**Appendix e-1**

**Antibody characterization and confirmation experiments**

**Indirect immunofluorescence assay (IFA) and dual staining by confocal microscopy**

Patient serums, absorbed with bovine liver powder to remove non organ-specific IgG (1:240), and CSFs (unabsorbed, 1:2), were tested on cryosections of composite adult mouse tissues: cerebellum, midbrain, cerebral cortex, hippocampus, thalamus, hypothalamus, kidney and gut as described previously.8 For dual staining of mouse tissue, a neurochondrin rabbit polyclonal IgG (1:50-1:100; ab224451 Abcam San Francisco, USA) was used. Secondary antibodies were fluorescein isothiocyanate (FITC)-conjugated anti-human (1:200) and tetramethylrhodamine isothiocyanate (TRITC)-conjugated anti-rabbit IgG (1:200; Southern Biotechnology, Birmingham, AL, USA). Confocal images were captured using a LSM780 microscope (20x, and 40x water immersion lenses, Carl Zeiss AG, Oberkochen, Germany).

**Western blot**

Mouse cytosolic cerebrum extract or glutathione S-transferase (GST)-tagged recombinant neurochondrin full-length protein (Abcam161548, SF, USA) was separated on 4-15% polyacrylamide gels, transblotted to nitrocellulose membranes and probed with serum IgGs from healthy subjects or patients (1:350 dilutions).

**Immunoprecipitation assay and sequencing by mass spectrometry**

Serum IgGs from 3 patients (1,4, and 6) and purified IgGs from patients 1 and 4 with two healthy controls were complexed to protein G magnetic beads (Dynabeads; Invitrogen, Carlsbad, CA; Thermo Fisher Scientific) and exposed to mouse cerebral protein extract (20 min, at room temperature). After washing, beads were boiled for 5 min in 2 × Laemmli sample buffer. The eluted proteins were electrophoresed in 5% polyacrylamide gel, and located by Coomassie G-250 staining (Bio-Rad) and western blot. Bands corresponding to immunoreactivity were excised and analyzed by high pressure liquid chromatography electrospray tandem mass spectrometry (Mayo Clinic Medical Genome Facility – Proteomics Core).

**Cell-binding assay (CBA)**

Euroimmun CBA protocol with recombinant expression of neurochondrin in HEK293 cells using human DNA: cells were grown on sterile cover glasses, transfected, and allowed to express neurochondrin for 48 hr. Cover glasses were washed with PBS, fixed with acetone for 10 min at room temperature, air-dried and cut into millimeter-sized fragments (biochips).