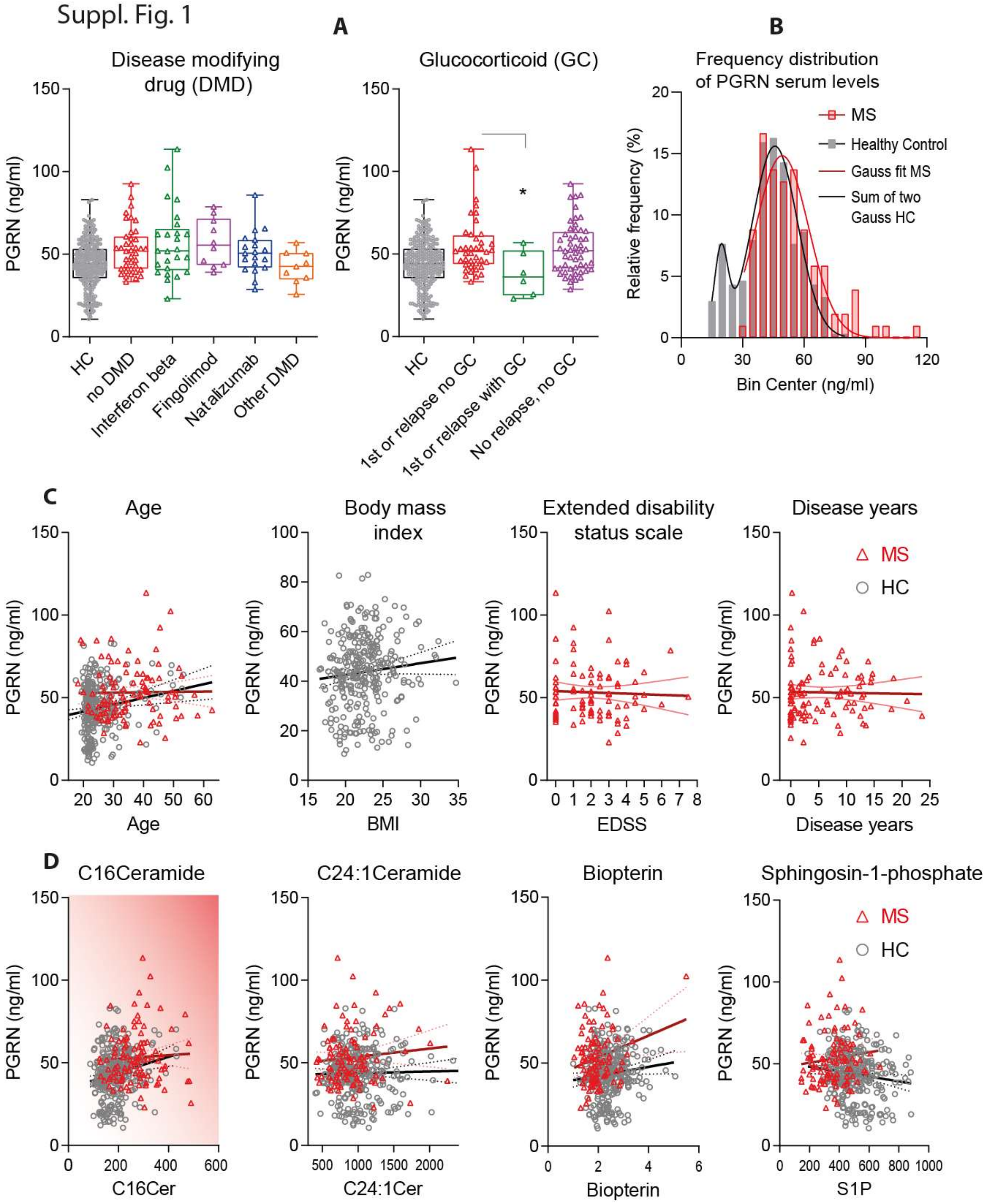
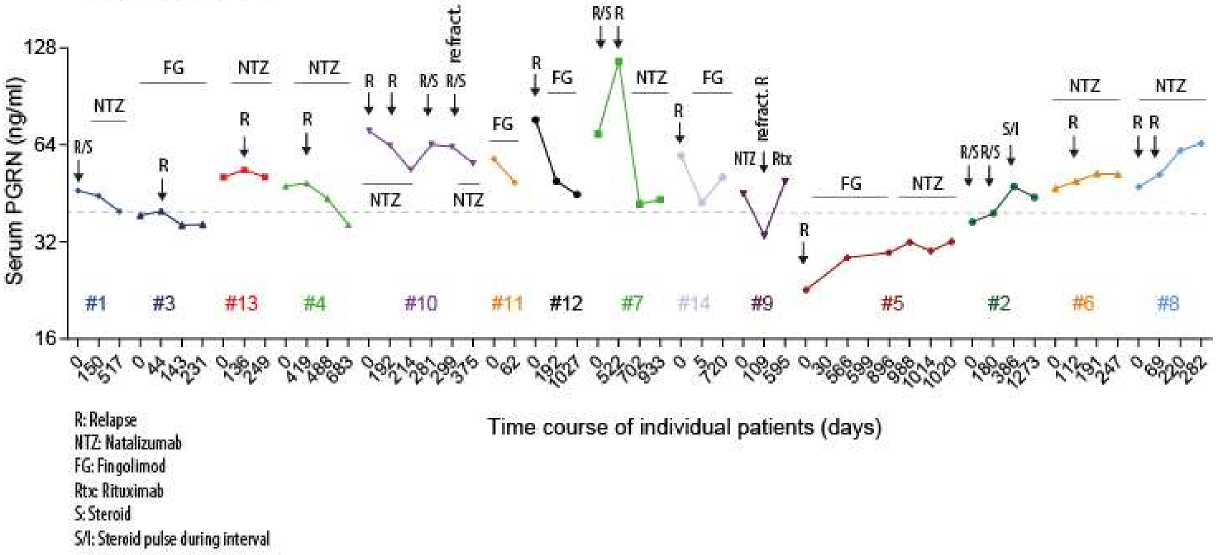
Supplementary Figures and Legends

