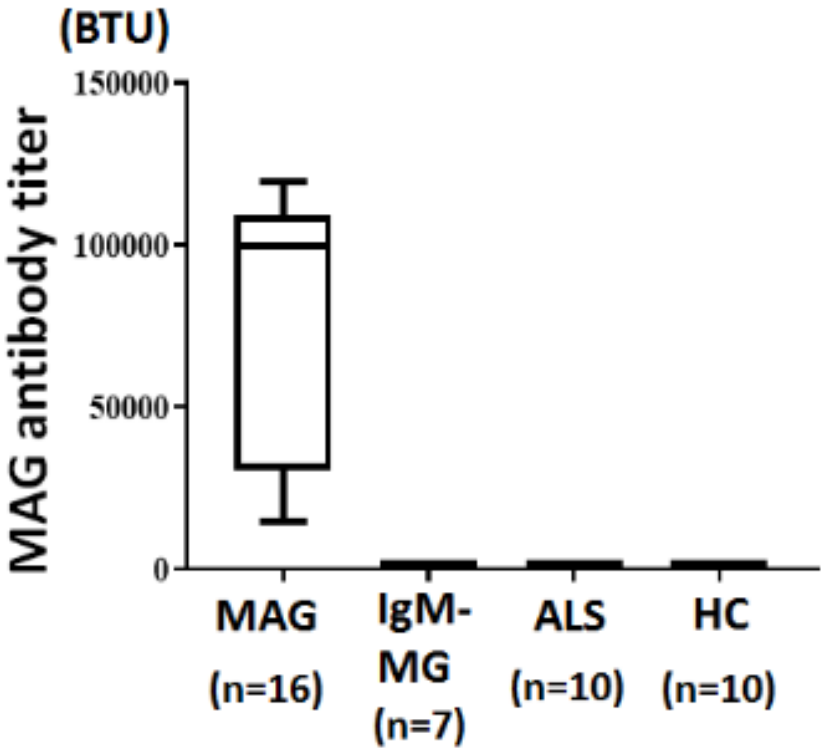
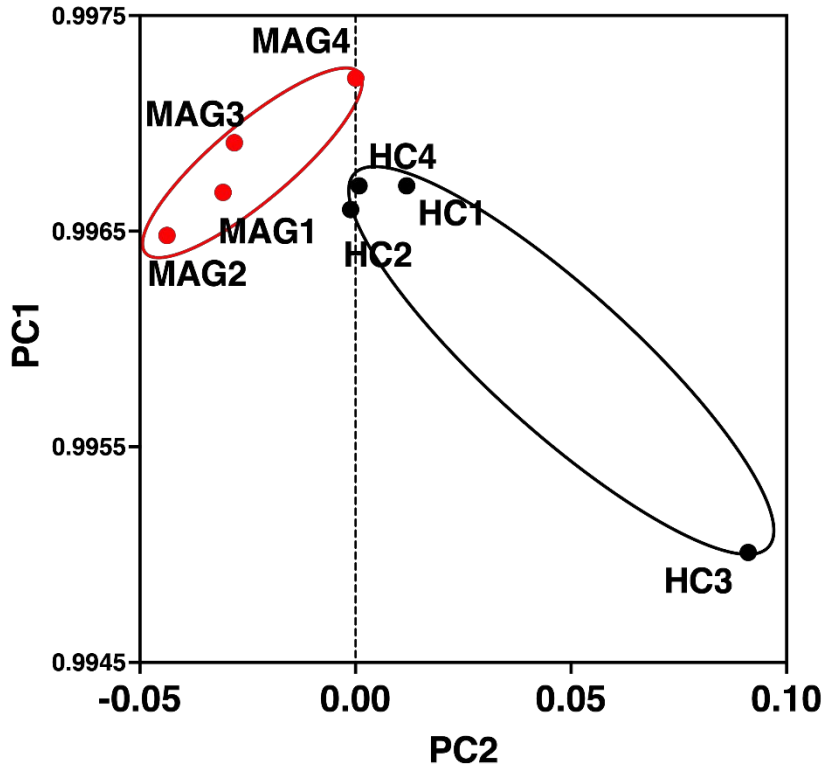
eFigure 1



