HDinHD: A Comprehensive Data Portal for Advancing Huntington's Disease Research (https://www.hdinhd.org/)

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Abstract

HDinHD (Huntington's Disease in High Definition; HDinHD.org) is an open online portal designed for Huntington's Disease (HD) researchers [1]. The platform provides a unified view of HD experimental data and features a federated set of visualization and analysis tools developed by HD scientists. Researchers can explore interconnected datasets, visualize analytical results, and download data for integration into local databases or computational pipelines.

To ensure the portal remains comprehensive and up-to-date, the HDinHD team continues to monitor the literature and community omics repositories to identify emerging HD experimental data. New HD studies are curated and analyzed according to established vocabularies, methods and pipelines before integration into the HDinHD environment. The recent 2.4 release includes dozens of previously unreleased CHDI studies, including characterization of genetically modified animal (GMA) models and power calculations for selected assays in GMA models.

HDinHD is committed to addressing the evolving needs of the research community. Feedback and suggestions are welcomed via the Feedback link on the HDinHD website or by contacting CHDI directly.

Downloads

Striatum Disease Signature	Manuscript describing generation of molecular disease signatures in HD mice and supplemental files detailing results [2].
Mouse Allelic Series	Raw, processed and analyzed molecular and behavioural data from the Mouse Allelic Series project.
GWAS Studies	Topic reports for genes implicated by early GeM-HD results.
DNA Repair and Handling	Topic reports plus visual and computable DNA repair pathways.
Causal Modeling Results	Simulation and other results from a series of causal models built from Mouse Allelic Series molecular and behavioural data.
Curated HD Datasets	Independent slices of HD experimental data that underlie the **HD Explorer**.

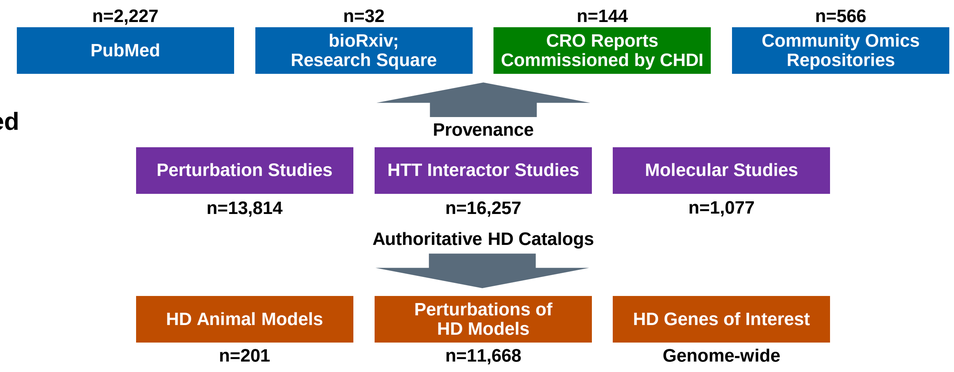
Federated Set of HD Tools Authored by the Community

CHDI	**HD Explorer**	Integrated network of HD experimental data curated and analyzed from the literature, community omics repositories and internal CHDI reports.
GeM-HD Consortium	**GeM Euro 9K**	Visualization tools and summary results of a genome-wide association study to identify genetic modifiers of Huntington's disease.
CHDI	**ASViewer**	Visualization of Q-length and age-dependent gene and protein expression data from brain and peripheral tissues of the Mouse Allelic Series.
Khakh Lab (UCLA)	**Adult Astrocyte RNAseq Explorer**	Visualization tool providing Astrocyte gene expression profiles across brain regions and HD disease models.
Neri Lab (INSERM)	**Brain-C lab HD Knowledge base**	Browsable knowledgebase of HD animal model data using precision machine-learning and 3D-visualization of RNAseq data in brain structures of HD model mice.
Ma'ayan Lab (Mt. Sinai)	**Enricher**	Gene set enrichment analysis tool operating over a large, diverse collection of gene set libraries including HDSigDB, a library containing HD and HD-related gene sets.
Yang Lab (UCLA)	**CoExMap Viewer**	Visualization tool for a large-scale Weighted Gene Co-expression Network Analysis (WGCNA) of 6-month mouse striatum data.

Tools: HD Explorer

HD and HD-related Experimental Data Curated and Analyzed from Internal and External Sources.

