

Supplementary Materials:

Supplementary Fig 1-3, Supplementary Table S1

Supplementary Figure Legends

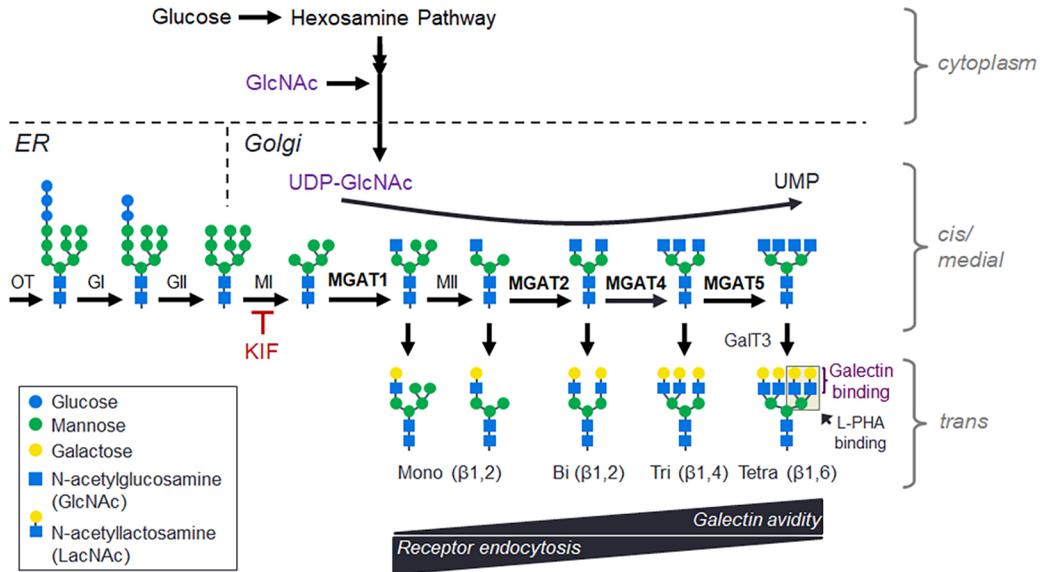
Supplementary Figure 1. GlcNAc promotes oligodendrogenesis from precursor cells. (A) UDP-GlcNAc, which is synthesized *de novo* from glucose or salvaged from GlcNAc, is the donor substrate utilized by the Mgat branching enzymes. **(B)** Immunofluorescence microscopy of E12.5 NSC's from CD1 mice cultured in growth media (FGF+EGF) \pm GlcNAc for 48 hours. **(C-G)** Flow cytometry of C57BL/6 mouse E12.5 NSC's of the indicated genotypes treated in either growth media (FGF+EGF, C), in differentiation media (FGF+PDGF-AA (10ng/mL)) (E-G) or as indicated **(D)** with/without GlcNAc 80 mM (C-E), kifunensine for 48hrs (F) or doxycycline pre-treatment for 8 days (G). Data are 3 technical replicates per group and representative of 2 experiments. P-values are by one-way ANOVA with Sidaks's multiple comparison test. (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

Supplementary Figure 2. GlcNAc and N-glycan branching promote primary myelination. (A) Flow cytometry of brains from PL/J pups whose mothers were treated with GlcNAc (1mg/mL) in drinking water from P5 or E12.5 to P8 (N=5,5 and 2, 11; one sided t-test). **(B)** *Mgat1^{f/f}Plp1-cre/ERTc⁺* mice were injected with or without tamoxifen (75mg/kg) daily for 3 days and brains analyzed by flow cytometry. Data is representative of 3 mice per group. **(C)** *Mgat1^{f/f}Plp1-cre/ERTc⁺* mice (10 weeks old) were treated with tamoxifen at week 0 and 4, sacrificed at week 8 and cerebellums were analyzed by immunofluorescence microscopy for MBP and myelin (fluoromyelin) (N=5 (2 male, 3 female),8 (6 male, 2 female); one sided t-test). Data points represents average fluorescence of area depicted from 2 slices per mouse. **(D-E)** The indicated mice (10 weeks old) were treated with tamoxifen at week 0 and then sacrificed at week 2 and brains were analyzed by immunofluorescence microscopy for MBP and myelin (fluoromyelin) (N=8 (4 male, 4 female), 6 (4 male, 2 female (D), N=8 (4 male, 4 female), 4 (1 male, 3 female) (E), one sided t-test. Data points represent average fluorescence of area highlighted in red in 2 slices per mouse.

