



Abstract

HDinHD (Huntington's Disease in High Definition; HDinHD.org) is an open online portal for Huntington's Disease (HD) researchers. HDinHD presents an integrated view of HD experimental data and highlights a federated set of visualization and analysis tools developed independently by HD scientists across the community. Researchers can interactively explore a richly-connected set of experimental data, visualize analytical results or download datasets locally to incorporate bulk data into their own databases and computational pipelines. 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 methods and pipelines and integrated into the HDinHD environment. HDinHD endeavors to be responsive to community needs. Input is welcomed and may be submitted either through the Feedback link on the HDinHD website or by contacting CHDI directly.

HDinHD Home Page



HDinHD: Open Source Science for the HD Research Community

The goal of HDinHD is to foster and support a collaborative community united in its drive to accelerate the development of therapeutics that will delay the onset and/or ameliorate the effects of Huntington's disease. HDinHD seeks to achieve this through:

- Sharing HD-related primary scientific data
- Sharing analyses and computational models built from HD-related scientific data
- Providing browsing and data interrogation tools over both primary and analyzed data that facilitate data exploration and hypothesis generation
- Building a forum for HD researchers to highlight their data, tools, know-how and insight to the community

The HDinHD website is currently a joint development effort by CHDI and UCLA, through the laboratory of Dr. Giovanni Coppola. As you will see when you Register for access, HDinHD highlights data and tools provided by the broader community. If you are interested in contributing data to HDinHD, suggest links to other HD-related scientific data or websites, or would otherwise like to provide feedback to us, we encourage you to do so. HDinHD is for the community; please help us tailor and grow HDinHD in a direction that can make a difference to your research, and ultimately, to improve the lives of HD families.

Want to learn more about HDinHD?

Watch a detailed video overview of HDinHD presented at the 18th Annual HD Therapeutics Conference (April 2021). The video outlines data resources and tools within HDinHD and provides a detailed demonstration of the new HD Explorer tool.

Read the following publication introducing HDinHD: HDinHD: A Rich Data Portal for Huntington's Disease Research, *J Huntington's Dis.*, 10, 405-412 (2021).

Latest news and publications from around the HD Ecosystem

HDBuzz	Literature	News
<ul style="list-style-type: none"> • Hunting for balance: how the huntingtin protein compensates in HD Source: HDBuzz Published on 2023-04-05 	<ul style="list-style-type: none"> • Animal models of Huntington's disease and their applicability to novel drug discovery and development Source: HD Explorer Published on 2023-04-11 	<ul style="list-style-type: none"> • Phosphorescent Pigments Industry Projected to Witness a Double-Digit CAGR During 2023 - 2030 Source: Google News Published on 2023-04-12

HDinHD home page content includes a video tutorial, RSS feeds from HDBuzz, HD-related literature aggregated from PubMed, bioRxiv and medRxiv and an HD-related news feed. Downloads, Tools, and New in HDinHD sections are available as independent tabs from the home page to registered users. Prospective users may register for an account directly from the homepage to gain full access.

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 & Handling	Topic report 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, including HDSigDB, underlying HD Explorer Tool.

Downloads: HDSigDB

To provide rich functional context for HD gene set enrichment analysis, we developed an HD-relevant gene set library called **HDSigDB**. The core of **HDSigDB** was derived from curation and analysis of HD and triplet-repeat expansion disease studies deposited in GEO, ArrayExpress, and PRIDE. Additional sources of gene sets include selected PubMed articles (publication-based) and DNA Damage Response pathways (CHDI reports). The lists of genes available in human and mouse symbols and Entrez gene IDs. **HDSigDB** is available within HDinHD Downloads and integrated within HD Explorer. **HDSigDB** is also included in the Enricher, a gene set enrichment analysis package from Ma'ayan Lab (Mt. Sinai) (<https://maayanlab.cloud/Enrichr/>) [3-5].