Suppl. Fig. 1



Suppl. Fig. 1E



Suppl. Fig. 1:

Associations of progranulin serum levels in MS patients with medication and demographic data

A: Box/scatter of progranulin serum concentrations in 102 patients with multiple sclerosis and 301 healthy controls. The box shows the interquartile range, the line is the median, the whisker show minimum to maximum. The asterisks indicate significant differences between groups, * $P < 0.05$, one-way ANOVA and subsequent posthoc t-tests versus each other using an adjustment of alpha according to Šidák).

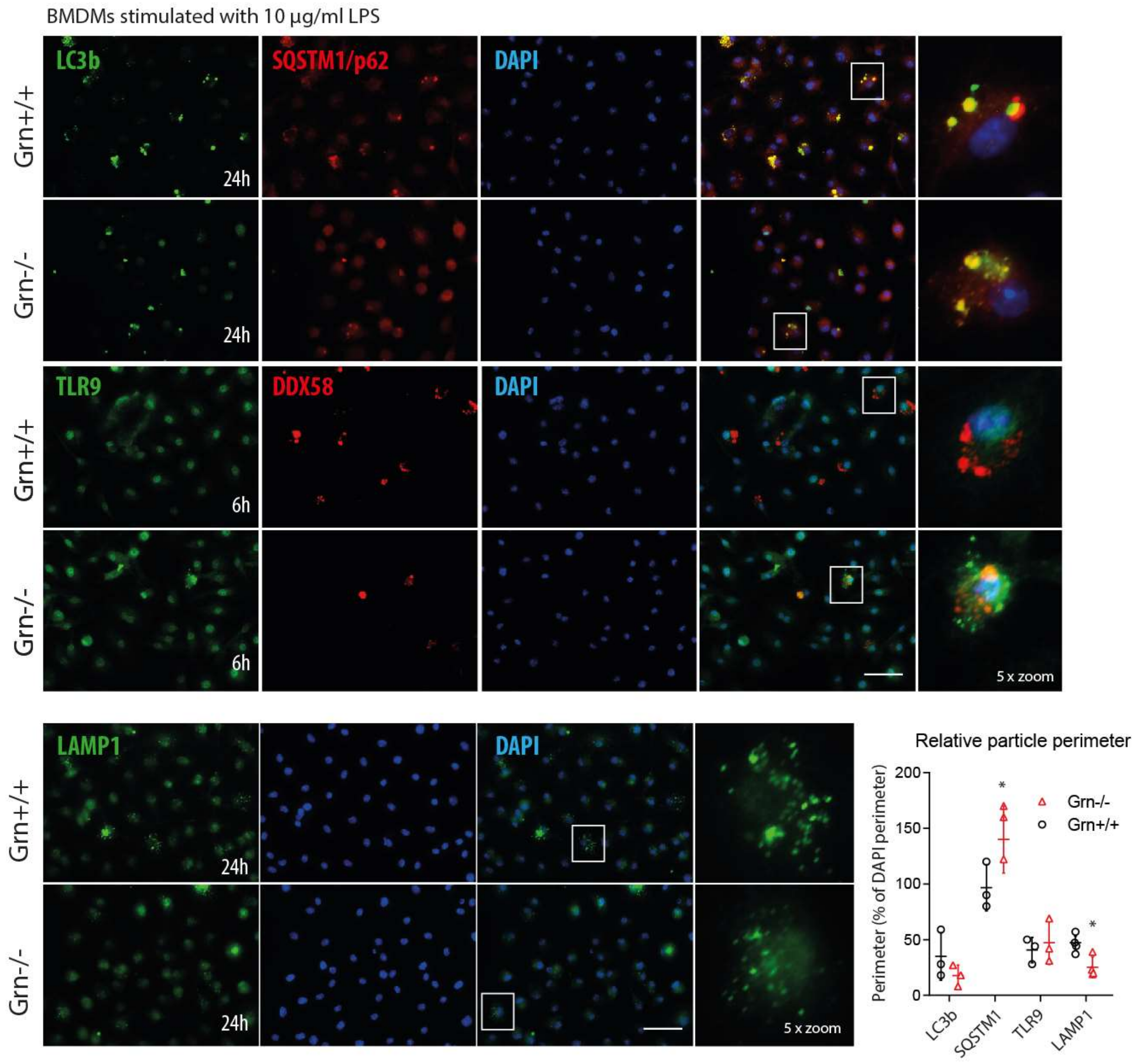
B: Frequency distribution of progranulin serum concentrations in MS patients and healthy controls (HC) and Gauss fit. The frequency distribution of progranulin serum levels in healthy controls follows a sum of two Gauss curves. i.e. it is biphasic.

C: Associations of progranulin serum levels with age, body mass index (BMI), extended disability status score (EDSS) and number of years since diagnosis of MS. The lines are the linear regression lines, the dotted lines show the 95% confidence intervals.

D: Associations of progranulin serum levels with other serum markers of disease activity. C16Cer is a ceramide with 16 C-atoms, which is increased in MS. C24:1Cer is a very long chain ceramide with 24 C-atoms and one unsaturated bond, which is reduced in MS. Biopterin is a marker of antioxidative capacity. The lines are the linear