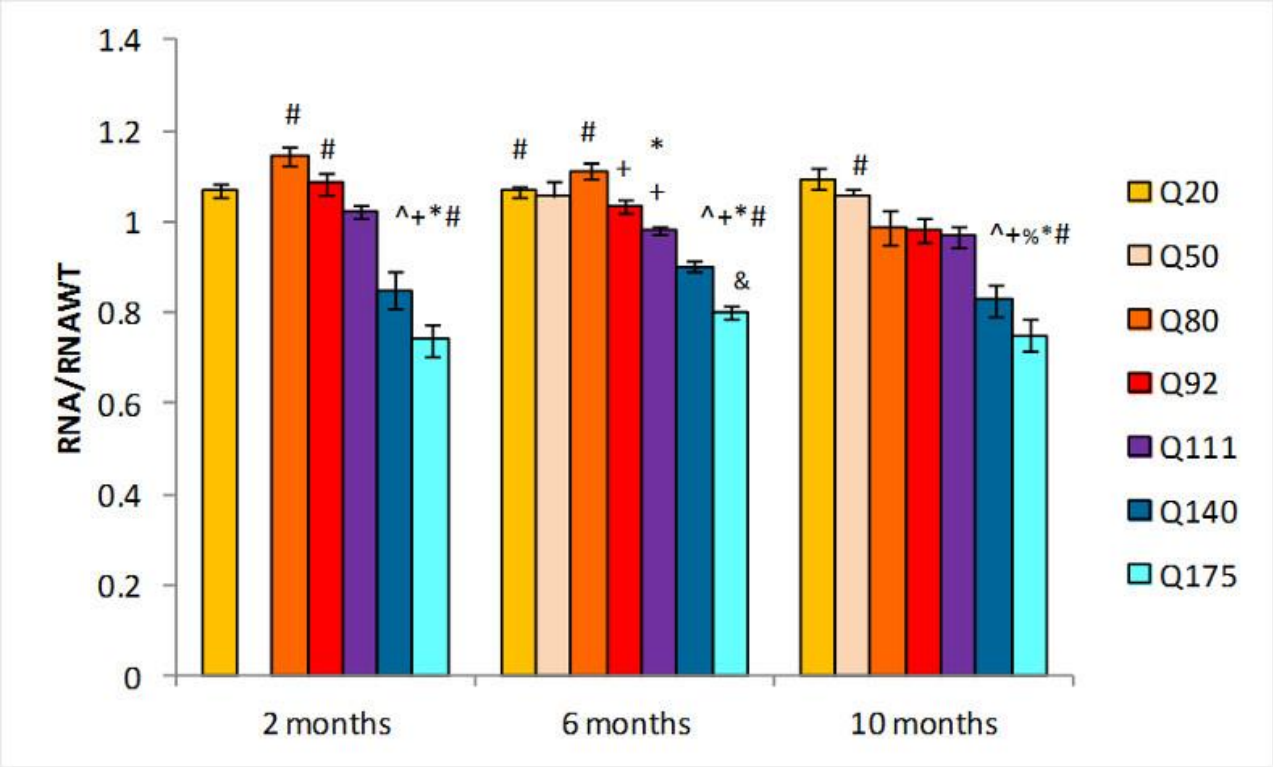


Supplementary Figure 1

Quantification of endogenous *Htt* mRNA by qPCR.

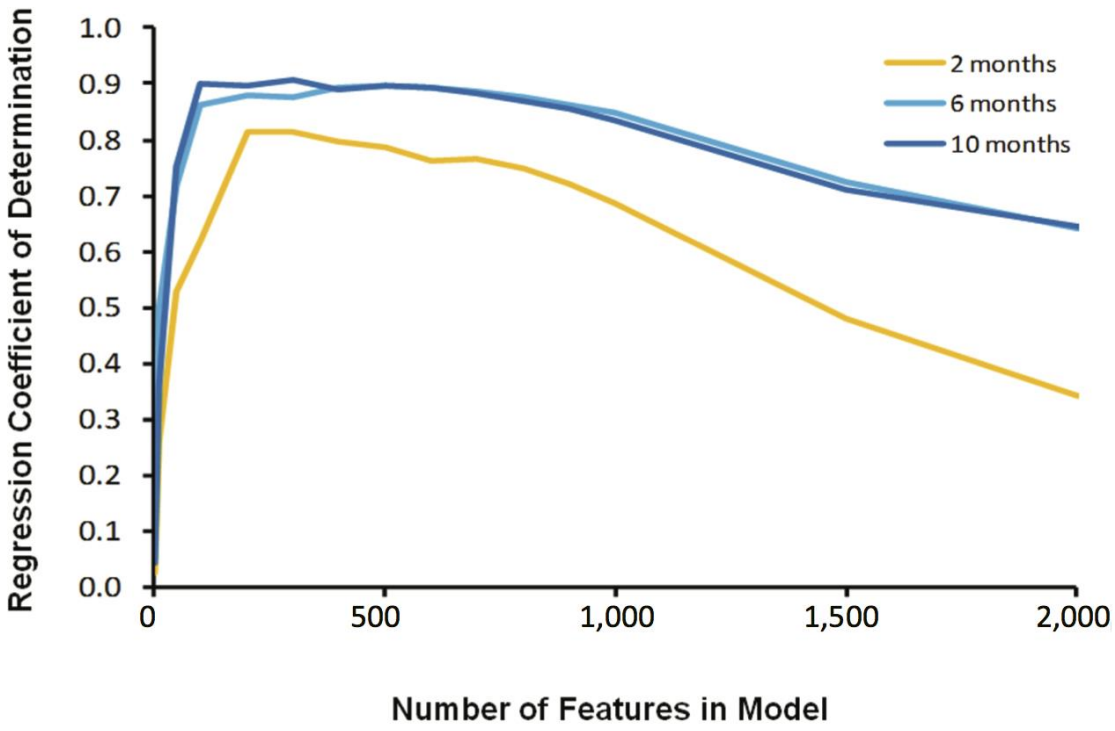
WT: wild type mice; Q20: HET mice from HdhQ^{20}line; Q50: HET mice from HdhQ^{50} line; Q80: HET mice from HdhQ^{80}line; Q92: HET mice from HdhQ^{92} line; Q111: HET mice from HdhQ^{111} line; Q140: HET mice from CAG 140 KI line; Q175: HET mice from zQ175 line; Q50neo: HET mice from HdhQ50neo in line. Asterisk (*) denote significant differences of the levels of mRNA of the endogenous Htt against the WT controls. Number symbols (#) denote significant differences of the levels of mRNA of the endogenouse Htt from HET mice from Q50 line against the HET mice from all the other lines. Data are expressed as mean ± S.E.M. n=4-8 per group.



Supplementary Figure 2

Quantification of *Htt* RNA by RNA-seq.