HDSigDB Gene Sets

Gene Set Category	Gene Set Sub-category	# of Gene Sets
Disease and Disease Model Signatures	Huntington's disease	1,797
	Ataxia (including Friedrich's, SCA1, SCA2, SCA3, SCA6, SCA7, SCA17)	487
	Muscular Dystrophy (including Becker, Duchenne, tibial, myotonic, facioscapulohumeral)	191
	Other diseases	131
Non-Disease Signatures	Tissue or cell type signatures (neurons, astrocytes, etc.)	778
	Pathways (DNA repair pathways, perturbation effects in WT, etc.)	256
	Protein localization (cytoplasm, nucleus, etc.)	15
Other		17

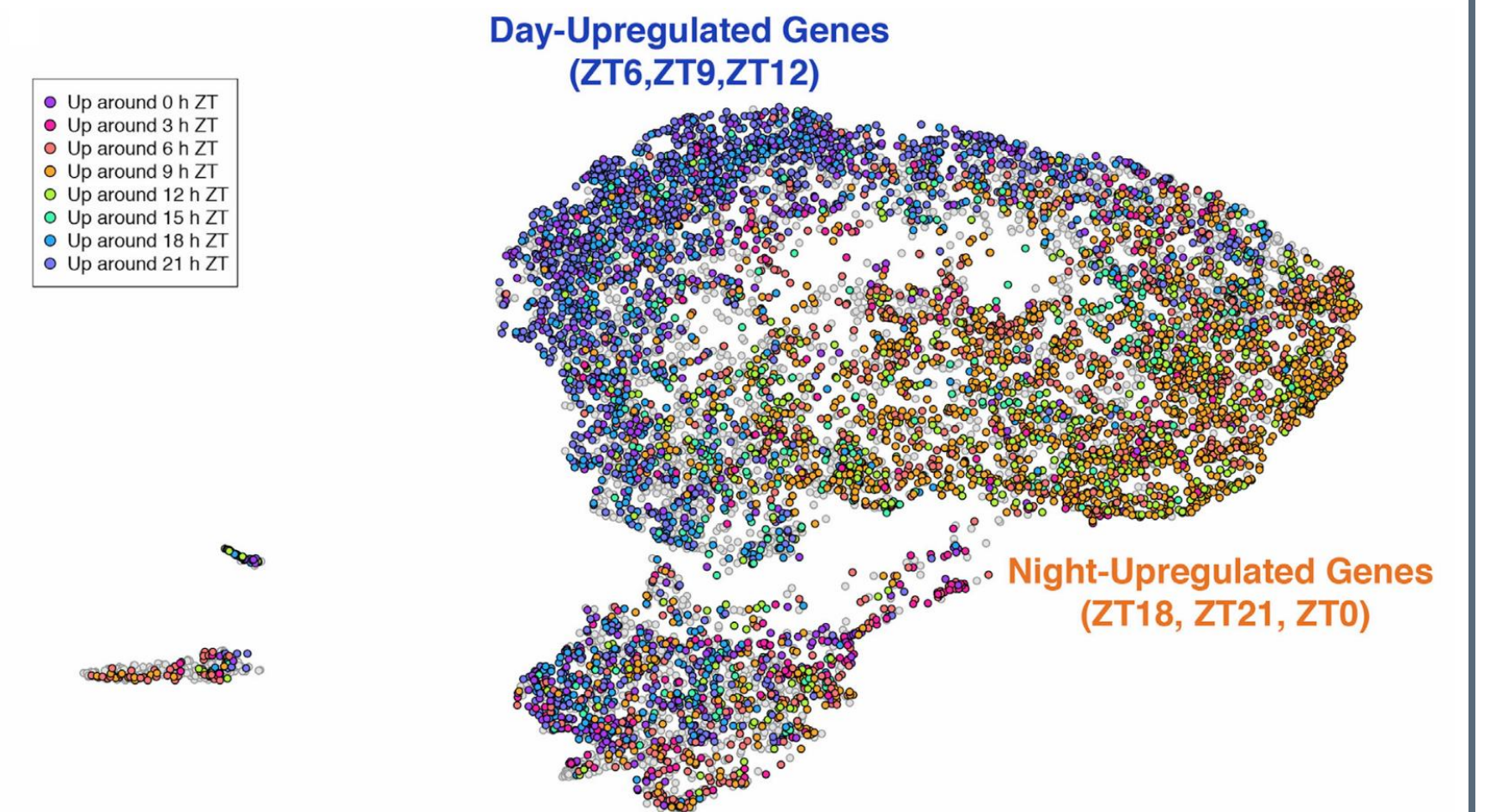
Federated Set of HD Tools Authored by the Community