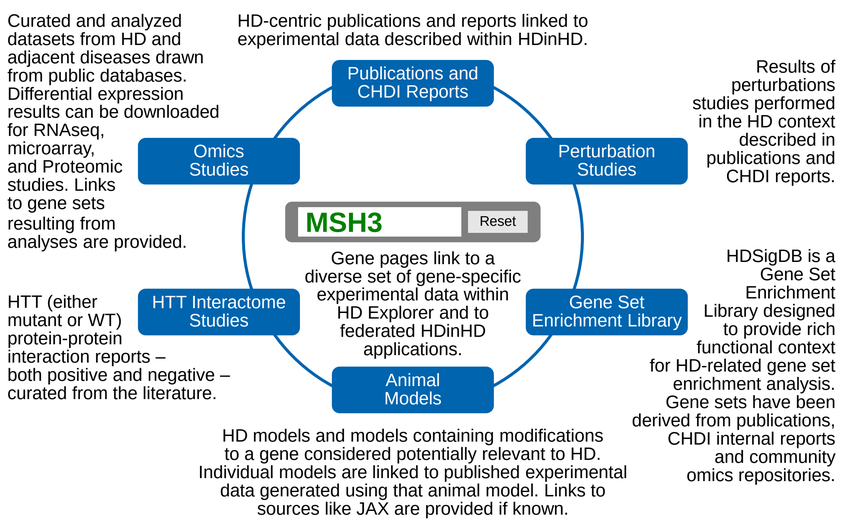
Shared HD Catalogs allow facile pivoting on Animal Models, Treatments and Genes/Targets.



HD Explorer Entry Portals

Each box on the Explorer entry circle as well as the central gene name search box provide distinct portals into the integrated HD Explorer application. Inside a portal, users can pivot via a rich set of semantic links to explore related HDinHD federated tools or adjacent HD Explorer data sections. After entering a gene name, users can check on the expression of that gene/protein in the Mouse Allelic Series and visit sets of experimental studies performed on that gene within the HD context.

The datasets are available for downloads to support incorporation of data from HD Explorer into internal databases and analytical pipelines.



HD Animal Models

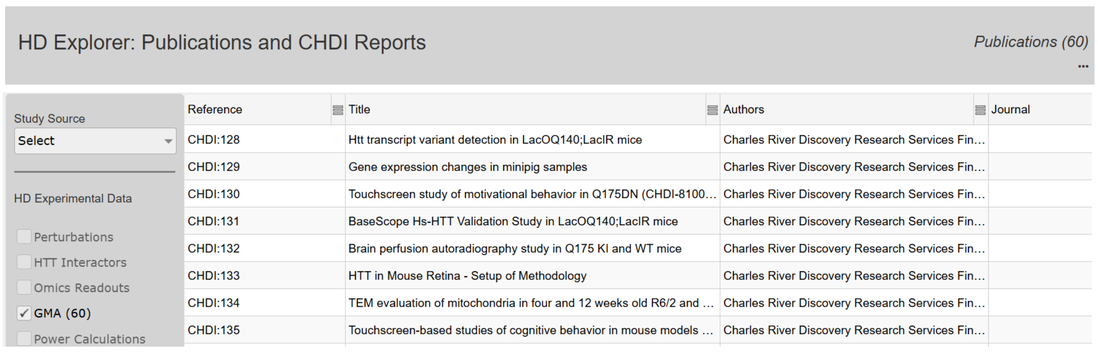
Animal models are essential tools for studying HD, as they provide a controlled system to investigate the complex mechanisms underlying this neurodegenerative disorder. These models enable researchers to simulate key genetic, molecular, and phenotypic aspects of the disease, offering insights that are not feasible to obtain from human studies alone.

A catalog of HD animal models within the HD Explorer is a valuable resource for researchers, facilitating the selection of appropriate models based on specific phenotypic features and research objectives.

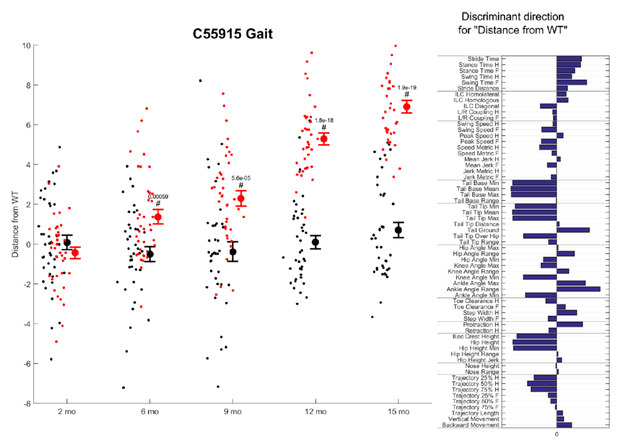
Phenotyping of HD Mouse Models

Phenotypic characterization of HD animal models contributes to understanding progression at behavioral, cellular, and molecular levels. This characterization informs selection of fit-for-purpose animal model(s) most appropriate for planned experiments and enables the identification of biomarkers, therapeutic targets, and the evaluation of potential treatments, improving translational success of preclinical research.

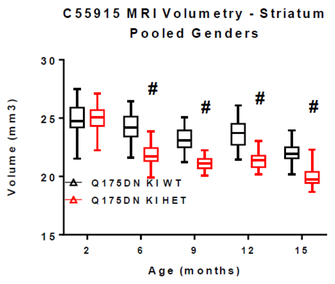
A set of previously unreleased CHDI GMA Phenotyping reports (n=60), prepared by Charles River Laboratories, has been added to HD Explorer in January 2025. These reports are accessible as collections within the **Publications and Reports** portal. Additionally, the HD animal models studied in these reports are organized into collections within the **HD Animal Models** portal, allowing researchers to explore relevant models efficiently. Individual HD animal model drilldown pages link to these reports, ensuring seamless access to valuable information for further study and analysis.



