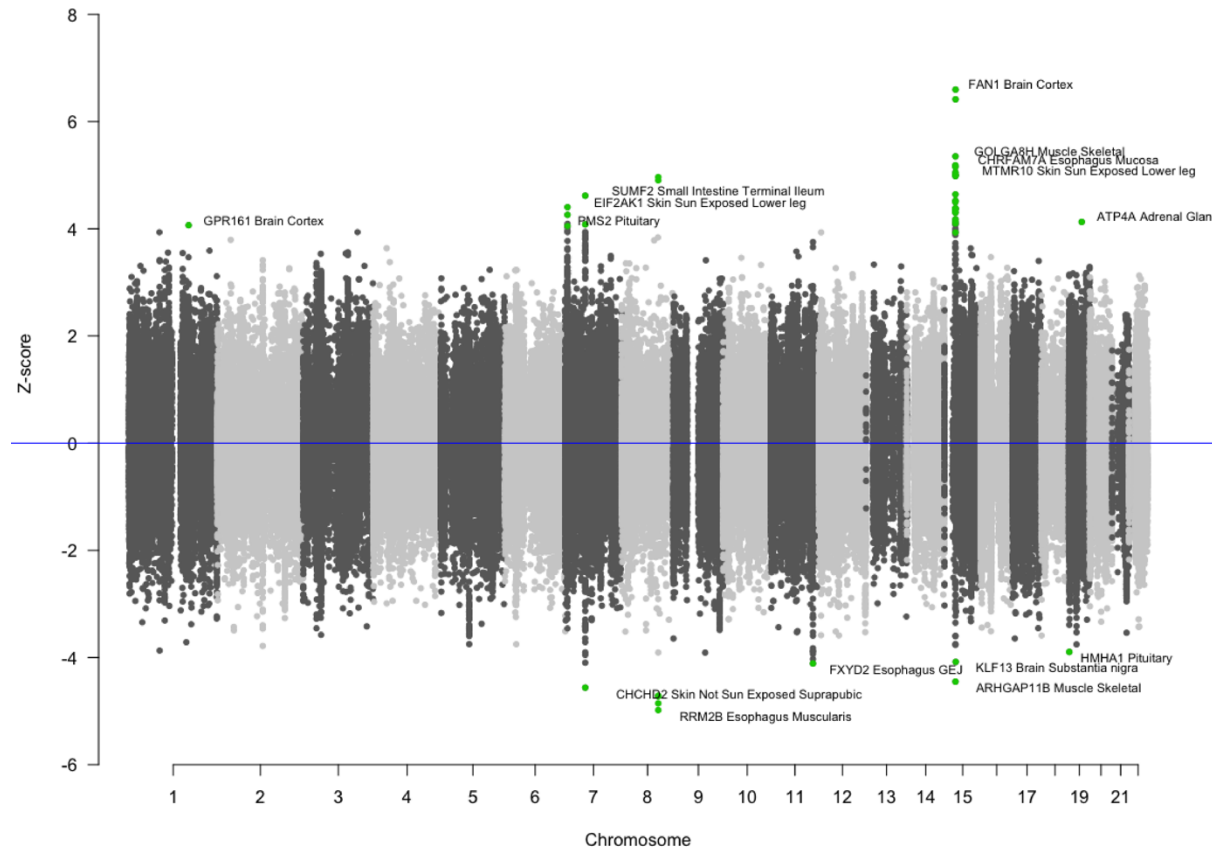
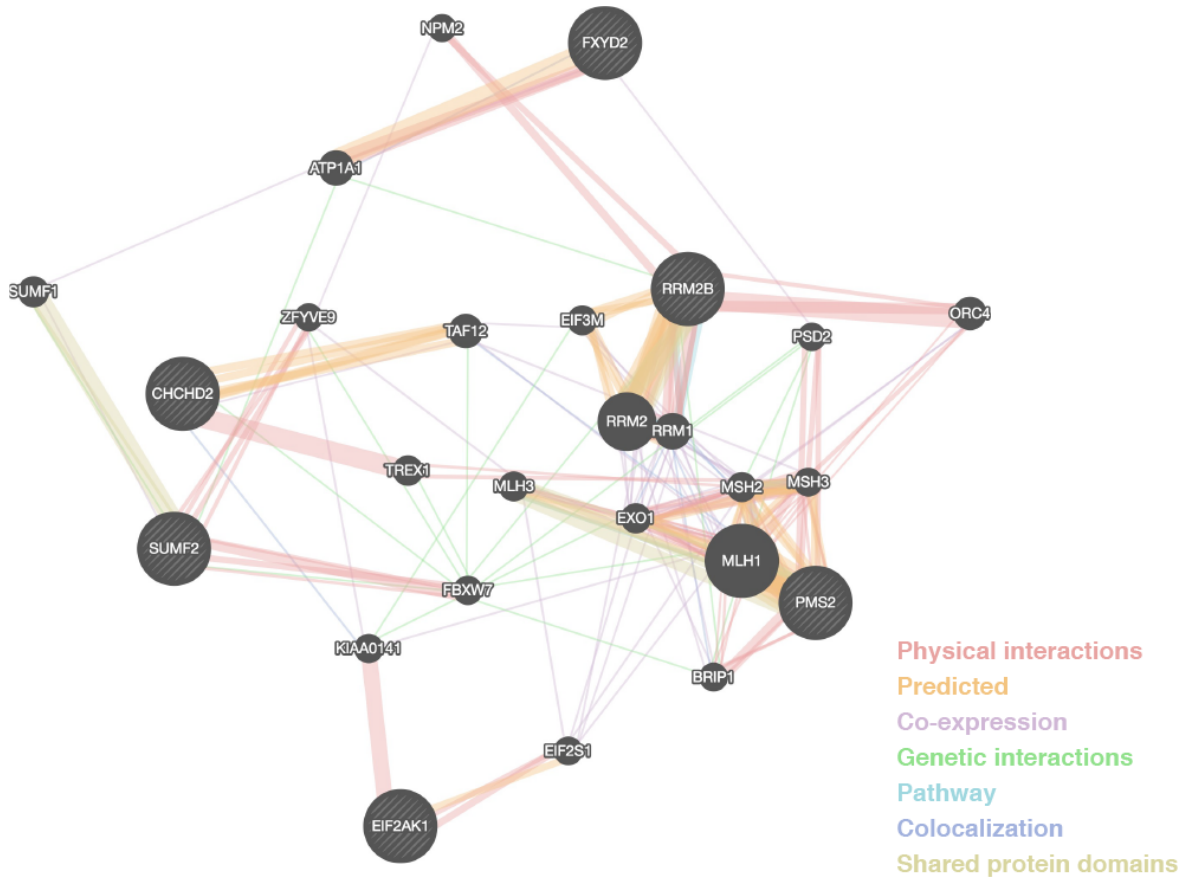


SUPPLEMENTARY INFORMATION



Supplementary Fig. 1 Miami plot displaying the association results from the HD clinical onset TWAS. S-PrediXcan Z-scores are indicated on the y-axis and chromosomal location of genes on the x-axis. The most significant gene-tissue association for each of the 15 prioritized transcriptomic modifier genes are annotated in green.



Supplementary Fig. 2 Gene-gene functional interaction network for candidate HD clinical modifier genes that were colocalized in GTEx. These colocalization analyses aided in refining Huntington disease modifier gene list as indicated by the tight connections observed in the gene-gene functional interaction network that was enriched for mismatch repair, DNA binding and ATPase activity.

Supplementary Table 1 Gene-tissue pairs for the genetic modifiers of the clinical onset of Huntington disease that passed the false discovery rate of 0.1 correction for multiple testing.

Tissue	Gene	GeM-HD Z-score	GeM-HD P-value
Brain Cortex	<i>FAN1</i>	6.60	4.25E-11
Adipose Subcutaneous	<i>FAN1</i>	6.42	1.41E-10
Muscle Skeletal	<i>GOLGA8H</i>	5.35	8.73E-08
Esophagus Mucosa	<i>CHRFAM7A</i>	5.18	2.19E-07
Heart Left Ventricle	<i>GOLGA8H</i>	5.15	2.55E-07
Nerve Tibial	<i>GOLGA8H</i>	5.05	4.42E-07
Breast Mammary Tissue	<i>GOLGA8H</i>	5.01	5.57E-07
Skin Sun Exposed Lower leg	<i>MTMR10</i>	5.00	5.79E-07
Artery Tibial	<i>GOLGA8H</i>	4.98	6.28E-07
Esophagus Muscularis	<i>RRM2B</i>	-4.98	6.29E-07
Esophagus Mucosa	<i>RRM2B</i>	4.96	6.91E-07
Muscle Skeletal	<i>RRM2B</i>	4.90	9.52E-07
Thyroid	<i>RRM2B</i>	-4.86	1.20E-06
Artery Tibial	<i>RRM2B</i>	-4.72	2.32E-06
Esophagus Gastroesophageal Junction	<i>RRM2B</i>	-4.71	2.44E-06
Adrenal Gland	<i>GOLGA8H</i>	4.64	3.46E-06
Small Intestine Terminal Ileum	<i>SUMF2</i>	4.62	3.89E-06
Skin Not Sun Exposed Suprapubic	<i>CHCHD2</i>	-4.56	5.10E-06
Esophagus Muscularis	<i>GOLGA8H</i>	4.52	6.08E-06
Artery Coronary	<i>CHRFAM7A</i>	4.50	6.82E-06
Muscle Skeletal	<i>ARHGAP11B</i>	-4.45	8.63E-06
Skin Sun Exposed Lower leg	<i>EIF2AK1</i>	4.40	1.07E-05
Pituitary	<i>GOLGA8H</i>	4.38	1.16E-05
Artery Coronary	<i>GOLGA8H</i>	4.37	1.22E-05

