SUPPLEMENTARY MATERIALS

Supplementary Table ST1: Clinical characterization of patients and SRM order of analysis.

Supplementary Table ST2: List of SRM transitions acquired and SRM assay parameters.

Supplementary Table ST3: Raw peak areas measured in the QQQ for each transition (MSstats input).

Supplementary Table ST4: Protein fold-changes among patient groups as calculated by MSstats.

Supplementary Table ST5: Training and validation iterations to select protein combinations with high classification power.

Supplementary Table ST6: Modified residues, post-translational modifications, natural variants, and sequence conflicts described for the proteins quantified in this study.

Supplementary Table ST7: Modified residues, post-translational modifications, natural variants, and sequence conflicts described for the peptides quantified in this study.
Supplementary Figure S1

Supplementary Figure S1: Detailed intensity profiles for each targeted mass spectrometric signals (SRM transitions) for the all the measured endogenous peptide and their corresponding isotopically-labeled references.

splO75326lSEM7A_HUMAN

Reference

Endogenous
Supplementary Figure S2

Supplementary Figure S2: Targeted mass spectrometric signals (SRM transitions) for all the measured endogenous peptide and their corresponding isotopically-labeled references.
Supplementary Figure S3

Supplementary Figure S3: Retention time drift of all measured peptides in the 73 patient samples.

CLU5_HUMAN (P10909) Clusterin
ASSIDELFQDR

CNDP1_HUMAN Beta-Ala-His dipeptidase
HLEDVFSK

A1AG1_HUMAN (P02763) Alpha-1-acid glycoprotein 1
TEDTIFLR

A1AG1_HUMAN (P02763) Alpha-1-acid glycoprotein 1
SDVVYTDWK

AACT_HUMAN (P01011-2) Isoform 2 of Alpha-1-antichymotrypsin
LYGSEAFATDFQDSAAAK

Retention Time (min)
SEM7A_HUMAN (O75326) Semaphorin 7A
IFAVWK
SEM7A_HUMAN (O75326) Semaphorin 7A
VYLFDFPEGK
SEM7A_HUMAN (O75326) Semaphorin 7A
LQDVFLLPDPSGQWR

Retention Time (min)

Retention Time (min)

Retention Time (min)
Supplementary Figure S4: Schematic representation of the statistical analysis used to select the protein classifications with the highest classification power.
Supplementary Figure S5: A) Volcano plots for protein abundance comparisons CIS vs. CDMS, CDMS vs. OND, and CIS vs. OND; B) Normalized intensities (log-scale) of selected proteins in each of the measured patient groups calculated with MSstats. CIS patients correspond to patients with a clinically isolated syndrome who did not convert to multiple sclerosis; CDMS refers to patients with a clinically isolated syndrome.
syndrome who developed to multiple sclerosis; and OND corresponds to patients with other neurological disorders.
spIP01011–2IAACT_HUMAN

Reference

Endogenous

CIS  CDMS  OND

CIS  CDMS  OND

Log2-intensities

MS runs

Reference

Endogenous

CIS  CDMS  OND

CIS  CDMS  OND

Log2-intensities

MS runs
The diagram shows the log2 intensities of sp|P01024|CO3_HUMAN for three conditions: CIS, CDMS, and OND. The intensities are compared between the reference and endogenous conditions. The x-axis represents MS runs, and the y-axis represents log2-intensities.
sp|P01034|CYTC_HUMAN

- ALDFAVGEYNK_2_y5
- ALDFAVGEYNK_2_y7
- ALDFAVGEYNK_2_y6
- ALDFAVGEYNK_2_y8

Endogenous
Log2 intensities for reference and endogenous samples.

- Reference: ANDESNEHSDV/DSQELSK_3_y3_NA, ANDESNEHSDV/DSQELSK_3_y6_NA, ANDESNEHSDV/DSQELSK_3_y4_NA, ANDESNEHSDV/DSQELSK_3_y7_NA.

- MS runs: 25, 49, 71.
sp|P13521|SCG2_HUMAN

![Graph showing log2 intensities for different conditions and MS runs.](image-url)
spI\text{Q96KN2|CNDP1\_HUMAN}

**MS runs**

**Log$_2$-intensities**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Endogenous</th>
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<tbody>
<tr>
<td>CIS</td>
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<td>CDMS</td>
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<tr>
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