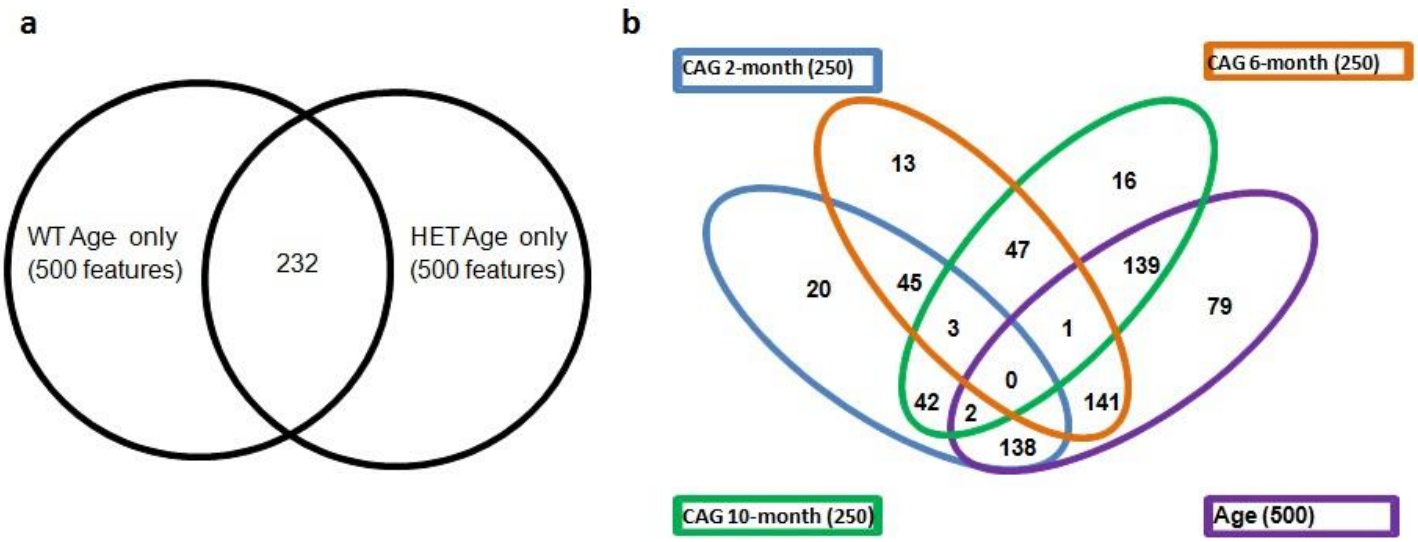
WT: wild type mice; Q20: HET mice from HdhQ^{20}line; Q50: HET mice from HdhQ^{50} line; Q80: HET mice from HdhQ^{80}line; Q92: HET mice from HdhQ^{92} line; Q111: HET mice from HdhQ^{111} line; Q140: HET mice from CAG 140 KI line; Q175: HET mice from zQ175 line. Number symbols (#) denote significant differences of the Htt mRNA levels compared to WT controls. Asterisks (*) denote significant differences of the Htt mRNA levels compared to Q20. Percents (%) denote significant differences of the Htt mRNA levels compared to Q50. Plus (+) denote significant difference of the Htt mRNA levels compared to Q80. Carets (^) denote significant difference of the Htt mRNA levels compared to Q92 and Q111. Ampersands (&) denote significant difference of the Htt mRNA levels compared to Q140. Htt mRNA levels appeared inversely proportional to Q length but independently of age. Data are expressed as mean ± S.E.M.. N of WTs per age=7-48, n of HETs per line per age=6-8. Note: At 6 and 10 months of age, HdhQ50 tissues were examined in a separated study from the one that assessed Q20, Q80, Q92, Q111, Q140 and Q175 HET tissues. Values from HETs animals were normalized to the values of the WT animals run concurrently.



Supplementary Figure 3

Performance of the CAG model, as measured by the coefficient of determination of the regression line (R2) fitted to the predicted versus observed CAG values, as a function of the number of features included.

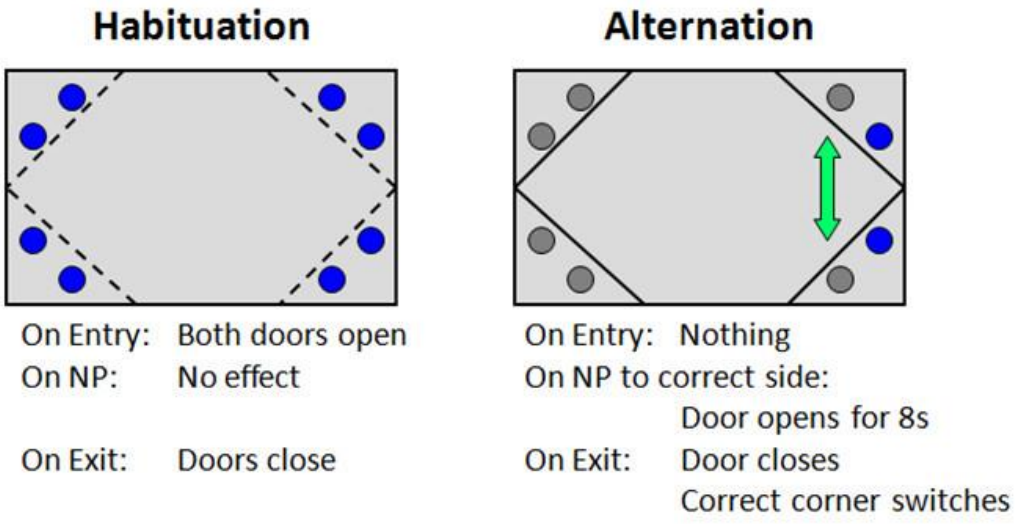
To reach accuracy larger than 0.8 requires more than 100 features for the 6 and 10 month old mice, and more than double that for the 2 month of age.



Supplementary Figure 4

Overlap of optimally predictive feature sets from various CAG and age models.

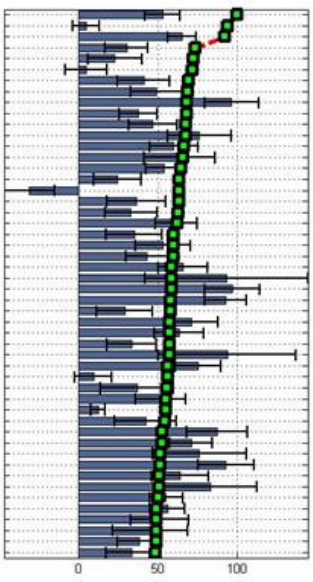
A. Overlap of features best modeling Age for WTs and HETs. A substantial decrease of overlap of age-specific features between WT and HETs age is an indication that HD affects ageing. B. Degree of overlap among -features comprising CAG model and Age model for HETs. Age-specific features continue to play important role in all CAG models (over 50% of features in each CAG model are Age-specific features). Also, CAG-specific features change substantially for each Age.



Supplementary Figure 5

Standard protocol phases in PhenoCube.