Skin Not Sun Exposed Suprapubic	<i>GOLGA8H</i>	4.37	1.26E-05
Esophagus Gastroesophageal Junction	<i>CHRFAM7A</i>	4.37	1.27E-05
Brain Putamen basal ganglia	<i>CHRFAM7A</i>	4.32	1.58E-05
Adipose Visceral Omentum	<i>GOLGA8H</i>	4.30	1.73E-05
Heart Atrial Appendage	<i>EIF2AK1</i>	4.26	2.04E-05
Adipose Subcutaneous	<i>GOLGA8H</i>	4.18	2.94E-05
Skin Sun Exposed Lower leg	<i>GOLGA8H</i>	4.13	3.57E-05
Adrenal Gland	<i>ATP4A</i>	4.13	3.67E-05
Esophagus Gastroesophageal Junction	<i>FXVD2</i>	-4.11	3.94E-05
Ovary	<i>GOLGA8H</i>	4.10	4.17E-05
Pituitary	<i>SUMF2</i>	4.08	4.50E-05
Brain Substantia nigra	<i>KLF13</i>	-4.08	4.50E-05
Brain Cortex	<i>GPR161</i>	4.06	4.82E-05
Pituitary	<i>PMS2</i>	4.05	5.09E-05
Brain Cortex	<i>GOLGA8H</i>	3.93	8.49E-05
Pituitary	<i>HMHA1</i>	-3.90	9.78E-05

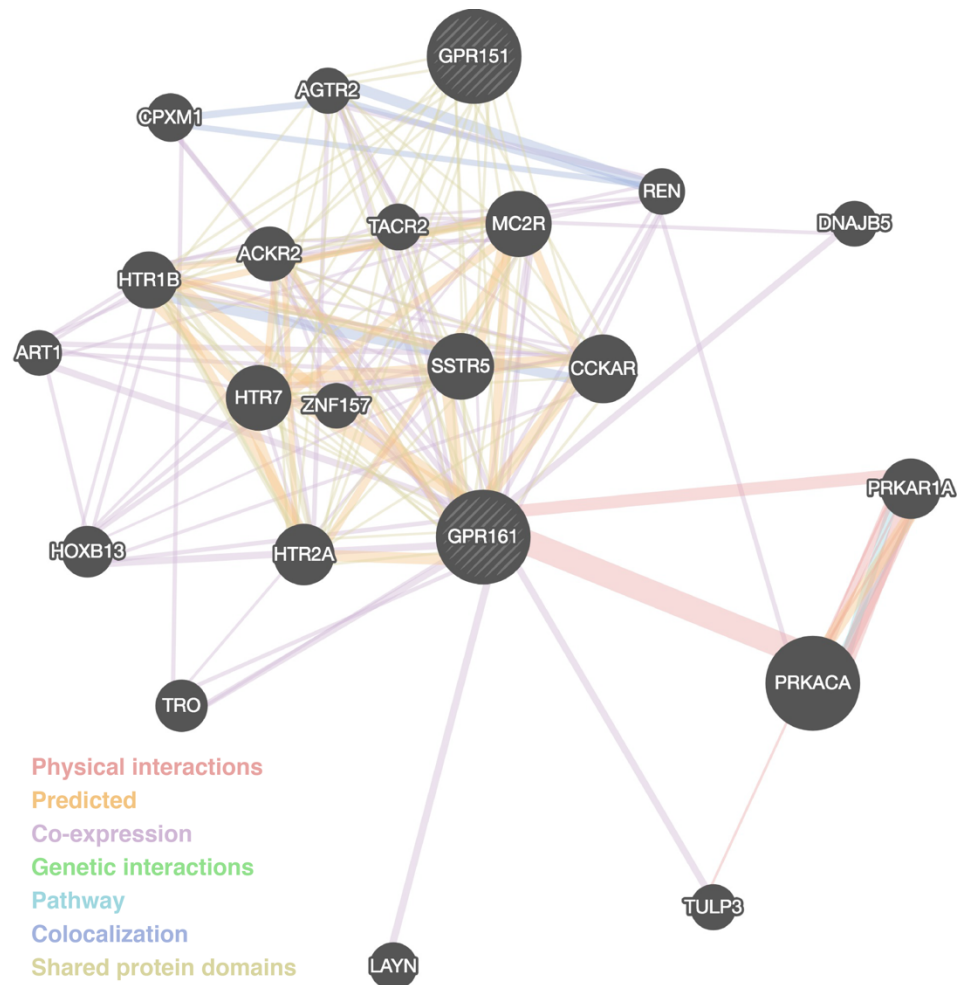
Supplementary Table 2 Top transcriptomic modifier HD genes that also displayed replication in the TRACK-HD cohort with effects in the same direction across cohorts.

Tissue	Gene	GeM-HD Z-score	GeM-HD P-value	TRACK-HD Z-score	TRACK-HD P-value
Heart Atrial Appendage	<i>EIF2AK1</i>	4.26	2.04E-05	2.68	7.33E-03
Cells EBV-transformed lymphocytes	<i>EIF2AK1</i>	4.09	4.30E-05	2.89	3.81E-03
Pituitary	<i>SUMF2</i>	4.08	4.50E-05	2.18	2.90E-02
Skin Not Sun Exposed Suprapubic	<i>EIF2AK1</i>	4.03	5.69E-05	2.22	2.61E-02
Adipose Subcutaneous	<i>CHCHD2</i>	-3.50	4.74E-04	-2.12	3.43E-02
Skin Sun Exposed Lower leg	<i>CHCHD2</i>	-3.38	7.38E-04	-2.29	2.19E-02
Uterus	<i>CHCHD2</i>	-3.29	9.91E-04	-2.13	3.33E-02
Adrenal Gland	<i>PMS2</i>	3.28	1.04E-03	2.87	4.13E-03
Artery Coronary	<i>PMS2</i>	3.28	1.04E-03	2.13	3.33E-02
Adrenal Gland	<i>EIF2AK1</i>	3.21	1.31E-03	2.69	7.19E-03
Cells Transformed fibroblasts	<i>EIF2AK1</i>	3.17	1.52E-03	2.00	4.53E-02
Adipose Visceral Omentum	<i>PMS2</i>	3.03	2.48E-03	2.23	2.55E-02
Artery Aorta	<i>EIF2AK1</i>	2.91	3.59E-03	3.23	1.25E-03
Adipose Subcutaneous	<i>EIF2AK1</i>	2.90	3.77E-03	2.60	9.43E-03
Adipose Visceral Omentum	<i>EIF2AK1</i>	2.88	4.03E-03	3.02	2.55E-03
Heart Atrial Appendage	<i>PMS2</i>	2.73	6.36E-03	2.06	3.93E-02
Testis	<i>EIF2AK1</i>	2.58	9.99E-03	2.19	2.88E-02
Whole Blood	<i>CHCHD2</i>	-2.40	1.64E-02	-2.03	4.19E-02
Esophagus Mucosa	<i>MTMR10</i>	-2.39	1.68E-02	-2.20	2.75E-02
Pancreas	<i>PMS2</i>	2.38	1.75E-02	2.02	4.38E-02
Cells Transformed fibroblasts	<i>PMS2</i>	2.35	1.89E-02	2.57	1.02E-02
Heart Atrial Appendage	<i>MTMR10</i>	-2.28	2.24E-02	-1.97	4.86E-02
Whole Blood	<i>PMS2</i>	1.96	4.96E-02	2.05	4.04E-02

Supplementary Table 3 Differences in protein levels of top HD modifiers ascertained by Western blotting in HD patient and age-matched control brain tissues.