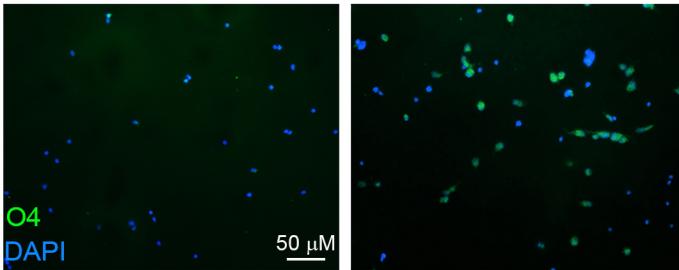
Supplementary Figure 3. Oral GlcNAc promotes oligodendrogenesis and re-myelination while limiting axonal injury. (A) Per mouse averages of g-ratio, total axons, myelinated axons, paranodes, and dystrophic axons as well number of degenerating axons from electron micrographs of the medial CC of the *Mgat5*^{+/-} mice from Fig. 3G (N=3,3 (2 male and 1 female per group)) with data obtained blind to treatment conditions and averaged from 2 fields (g-ratio) or 6 fields per mouse (105 μ m/field). Degenerating axons highlighted by red arrows and paranodes denoted by blue asterisks. Mice were treated \pm GlcNAc for 4 weeks after 5 weeks of cuprizone. P-value by one-sided t-test and chi-square test. Scale bar = 1 μ m (B) Electron micrographs of 10-week old *Mgat5*^{+/+} and *Mgat5*^{+/-} littermates were analyzed for number of myelinated axons per field (N=12, 12 fields; 6 fields per mouse, 105 μ m/field, one-sided t-test) and g-ratio (N=839 axons over 6 fields). Scale bar = 1 μ m. (C) Fluoromyelin staining of medial CC of *Mgat5*^{+/-} mice who were treated \pm GlcNAc for 6 weeks after 5 weeks of cuprizone starting at 10 weeks of age (N=3 (3 male), 6 (4 male, 2 female); one sided t-test). Data points represent average of 4 slices per mouse.