	HD Explorer	
GeM-HD Consortium	GeM MOA SNP Viewer	Integrated network of HD experimental data curated and analyzed from the literature, community omics repositories and newly-released internal CHDI reports.
GeM-HD Consortium	GeM Euro 9K	Summary findings from Huntington's disease genome-wide association studies that seek out genes influencing the pathogenesis and expression of Huntington's disease.
	ASViewer	Visualization tools and summary results of a genome-wide association study to identify genetic modifiers of Huntington's disease.
Khakh Lab (UCLA)	Adult Astrocyte RNAseq Explorer	Visualization of Q-length and age dependent gene and protein expression data from brain and peripheral tissues of the Mouse Allelic Series.
Schaab (Evotec)	HD Proteome Base	Visualization tool providing Astrocyte gene expression profiles across brain regions and HD disease models.
Neri Lab (INSERM)	BioGemix Suite	Proteomics query tool displaying differential expression data from brain and peripheral tissues of the Mouse Allelic Series as well as baseline proteomic and phosphoproteomic data from the R6/2 mouse model.
Ma'ayan Lab (Mt. Sinai)	Enricher	Browsable knowledgebase of integrated HD animal model data using precision machine-learning and 3D-visualisation of RNA-seq data in brain structures of HD model mice.
Yang Lab (UCLA)	CoExMap Viewer	Gene set enrichment analysis tool operating over a large, diverse collection of gene set libraries including HDSigDB, a gene set library containing HD and HD-related gene sets.
		Visualization tool allowing exploration of results and underlying data of a large-scale Weighted Gene Co-expression Network Analysis (WGCNA) of hundreds of samples from intact mouse striatum at 6-month of age as well as from gene set enrichment analysis of transcriptomic signatures of differentially expressed genes from 52 heterozygous HD knockout mice and wildtype controls.

Tools: CoExMap Viewer

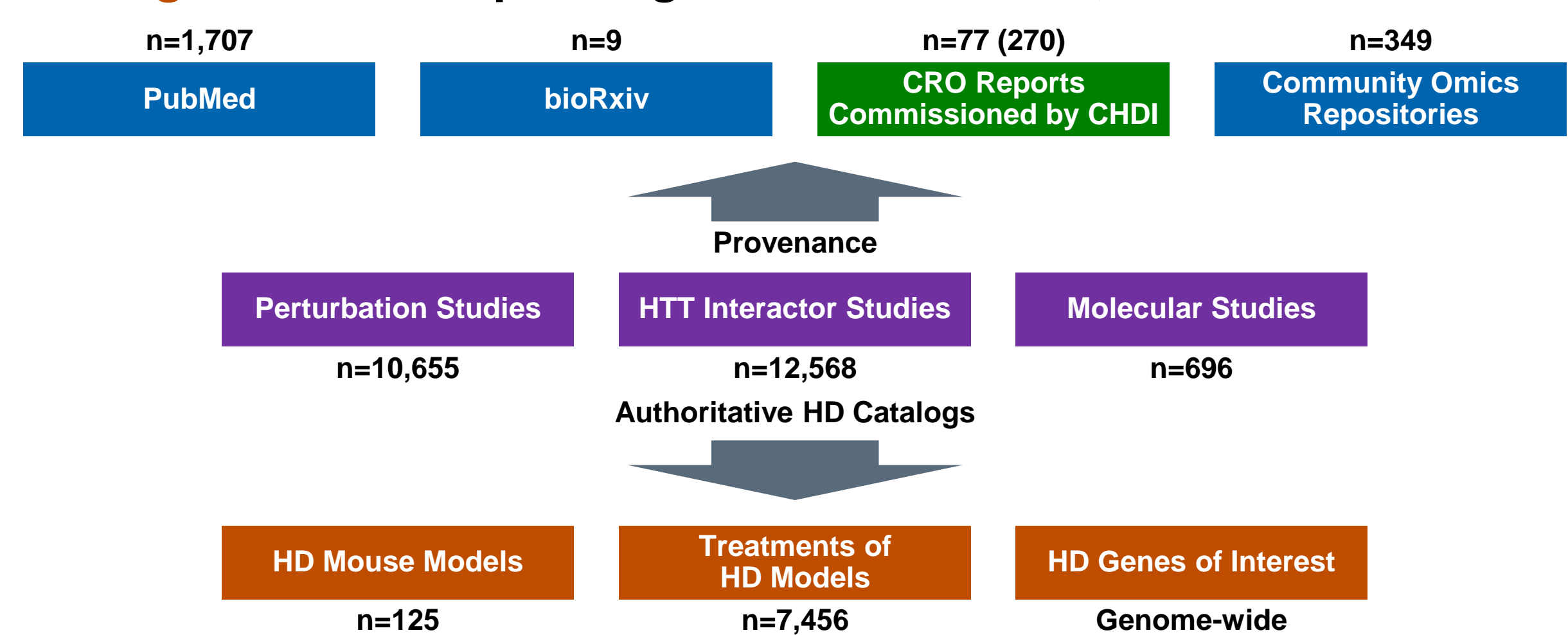
CoExMap Viewer is now available as a federated application within HDinHD's Tools section [6]. CoExMap Viewer offers two major interactive components:

