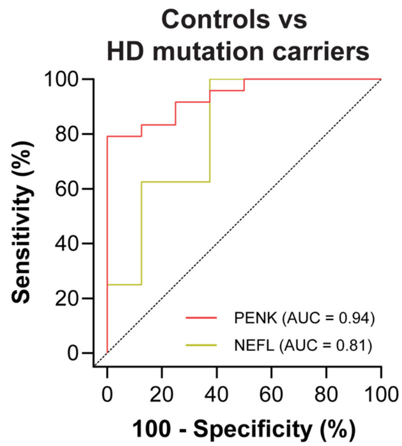
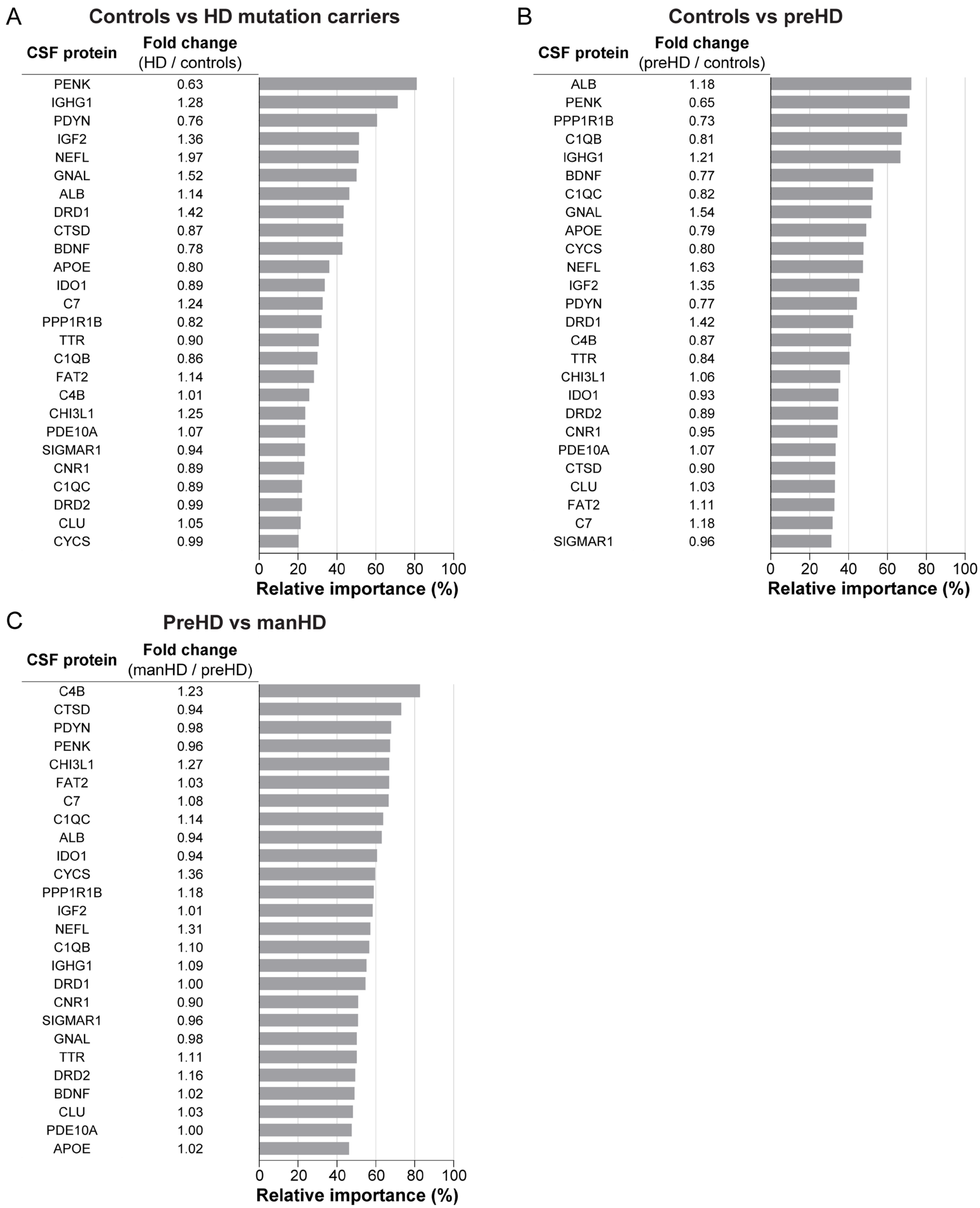
Supplementary Figure 1: Comparison of NEFL and PENK for discriminating HD mutation carriers from controls. ROC curve and AUC values comparing the discriminatory ability of NEFL and PENK for distinguishing between HD mutation carriers and controls.