eFigure 2



eTable 1

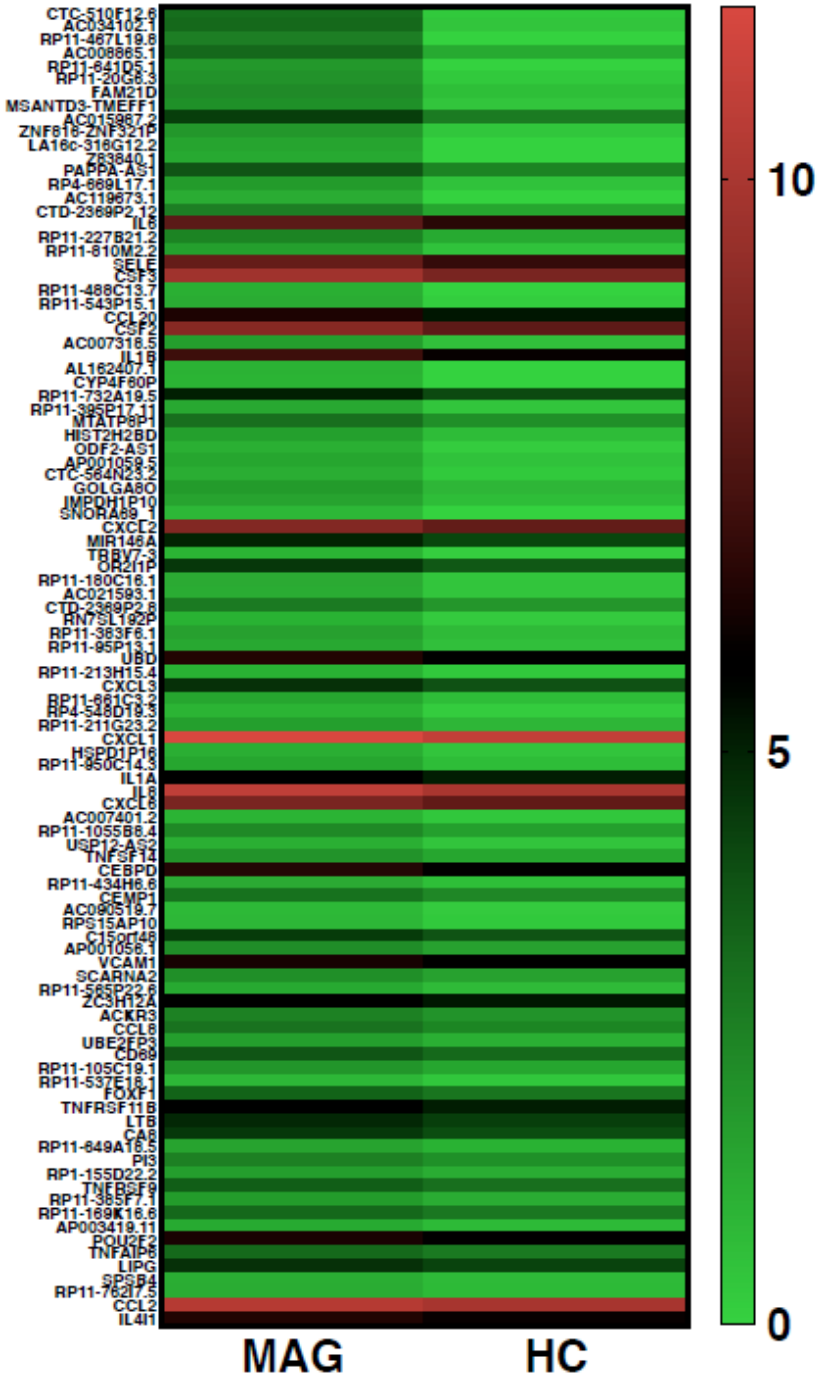
The cerebrospinal fluid (CSF) data from 4 patients with anti-MAG neuropathy who received sural nerve biopsy

Pt Nos.	Age	Sex	Cell count	CSF protein	Q Alb	BNB damage
1	73	M	5	55	N/A	N/A
2	59	M	1	165	25	moderate
3	82	M	1	82	13	mild
4	72	M	16	62	9	mild