1. A Table Browser that allows users to sort striatal gene signatures, cell type, and/or diurnal markers based on their enrichment in any CoExMap module as well as the converse, to sort the CoExMap modules by relevance to any particular gene signature, cell type or diurnal marker.
2. A UMAP (uniform manifold approximation and projection) visualization that depicts a 2-dimensional projection of co-expression modules that reflects intramodular connectivity. Users can visualize the location of their own set of genes on the UMAP, and gain insight based on functional annotation of distinct regions within the UMAP.



Tools: HD Explorer

HD and HD-related Experimental Data Curated & Analyzed from Internal and External Sources. Shared HD Catalogs allow facile pivoting on Mouse Models, Treatments and Genes/Targets.



HD Explorer Entry Portals

Contains >1,790 PubMed articles and CHDI reports referred to within the HDinHD ecosystem. Most publications are bi-directionally linked to experimental data detailed across HDinHD.

Includes >690 HD and HD-related datasets drawn from >340 GEO, PRIDE and ArrayExpress molecular studies. Datasets are curated and analyzed, and links are provided to gene sets resulting from these analyses.

Includes results of perturbations studies performed in the HD context that have been curated from >1270 PubMed articles and CHDI reports.

HDSigDB is a Gene Set Enrichment Library designed to provide rich functional context for HD-related gene set enrichment analysis. >3,670 gene sets have been derived from publications, CHDI internal reports and community omics repositories.

Provides a catalog of >120 HD Mouse models described in the literature. Individual mouse model lines are bi-directionally linked within HD Explorer to/from published experimental data generated using that mouse model.

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. Once 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. For example, after entering a gene name, users check on the expression of that gene/protein in the Mouse Allelic Series and can visit sets of experimental studies performed on that gene within the HD context. Component datasets are available on the HDinHD Downloads tab for labs who wish to incorporate HD Explorer batch data to facilitate internal data mining efforts.

Acknowledgements

HDinHD is funded and developed by CHDI Foundation, Inc., a nonprofit biomedical research organization exclusively dedicated to collaboratively developing therapeutics that will substantially improve the lives of those affected by Huntington's disease. HDinHD was launched in 2015 in partnership with the laboratory of Giovanni Coppola (UCLA). Colleagues at Rancho BioSciences contributed data curation, data analysis, data modeling and software/data engineering support, and Bridlewood Consulting contributed solutions architecture, systems and software engineering support. CHDI thanks the investigators who have kindly contributed to HDinHD's federated set of community-developed tools.

References

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