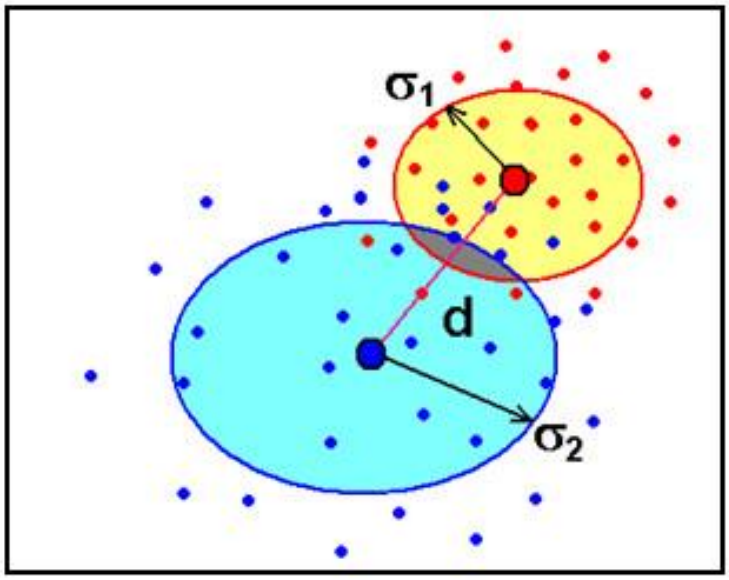
The Habituation phase (left panel) is employed for the first 6 hrs of the experiment where both doors are open upon entry to any of the 4 corners, allowing for free access to the water bottles. Following the Habituation phase the Alternation phase is employed (right panel), where a mouse would be required to visit one of the 2 assigned active corners and nose poke into the correct recess in order for the door within that recess to open and allow for access to that water bottle for 8 seconds. The green arrow indicates the alternation or switch of the correct corner identity to the adjacent active corner following a correct visit in which reinforcement was available.



Supplementary Figure 6

Difference in feature values and feature ranks (red curve with green squares).

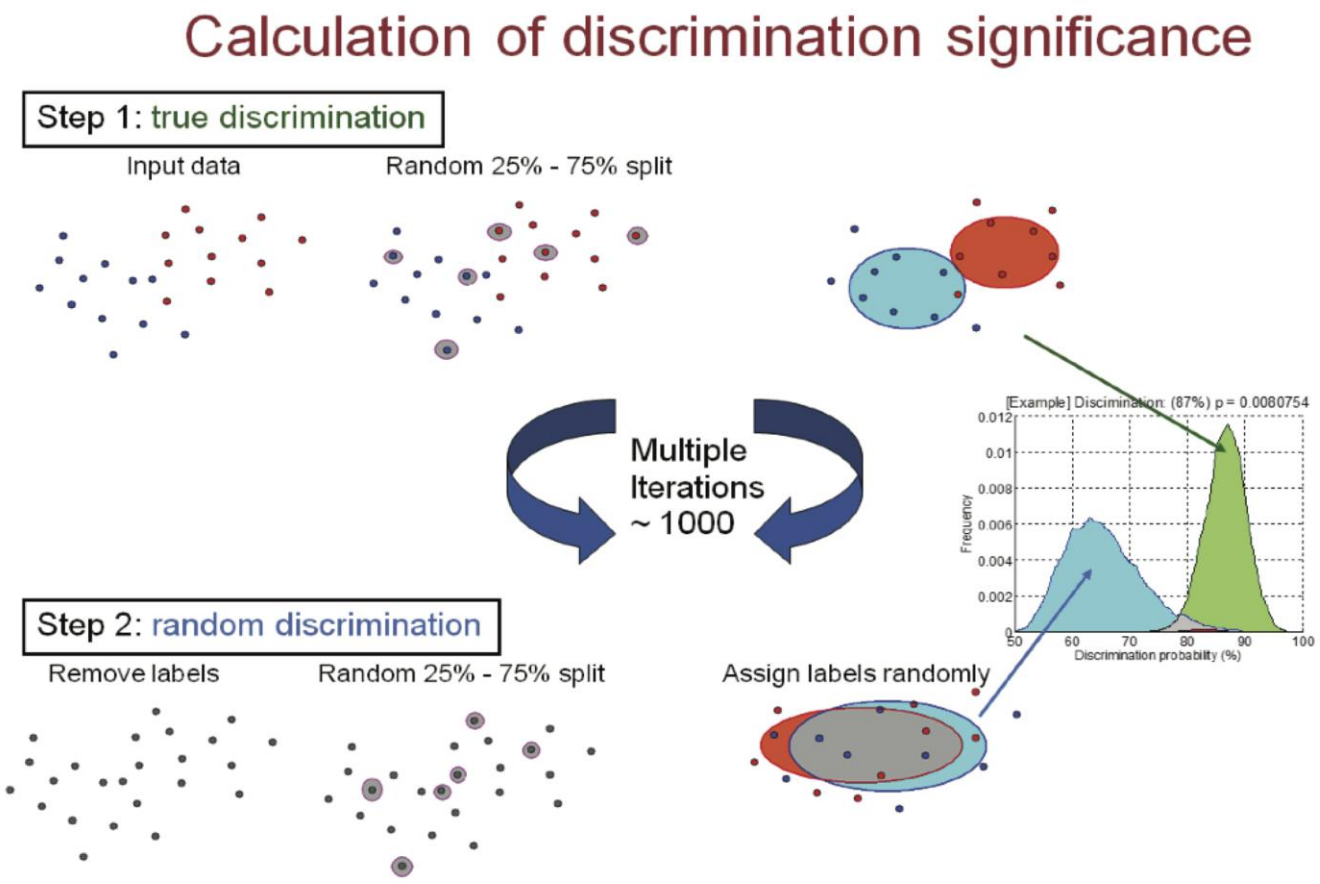
Relative difference (%) between feature values in two different sets is calculated and plotted in the order corresponding to feature ranks together with their ranks varying from 0 to 100.



