**Supplementary materials and methods**

*In vitro isotope peptide labelling*

400µg of total extracts from four pooled control (100µg/each) and four pooled schizophrenia (100µg/each) lysates were reduced with 5mM dithiothreitol at 56ºC for 30 minutes and alkylated with 15mM iodoacetamide in 50mM Tris pH 8 in the dark at room temperature for 30 minutes. Each extract was digested with 5ng/µL trypsin in Tris 50mM, 1mM CaCl2 pH 8 at 37ºC for 16 h. Peptides were desalted by reversed-phase in a Sep-Pak C18 cartridge (100mg, Waters). Peptide mixtures were resuspended in 500 µl of 1M HEPES pH 7.5 and subjected to a reductive dimethylation reaction as described previously (Khidekel et al., 2007). Briefly, 20µl of a 600mM stock of NaCNBH3 or NaCNBD3 in water and 20µl of 4% aqueous formaldehyde-d0 (light labelling reaction) or 20µl of 4% aqueous formaldehyde-d2 (heavy labelling reaction) for the control or SZ samples respectively were added to the peptide solution, incubated for 10 minutes at room temperature and then quenched by adding 450µl of 10% Trifluoroacetic acid (TFA) (pH<3-4) and incubated for 1 hour. The light and heavy dimethylated peptide solutions were mixed 1:1. Peptides were desalted by reversed-phase in a Sep-Pak C18 cartridge. Peptide mixtures were resuspended in 5% acetonitrile (ACN) and 4% formic acid.

*Mass spectrometry analysis*

Dimethylated peptide mixtures were subjected to strong cation exchange chromatography on a polysulphoethyl A column. Twelve fractions were collected over 48 minutes in a gradient of KCl in 5mM potassium phosphate, 30% ACN, and dried by vacuum centrifugation. Peptides were resuspended in 1ml 0.1% trifluoroacetic acid, desalted by reversed-phase in a Sep-Pak C18 cartridge and dried by vacuum centrifugation. Peptide mixtures were resuspended in 5% ACN and 4% formic acid for LC-MS/MS analysis. Each peptide fraction was separated by reverse phase chromatography on a capillary column and analysed online on a hybrid linear ion trap Orbitrap (LTQ-Orbitrap XL, Thermo Scientific) mass spectrometer. For each cycle, one full MS scan acquired at high mass resolution (AGC target = 1 × 106, maximum ion injection time = 1,000 ms) in the Orbitrap analyser was followed by 10 MS/MS spectra on the linear ion trap (AGC target = 5 × 103, maximum ion injection time = 120 ms) for the ten most abundant ions. Fragmented precursor ions were dynamically excluded from further selection for 35s. Ions were also excluded if their charge was either <2 or unassigned. All spectra were acquired in centroid mode.

*Protein database searches, peptide quantification and data analysis*

Raw files were converted to mzXML format using ReAdW 2015.1.0 and default parameters. MS/MS spectra were searched against a concatenated target-decoy Uniprot human protein database (UP000005640 version 05-23-2017, n=71,567 target sequences) using the Comet search algorithm (version 2015025). Search parameters included full tryptic enzyme specificity with up to two missed cleavages permitted, mass tolerance of 50 ppm for the precursor and 1 Da for fragments ions, fixed modifications of carboxamidomethylation on cysteines (+57.02146) and dimethylation on lysines and peptide N-termini (+28.03130), and as variable modifications methionine oxidation (+15.99491) and the difference between heavy (6 hydrogen to deuterium) and light dimethyl on lysines and peptide N-termini (+6.03766). The RAW mass spectrometry proteomics data have been deposited in the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD008216 (Vizcaíno et al. 2016). Peptide matches were filtered to <1% false-discovery rate, the accepted threshold in the field, using the target-decoy database strategy and Percolator 3.1.2. Protein inference was carried out using Protein Prophet (contained in the Trans Proteomic Pipeline v4.8.0) and protein groups were filtered at ≥90 % probability score. Peptides were quantified using in-house software by peak-area integration, heavy and light peptide intensities were combined for every protein group and a log2 heavy/light ratio determined (Supplementary Data 1).

The log2 heavy/light ratio for each protein was transformed to a z-score for asymmetrical standard deviations of the main distribution as described previously (Graumann et al. 2008). A significance value (p-value) for each protein ratio was calculated from the complementary error function for the normalized distribution of the z-scores. To minimize the risk of type I errors and to estimate the proportion of true null hypotheses in our study, a False Discovery Rate (FDR) using the Benjamini and Hochberg method (Benjamini and Hochberg 1995) was also computed for all the p-values. The FDR threshold was set at 0.1. Significant proteins with consistent changes amongst peptides were then selected. Proteins were classified according to their biological function using the Human Protein Reference Database (HPRD-http://www.hprd.org). Up-regulated proteins were those with a z-score >0 and an FDR p-value <0.1 and down-regulated proteins were those with a z-score <0 and an FDR p-value <0.1. From these significantly altered proteins a panel of candidate proteins was then selected to be further validated by immunoblot following these criteria: (i) the change had been identified in more than 4 peptides; (ii) a greater than 2-fold increase or decrease.

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