Protein	Tissue	P-value	Mean controls (SEM)	Mean HD (SEM)
<i>CHCHD2</i>	Caudate nucleus	0.9717	1.000 ± 0.2874 N=5	0.9855 ± 0.2720 N=5
<i>EIF2AK1</i>	Caudate nucleus	0.0015	1.000 ± 0.1441 N=9	0.3635 ± 0.08275 N=9
<i>FAN1</i> (67 KDa)	Caudate nucleus	0.1974	1.000 ± 0.09031 N=5	0.7648 ± 0.1408 N=5
<i>FAN1</i> (150 KDa)	Caudate nucleus	0.0537	1.000 ± 0.2186 N=5	0.3878 ± 0.1598 N=5
<i>GPR161</i>	Caudate nucleus	0.005	1.000 ± 0.1061 N=5	0.4514 ± 0.09592 N=5
<i>MSH3</i>	Caudate nucleus	0.0399	1.000 ± 0.1758 N=10	0.5389 ± 0.06528 N=8
<i>MTMR10</i>	Caudate nucleus	0.0098	1.000 ± 0.1557 N=9	2.027 ± 0.4595 N=8
<i>RRM2B</i>	Caudate nucleus	0.2076	1.000 ± 0.1634 N=10	0.7273 ± 0.1230 N=9
<i>SUMF2</i>	Caudate nucleus	0.1861	1.000 ± 0.1025 N=10	0.8275 ± 0.06616 N=9
<i>PMS2</i>	Caudate nucleus	0.1104	1.000 ± 0.3046 N=5	0.3972 ± 0.1413 N=5
<i>CHCHD2</i>	Cortex	0.3069	1.000 ± 0.2875 N=5	1.517 ± 0.3763 N=5
<i>EIF2AK1</i>	Cortex	0.8529	1.000 ± 0.1051 N=8	0.9685 ± 0.1294 N=8
<i>FAN1</i> (67 KDa)	Cortex	0.0004	1.000 ± 0.06128 N=5	0.5207 ± 0.03467 N=4
<i>FAN1</i> (150 KDa)	Cortex	0.0491	1.000 ± 0.1111 N=5	0.6642 ± 0.07271 N=4
<i>GPR161</i>	Cortex	0.1359	1.000 ± 0.1401 N=5	0.6592 ± 0.1426 N=4
<i>MSH3</i>	Cortex	0.9874	1.000 ± 0.1928 N=8	0.9952 ± 0.2292 N=7
<i>MTMR10</i>	Cortex	0.0071	1.000 ± 0.08882 N=8	0.6145 ± 0.08408 N=8
<i>RRM2B</i>	Cortex	0.0702	1.000 ± 0.1748 N=8	0.6031 ± 0.07778 N=7
<i>SUMF2</i>	Cortex	0.0321	1.000 ± 0.09093 N=8	0.6993 ± 0.08441 N=7
<i>PMS2</i>	Cortex	0.017	1.000 ± 0.1214 N=7	0.6348 ± 0.05137 N=7

N, sample size; SEM, standard error of the mean

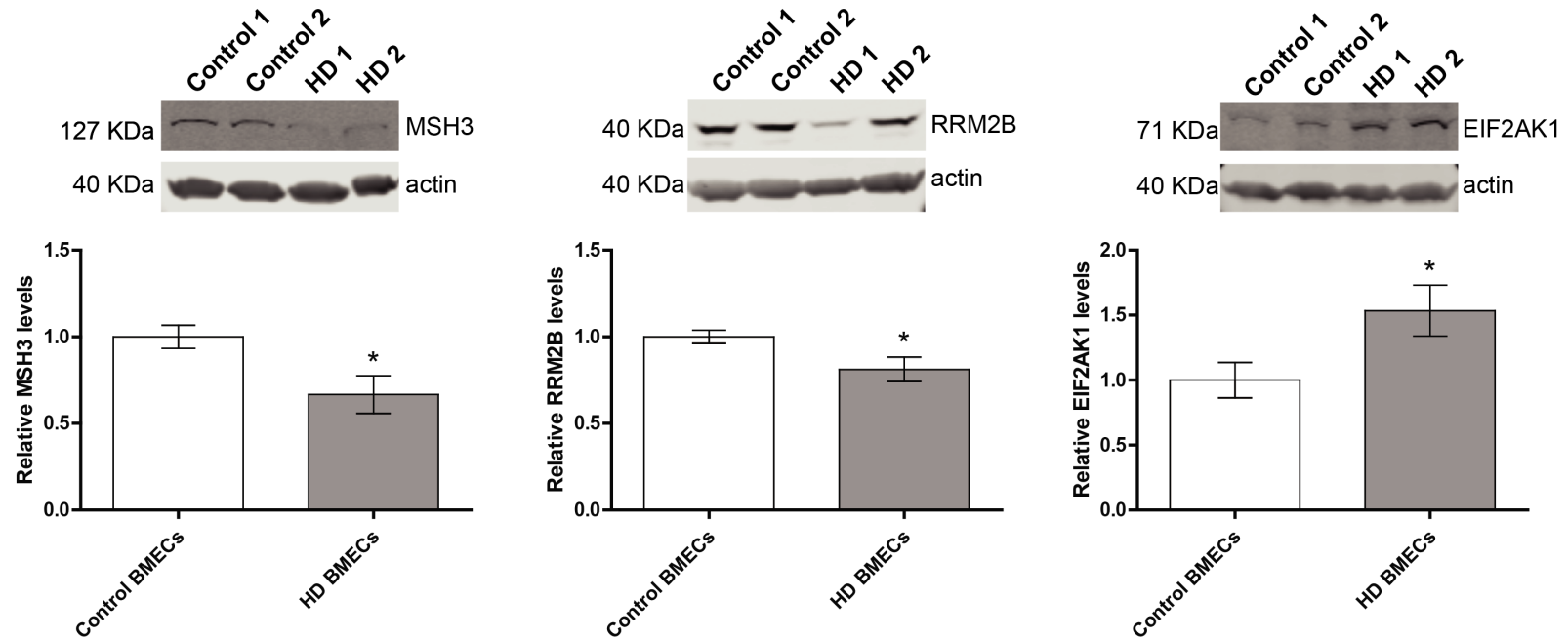


Supplementary Fig. 3 Gene-gene functional interaction network for *GPR151* and *GPR161* to identify potential shared biological pathways between these two candidate HD clinical modifier genes. GeneMania network analysis of these two G protein-coupled receptors indicated enrichment activation of phospholipase C activity and the serotonin receptor signaling pathway.

Supplementary Table 4 Differences in protein levels of top HD modifiers ascertained by Western blotting in HD and control brain microvascular endothelial cells (BMECs).

Protein	P-value	Mean controls (SEM)	Mean HD (SEM)
CHCHD2	0.4491	1.000 ± 0.2146 N=6	0.7545 ± 0.2259 N=6
EIF2AK1	0.0355	1.000 ± 0.1357 N=12	1.535 ± 0.1966 N=12
FAN1	0.6431	1.000 ± 0.06735 N=12	0.9434 ± 0.09993 N=12
GPR161	0.526	1.000 ± 0.04335 N=11	1.070 ± 0.09644 N=12
MSH3	0.0134	1.000 ± 0.06632 N=12	0.6667 ± 0.1089 N=10
MTMR10	0.161	1.000 ± 0.05193 N=12	0.7575 ± 0.1589 N=12
RRM2B	0.0291	1.000 ± 0.03859 N=12	0.8124 ± 0.07049 N=12
SUMF2	0.291	1.000 ± 0.08431 N=12	0.8720 ± 0.08294 N=12
PMS2	0.2306	1.000 ± 0.1012 N=12	0.8151 ± 0.1101 N=11

N, sample size; SEM, standard error of the mean



Supplementary Fig. 4 Top candidate HD modifier proteins are dysregulated in brain microvascular endothelial cells (BMECs) derived from human pluripotent stem cells. Relative protein levels of MSH3 and RRM2B are significantly decreased in HD patient derived BMECS compared to controls, while EIF2AK1 is significantly upregulated in HD BMECs. Asterisks indicate $P < 0.05$.

Supplementary Table 5 Enrichment analyses of S-PrediXcan associations for modifiers of the clinical onset of Huntington disease for diverse gene sets arranged by significance levels.

Gene list	Description*	Reference(s) ^a	Top 5 genes ^b	Genes in set	Mean Z ² -score of gene set members	Mean Z ² -score of other genes	P-value	Corrected P-value
GWAS Catalog	Closest gene 3' and 5' of GWAS hits in the NHGRI GWAS Catalog as of Feb 9, 2015	www.genome.gov/gwastudies PMID: 24316577	<i>HCN4</i> <i>RBM6</i> <i>AKR1C4</i> <i>CYP27C1</i> <i>STX2</i>	4081	0.95	0.97	7.6 x 10 ⁻⁸	1.3 x 10⁻⁶
Drug targets (Nelson <i>et al.</i>)	Drug targets according to Nelson <i>et al.</i> 2012	PMID: 16376820 PMID: 22604722	<i>CHRNA5</i> <i>NOS2</i> <i>GSK3B</i> <i>TRPM8</i> <i>CTLA4</i>	201	1.18	0.97	1.7 x 10 ⁻⁶	2.9 x 10⁻⁵
DNA Repair Genes (Wood <i>et al.</i>)	Human DNA repair genes from Wood <i>et al.</i>	PMID: 15922366	<i>MSH3</i> <i>PMS1</i> <i>PMS2</i> <i>ERCC3</i> <i>UBE2B</i>	178	1.27	0.96	3.5 x 10 ⁻⁵	0.00059
ClinGen haplo-insufficient genes	Genes with sufficient evidence for dosage pathogenicity (level 3) as determined by the ClinGen Dosage Sensitivity Map	www.ncbi.nlm.nih.gov/projects/dbvar/clingen/	<i>SETD5</i> <i>PTCH1</i> <i>TWIST1</i> <i>NR5A1</i> <i>PTPN11</i>	221	1.08	0.97	0.00012	0.002
Genes with any disease association reported in ClinVar	Genes where there is at least one variant with an assertion of pathogenic or likely pathogenic in ClinVar	PMID: 24234437	<i>HCN4</i> <i>MSH3</i> <i>DPM2</i> <i>PMS1</i> <i>SQSTM1</i>	3078	1.01	0.96	0.00041	0.007
All autosomal dominant	Autosomal dominant genes according to	PMID: 22995991	<i>HCN4</i> <i>FXVD2</i> <i>PMS1</i>	709	1.09	0.96	0.0011	0.019