Supplementary Figure 7

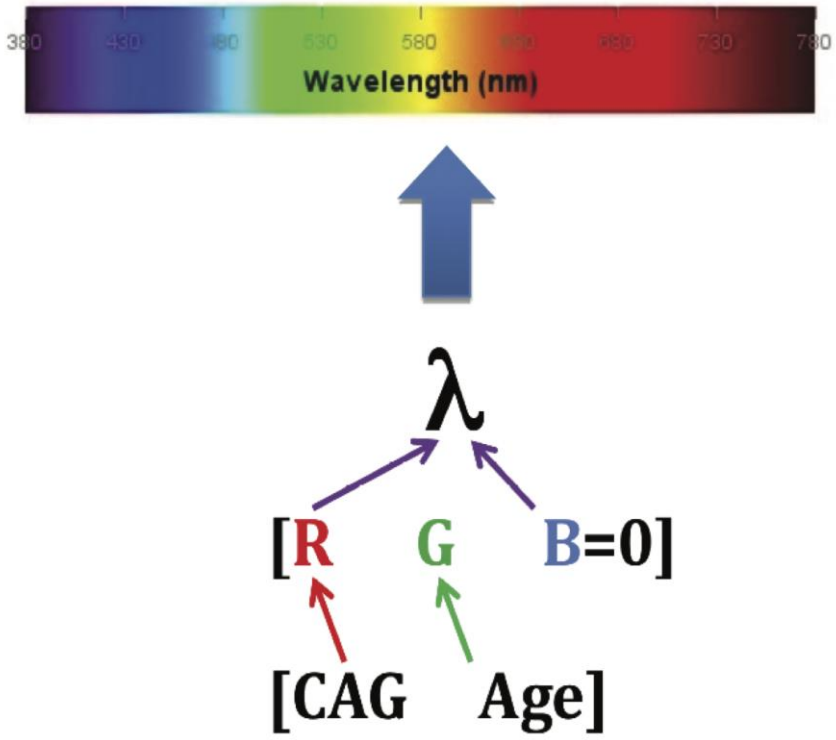
Visualization of binary discrimination in the ranked decorrelated feature space.

The two highest ranked de-correlated features are chosen to form the 2D coordinate plane for visualization purposes. Each dot represents a mouse. Mice from the control group are shown as blue dots and mice from the disease group are plotted in red. The other convenient (from a scale perspective) but equivalent measure derived from the cloud overlap is discrimination probability = 1 – overlap which measures how reliably a classifier can be trained to discriminate between groups A and B above the chance level zero corresponding to 100% overlap and no ability to distinguish the two groups above the chance level whereas 100% meaning the error free discrimination.



Supplementary Figure 8

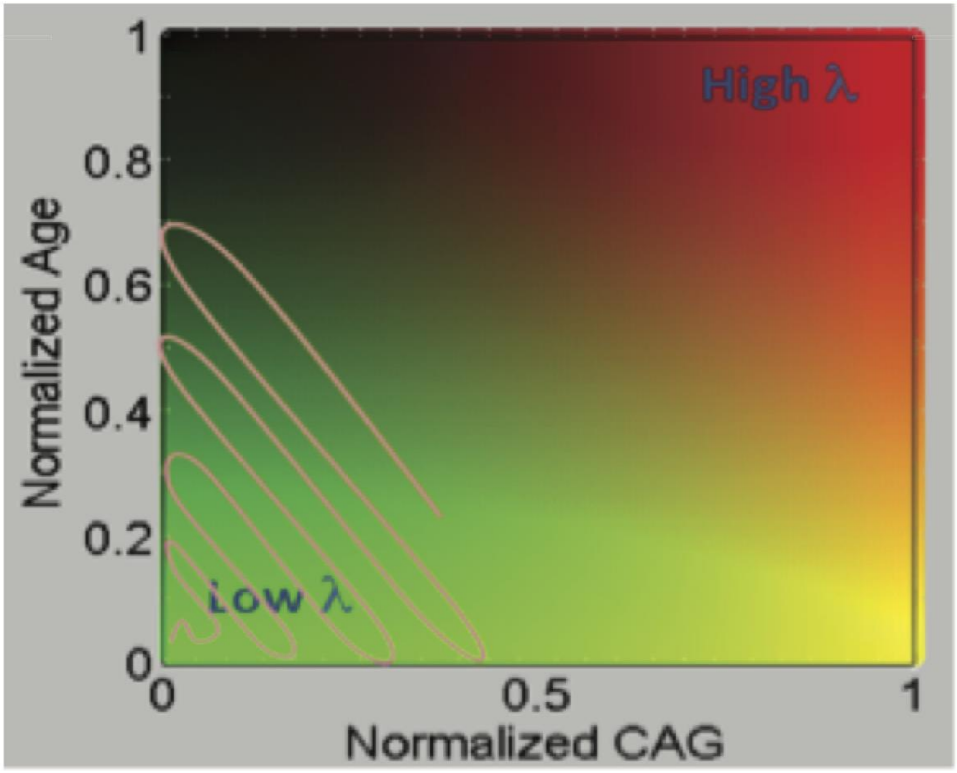
Calculation of discrimination significance.



Supplementary Figure 9

Mapping a multidimensional dependent variable into a fully equivalent one-dimensional one.

The figure shows the wavelength transformation mapping 2-dimensional CAG/Age pairs to a 1-dimensional dependent variable: normalized to [0..1] range CAG length and Age get uniquely encoded as the values of the R (red) and G (green) channels respectively in the RGB (B=0) colormap notation.



Supplementary Figure 10

Building a λ → CAG/age lookup table.

The figure outlines the procedure for building a reverse map connecting the 1-dimensional values of the dependent variable (λ) back to the corresponding values of (normalized) CAG length and Age, which is achieved by constructing a lookup table. Each pixel (R/G/B=0 pair) is enumerated, i.e. assigned a value from 1 to N in a continuous manner as shown in the figure. The normalized [CAG,Age] (i.e. [R,G]) matrix is traversed from the lower left to the upper right corner along each subsequent diagonal enumerating (assigning next available integer value) every coordinate pair. At the end, the resulting 1D array is also normalized to the [0..1] range. Note that small λ (around 0) in this enumeration scheme correspond to the low CAG and low Age values, whereas high λ (around 1) correspond to high CAG and high Age.

SUPPLEMENTARY INFORMATION

Supplementary Table 1

	CAG repeat mean	Standard deviation	Min CAG repeat	Max CAG repeat
HdhQ20	20.01	0.25	18	21
HdhQ50	50.34	0.58	49	52
HdhQ50neo	50.19	0.36	49	51
HdhQ80	87.08	2.26	80	92
HdhQ92	102.60	2.13	98	110
HdhQ111	125.35	3.90	110	134
CAG 140	147.58	6.18	136	181
zQ175	204.08	5.02	189	215

Supplementary Table 1 presents the CAG repeat mean, standard deviation and range for the HET mice of the different lines tested at each age. These animals carry pure CAG repeats followed by CAGCAA as humans do. In WTs mice huntingtin always contains a stable CAGCAGCAACAGCAGCAGCAG (n=7 CAG/CAA) sequence, in all cohorts and lines.