Overall Gait analysis score of pooled genders of KI Q175DN mice from 2-15 months of age. The score is based on differences between heterozygote and wild-type mice in all the PC scores. Identified "fingerprint" (combination) of original variables, which best characterizes the disease model is seen in the Discriminant direction vector bar graph. The bar length and direction corresponds to the weight of individual parameters in the Overall Gait analysis score. (Q175DN KI WT n=40-39; Q175DN KI HET n=40-39). # p<0.05, Q175DN KI HET vs. Q175DN KI WT from report CHDI:157.



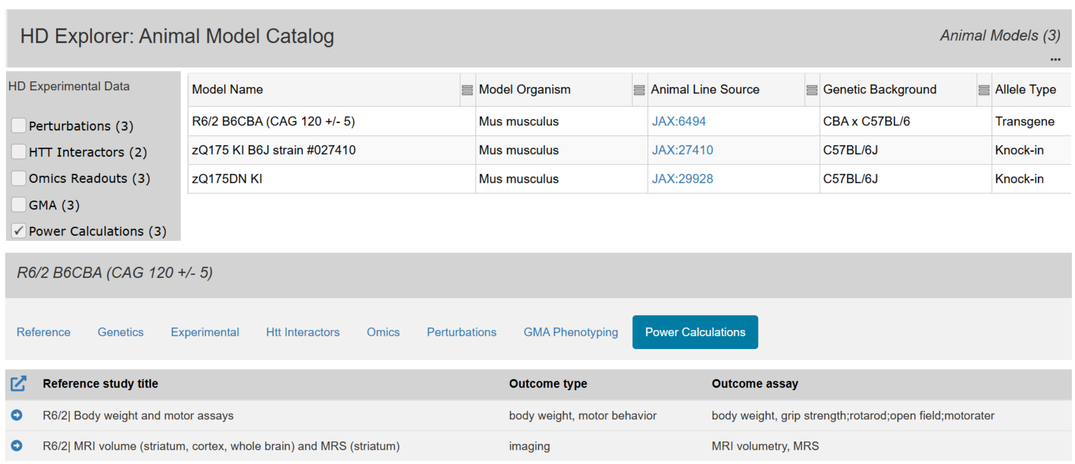
Striatum volumes of pooled genders of KI Q175DN mice from 2-15 months of age. Data are presented as quartiles, center line as median, whiskers as minimum and maximum of all of the data (Q175DN KI WT n=40-39; Q175DN KI HET n=40-39). # p<0.05, Q175DN KI HET vs. Q175DN KI WT from report CHDI:157.



Power Calculation Reports

Ensuring a study is appropriately powered (i.e., ≥80%) is an important component of generating robust and meaningful results. To facilitate the conduct of robust preclinical studies, CHDI has commissioned the generation of several statistical power reports, leveraging historic data from the GMA reports. Each report is focused on a single mouse model (e.g., R6/2) and a set of assays (e.g., motor), and presents the results from a series of power calculations in tables, which show power for each assay based on manipulation of various parameters: design (i.e., fixed time point; repeated measures), time point or time points (e.g., 10 weeks; 4-10 weeks), sex (i.e., male, female, mixed), expected rescue towards WT control phenotype (i.e., 100%; 50%; 30%), and sample size per group (i.e., N=6-30).

These reports are valuable for robust study planning, pointing to an appropriate sample size for a specific design to achieve adequate power (i.e., ≥80%). They also enable exploration of the impact of manipulating sample size and study duration on study power, achieving desired power while optimizing cost. These reports, prepared by the ISSC and Prioris.ai, have been added to HD Explorer alongside the GMA reports.



Power Calculation Table from Report CHDI:124

MotoRater walking (mixed sex): cross-sectional power (genotype effect) for R6/2

rescue	week	effect_size	sigma	N_6	N_8	N_10	N_12	N_14	N_16	N_20	N_24	N_30
100%	4	-1.74	1.86	0.48	0.54	0.57	0.58	0.60	0.61	0.63	0.66	0.69
100%	10	-4.73	2.43	0.86	0.95	0.98	1.00	1.00	1.00	1.00	1.00	1.00
50%	4	-0.87	1.86	0.19	0.25	0.31	0.35	0.39	0.43	0.48	0.51	0.55
50%	10	-2.36	2.43	0.33	0.44	0.54	0.62	0.70	0.76	0.85	0.91	0.96
30%	4	-0.52	1.86	0.10	0.12	0.14	0.16	0.19	0.21	0.25	0.29	0.34
30%	10	-1.42	2.43	0.15	0.19	0.23	0.28	0.32	0.36	0.43	0.51	0.60

Acknowledgements

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Go to HDinHD

References

1. Aaronson J et al, *J Huntington's Dis* 2021,10(3):405-412.
2. Obenauer J et al, bioRxiv, https://doi.org/10.1101/2022.02.04.479180.