regression lines, the dotted lines show the 95% confidence intervals The red colored graph indicates that the regression line for MS patients was significantly deviant from zero, i.e. progranulin was positively associated with C16Cer.

E: Time course of progranulin serum concentrations in individual MS patients with serious courses of the disease. They were observed up to 3 years after taking the initial blood sample (referred to as time zero). Patients on the left side (#1-#9) rather have high levels during relapses, patients #5-#8 have rather low levels during relapse.

Suppl. Fig. 2



Suppl. Figure 2:

Autophagy and lysosome markers and TLR9 in progranulin deficient BMDMs

Exemplary immunofluorescence images of LPS-stimulated BMDMs showing the autophagy markers microtubule associated protein 1 light chain 3 beta (MAP1LC3B/LC3b), sequestosome 1 (SQSTM1/p62) (upper panel), Toll like receptor 9 (TLR9) and retinoic acid-inducible gene I protein (DDX58/RIG-I) and the lysosome marker LAMP1. For quantification, particle areas and perimeters were normalized on DAPI perimeters and were analyzed with ImageJ. Data of different time points (3, 6 and 24 h) were combined to gain power. Each dot represents one culture (n = 4), the line is the mean, the whisker show the SD. The relative areas of LAMP1 positive particles were reduced in Grn$^{-/-}$, whereas SQSTM1 particles were increased (2-sided, unpaired t-test, P <0.05).