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Supplementary Table 2

	Number of animals available for testing the week before testing began(1)	Number of animals tested in PC (2)	Number of animals included in the 2-class analysis (3)	Number of animals included in modeling (4)
2-mo cohort				
HdhQ20	16/16/16/16	16/16/16/14	16/14/14/12	16/14/14/12
HdhQ80	16/16/16/16	16/16/15/14	15/13/14/11	15/13/14/11
HdhQ92	16/16/16/16	15/16/16/16	11/13/15/16	11/13/15/16
HdhQ111	16/16/16/16	16/16/16/16	15/13/13/12	15/13/13/12
CAG 140	16/16/16/16	16/16/16/15	16/14/14/12	16/14/14/11
zQ175	16/16/16/16	15/16/16/16	15/16/16/12	15/16/16/12
6-mo cohort				
HdhQ20	16/16/16/16	13/15/16/14	8/14/13/14	8/14/13/14
HdhQ80	16/16/15/16	15/12/15/15	13/11/13/14	13/11/13/14
HdhQ92	16/16/16/15	15/16/15/12	11/16/10/10	11/16/6/8
HdhQ111	16/16/16/16	16/16/14/15	15/16/9/14	15/16/7/13
CAG 140	16/16/16/16	16/15/16/14	12/14/13/13	12/14/9/13
zQ175	16/16/16/16	15/15/14/16	9/13/13/15	9/13/13/15
HdhQ50neo	16/16/16/16	13/14/16/13	11/14/15/13	11/14/15/13
10-mo cohort				
HdhQ20	15/16/16/16	14/9/14/15	11/8/13/15	11/8/10/15
HdhQ80	16/16/16/16	16/12/16/11	16/11/14/9	16/11/14/8
HdhQ92	16/16/16/14	16/12/14/12	11/10/11/12	11/10/9/12
HdhQ111	16/16/16/15	15/13/16/10	14/12/14/8	14/12/14/7
CAG 140	16/16/16/16	15/12/16/12	13/10/13/9	13/10/13/7
zQ175	16/16/16/16	16/10/16/15	16/6/11/12	16/6/11/9
Second cohort				

6-month				
HdhQ20	16/16/16/16	13/13/15/15	13/16/15/15	13/16/15/15
HdhQ50	15/16/16/16	13/16/12/14	13/15/12/14	13/15/12/14
CAG 140	16/16/16/16	12/14/15/16	12/14/15/16	12/14/15/16
Mystery line	16/15/16/16	13/15/13/13	13/15/13/13	13/15/12/13
Second cohort				
10-month	-			
HdhQ20	16/16/16/16	16/13/13/16	16/12/13/15	16/14/13/13
HdhQ50	16/15/16/16	16/13/14/15	16/13/14/15	16/13/14/15
CAG 140	16/16/16/16	15/15/12/15	14/15/12/15	14/15/12/15
Mystery line	16/16/16/16	15/14/13/13	15/14/13/12	15/14/13/12

Nature Biotechnology: doi:10.1038/nbt.3587

Supplemental Table 2 presents the number of animals per age/line/genotype/sex available for testing and/or analysis. Table presents the number of animals in the following order: WT-F / WT-M / HET-F / HET-M. (1) Although we targeted to test 16 animals, in some groups animals were excluded animals due to dermatitis, aggression or aggression-related wounds. (2) A subset of animals did not complete PhenoCube testing due to failure of chips, aggression/aggression-related wounds or lack of licking behavior. In brief, if an animal failed to lick within the first 16 h, its protocol was switched back to habituation to allow free access to water. If the animal failed to drink under this condition during 6 h, it was removed from the system and set back into its homecage. (3) Only animals that were tested in the 3 systems and completed all the phased in the PC, were included in the 2-class analysis. (4) Few animals from the dataset utilized in the 2 class analysis were excluded in the modeling exercise because they were not recognized by the very model which would include such animals in that model's training set (1 from the 2 mo cohort, 12 from the 6 mo cohort and 12 from the 10 mo cohort). In addition, genotyping after tissue collection was inconclusive for few animals (n=6) and therefore they were removed from the analysis.

Supplementary Table 3

Mouse Gene ID	5' Primer Sequence	3' Primer Sequence	Universal Probe Library #	Hydrolysis Probe	PCR Efficiency	R^2 Value of Standard Curve
***Htt* (exon1-exon 2)**	**GCTTTCGAGTCGCTCAAGTC**	**TGGTGGCTGAGAGTTCCTTC**	**N/A**	**6 FAM Labeled-CAGGTCCGGC-AGAGGAAC-TAMRA**	**1.92**	**0.998**
ATP5B	**GGCACAATGCAGGAAAGG**	**TCAGCAGGCACATAGATAGCC**	**77**	**N/A**	**1.92**	**0.999**
CANX	**TTCCAGACCCTGATGCAGA**	**TCCCATTCTCCGTCCATATC**	**106**	**N/A**	**1.99**	**0.999**
RPL13A	**TTGTGGCCAAGCAGGTACT**	**GTTGATGCCTTCACAGCGTA**	**77**	**N/A**	**1.98**	**1.000**

Supplementary Table 3. Qualitative Polymerase Chain Reaction (qPCR) information

Analysis of the complexity of the trajectory

For post-hoc tests we used a Bonferroni correction for the critical alpha value, which yields α=0.05/6=0.0083, considering only 6 comparisons against the WT line.

2 months of age

ANOVA Table for TimeB_1
Split By: Age
Cell: 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	.072	.012	3.036	.0065	18.215	.917
Residual	403	1.593	.004				

Bonferroni/Dunn for TimeB_1
Effect: Line
Significance Level: 5 %
Split By: Age
Cell: 2

	Mean Diff.	Crit. Diff.	P-Value
Q111B, Q140B	.033	.035	.0036
Q111B, Q175B	.037	.035	.0011
Q111B, Q20B	.012	.043	.4124
Q111B, Q80B	.017	.042	.2201
Q111B, Q92B	.004	.042	.7637
Q111B, WT	.010	.030	.2991
Q140B, Q175B	.004	.034	.7259
Q140B, Q20B	-.022	.043	.1196
Q140B, Q80B	-.016	.042	.2303
Q140B, Q92B	-.029	.042	.0335
Q140B, WT	-.023	.030	.0174
Q175B, Q20B	-.026	.043	.0655
Q175B, Q80B	-.020	.042	.1360
Q175B, Q92B	-.033	.042	.0156
Q175B, WT	-.027	.029	.0052
Q20B, Q80B	.005	.049	.7371
Q20B, Q92B	-.007	.049	.6438
Q20B, WT	-.001	.039	.9159
Q80B, Q92B	-.013	.048	.4173
Q80B, WT	-.007	.038	.5885
Q92B, WT	.006	.038	.6258

Means Table for TimeB_1
Effect: Line
Split By: Age
Cell: 2

	Count	Mean	Std. Dev.	Std. Err.
Q111B	60	3.025	.067	.009
Q140B	62	2.992	.064	.008
Q175B	63	2.988	.066	.008
Q20B	30	3.013	.056	.010
Q80B	32	3.008	.054	.009
Q92B	32	3.021	.055	.010
WT	131	3.015	.064	.006

6 months of age

ANOVA Table for TimeB_1
Split By: Age
Cell: 6

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	.444	.074	16.341	<.0001	98.049	1.000
Residual	402	1.819	.005				

Bonferroni/Dunn for TimeB_1
Effect: Line
Significance Level: 5 %
Split By: Age
Cell: 6