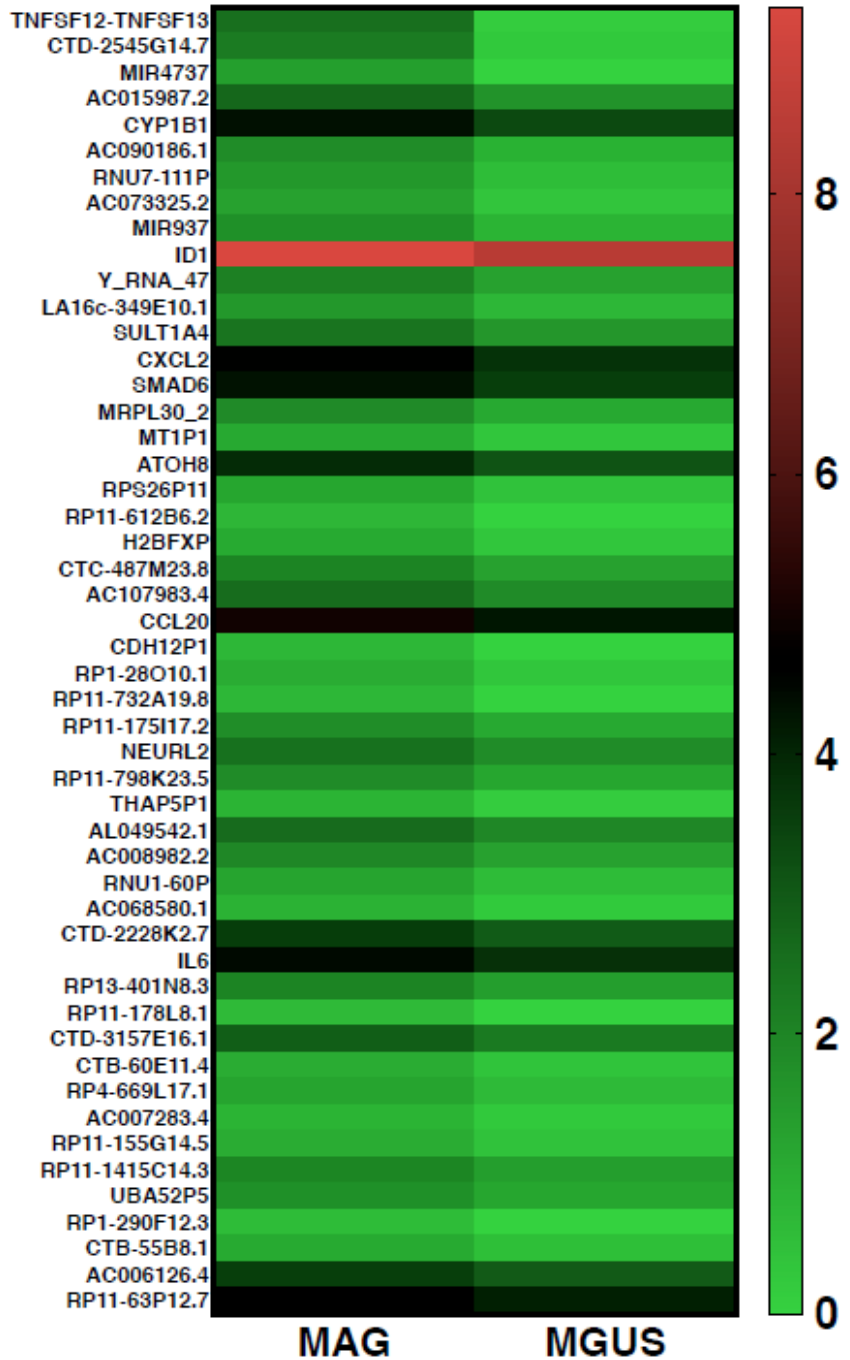
Pt Nos: patient numbers; Cell count: Cerebrospinal fluid cell count; CSF protein: Cerebrospinal fluid protein; Q Alb: CSF/serum albumin ratio.

CSF protein was elevated in all 4 patients and the IgG index was increased in 2 patients. The CSF/serum albumin ratio (Q Alb) was increased in 3 patients. Q Alb LIM was calculated as [(age/15)+4] as the cut-off value. The BNB damage was classified into 4 patterns (1. absent, QALB<QAlbLIM; 2. mild BNB damage, QALB/QAlbLIM 1.0-2.0; 3. moderate BNB damage, QALB/QAlbLIM 2.0-5.0; 4. severe BNB damage, QALB/QAlbLIM >5.0). According to this formula, the patient showed moderate BNB damage and 2 patients showed mild BNB damage.