Supplementary Figure 1

A



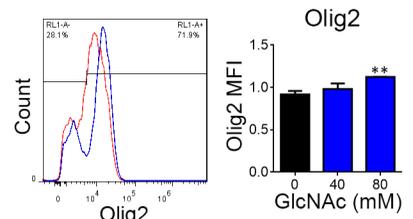
B



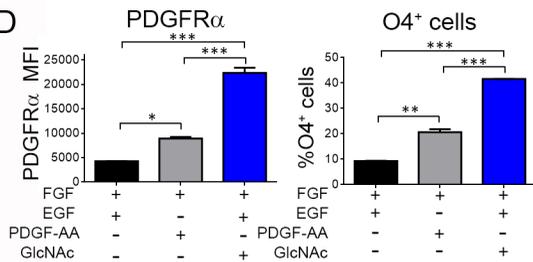
GlcNAc (mM) 0

80

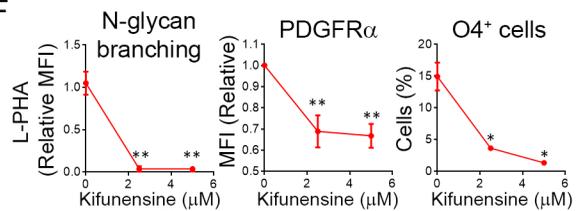
C



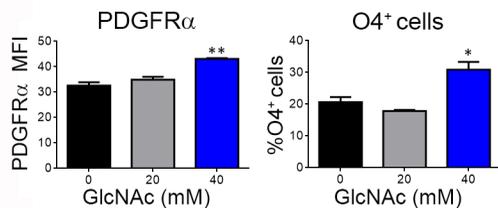