	either Berg <i>et al.</i> or Blekhman <i>et al.</i>	PMID: 18571414	<i>SQSTM1</i> <i>PMS2</i>					
DNA Repair Genes (Kang <i>et al.</i>)	DNA repair genes from DNA repair pathways: ATM, BER, FA/HR, MMR, NHEJ, NER, TLS, XLR, RECQ, and other.	PMID: 22505474	<i>MSH3</i> <i>PMS1</i> <i>PMS2</i> <i>ERCC3</i> <i>UBE2B</i>	151	1.22	0.97	0.0032	0.054
GPCRs	GPCR list from guidetopharmacology.org	PMID: 24234439	<i>HCN4</i> <i>FXVD2</i> <i>KCNK16</i> <i>MST1R</i> <i>NR1I2</i>	1705	0.94	0.97	0.0043	0.072
Kinases	From UniProt (pkinfam)	PMID: 10647936 PMID: 12471243 PMID: 17557329	<i>MST1R</i> <i>PHKG1</i> <i>CAMKV</i> <i>ULK3</i> <i>GRK6</i>	351	0.94	0.97	0.0045	0.076
All autosomal recessive	Autosomal recessive genes according to either Berg <i>et al.</i> or Blekhman <i>et al.</i>	PMID: 22995991 PMID: 18571414	<i>ERCC3</i> <i>NDUFAF3</i> <i>AMT</i> <i>MPI</i> <i>ASH1L</i>	1183	0.98	0.97	0.045	0.76
Olfactory receptors	Olfactory receptors from the Mainland <i>et al.</i> 2015	PMID: 25977809	<i>OR52D1</i> <i>OR56B1</i> <i>OR6T1</i> <i>OR51S1</i> <i>OR51I2</i>	371	0.87	0.97	0.047	0.8
Natural product targets	List of hand-curated targets of natural products	PMID: 20565092	<i>GSK3B</i> <i>MAP2K1</i> <i>JAK1</i> <i>PPIA</i> <i>POLD1</i>	37	0.86	0.97	0.24	1

Essential in mice	Genes where homozygous knockout in mice results in pre-, peri- or post-natal lethality	PMID: 21051359 PMID: 23675308 PMID: 23843252	<i>HCN4</i> <i>NKX2-2</i> <i>SRSF3</i> <i>DDX20</i> <i>ERCC3</i>	2454	0.97	0.97	0.25	1
BROCA Cancer Risk Panel	Panel used for the evaluation of patients with a suspected hereditary cancer predisposition	http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm	<i>PMS2</i> <i>PTCH1</i> <i>CTNNA1</i> <i>FLCN</i> <i>PDGFRA</i>	66	1.25	0.97	0.36	1
FDA-approved drug targets	Genes whose protein products are known to be the mechanistic targets of FDA-approved drugs	PMID: 24203711 PMID: 21059682 PMID: 18048412 PMID: 16381955	<i>FXRD2</i> <i>ATP4A</i> <i>TRPM8</i> <i>P2RY12</i> <i>CTLA4</i>	286	0.96	0.97	0.4	1
Essential in culture	Genes deemed essential in multiple cultured cell lines based on shRNA screen data	PMID: 24987113	<i>SRSF3</i> <i>NAPSA</i> <i>EIF2S2</i> <i>HSPG2</i> <i>NAPG</i>	285	0.97	0.97	0.62	1
ACMG V2.0	Recommended for reporting of secondary findings in clinical sequencing by ACMG	PMID: 27854360	<i>PMS2</i> <i>BRCA2</i> <i>TSC1</i> <i>MUTYH</i> <i>BMPR1A</i>	59	1.34	0.97	0.85	1

Significantly enriched gene lists after Bonferroni correction for multiple testing are indicated in bold. **Abbreviations:** ACMG, American College of Medical Genetics and Genomics; FDA, Food and Drug Administration; GPCR, G-protein-coupled receptor; GWAS, genome-wide association study; NHGRI, National Human Genome Research Institute; PMID, PubMed identifier. ^aDerived from https://github.com/macarthur-lab/gene_lists (downloaded November 2017) ^bAccording to absolute mean Z-score across all tissues.

Supplementary Table 6 Analysis of *Htt* CAG length and age dependent gene expression modules for enrichment of S-PrediXcan associations for modifiers of the clinical onset of Huntington disease. Striatal modules M1 and M20, both associated with increased expression at higher CAG lengths at increased ages were significantly enriched.

Module	Number of genes in module	Top 5 genes ^a	Mean Z ² -score of module list members	Mean Z ² -score of other genes	P-value	Corrected P-value
Striatum M1	185	<i>EIF2AK1</i> <i>TRAP1</i> <i>LRPPRC</i> <i>NAPG</i> <i>RNF14</i>	1.26	0.96	8.70 x 10 ⁻¹²	1.60 x 10⁻¹⁰
Striatum M20	652	<i>SUMF2</i> <i>MSH3</i> <i>FAM219B</i> <i>C22orf23</i> <i>ERCC3</i>	1.08	0.96	0.00017	0.003
Striatum M34	142	<i>SRR</i> <i>ZNF667</i> <i>RUNX1T1</i> <i>ZSCAN20</i> <i>TBL1XR1</i>	0.89	0.97	0.0065	0.12
Cortex M4	282	<i>ODF4</i> <i>RHOQ</i> <i>CINP</i> <i>GPR126</i> <i>CPNE9</i>	0.92	0.97	0.0075	0.13
Striatum M43	197	<i>NICN1</i> <i>TEPP</i> <i>FUCA2</i> <i>POLR3C</i> <i>TLL12</i>	0.99	0.96	0.01	0.19
Cortex M2	76	<i>ANKRD63</i> <i>NFATC2</i> <i>EPYC</i> <i>SUSD2</i>	1.03	0.97	0.039	0.7

		<i>SH3RF2</i>				
Striatum M52	79	<i>CPT1A</i> <i>OGDH</i> <i>NT5C1A</i> <i>FNIP2</i> <i>PTPN22</i>	0.87	0.97	0.2	1
Cortex M6	226	<i>HCN4</i> <i>CPA6</i> <i>FAM19A3</i> <i>RD3L</i> <i>SH3BGR</i>	0.98	0.97	0.22	1
Striatum M11	203	<i>PHKG1</i> <i>TENC1</i> <i>DCN</i> <i>JUN</i> <i>PARP3</i>	0.91	0.97	0.23	1
Striatum M25	116	<i>RHOQ</i> <i>CD93</i> <i>PRICKLE1</i> <i>FLYWCH1</i> <i>LRRFIP2</i>	0.99	0.97	0.34	1
Striatum M7	224	<i>NKX2-2</i> <i>LARS</i> <i>HSPB6</i> <i>SCCPDH</i> <i>FGL2</i>	0.96	0.97	0.43	1
Striatum M2	1583	<i>WRB</i> <i>PARS2</i> <i>AMT</i> <i>ANKRD63</i>	0.94	0.97	0.57	1
Striatum M46	143	<i>ZC3H14</i> <i>ADNP</i> <i>SLC35A3</i> <i>FAM120B</i>	0.92	0.97	0.66	1

		<i>DHX57</i>				
Striatum M39	245	<i>AP3S2</i> <i>DPYSL3</i> <i>ANKRD61</i> <i>ABCA7</i> <i>PCDHB2</i>	0.96	0.97	0.71	1
Striatum M9	328	<i>SQSTM1</i> <i>ORMDL1</i> <i>EIF2B2</i> <i>ATP5G1</i> <i>P4HTM</i>	0.94	0.97	0.76	1
Cortex M45	87	<i>PHKG1</i> <i>GRAMD3</i> <i>C1orf110</i> <i>DDAH1</i> <i>CHPT1</i>	0.99	0.97	0.77	1
Striatum M10	145	<i>CCT6A</i> <i>GPM6A</i> <i>PTPN9</i> <i>KPNA4</i> <i>KLHL7</i>	0.90	0.97	0.81	1
Cortex M7	101	<i>CLIC4</i> <i>GALNT6</i> <i>PSAT1</i> <i>MARCH8</i> <i>TMEM88B</i>	0.89	0.97	0.94	1

Significantly enriched modules after Bonferroni correction for multiple testing are highlighted in grey. ^aAccording to absolute mean Z-score across all tissues.

