Supplemental data

Mutant huntingtin protein in Huntington's disease cerebrospinal fluid

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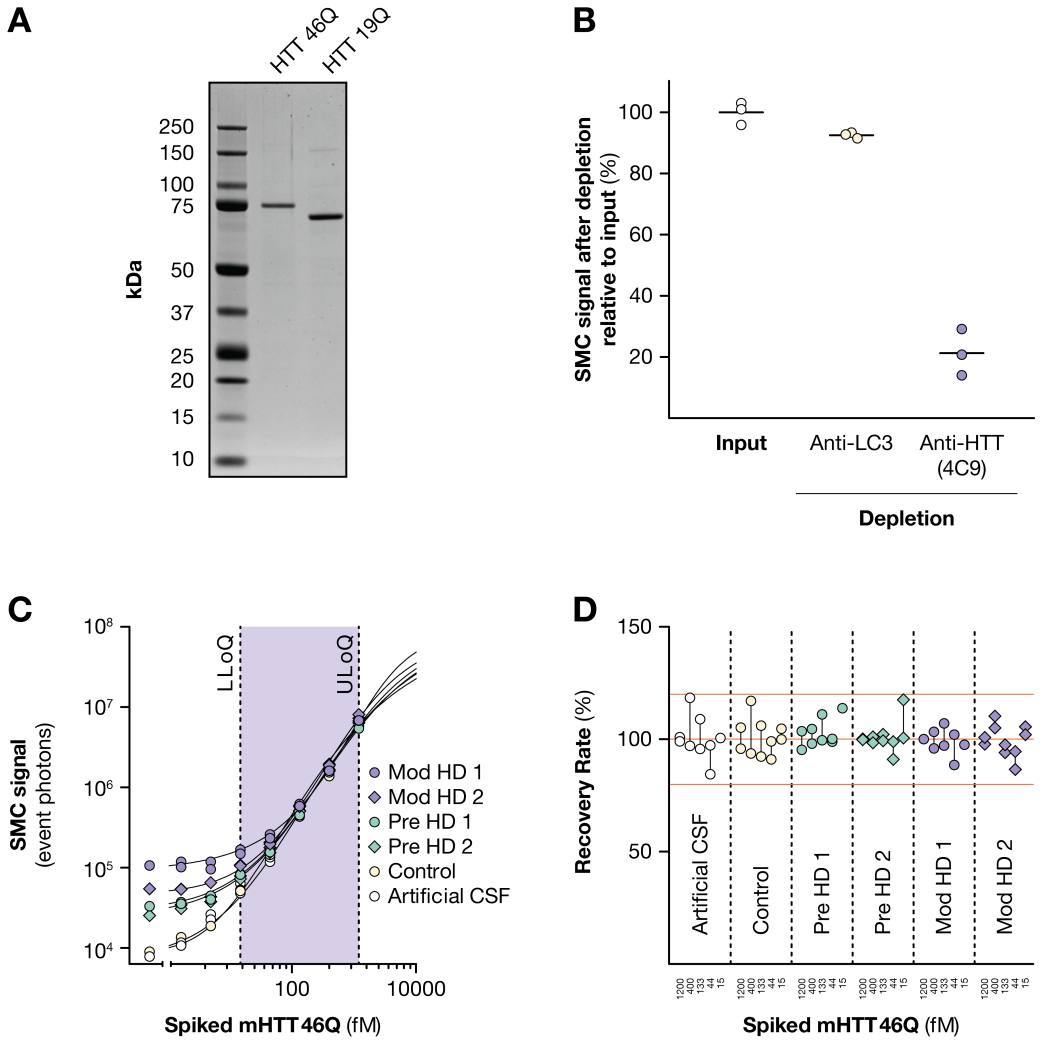
Supplemental data