	Mean Diff.	Crit. Diff.	P-Value
Q111B, Q140B	.062	.052	.0003
Q111B, Q175B	.090	.051	<.0001
Q111B, Q20B	-.017	.051	.3213
Q111B, Q80B	-.021	.052	.2104
Q111B, Q92B	-.009	.052	.6181
Q111B, WT	-.014	.039	.2682
Q140B, Q175B	.028	.052	.1002
Q140B, Q20B	-.078	.052	<.0001
Q140B, Q80B	-.083	.052	<.0001
Q140B, Q92B	-.070	.053	<.0001
Q140B, WT	-.076	.039	<.0001
Q175B, Q20B	-.106	.051	<.0001
Q175B, Q80B	-.111	.052	<.0001
Q175B, Q92B	-.098	.052	<.0001
Q175B, WT	-.104	.039	<.0001
Q20B, Q80B	-.005	.052	.7878
Q20B, Q92B	.008	.052	.6329
Q20B, WT	.003	.039	.8386
Q80B, Q92B	.013	.053	.4602
Q80B, WT	.007	.039	.5793
Q92B, WT	-.006	.040	.6702

Means Table for TimeB_1
Effect: Line
Split By: Age
Cell: 6

	Count	Mean	Std. Dev.	Std. Err.
Q111B	32	2.979	.050	.009
Q140B	31	2.917	.067	.012
Q175B	32	2.889	.067	.012
Q20B	32	2.995	.055	.010
Q80B	31	3.000	.065	.012
Q92B	30	2.987	.072	.013
WT	221	2.993	.070	.005

10 months of age

ANOVA Table for TimeB_1
Split By: Age
Cell: 10

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	.257	.043	8.526	<.0001	51.155	1.000
Residual	385	1.933	.005				

Bonferroni/Dunn for TimeB_1
Effect: Line
Significance Level: 5 %
Split By: Age
Cell: 10

	Mean Diff.	Crit. Diff.	P-Value
Q111B, Q140B	-.005	.055	.7891
Q111B, Q175B	.071	.072	.0025
Q111B, Q20B	-.052	.055	.0036
Q111B, Q80B	-.035	.055	.0519
Q111B, Q92B	-.041	.056	.0241
Q111B, WT	-.047	.042	.0006
Q140B, Q175B	.076	.071	.0012
Q140B, Q20B	-.047	.054	.0077
Q140B, Q80B	-.031	.055	.0900
Q140B, Q92B	-.037	.056	.0442
Q140B, WT	-.042	.041	.0017
Q175B, Q20B	-.123	.071	<.0001
Q175B, Q80B	-.107	.072	<.0001
Q175B, Q92B	-.113	.072	<.0001
Q175B, WT	-.118	.062	<.0001
Q20B, Q80B	.017	.055	.3494
Q20B, Q92B	.011	.056	.5523
Q20B, WT	.005	.041	.6933
Q80B, Q92B	-.006	.056	.7425
Q80B, WT	-.012	.042	.4006
Q92B, WT	-.006	.043	.6930

Means Table for TimeB_1
Effect: Line
Split By: Age
Cell: 2

	Count	Mean	Std. Dev.	Std. Err.
Q111B	60	3.025	.067	.009
Q140B	62	2.992	.064	.008
Q175B	63	2.988	.066	.008
Q20B	30	3.013	.056	.010
Q80B	32	3.008	.054	.009
Q92B	32	3.021	.055	.010
WT	131	3.015	.064	.006

Analysis of percent duration clustering

Analyses were done by ANOVA. For post-hoc tests we used a Bonferroni correction for the critical alpha value, which yields α=0.05/6=0.0083, considering only 6 comparisons against the WT line.

2 months of age

ANOVA Table for Night
Split By: age
Cell: M 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	187.997	31.333	2.984	.0073	17.904	.911
Residual	402	4221.211	10.501				

Bonferroni/Dunn for Night
Effect: Line
Significance Level: 5 %
Split By: age
Cell: M 2

	Mean Diff.	Crit. Diff.	P-Value	
HD_KI_WT, Q111B	1.941	1.899	.0019	S
HD_KI_WT, Q140B	-.994	1.899	.1102	
HD_KI_WT, Q175B	.327	1.873	.5935	
HD_KI_WT, Q20B	.296	1.927	.6389	
HD_KI_WT, Q80B	1.346	1.927	.0333	
HD_KI_WT, Q92B	.437	1.873	.4764	
Q111B, Q140B	-2.935	2.517	.0004	S
Q111B, Q175B	-1.614	2.497	.0488	
Q111B, Q20B	-1.645	2.537	.0481	
Q111B, Q80B	-.595	2.537	.4737	
Q111B, Q92B	-1.505	2.497	.0662	
Q140B, Q175B	1.322	2.497	.1064	
Q140B, Q20B	1.290	2.537	.1208	
Q140B, Q80B	2.340	2.537	.0050	
Q140B, Q92B	1.431	2.497	.0805	
Q175B, Q20B	-.031	2.518	.9697	
Q175B, Q80B	1.019	2.518	.2168	
Q175B, Q92B	.109	2.477	.8927	
Q20B, Q80B	1.050	2.558	.2102	
Q20B, Q92B	.141	2.518	.8645	
Q80B, Q92B	-.909	2.518	.2701	

6 months of age

ANOVA Table for Night
Split By: age
Cell: M6

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	573.365	95.561	5.277	<.0001	31.663	.997
Residual	381	6899.317	18.108				

Bonferroni/Dunn for Night
Effect: Line
Significance Level: 5 %
Split By: age
Cell: M6

	Mean Diff.	Crit. Diff.	P-Value	
HD_KI_WT, Q111B	.327	2.577	.6979	
HD_KI_WT, Q140B	-.154	2.539	.8531	
HD_KI_WT, Q175B	3.630	2.539	<.0001	S
HD_KI_WT, Q20B	-1.537	2.539	.0648	
HD_KI_WT, Q80B	-1.837	2.539	.0275	
HD_KI_WT, Q92B	.359	2.660	.6798	
Q111B, Q140B	-.481	3.389	.6645	
Q111B, Q175B	3.302	3.389	.0031	
Q111B, Q20B	-1.864	3.389	.0933	
Q111B, Q80B	-2.164	3.389	.0515	
Q111B, Q92B	.032	3.481	.9776	
Q140B, Q175B	3.783	3.361	.0006	S
Q140B, Q20B	-1.383	3.361	.2088	
Q140B, Q80B	-1.683	3.361	.1263	
Q140B, Q92B	.513	3.453	.6498	
Q175B, Q20B	-5.167	3.361	<.0001	S
Q175B, Q80B	-5.467	3.361	<.0001	S
Q175B, Q92B	-3.270	3.453	.0040	
Q20B, Q80B	-.300	3.361	.7850	
Q20B, Q92B	1.896	3.453	.0938	
Q80B, Q92B	2.196	3.453	.0524	

10 months of age

ANOVA Table for Night
Split By: age
Cell: M 10

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Line	6	505.006	84.168	2.531	.0207	15.188	.845
Residual	338	11238.722	33.251				

Bonferroni/Dunn for Night
Effect: Line
Significance Level: 5 %
Split By: age
Cell: M 10