Gene functional enrichment analyses for significantly associated modules (from Langvelder et al. 2016):

M1 striatum IPA: Protein ubiquitination pathway; tRNA charging; Huntington's disease signaling.

Gene ontology (GO): Purine nucleotide binding; Cellular protein localization; Ubl conjugation pathway.

M20 striatum IPA: p53 signaling; *Brca1* in DNA damage response.

GO: Cell division; Protocadherin beta; Zinc finger, CH2H-like

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Supplementary Table 7 Analysis gene expression consensus modules ($n=47$) from postmortem dorsal lateral prefrontal cortex in ROSMAP participants (Mostafavi *et al.* 2018) identified 15 modules with significant differences S-PrediXcan mean Z^2 -scores for modifiers of the clinical onset of Huntington disease. The table is sorted by strength of association with modules enriched in the Huntington disease related associations highlighted in grey.

Module	Number of genes in module	Top 5 genes ^a	Mean Z^2 score of module list members	Mean Z^2 score of other genes	P -value	Corrected P -value
107	376	<i>RHOA</i> <i>FAM219B</i> <i>PFKFB2</i> <i>TMEM100</i> <i>SCRG1</i>	0.84	0.97	1.1×10^{-12}	5.5×10^{-11}
109	335	<i>NKX2-2</i> <i>MED1</i> <i>RHOQ</i> <i>HEY2</i> <i>FLCN</i>	0.83	0.97	1.1×10^{-11}	5.2×10^{-10}
106	411	<i>PHKG1</i> <i>AMT</i> <i>CCDC82</i> <i>CMTM8</i> <i>DBT</i>	1.05	0.97	3.1×10^{-9}	1.5×10^{-7}
108	255	<i>TRIOBP</i> <i>PTCH1</i> <i>TUFM</i> <i>TMEM216</i> <i>NWD1</i>	1.11	0.97	2.5×10^{-7}	1.2×10^{-5}
1	427	<i>DPM2</i> <i>P4HTM</i> <i>LSMD1</i> <i>LSM7</i> <i>SH3GLB2</i>	0.89	0.97	3.6×10^{-7}	1.8×10^{-5}

114	232	<i>STX2</i> <i>DLL4</i> <i>MYL6</i> <i>SH3BGR</i> <i>HEATR2</i>	1.11	0.97	2.1×10^{-6}	0.0001
131	25	<i>MDH1</i> <i>SEC31A</i> <i>TOMM70A</i> <i>CD200</i> <i>CMAS</i>	1.43	0.97	4.1×10^{-6}	0.0002
257	37	<i>CYB561D2</i> <i>IFT52</i> <i>DOPEY1</i> <i>PIGT</i> <i>POLDIP2</i>	0.79	0.97	1.5×10^{-5}	0.0007
14	277	<i>ATP5G1</i> <i>DSCAML1</i> <i>ANKRD39</i> <i>ASNS</i> <i>BNIP1</i>	0.85	0.97	3.7×10^{-5}	0.002
233	39	<i>MRPS18A</i> <i>EIF1AD</i> <i>BRK1</i> <i>HMGA1</i> <i>ZNF622</i>	0.68	0.97	4.1×10^{-5}	0.002
16	305	<i>CAMKV</i> <i>C1QTNF4</i> <i>ZER1</i> <i>FBLL1</i> <i>FAM212B</i>	1	0.97	4.5×10^{-5}	0.002
122	306	<i>EIF2AK1</i> <i>PMS2</i> <i>ERCC3</i> <i>QRICH1</i> <i>CCZ1</i>	1.16	0.96	4.8×10^{-5}	0.002

117	373	<i>SRSF3</i> <i>ASNSD1</i> <i>EIF2B2</i> <i>TIGD7</i> <i>MOB1B</i>	0.89	0.97	1.9×10^{-4}	0.009
11	13	<i>DCLRE1C</i> <i>CNOT2</i> <i>ZNF232</i> <i>RHOA</i> <i>ADAL</i>	0.66	0.97	2.0×10^{-4}	0.010
2	412	<i>SUMF2</i> <i>ZNF75A</i> <i>AP3S2</i> <i>MAP3K13</i> <i>CCZ1B</i>	1.02	0.97	0.0003	0.013

Significantly enriched modules after Bonferroni correction for multiple testing are highlighted in grey.

^aAccording to absolute mean Z-score across all tissues.

Supplementary Table 8 Associations between ROSMAP cortical coexpression modules and phenotypes that passed within trait Bonferroni correction for multiple testing.

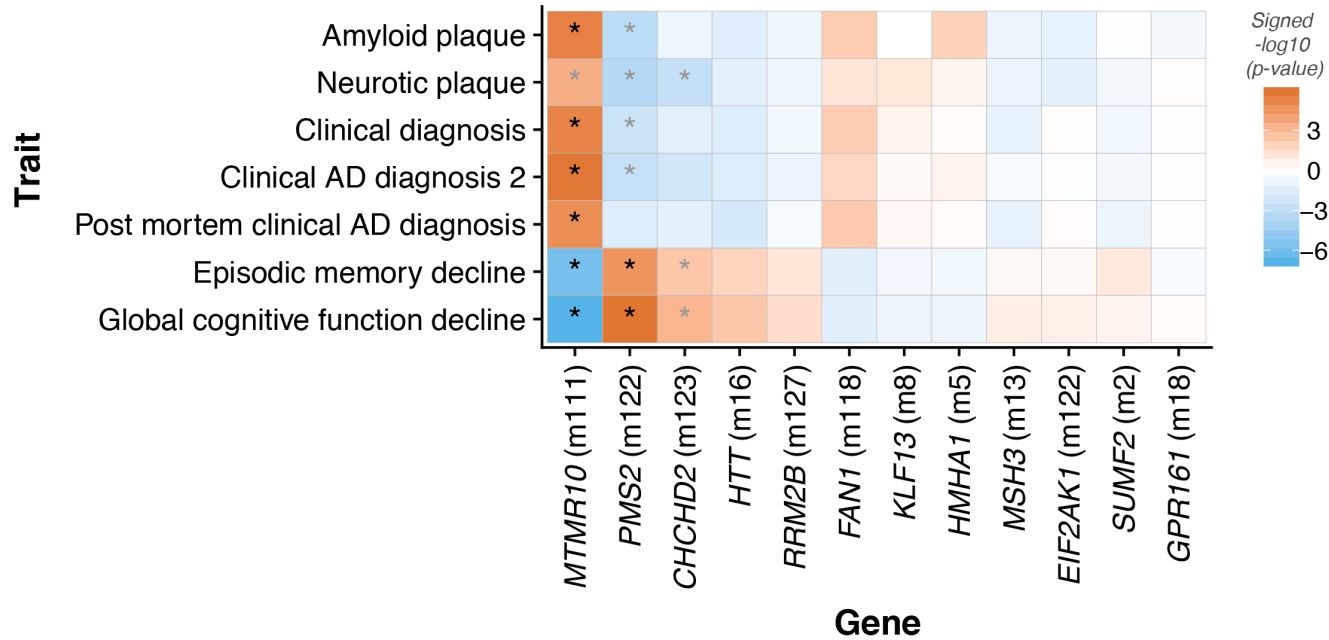
Module	Trait	Category	N	Estimate	SE	Statistic	P-value
m131	Estimated slope from random effects model for working memory	Cognitive Decline	470	0.35	0.06	5.91	6.72E-09
m131	Mini-Mental State Exam, 30 item	Cognitive Decline	494	53	10	5.12	4.46E-07
m122	Global burden of AD pathology based on 5 regions	Pathology	494	-5.8	1.2	-4.9	1.31E-06
m131	Global cognitive function - Average of 19 tests	Cognitive Decline	493	6.5	1.3	4.89	1.35E-06
m131	Estimated slope from random effects model for perceptual speed	Cognitive Decline	457	0.43	0.094	4.57	6.41E-06
m114	Estimated slope from random effects model for working memory	Cognitive Decline	470	-0.37	0.086	-4.31	2.02E-05
m122	Estimated slope from random effects model for semantic memory	Cognitive Decline	461	1	0.23	4.3	2.08E-05
m114	Estimated slope from random effects model for perceptual speed	Cognitive Decline	457	-0.57	0.13	-4.3	2.13E-05
m114	Mini-Mental State Exam, 30 item	Cognitive Decline	494	-63	15	-4.26	2.47E-05
m131	Estimated slope from random effects model for global cognition	Cognitive Decline	470	0.52	0.12	4.25	2.60E-05
m122	NIA Reagan Diagnosis of Alzheimer's disease - 4 levels (none to high likelihood)	Pathology	494	6	1.4	4.23	2.78E-05
m122	Global cognitive function - Average of 19 tests	Cognitive Decline	493	9.1	2.2	4.18	3.48E-05
m122	Estimated slope from random effects model for global cognition	Cognitive Decline	470	0.84	0.2	4.18	3.50E-05
m122	Neuritic plaque summary based on 5 regions	Pathology	494	-26	6.2	-4.14	4.07E-05
m122	Diffuse plaque summary based on 5 regions	Pathology	494	-26	6.5	-4.1	4.92E-05