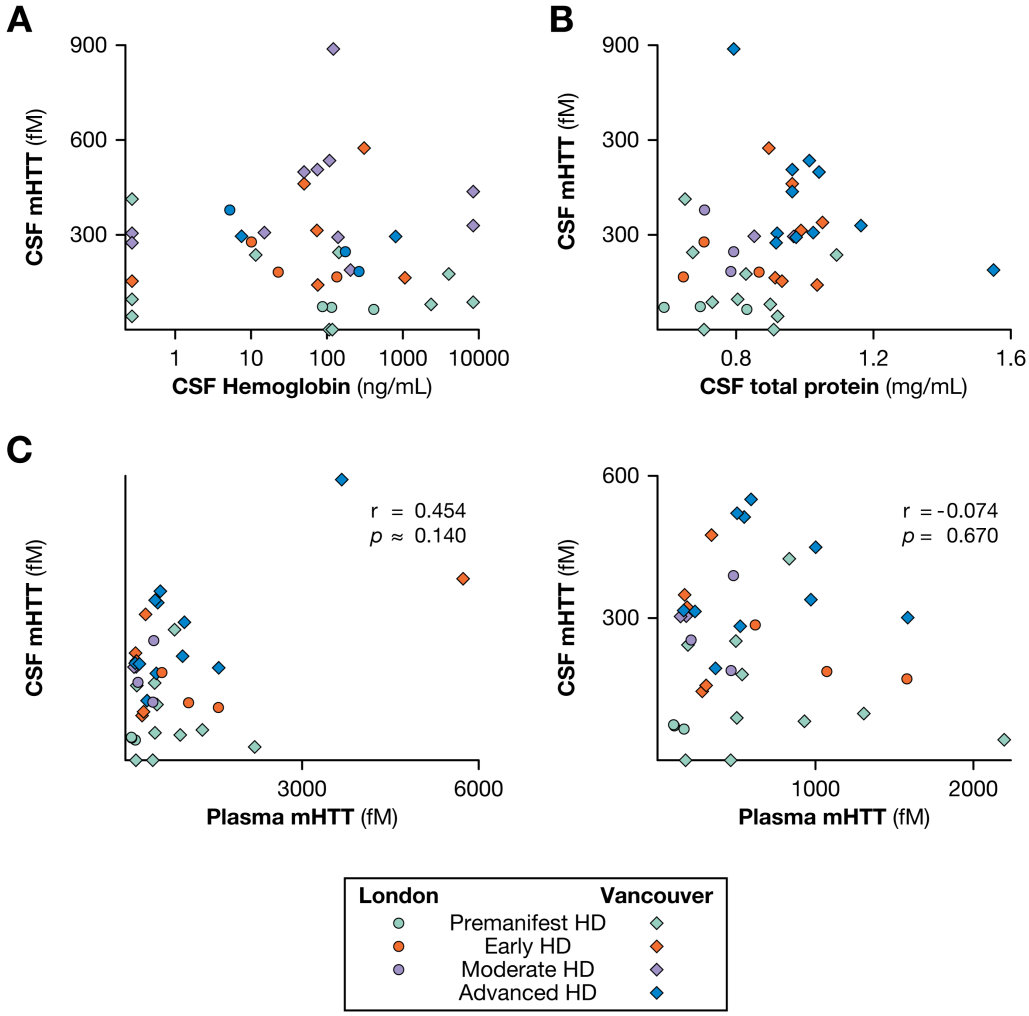
Supplemental figure 1



Supplemental Figure 1. A) Purity and quality control of recombinant N-terminal (N458) human wild-type (HTT 19Q) and mutant (HTT 46Q) huntingtin proteins shown by Coomassie blue SDS page gel. **B)** Immunodepletion experiment with a non-huntingtin control antibody (anti-LC3) and the anti-huntingtin antibody 4C9, designed against an epitope that is not recognized by either of the antibodies used in the detection assay, shows the specific detection of huntingtin protein by the assay (n=3 replications per experiment). **C-D)** Recovery rates of purified mutant huntingtin protein spiked into independent human CSF samples from healthy control,

premanifest Huntington's disease and moderate Huntington's disease patients (n=2 replications per sample).

Supplemental figure 2



Supplemental Figure 2. A) Relationship between CSF mHTT and CSF hemoglobin. Values outside the quantifiable range of the assay are shown as having the lower (n=6) and upper (n=3) quantifiable values. Spearman Rank analysis: n=9, r=-0.55, *p*=0.125 for London; n=29, r=0.01, *p*=0.945 for Vancouver. There was no statistically significant difference in hemoglobin values between the London and Vancouver cohorts (*p*=0.63 by Wilcoxon test). **B)** Relationship between CSF mHTT protein and CSF total protein. Linear regression: n=9, R=0.0816, *p*=0.835 for London; n=30, R=0.0376, *p*=0.844 for Vancouver. **C-D)** Relationship between matched CSF and plasma mHTT concentrations. No significant association was seen between CSF and

matched plasma mHTT concentrations **(C)** in the whole dataset (linear regression with 95% bootstrap confidence interval -0.145 to 0.740; n=38) or **(D)** after the exclusion of two extreme outliers (Linear regression: r=-0.074. *p*=0.670; n=36).

Supplemental table 1

A. Before controlling for disease burden score

CSF protein		SDMT	Stroop Color	Stroop Word	Stroop Interference
mHTT	R	-0.565	-0.620	-0.612	-0.505
	p	**0.0062**	**0.0012**	**0.0015**	**0.012**
	q	0.083	0.030	0.030	0.012
	n	22	24	24	24
Tau	R	-0.437	-0.382	-0.363	-0.30168
	p	**0.042**	0.065	0.082	0.15
	q	0.11	0.11	0.11	0.15
	n	22	24	24	24
NFL	R	-0.699	-0.838	-0.744	-0.792
	p	**0.012**	**0.0002**	**0.0023**	**0.0007**
	q	**0.012**	**0.0008**	**0.0031**	**0.0014**
	n	12	14	14	14

B. After controlling for disease burden score

CSF protein		SDMT	Stroop Color	Stroop Word	Stroop Interference
mHTT	R	-0.440	-0.512	-0.500	-0.331
	p	**0.046**	**0.012**	**0.015**	0.12
	p_{FDR}	0.061	**0.038**	**0.038**	0.096
	n	22	24	24	24
Tau	R	-0.376	-0.343	-0.321	-0.251
	p	0.093	0.11	0.14	0.25
	p_{FDR}	0.18	0.18	0.18	0.25
	n	22	24	24	24
NFL	R	-0.553	-0.626	-0.449	-0.547
	p	0.078	**0.022**	0.124	0.053
	p_{FDR}	0.10	0.08	0.12	0.10
	n	12	14	14	14

Supplemental table 2. Associations between individual CSF proteins and cognitive scores (A) before and (B) after adjustment for disease burden score. Linear regression analysis. p-values below the 0.05 significance threshold are in bold. *q*, FDR value accounting for multiple comparisons.