D



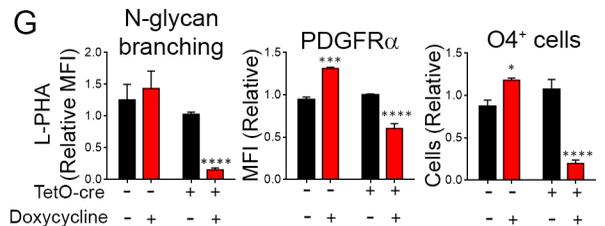
F



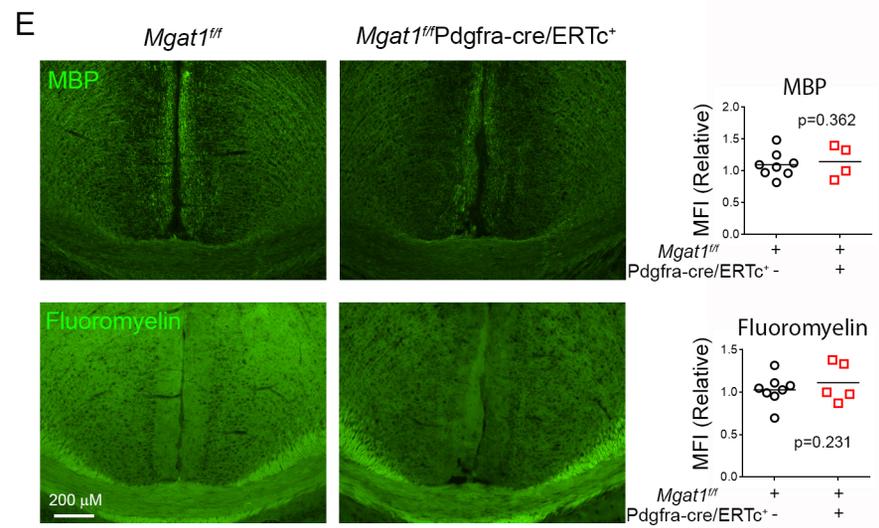
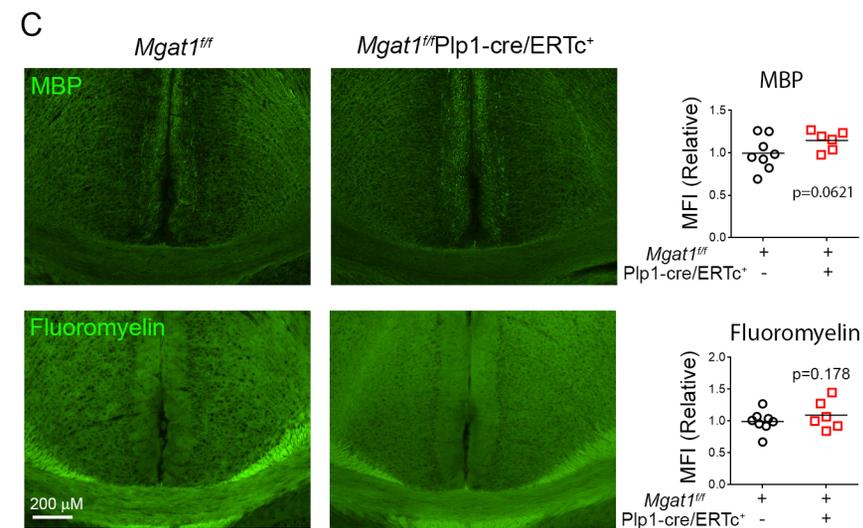
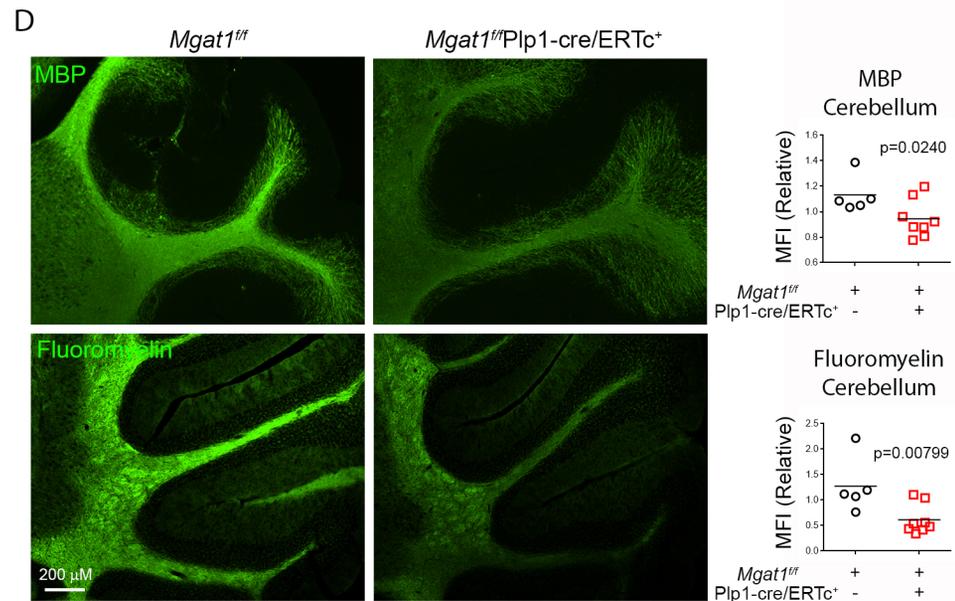
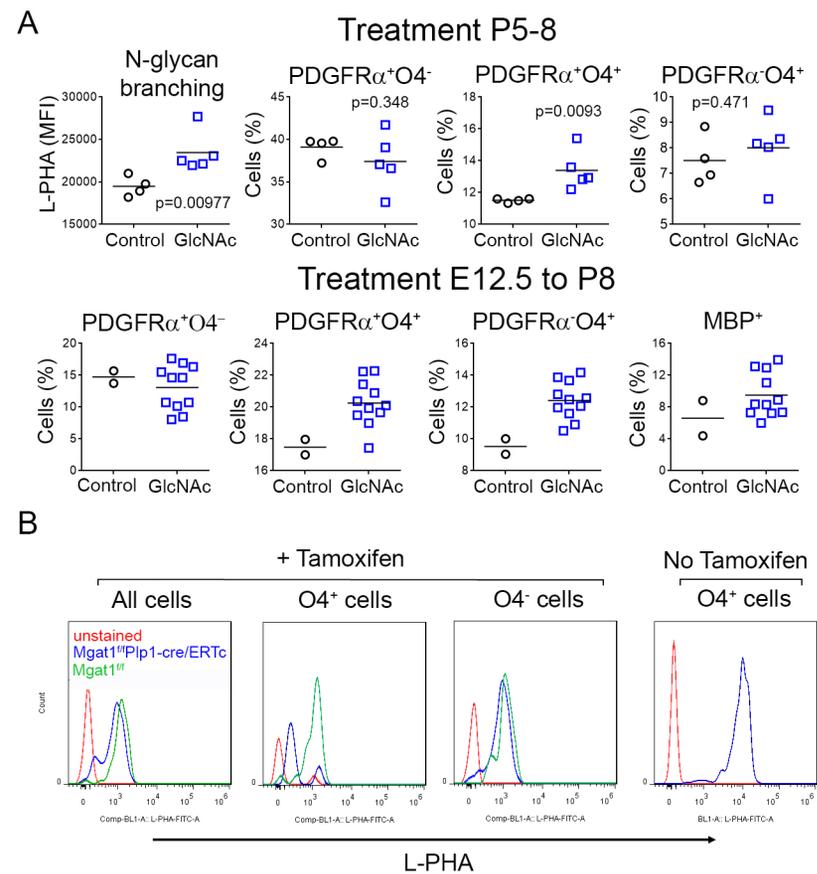
E