m108	Estimated slope from random effects model for working memory	Cognitive Decline	470	-0.32	0.078	-4.08	5.40E-05
m122	Estimated slope from random effects model for perceptual speed	Cognitive Decline	457	0.62	0.15	4	7.38E-05
m131	Parkinsonian signs domain: Gait	Motor and Gait	491	-100	26	-3.88	0.00012
m16	Motor function partial composite: Hand strength	Motor and Gait	465	1.7	0.45	3.81	0.00016
m114	Global cognitive function - Average of 19 tests	Cognitive Decline	493	-7.1	1.9	-3.73	0.000215
m122	Mini-Mental State Exam, 30 item	Cognitive Decline	494	63	17	3.72	0.000223
m122	Estimated slope from random effects model for episodic memory	Cognitive Decline	469	0.76	0.21	3.7	0.00024
m114	Estimated slope from random effects model for global cognition	Cognitive Decline	470	-0.64	0.17	-3.67	0.00027
m106	Motor function partial composite: Hand strength	Motor and Gait	465	-2.1	0.57	-3.64	0.000304
m16	Perceived social isolation (loneliness)	Lifestyle, Personality	202	-5	1.4	-3.58	0.000428
m108	Motor function partial composite: Hand strength	Motor and Gait	465	-1.7	0.48	-3.44	0.00064
m131	Estimated slope from random effects model for episodic memory	Cognitive Decline	469	0.43	0.13	3.43	0.000667
m131	Perceived social isolation (loneliness)	Lifestyle, Personality	202	-4.3	1.2	-3.45	0.00069
m131	Global burden of AD pathology based on 5 regions	Pathology	494	-2.4	0.74	-3.31	0.00101
m114	Perceived social isolation (loneliness)	Lifestyle, Personality	202	6.1	1.8	3.34	0.00102
m131	Estimated slope from random effects model for semantic memory	Cognitive Decline	461	0.47	0.14	3.25	0.00122
m108	Mini-Mental State Exam, 30 item	Cognitive Decline	494	-44	13	-3.25	0.00123
m114	NIA Reagan Diagnosis of Alzheimer's disease - 4 levels (none to high likelihood)	Pathology	494	-4	1.2	-3.22	0.00138

m114	Estimated slope from random effects model for semantic memory	Cognitive Decline	461	-0.65	0.2	-3.18	0.00157
m114	Estimated slope from random effects model for episodic memory	Cognitive Decline	469	-0.57	0.18	-3.17	0.00162
m131	NIA Reagan Diagnosis of Alzheimer's disease - 4 levels (none to high likelihood)	Pathology	494	2.7	0.87	3.14	0.00177
m108	Global cognitive function - Average of 19 tests	Cognitive Decline	493	-5.4	1.7	-3.14	0.00182
m114	Actical sleep measure - Probability of transitioning from rest state to active state	Sleep and Circadian Rhythms	95	0.13	0.04	3.17	0.00204
m131	Neuritic plaque summary based on 5 regions	Pathology	494	-12	3.8	-3.05	0.00242
m131	Diffuse plaque summary based on 5 regions	Pathology	494	-12	4	-3.02	0.00262
m122	Estimated slope from random effects model for working memory	Cognitive Decline	470	0.3	0.1	2.99	0.00291
m114	Neuritic plaque summary based on 5 regions	Pathology	494	16	5.4	2.98	0.00303
m114	Diffuse plaque summary based on 5 regions	Pathology	494	17	5.7	2.96	0.00321
m114	Global burden of AD pathology based on 5 regions	Pathology	494	3	1.1	2.86	0.00441

Supplementary Table 9 Associations between expression of top transcriptomic modifier genes in the ROSMAP cortical samples and phenotypes that passed within trait Bonferroni correction for multiple testing.

Gene	Trait	Signed $-\log_{10}(P\text{-value})$	<i>P</i>-value
<i>MTMR10</i>	Global cognitive function decline	-6.91	1.24E-07
<i>PMS2</i>	Global cognitive function decline	5.89	1.28E-06
<i>MTMR10</i>	Episodic memory decline	-5.87	1.35E-06
<i>MTMR10</i>	Clinical AD diagnosis 2	5.83	1.48E-06
<i>MTMR10</i>	Amyloid plaque	5.41	3.86E-06
<i>MTMR10</i>	Clinical diagnosis	5.27	5.32E-06
<i>MTMR10</i>	Post mortem clinical AD diagnosis	4.82	1.50E-05
<i>PMS2</i>	Episodic memory decline	4.58	2.63E-05
<i>MTMR10</i>	Neurotic plaque	3.47	0.000341
<i>PMS2</i>	Neurotic plaque	-3.40	0.000398
<i>PMS2</i>	Amyloid plaque	-3.17	0.000684
<i>CHCHD2</i>	Global cognitive function decline	3.15	0.000708
<i>CHCHD2</i>	Neurotic plaque	-2.76	0.00172
<i>PMS2</i>	Clinical AD diagnosis 2	-2.73	0.00188
<i>PMS2</i>	Clinical diagnosis	-2.53	0.00292
<i>CHCHD2</i>	Episodic memory decline	2.43	0.0036



Supplementary Fig. 5 Analysis of top transcriptomic modifier genes for Huntington disease clinical onset, as well as *HTT*, with regards to a subset of the phenotypes. Expression of *MTMR10* and *PMS2* was associated with a variety of phenotypes, decline in global cognitive function achieving greatest statistical significance. Black asterisks: significant after correcting for all comparisons, grey asterisks: significant after adjusting for within trait comparisons. AD, Alzheimer's disease.

Supplementary Table 10. Top perturbagens similar (>95%) and dissimilar (<95%) perturbagens in the signature matching analyses of HD gene expression TWAS profiles to the Connectivity Map database.

Type	Name	Median tau	PC3	VCAP	A375	A549	HA1E	HCC515	HT29	MCF7	HEPG2	Summary
CP	CGP-60474	99.69	99.56	99.96	99.63	99.74	98.42	99.73	99.85	99.65	99.74	99.05
KD	SLC25A28	99.67	99.82	NA	86.75	67.58	99.73	NA	65.72	99.61	99.95	99.92
CP	chromomycin-a3	99.64	99.71	60.31	99.81	99.19	99.65	99.54	99.63	99.76	99.86	99.01
CP	ER-27319	99.62	99.66	99.34	91.77	99.63	99.61	99.62	99.61	99.62	99.63	98.73
CP	mitoxantrone	99.6	99.6	99.03	99.63	83.06	99.6	99.75	99.76	99.43	NA	98.87
CP	alvocidib	99.59	99.56	92.28	99.66	99.64	99.64	99.34	99.63	99.48	99.66	98.66
CP	daunorubicin	99.58	99.24	99.85	99.65	99.76	98.85	99.87	99.6	99.53	99.56	98.63
CP	daunorubicin	99.57	99.6	95.74	99.65	99.79	99.58	99.45	99.6	99.55	99.42	98.63
CP	BRD-K77681376	99.56	99.34	NA	99.58	99.66	NA	99.53	99.65	98.14	99.66	98.66
CP	bisindolylmaleimide-ix	99.56	99.22	69.45	99.72	99.55	99.57	99.57	99.68	99.49	99.56	98.63
CP	triptolide	99.56	99.63	99.93	97.25	99.68	99.51	99.61	99.44	99.48	99.67	98.59
CP	AT-7519	99.54	99.52	98.8	99.67	99.56	99.68	99.63	99.9	99.42	99.4	98.77
CP	PIK-75	99.53	99.6	-91.14	99.81	97.72	99.87	99.51	99.61	99.53	99.54	98.66
CP	JNK-9L	99.53	99.66	97.16	99.47	99.62	99.68	99.51	99.55	99.26	99.7	98.66
CP	doxorubicin	99.52	99.52	85.76	99.95	93.95	99.65	99.63	86.24	99.72	NA	98.94
CP	daunorubicin	99.52	99.57	99.19	99.72	94.53	99.78	99.54	99.5	99.27	99.73	98.8
CP	pidorubicine	99.52	99.65	84.87	99.5	85.74	99.64	99.5	99.55	99.81	99.54	98.7
CP	triptolide	99.51	99.52	60.34	99.5	99.2	99.68	NA	99.93	99.68	NA	98.87
CP	dactinomycin	99.51	99.53	89.19	99.88	95.14	99.51	99.56	99.51	99.59	99.37	98.63
CP	PF-562271	99.51	99.63	NA	99.65	99.25	99.61	99.51	99.5	95.99	99.54	98.63
CP	ZG-10	99.51	99.53	99.87	99.59	95.02	99.64	99.48	99.64	99.49	99.46	98.56
CP	A-443644	99.43	99.66	61.92	95.42	99.73	99.38	99.69	99.59	72.21	99.48	98.66
CP	dactinomycin	99.43	99.62	92.65	99.39	99.62	99.77	97.84	99.73	93.78	99.47	98.56
CP	BRD-K85853281	99.4	99.59	80.7	99.42	99.66	91.83	99.37	99.68	99.32	99.54	98.63
KD	PLS1	99.38	99.92	NA	99.98	98.61	-86.05	99.96	30.51	99.38	90.58	99.95