	Mean Diff.	Crit. Diff.	P-Value
HD_KI_WT, Q111B	1.629	3.983	.2114
HD_KI_WT, Q140B	2.395	3.582	.0414
HD_KI_WT, Q175B	3.087	3.428	.0062
HD_KI_WT, Q20B	.422	3.477	.7107
HD_KI_WT, Q80B	-1.202	3.764	.3291
HD_KI_WT, Q92B	-.904	3.700	.4549
Q111B, Q140B	.766	5.029	.6412
Q111B, Q175B	1.457	4.921	.3652
Q111B, Q20B	-1.208	4.955	.4561
Q111B, Q80B	-2.831	5.160	.0940
Q111B, Q92B	-2.533	5.113	.1303
Q140B, Q175B	.691	4.602	.6460
Q140B, Q20B	-1.974	4.638	.1936
Q140B, Q80B	-3.597	4.857	.0240
Q140B, Q92B	-3.299	4.808	.0364
Q175B, Q20B	-2.665	4.521	.0720
Q175B, Q80B	-4.288	4.745	.0060
Q175B, Q92B	-3.991	4.694	.0097
Q20B, Q80B	-1.623	4.780	.2993
Q20B, Q92B	-1.326	4.730	.3915
Q80B, Q92B	.298	4.945	.8539

Supplementary Figure 7

Analysis of Variance of qPCR results

Bonferroni correction for comparison against WT only (endogenous *Htt*) yield α=0.000625 and for comparison between HET lines yield α=0.0025

ANOVA Table for levels

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
geno	8	2.195	.274	122.076	<.0001	976.604	1.000
Residual	57	.128	.002				

Bonferroni/Dunn for levels
Effect: geno
Significance Level: 5 %

	Mean Diff.	Crit. Diff.	P-Value	
Q111, Q140	.060	.080	.0138	
Q111, Q175	.056	.080	.0216	
Q111, Q20	.058	.080	.0171	
Q111, Q50	-.092	.098	.0024	
Q111, Q50neo	.061	.080	.0130	
Q111, Q80	.070	.080	.0044	
Q111, Q92	.041	.086	.1145	
Q111, WT	-.506	.080	<.0001	S
Q140, Q175	-.004	.080	.8583	
Q140, Q20	-.002	.080	.9331	
Q140, Q50	-.152	.098	<.0001	S
Q140, Q50neo	.001	.080	.9825	
Q140, Q80	.010	.080	.6709	
Q140, Q92	-.019	.086	.4562	
Q140, WT	-.566	.080	<.0001	S
Q175, Q20	.002	.080	.9247	
Q175, Q50	-.148	.098	<.0001	S
Q175, Q50neo	.005	.080	.8412	
Q175, Q80	.014	.080	.5466	
Q175, Q92	-.015	.086	.5614	
Q175, WT	-.562	.080	<.0001	S
Q20, Q50	-.150	.098	<.0001	S
Q20, Q50neo	.003	.080	.9157	
Q20, Q80	.012	.080	.6110	
Q20, Q92	-.017	.086	.5042	
Q20, WT	-.564	.080	<.0001	S
Q50, Q50neo	.153	.098	<.0001	S
Q50, Q80	.163	.098	<.0001	S
Q50, Q92	.133	.103	<.0001	S
Q50, WT	-.413	.098	<.0001	S
Q50neo, Q80	.010	.080	.6869	
Q50neo, Q92	-.020	.086	.4441	
Q50neo, WT	-.566	.080	<.0001	S
Q80, Q92	-.029	.086	.2567	
Q80, WT	-.576	.080	<.0001	S
Q92, WT	-.547	.086	<.0001	S

Analysis of Variance of RNA-Seq results

2 months of age

Bonferroni correction for comparisons against WT only yield α=0.0083.

For multiple comparisons, α=0.003.

ANOVA Table for normalized to WT

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Geno line	6	.905	.151	26.392	<.0001	158.354	1.000
Residual	42	.240	.006				

Bonferroni/Dunn for normalized to WT
Effect: Geno line
Significance Level: 5 %

	Mean Diff.	Crit. Diff.	P-Value	
Q111 HET, Q140 HET	.170	.127	<.0001	S
Q111 HET, Q175 HET	.279	.127	<.0001	S
Q111 HET, Q20 HET	-.050	.136	.2458	
Q111 HET, Q20 WT	.020	.131	.6215	
Q111 HET, Q80 HET	-.124	.131	.0038	
Q111 HET, Q92 HET	-.064	.136	.1370	
Q140 HET, Q175 HET	.109	.122	.0063	
Q140 HET, Q20 HET	-.220	.132	<.0001	S
Q140 HET, Q20 WT	-.150	.127	.0004	S
Q140 HET, Q80 HET	-.294	.127	<.0001	S
Q140 HET, Q92 HET	-.234	.132	<.0001	S
Q175 HET, Q20 HET	-.328	.132	<.0001	S
Q175 HET, Q20 WT	-.259	.127	<.0001	S
Q175 HET, Q80 HET	-.403	.127	<.0001	S
Q175 HET, Q92 HET	-.343	.132	<.0001	S
Q20 HET, Q20 WT	.070	.136	.1054	
Q20 HET, Q80 HET	-.074	.136	.0847	
Q20 HET, Q92 HET	-.014	.141	.7454	
Q20 WT, Q80 HET	-.144	.131	.0009	S
Q20 WT, Q92 HET	-.084	.136	.0527	
Q80 HET, Q92 HET	.060	.136	.1610	

6 months of age

Bonferroni correction for comparisons between Q20, Q80, Q92, Q111, Q140 and Q175 against WT only yield α=0.0083.

ANOVA Table for Normalized to WT

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
genotype	6	.536	.089	62.655	<.0001	375.929	1.000
Residual	89	.127	.001				

Bonferroni/Dunn for Normalized to WT
Effect: genotype
Significance Level: 5 %

	Mean Diff.	Crit. Diff.	P-Value	
Q111 HET, Q140 HET	.081	.059	<.0001	S
Q111 HET, Q175 HET	.181	.059	<.0001	S
Q111 HET, Q20 HET	-.085	.059	<.0001	S
Q111 HET, Q80 HET	-.130	.059	<.0001	S
Q111 HET, Q92 HET	-.051	.059	.0079	
Q111 HET, WT	-.017	.045	.2379	
Q140 HET, Q175 HET	.101	.059	<.0001	S
Q140 HET, Q20 HET	-.166	.059	<.0001	S
Q140 HET, Q80 HET	-.210	.059	<.0001	S
Q140 HET, Q92 HET	-.132	.059	<.0001	S
Q140 HET, WT	-.098	.045	<.0001	S
Q175 HET, Q20 HET	-.267	.059	<.0001	S
Q175 HET, Q80 HET	-.311	.059	<.0001	S
Q175 HET, Q92 HET	-.233	.059	<.0001	S
Q175 HET, WT	-.199	.045	<.0001	S
Q20 HET, Q80 HET	-.044	.059	.0212	
Q20 HET, Q92 HET	.034	.059	.0741	
Q20 HET, WT	.068	.045	<.0001	S
Q80 HET, Q92 HET	.078	.059	<.0001	S
Q80 HET, WT	.113	.045	<.0001	S
Q92 HET, WT	.034	.045	.0200	

Unpaired t-test for normalized level to Wt
Grouping Variable: genotypes
Hypothesized Difference = 0
Row exclusion: Untitled Dataset #1

	Mean Diff.	DF	t-Value	P-Value
Q20_WT_6, Q50_HET_6	-.056	14	-1.279	.2217

Group Info for normalized level to Wt
Grouping Variable: genotypes
Row exclusion: Untitled Dataset #1

	Count	Mean	Variance	Std. Dev.	Std. Err
Q20_WT_6	8	1.000	.007	.084	.030
Q50_HET_6	8	1.056	.008	.091	.032

For multiple comparisons between HET groups, α=0.0023.