eFigure 3

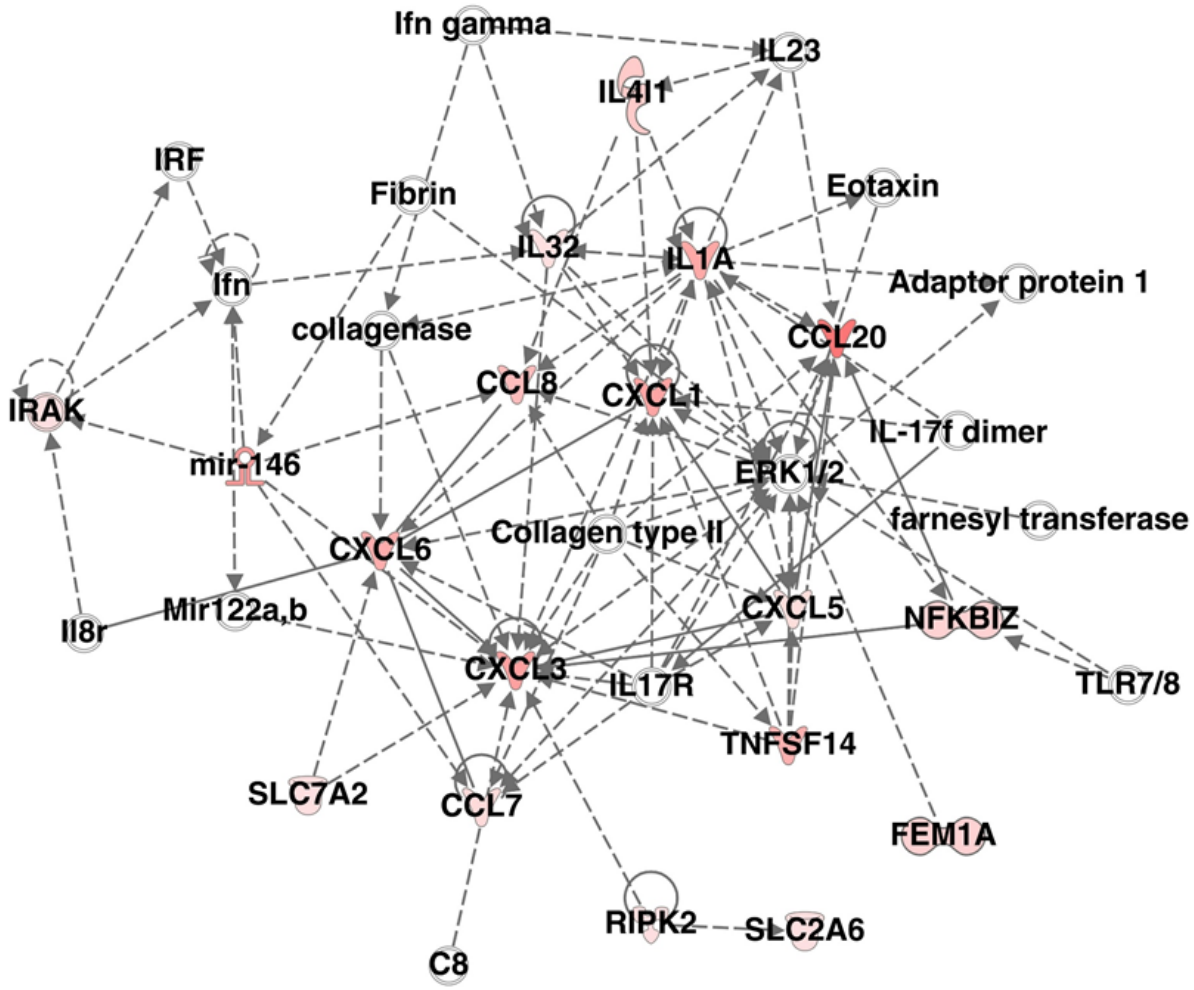


eFigure 4



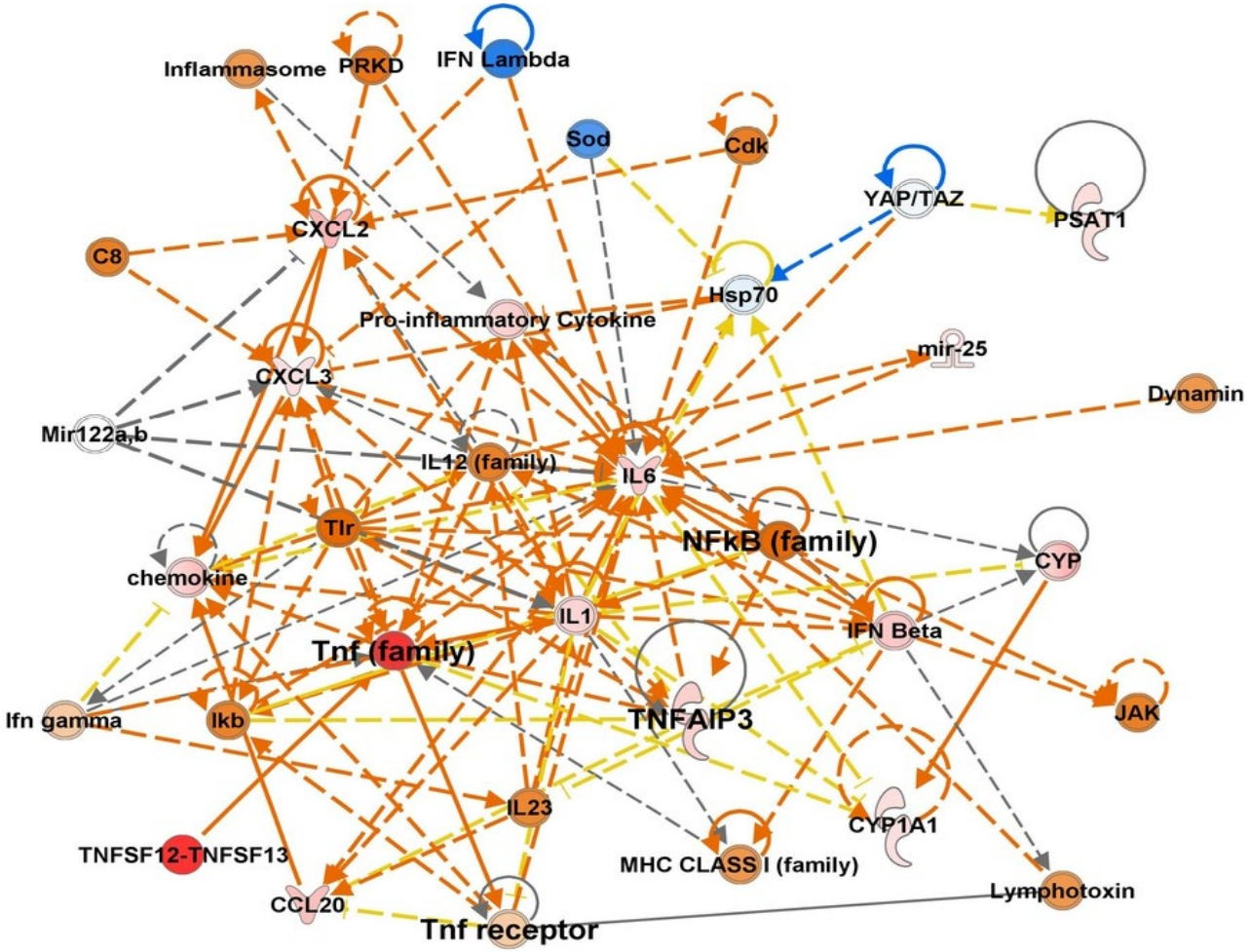
eFigure 5

Anti-MAG vs HC



eFigure 6

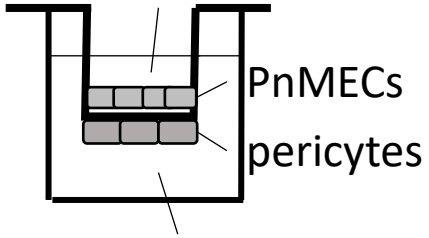
Anti-MAG vs IgM-MG



eFigure 7

in vitro BNB
co-culture model

upper chamber:
MCBD medium
with 10% sera

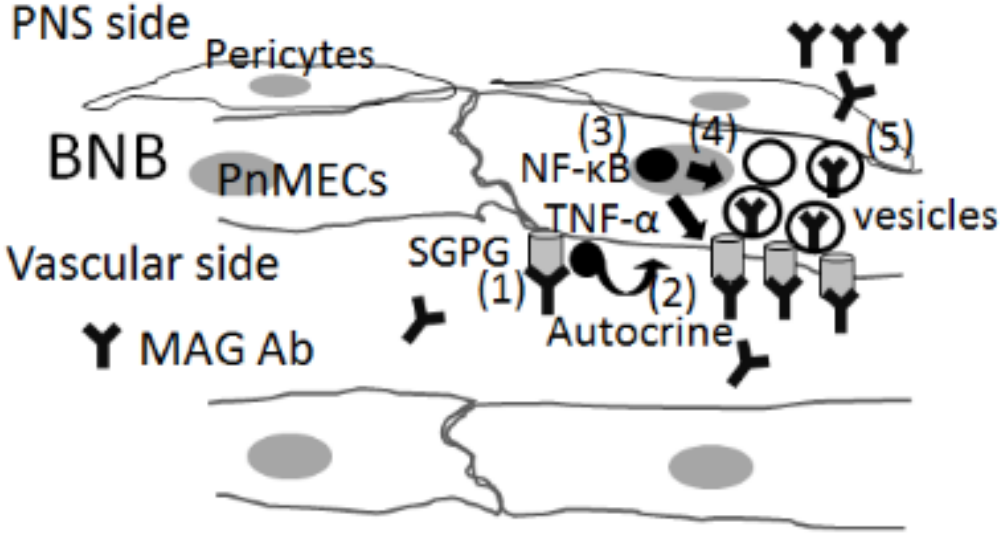


lower chamber:
MCBD medium

IgM permeability index:
IgM concentration in chamber
(=lower/upper)

MAG antibody permeability index:
MAG antibody concentration in
lower chamber (BTU)

eFigure 8



(1) Bound of MAG Ab to SGPG on the PnMECs
(2) Increase of TNF-α secretion and autocrine effect on the PnMECs
(3) Upregulation of NF-κB signal
(4) Increase of SGPG expression and vesicles including MAG Ab
(5) Penetration of MAG Ab through receptor mediated-transcytosis

eFigure 1

Anti-MAG antibodies titer from each samples. MAG, anti-MAG neuropathy (n=16); IgM-ML, IgM-monoclonal gammopathy neuropathy (n=7); ALS, amyotrophic lateral sclerosis (n=10); HCs; healthy controls (n=10). The dashed lines indicate the upper limits of the anti-MAG antibody titer in the healthy control group (mean+3 SD).

eFigure 2