Supplementary Information 25

KD	NFKBIB	99.37	99.98	100	99.62	94.05	96.27	86.29	99.61	99.13	99.12	99.82
CP	NVP-BEZ235	99.22	99.1	99.34	99.56	88.61	99.46	99.44	99.81	85.99	32.58	98.84
CP	lestaurtinib	99.19	99.66	99.91	85.7	99.86	98.89	99.5	98.81	97.43	99.5	98.7
CP	JNJ-7706621	99.18	99.45	97.25	99.59	77.57	93.51	98.92	99.56	99.53	99.59	98.52
CP	BRD-K53780220	99.17	92.01	88.67	99.17	32.89	NA	99.54	99.79	99.78	99.77	98.84
CP	idarubicin	99.16	99.5	90.32	99.67	99.33	99.58	NA	98.99	89.65	NA	98.63
CP	AZD-8055	99.08	99.8	99.43	99.89	74.58	99.11	99.57	98.52	99.05	93.96	98.79
CP	KU-0063794	99.03	99.11	99.67	97.07	50.14	98.42	99.69	99.25	99.76	-56.51	98.94
PCL	PI3K inhibitor	99	99.17	99.45	96.47	90.47	99.5	99.2	98.83	96.42	85.11	99.2
PCL	Topoisomerase inhibitor	98.98	99.49	89.67	98.62	91.59	96.78	99.57	99.4	95.6	99.52	99.33
CP	BMS-345541	98.92	43.56	95.19	-59.08	99.79	99.63	99.44	99.08	-93.03	99.75	98.77
KD	NUCKS1	98.91	94.97	45.69	99.66	65.91	83.06	NA	98.91	99.7	99.66	99.66
PCL	MTOR inhibitor	98.9	98.99	99.39	95.1	83.65	99.29	99.5	98.82	98.73	-72.56	99.22
CP	pirarubicin	98.87	98.87	78.79	99.49	93.09	96.55	99.47	98.87	99.71	99.44	98.38
CP	AS-601245	98.85	99.52	96.96	99.72	92.27	92.1	99.26	99.48	78.81	99.43	98.45
KD	PLAT	98.82	99.01	99.21	35.64	67.89	56.61	NA	37.43	98.91	98.82	99
KD	PLAUR	98.66	-60	NA	41.68	NA	98.85	NA	98.66	99.9	64.67	98.87
CP	5-iodotubercidin	98.65	99.89	81.51	99.8	98.73	88.77	99.41	99.62	76.17	94.22	98.56
KD	CTDSP1	98.64	-36	69.44	99.11	99.95	98.64	-71.1	-20.77	NA	99.81	99.82
CP	ISOX	98.52	85.03	98.84	94.62	98.24	94.99	99.25	99.14	50.64	99.5	98.8
KD	IL10RB	98.36	84.15	NA	66.49	NA	99.87	NA	98.36	99.75	65.38	99.89
KD	TNIP1	98.32	-28.03	54.95	-29.73	83.22	97.63	99.71	99.82	99.02	99.58	99.71
CP	PI-828	98.29	99.72	99.5	98.38	89.66	98.47	99.85	90.04	70.04	43.13	98.2
CP	apicidin	98.24	77.62	52.07	93.34	98.99	99.31	98.92	99.38	32.02	98.6	97.89
PCL	CDK inhibitor	98.2	99.95	66.89	92.12	73.37	99.54	99.44	97.24	99.17	84.96	99.55
CP	PHA-793887	98.15	99.65	58.51	95.71	69.02	98.81	98.19	99.5	99.09	84.92	98.1
CP	staurosporine	98.06	99.58	81.28	94.72	99.63	97.55	99.47	99.56	97.01	97.05	98.56
CP	purvalanol-a	97.99	98.4	90.69	24.29	66.23	98.98	99.18	-38.76	99.71	NA	97.99
CP	doxorubicin	97.97	99.57	77.44	98.62	69.48	99.52	99.9	97.59	91.56	97.64	98.31

Supplementary Information 26

KD	GTF2A2	97.82	99.53	-90.1	-72.83	99.15	99.73	NA	42.71	-18.11	97.82	99.82
KD	GMPS	97.81	97.45	98.16	99.26	83.02	91.75	96.39	98.94	99.79	97.13	99.55
CP	TPCA-1	97.72	96.2	99.91	98.42	45.83	98.42	98.57	97.67	-49.3	40.3	97.78
CP	AZD-7762	97.69	99.35	77.78	79.5	99.35	98.95	78.12	97.3	98.07	77.1	98.27
KD	PSEN1	97.67	99.96	97.67	79.38	99.93	44.07	62.69	99.96	NA	20.26	99.95
CP	fludarabine	97.67	99.12	NA	96.93	90.59	95.51	98.72	98.93	93.04	NA	98.41
KD	RALBP1	97.42	99.35	97.26	63.47	99.13	97.58	49.89	93.18	99.81	81.93	98.98
CP	L-690488	97.26	96.43	96.78	92.19	37.92	99.31	97.73	99.94	20.01	99.66	99.08
KD	RPS3	97.17	97.38	-99.14	96.97	99.78	84.9	65.08	99.23	-35.46	99.96	99.31
CP	fostamatinib	97.15	99.77	96.06	98.23	99.09	91.07	95.95	99.91	-85.51	-66.63	98.98
KD	RASA1	97.11	39.86	NA	98.13	31.33	37.65	NA	NA	98.32	97.11	99.53
KD	ZNF274	97.05	86.5	23.79	97.05	-83.49	56.82	99.34	NA	99.83	97.85	99.61
CP	PI-103	97.03	98.65	97.29	93.43	96.78	99.19	99.11	44.72	86.73	82.72	98.29
KD	IL2RB	96.89	99.35	100	63.14	68.2	99.82	50.66	70.18	96.89	NA	99.61
KD	UVRAG	96.84	-94.38	NA	96.84	99.29	99.98	-35.08	30	99.91	34.38	99.79
PCL	FLT3 inhibitor	96.81	99.69	97.86	91.36	91.88	96.86	99.81	94.08	99.37	-30.1	96.76
KD	NPTN	96.73	37.76	52.8	96.73	87.82	99.67	99.4	99.32	85.84	NA	99.53
KD	CBX6	96.69	96.69	81.2	22.24	96.43	99.89	NA	99.6	92.44	99.32	99.87
CP	U-0126	96.69	74.39	69.85	99.55	97.02	59.17	87.44	96.37	99.65	97.84	99.21
CP	temsirolimus	96.58	99.33	98.21	93.33	96.11	99	98.82	76.76	91.7	-40.57	97.04
KD	MED28	96.5	96.99	NA	95.84	27.88	96.01	NA	98.95	99.9	-39.55	98.82
CP	topotecan	96.48	99.45	95.81	98.25	70.99	36.68	99.48	96.48	90.29	NA	97.57
KD	CREBL2	96.47	92.23	NA	96.85	99.95	79.56	NA	91.06	99.36	96.08	98.67
KD	TARDBP	96.44	93.8	94.05	71.03	99.55	99.86	98.84	99.98	84.23	60.57	99.92
CP	trichostatin-a	96.44	91.81	81.8	96.63	98.77	98.23	96.25	91.7	75.96	99.13	97.08
KD	ZNF219	96.35	51.3	-95.84	93.44	98.59	97.56	NA	96.83	78.79	98.23	96.35
KD	NR2C2	96.02	96.02	NA	53.58	38.69	97.97	NA	NA	98.43	87.34	97.29
KD	ETV1	96.01	28.55	48.08	38.16	99.76	99.34	33.01	99.45	93.28	98.73	99.84
CP	doxorubicin	96	93.86	81.04	95.74	96.26	76.99	92.94	98.78	98.12	98.39	97.18