Supplementary Figure 2: Discriminatory importance of CSF proteins for stratification of HD stages. CSF proteins ranked based on their relative importance for discriminating (**A**) HD mutation carriers from controls, (**B**) preHD from controls and (**C**) manHD from preHD groups. Fold changes represent the ratio of age-adjusted means between groups. Grey bars represent the percentage of events a variable was selected by sPLS-DA in the bootstrapped samples.



Supplementary Figure 3: Multi-marker CSF protein panels for stratifying subjects based on HD mutation status and disease severity. AUC values of individual and combinations of CSF proteins with the highest discriminatory ability for distinguishing (**A**) HD mutation carriers from controls, (**B**) preHD from controls, (**C**) manHD from preHD, (**D**) early/mid HD from preHD, and (**E**) late HD from early/mid HD.

A

Controls vs HD mutation carriers

1 marker		2 markers				3 markers	
Individual protein		Combination 2A		Combination 2B		Combination 3	
Protein	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
PENK	0.94	PENK	0.96	PENK	0.96	PENK	
		NEFL		IGHG1		GNAL	0.98
						IGHG1	

B

Controls vs preHD

1 marker		2 markers		3 markers															
Individual protein		Combination 2		Combination 3A		Combination 3B		Combination 3C		Combination 3D		Combination 3E		Combination 3F		Combination 3G		Combination 3H	
Protein	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
PENK	0.92	PENK	0.98	PENK		PENK		PENK		PENK		PENK		PENK		PENK		PENK	
		ALB		ALB	1	ALB	1	ALB	1	ALB	1	ALB	1	ALB	1	IGHG1	1	IGF2	1
				NEFL		IGF2		C7		BDNF		APOE		IGHG1		NEFL		C7	

C

PreHD vs manHD

1 marker		2 markers		3 markers		4 markers	
Individual protein		Combination 2		Combination 3		Combination 4	
Protein	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
CHI3L1	0.70	C4B	0.84	C4B		CHI3L1	
		IGHG1		IGHG1	0.87	C4B	
				NEFL		IGHG1	0.91
						ALB	

D

PreHD vs early/mid HD

1 marker		2 markers		3 markers						4 markers							
Individual protein		Combination 2		Combination 3A		Combination 3B		Combination 3C		Combination 4A		Combination 4B		Combination 4C		Combination 4D	
Protein	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
PPP1R1B	0.78	PPP1R1B	0.89	PPP1R1B		TTR		C4B		PPP1R1B		PPP1R1B		TTR		TTR	
		TTR		TTR	0.95	CHI3L1	0.95	TTR	0.95	TTR	1	TTR	1	ALB	1	CHI3L1	1
				CHI3L1		CTSD		CNR1		CHI3L1		ALB		CTSD		ALB	
										CTSD		CTSD		CYCS		CTSD	

4 markers																			
Combination 4E		Combination 4F		Combination 4G		Combination 4H		Combination 4I		Combination 4J		Combination 4K		Combination 4L		Combination 4M		Combination 4N	
Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
C4B		PPP1R1B		TTR		PPP1R1B		TTR		C4B		PPP1R1B		C1QB		C1QB		C1QB	
TTR	1	TTR	1	CHI3L1	1	C4B	1	CHI3L1	1	TTR	1	C1QB	1	TTR	1	TTR	1	TTR	1
ALB		ALB		CTSD		TTR		CTSD		CTSD		TTR		CTSD		CTSD		CHI3L1	
CYCS		CYCS		CYCS		CTSD		CNR1		CNR1		CTSD		CYCS		CNR1		CTSD	

E

Early/mid HD vs late HD

1 marker		2 markers		3 markers								4 markers		5 markers			
Individual protein		Combination 2		Combination 3A		Combination 3B		Combination 3C		Combination 3D		Combination 4		Combination 5A		Combination 5B	
Protein	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC	Proteins	AUC
PDYN	0.84	PDYN	0.88	PDYN		PDYN		PENK		CNR1		CNR1		CNR1		CNR1	
		PENK		PENK	0.91	C1QB	0.91	CNR1	0.91	C1QB	0.91	PPP1R1B	0.97	PPP1R1B		BDNF	
				IGHG1		IGHG1		IGF2		IGHG1		APOE		BDNF	1	APOE	1
												IGHG1		APOE		IGF2	
														IGHG1		IDO1	

5 markers					
Combination 5C		Combination 5D		Combination 5E	
Proteins	AUC	Proteins	AUC	Proteins	AUC
CNR1		CNR1		PDYN	
BDNF		PPP1R1B		CNR1	
C1QB	1	BDNF	1	PPP1R1B	1
IGF2		C1QB		C1QB	
IDO1		IGHG1		IGHG1	