PCA revealed the separation on PC2 between the MAG-Abs-associated disorder patients (n=4) and HC/control groups (n=4).

eFigure 3

The heatmap shows the gene expression of up-regulated gene in mean value between anti-MAG neuropathy (n=4) and healthy controls (n=4). Green indicates a relatively low expression and red arelatively high expression.

eFigure 4

The heatmap shows the gene expression of up-regulated gene in mean value between anti-MAG neuropathy (n=4) and IgM-monoclonal gammopathy neuropathy (n=4). Green indicates a relatively low expression and red a relatively high expression.

eFigure 5

Whole transcriptome analysis (using RNA-seq) of PnMECs after exposure to sera from patients with anti-MAG neuropathy. CCL20, IL1A, CXCL1, CXCL3 and CXCL5 were identified as downstream molecules of NF-κB signal in MAG neuropathy in comparison to in HCs. The red nodes show the upregulated genes in the RNA seq analysis (FC>1.5; P<0.05). Anti-MAG, Anti-MAG neuropathy; IgM-MG, IgM-monoclonal gammopathy neuropathy; HC, healthy control.

eFigure 6

Whole transcriptome analysis (using RNA-seq) of PnMECs after exposure to sera from patients with anti-MAG neuropathy. The IL-6, IL-12, CXCL2 and CXCL3 were observed as downstream molecules of NF-κB signaling in MAG neuropathy patients in comparison to patients with IgM-MG neuropathy (F). The red nodes show the upregulated genes in the RNA seq analysis (FC>1.5; P<0.05). Anti-MAG, Anti-MAG neuropathy; IgM-MG, IgM-monoclonal gammopathy neuropathy; HC, healthy control.

eFigure 7

Schematic illustration of the BNB *in vitro* co-culture model to investigate IgM and MAG antibody permeability. The IgM permeability index was calculated by measuring the IgM concentration in the lower and upper chamber (=lower/upper chamber). MAG antibody permeability index was assayed by measuring the MAG antibody concentration in the lower and upper chamber (=lower/upper chamber).

eFigure 8

Pathomechanism of anti-MAG antibody penetration across the blood-nerve barrier in anti-MAG neuropathy. Anti-MAG antibodies firstly bound SGPG on PnMECs and stimulated TNF-α secretion from PnMECs. Next, autocrine/paracrine TNF-α stimulated NF-κB signaling and increased the SGPG expression and vesicles in PnMECs. TNF-α/NF-κB signaling then activated the receptor-mediated transcytosis of MAG IgM antibodies across the BNB through SGPG.