Supplementary Information 27

KD	CLCN5	95.98	98.02	100	93.82	93.94	80.13	NA	-23.74	NA	99.25	99.45
KD	ERGIC2	95.96	99.54	99.8	-33.76	92.62	28.14	85.78	NA	99.51	NA	99.29
KD	P4HA1	95.84	97.24	95.39	99.4	91.02	62.93	99.04	78.64	95.84	NA	99.53
KD	EIF2AK2	95.7	97.41	NA	98.62	NA	-93.74	NA	29.45	95.7	86.95	98.11
OE	PRAME	95.68	52.2	99.3	-26.5	92.73	99.96	98.63	99.96	-82.67	-81.88	99.91
KD	TACC3	95.68	63.25	27.85	99.36	97.86	99.12	NA	26	95.68	48.53	99.28
CP	PP-30	95.68	93.71	99.91	97.65	71.92	75.55	84.88	99.66	99.42	67.83	98.73
KD	ATP1A3	95.68	95.68	97.65	58.72	61.95	74.28	NA	97.75	91.58	97.89	97.8
KD	FZD5	95.61	98.78	100	84.3	-65.07	95.73	95.48	99.98	77.79	-76.59	98.97
KD	IRAK1	95.55	95.8	-99.17	74.69	NA	99.2	NA	20.76	95.29	97.9	97.61
CP	methotrexate	95.42	97.47	99.26	37.08	82.81	-45.53	NA	97.75	93.37	NA	97.78
CP	guanabenz	95.41	36.56	98.62	-32.95	-83.85	91.62	95.55	99.04	95.41	NA	98.13
KD	PSEN2	95.26	-41.11	34.83	NA	94.1	98.26	99.06	26.17	96.43	NA	98.47
KD	ZNF791	-95.11	-91.8	-46.84	-99.91	39.96	-98.6	-93.15	-99.45	-97.07	-36.98	-99.71
KD	LEPRE1	-95.21	-99.22	83.02	NA	-99.3	-67.41	NA	-77.69	-96.48	-93.94	-99.5
KD	UGT1A6	-95.26	62.74	-95.26	NA	-98.59	99.82	-97.88	-50.79	-34.29	-99.56	-97.74
KD	IRS2	-95.34	-58.82	NA	-20.09	-95.34	-94.75	NA	NA	-97.87	-97.13	-97.79
KD	UBE2C	-95.38	-98.95	-38.59	-93.62	-94.71	-91.75	-96.04	-99.13	-98.77	-20.85	-98.44
KD	SLC7A11	-95.56	-91.74	-99.39	-91.85	-84.24	-99.48	NA	NA	NA	NA	-99.28
KD	NCF2	-95.67	-99.17	NA	55.7	-82.34	-99.19	NA	-96.57	-94.78	-41.77	-99.76
KD	GPATCH8	-95.69	NA	NA	-97.25	-54	-99.58	-94.13	-99.16	-61.54	-84.48	-99.74
KD	GCDH	-95.8	-99.98	41.54	24.69	-95.8	-96.45	-98.47	-60.53	NA	-92.78	-98.47
KD	FOXA1	-95.85	-99.52	-95.85	44.77	-96.81	-68.75	-99.56	-51.33	-25.38	NA	-99.35
KD	MAP2K2	-95.87	-95.83	-98.49	39.01	-43.99	27.13	-95.9	-99.22	-98.77	-60.87	-99.21
CP	vinorelbine	-95.9	-61.1	-98.95	-95.61	-12.87	38.39	-96.52	-96.2	-99.65	46.62	-98.48
CP	diprotin-a	-95.91	-95.91	-70.2	NA	NA	-18.89	-98.44	NA	NA	NA	-97.13
KD	CAST	-95.95	-88.06	97.76	53.73	-99.26	-98.35	NA	81.07	-95.95	-98.88	-98.68
CP	NSC-632839	-95.98	-75.25	-98.61	-98.5	-82.67	-62.01	-97.41	-65.38	-99.84	-96.75	-95.21
KD	KCNN4	-95.98	-45.13	43.32	-99.34	-99.95	-93.39	NA	-75.53	-99.79	-95.98	-99.74

Supplementary Information 28

KD	GPSM2	-96.03	-98.13	-47.92	-85.19	-94.47	-99.41	NA	NA	-98.58	-36.55	-97.59
KD	ETV5	-96.05	91.51	-55.6	38.14	-99.47	-99.43	NA	-97.31	-96.05	-38.92	-99.79
KD	GAS7	-96.1	-90.92	-99.89	-58.44	NA	-94.49	NA	-97.71	-64.22	-99.92	-99.58
KD	CDC7	-96.14	-37.9	-26.5	-99.98	NA	NA	NA	-96.14	-84.26	-98.32	-98.63
CP	VU-0365114-2	-96.15	-99.78	-99.43	-36.81	-96.15	NA	-51.02	-98.04	57.02	-85.45	-98.45
CP	dihydroergotamine	-96.28	-50.48	-98.21	61.04	-89.8	-96.89	-64.85	-95.66	-99.98	-98.07	-99.93
KD	CARD11	-96.52	-96.34	91.89	-98.78	-90.81	-98.87	-52.66	-31.15	-96.71	-99.29	-99.75
KD	MCM7	-96.6	-99.62	-98.36	15.61	-99.86	-52.53	-23.64	-85.73	-94.84	-99.52	-99.92
CP	ruxolitinib	-96.66	-75.45	20.69	14.47	-98.26	-99.89	22.27	-99.23	-95.05	-99.88	-99.86
KD	FGFR4	-96.78	-97.59	99.42	-93.68	-99.84	NA	NA	-84.81	-95.97	-99.96	-99.4
KD	GNAQ	-96.92	-35.12	-94.13	-99.96	-95.24	-98.6	NA	NA	-81.64	-98.94	-99.61
KD	KSR2	-96.95	-96.95	-35.95	-29.2	60.33	-97.08	NA	37.55	-97.65	-99.69	-97.55
KD	METRN	-97.09	-99.83	24.46	-98.52	-95.66	51.55	-84.48	-99.96	-99.96	-92.76	-99.95
KD	APOC3	-97.23	-99.46	-99.93	-97.23	NA	-63.62	-99.07	28.87	-39.49	-20.55	-99.61
KD	HES5	-97.25	-69.37	-28.69	-99.4	-60.83	-37.7	-98.22	-99.96	-97.25	NA	-99.34
KD	HOXA9	-97.4	-98.01	NA	-96.79	-92.59	-82.5	NA	-99.98	-99.84	-83.83	-99.82
KD	IGSF8	-97.54	-66.41	-100	-98.16	-95.95	-73.67	-34.07	-96.91	-98.63	-99.97	-99.84
CP	tricitiribine	-97.56	-95.7	-99.63	-93.34	98.93	-35.27	-99.85	-26.97	-99.61	-99.41	-99.72
KD	KBTBD2	-97.7	NA	-96.45	-98.15	-97.7	-93.27	NA	NA	55.87	-99.46	-99.47
KD	CAPN1	-97.78	41.69	24.1	-98.38	-97.69	-97.86	-48.85	-99.98	-93.43	-99.93	-99.79
KD	ARHGEF2	-97.83	45.44	-76.34	-99.93	-99.95	-94.81	NA	-89.65	-97.83	-99.47	-99.87
CP	emetine	-97.91	-99.09	-99.69	-54.38	-98.85	-92.84	-97.3	-97.79	-99.58	-96.04	-98.03
CP	tricitiribine	-97.97	-97.92	73	-99.25	49.35	-98.03	-99.84	27.64	-90.44	-98.67	-99.44
KD	PCK2	-98.06	-38.64	-98.15	-98.06	-69.62	-47.87	-99.97	-99.94	-97.53	-98.05	-99.87
CP	MST-312	-98.24	-86.19	-98.18	-99.42	-99.83	-89	-43.09	-26.14	-99.92	-98.31	-99.33
KD	STUB1	-98.3	-98.3	-20.37	-98.17	-99.22	-98.46	55.94	NA	-98.21	-99.89	-99.74
KD	PCGF1	-98.42	-98.42	-87.04	71.82	-55.16	-99.64	NA	-99.83	-99.31	37.15	-99.92
KD	BCL2L1	-98.59	-99.6	-30.77	-99.86	-83.79	29.82	NA	-98.59	-32.19	-98.71	-99.92
KD	RXRB	-98.6	-90.88	-100	-99.79	-98.6	-99.95	NA	-66.17	28.11	-76.19	-99.95

Supplementary Information 29

KD	ARF6	-98.64	-99.95	26.07	-97.87	-93.08	-21.62	85.81	-99.98	-99.73	-99.4	-99.95
OE	PPIA	-98.65	51.32	-93.13	-99.42	65.73	-98.29	-99	-99.95	82.49	-99.96	-99.91
KD	GAS6	-98.81	-99.13	46.01	-98.86	-99.93	-98.77	59.08	38.71	-99.89	-71.92	-99.79
KD	LSP1	-98.83	-99.6	NA	-99.88	-98.83	-99.93	56.89	-71.12	-97.01	42.38	-99.92
CP	GW-843682X	-98.98	-99.84	-95.66	-99.76	-99.58	-97.72	-97.86	-75.84	-99.95	-98.38	-99.61
CP	kinetin-riboside	-99.23	-99.45	-77.29	-92.7	-99.48	-99.26	-99.87	-99.88	-97.11	-98.45	-99.19
KD	PTK2B	-99.34	-54.87	-99.15	-99.53	NA	NA	-35.39	-51.18	-99.82	-99.81	-99.67
KD	RTCD1	-99.69	-99.57	-99.89	-99.8	-96.69	-92.99	-99.91	49.8	-99.88	-36.08	-99.89
KD	SMARCA2	-99.85	-26.1	-100	NA	-91.96	-99.87	NA	63.61	-99.98	-99.82	-99.95

CP, compound; KD, gene knock-down; OE, gene overexpression; PCL, perturbational class