Bonferroni/Dunn for normalized level to Wt
Effect: gen - line
Significance Level: 5 %
Row exclusion: Untitled Dataset #1

	Mean Diff.	Crit. Diff.	P-Value	
Q111 HET, Q140 HET	.081	.078	.0017	S
Q111 HET, Q175 HET	.181	.078	<.0001	S
Q111 HET, Q20 HET	-.085	.078	.0010	S
Q111 HET, Q50 HET	-.073	.078	.0042	
Q111 HET, Q80 HET	-.130	.078	<.0001	S
Q111 HET, Q92 HET	-.051	.078	.0405	
Q140 HET, Q175 HET	.101	.078	.0001	S
Q140 HET, Q20 HET	-.166	.078	<.0001	S
Q140 HET, Q50 HET	-.154	.078	<.0001	S
Q140 HET, Q80 HET	-.210	.078	<.0001	S
Q140 HET, Q92 HET	-.132	.078	<.0001	S
Q175 HET, Q20 HET	-.267	.078	<.0001	S
Q175 HET, Q50 HET	-.255	.078	<.0001	S
Q175 HET, Q80 HET	-.311	.078	<.0001	S
Q175 HET, Q92 HET	-.233	.078	<.0001	S
Q20 HET, Q50 HET	.012	.078	.6191	
Q20 HET, Q80 HET	-.044	.078	.0753	
Q20 HET, Q92 HET	.034	.078	.1677	
Q50 HET, Q80 HET	-.056	.078	.0247	
Q50 HET, Q92 HET	.022	.078	.3725	
Q80 HET, Q92 HET	.078	.078	.0023	S

Comparisons in this table are not significant unless the corresponding p-value is less than .0024.

10 months of age

Bonferroni correction for comparisons between Q20, Q80, Q92, Q111, Q140 and Q175 against WT only yield α=0.0083.

ANOVA Table for Normalized to WT

	DF	Sum of Squares	Mean Square	F-Value	P-Value	Lambda	Power
Geno type	6	.644	.107	11.861	<.0001	71.168	1.000
Residual	49	.444	.009				

Bonferroni/Dunn for Normalized to WT
Effect: Geno type
Significance Level: 5 %

	Mean Diff.	Crit. Diff.	P-Value	
Q111 HET, Q140 HET	.140	.152	.0049	
Q111 HET, Q175 HET	.217	.152	<.0001	S
Q111 HET, Q20 HET	-.127	.152	.0105	
Q111 HET, Q20 WT	-.033	.152	.4971	
Q111 HET, Q80 HET	-.017	.152	.7173	
Q111 HET, Q92 HET	-.015	.152	.7476	
Q140 HET, Q175 HET	.077	.152	.1112	
Q140 HET, Q20 HET	-.267	.152	<.0001	S
Q140 HET, Q20 WT	-.173	.152	.0007	S
Q140 HET, Q80 HET	-.157	.152	.0018	S
Q140 HET, Q92 HET	-.155	.152	.0020	S
Q175 HET, Q20 HET	-.344	.152	<.0001	S
Q175 HET, Q20 WT	-.250	.152	<.0001	S
Q175 HET, Q80 HET	-.235	.152	<.0001	S
Q175 HET, Q92 HET	-.233	.152	<.0001	S
Q20 HET, Q20 WT	.094	.152	.0537	
Q20 HET, Q80 HET	.109	.152	.0260	
Q20 HET, Q92 HET	.111	.152	.0236	
Q20 WT, Q80 HET	.015	.152	.7503	
Q20 WT, Q92 HET	.017	.152	.7201	
Q80 HET, Q92 HET	.002	.152	.9679	

Unpaired t-test for normalized to WT
Grouping Variable: geno line
Hypothesized Difference = 0
Row exclusion: Untitled Dataset #1

	Mean Diff.	DF	t-Value	P-Value
Q20_WT_10, Q50_HET_10	-.059	14	-3.187	.0066

Group Info for normalized to WT
Grouping Variable: geno line
Row exclusion: Untitled Dataset #1

	Count	Mean	Variance	Std. Dev.	Std. Err
Q20_WT_10	8	1.000	.001	.032	.011
Q50_HET_10	8	1.059	.002	.042	.015

For multiple comparisons between HET groups, α=0.002.

Bonferroni/Dunn for normalized to WT
Effect: geno line
Significance Level: 5 %
Row exclusion: Untitled Dataset #1

	Mean Diff.	Crit. Diff.	P-Value	
Q111 HET, Q140 HET	.140	.131	.0012	S
Q111 HET, Q175 HET	.217	.131	<.0001	S
Q111 HET, Q20 HET	-.127	.131	.0032	
Q111 HET, Q50_HET_10	-.092	.131	.0296	
Q111 HET, Q80 HET	-.017	.131	.6735	
Q111 HET, Q92 HET	-.015	.131	.7079	
Q140 HET, Q175 HET	.077	.131	.0649	
Q140 HET, Q20 HET	-.267	.131	<.0001	S
Q140 HET, Q50_HET_10	-.232	.131	<.0001	S
Q140 HET, Q80 HET	-.157	.131	.0003	S
Q140 HET, Q92 HET	-.155	.131	.0004	S
Q175 HET, Q20 HET	-.344	.131	<.0001	S
Q175 HET, Q50_HET_10	-.309	.131	<.0001	S
Q175 HET, Q80 HET	-.235	.131	<.0001	S
Q175 HET, Q92 HET	-.233	.131	<.0001	S
Q20 HET, Q50_HET_10	.035	.131	.3958	
Q20 HET, Q80 HET	.109	.131	.0102	
Q20 HET, Q92 HET	.111	.131	.0090	
Q50_HET_10, Q80 HET	.074	.131	.0753	
Q50_HET_10, Q92 HET	.076	.131	.0683	
Q80 HET, Q92 HET	.002	.131	.9626	

Comparisons in this table are not significant unless the corresponding p-value is less than .0024.