G

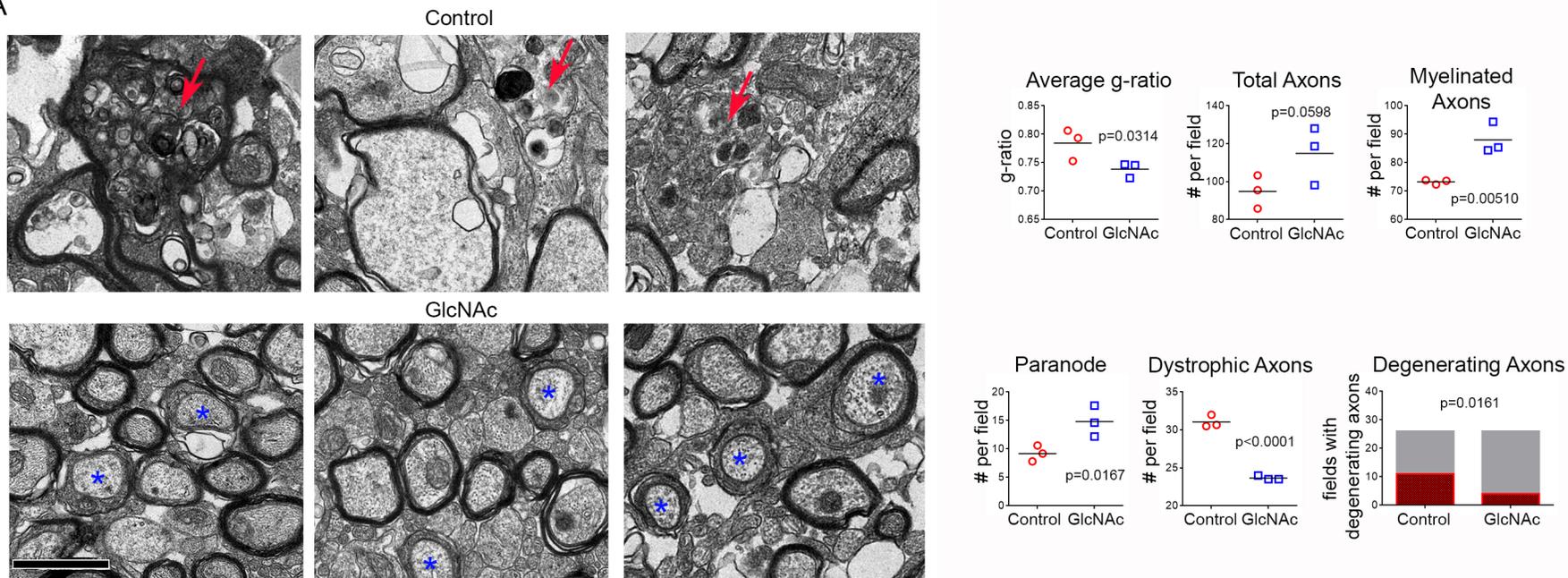


Supplementary Figure 2

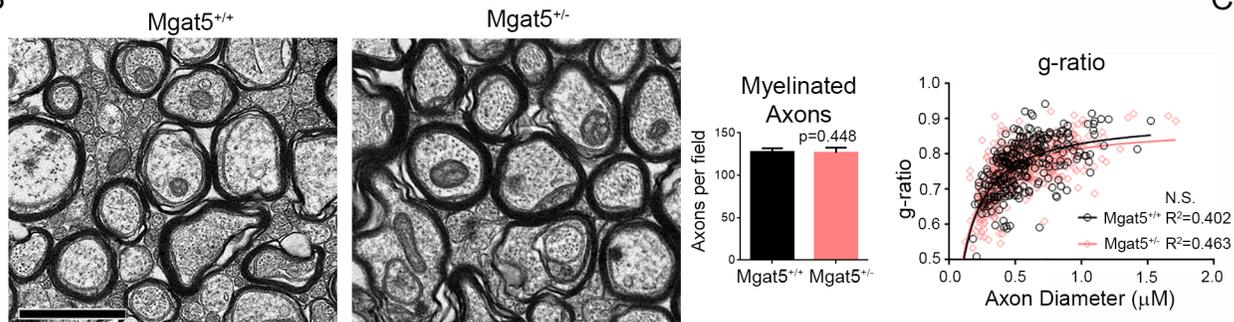


Supplementary Figure 3

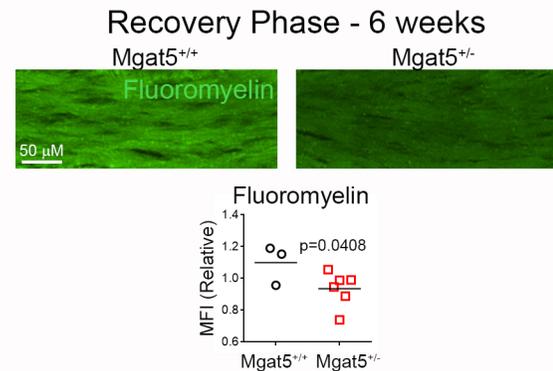
A



B



C



Supplementary Data Table 1 – MS cohort

MS patients	<i>n</i>	180
<i>RRMS</i>	<i>n</i>	<i>125</i>
<i>PPMS</i>	<i>n</i>	<i>23</i>
<i>SPMS</i>	<i>n</i>	<i>32</i>
Age (years)	Mean±SD	42.7±9.4
Sex (M/F)	<i>n/n</i>	73/107
Time since diagnosis (months)	Mean±SD	118.2±87.6
EDSS	Median (Min - Max)	3.0 (0.0-8.0)
T2LC	Median (Min - Max)	29 (0 – 162)
T2LV (ml)	Median (Min - Max)	2790 (0 – 54,900)
CELC	Median (Min - Max)	0 (0 – 6)

Abbreviations: MS, multiple sclerosis; RRMS, relapsing-remitting MS; PPMS, primary progressive MS; SPMS, secondary progressive MS; SD, standard deviation; EDSS, Expanded Disability Status Scale; T2LC, T2w lesion count; T2LV, T2w lesion volume; CELC, contrast enhancing lesion count.