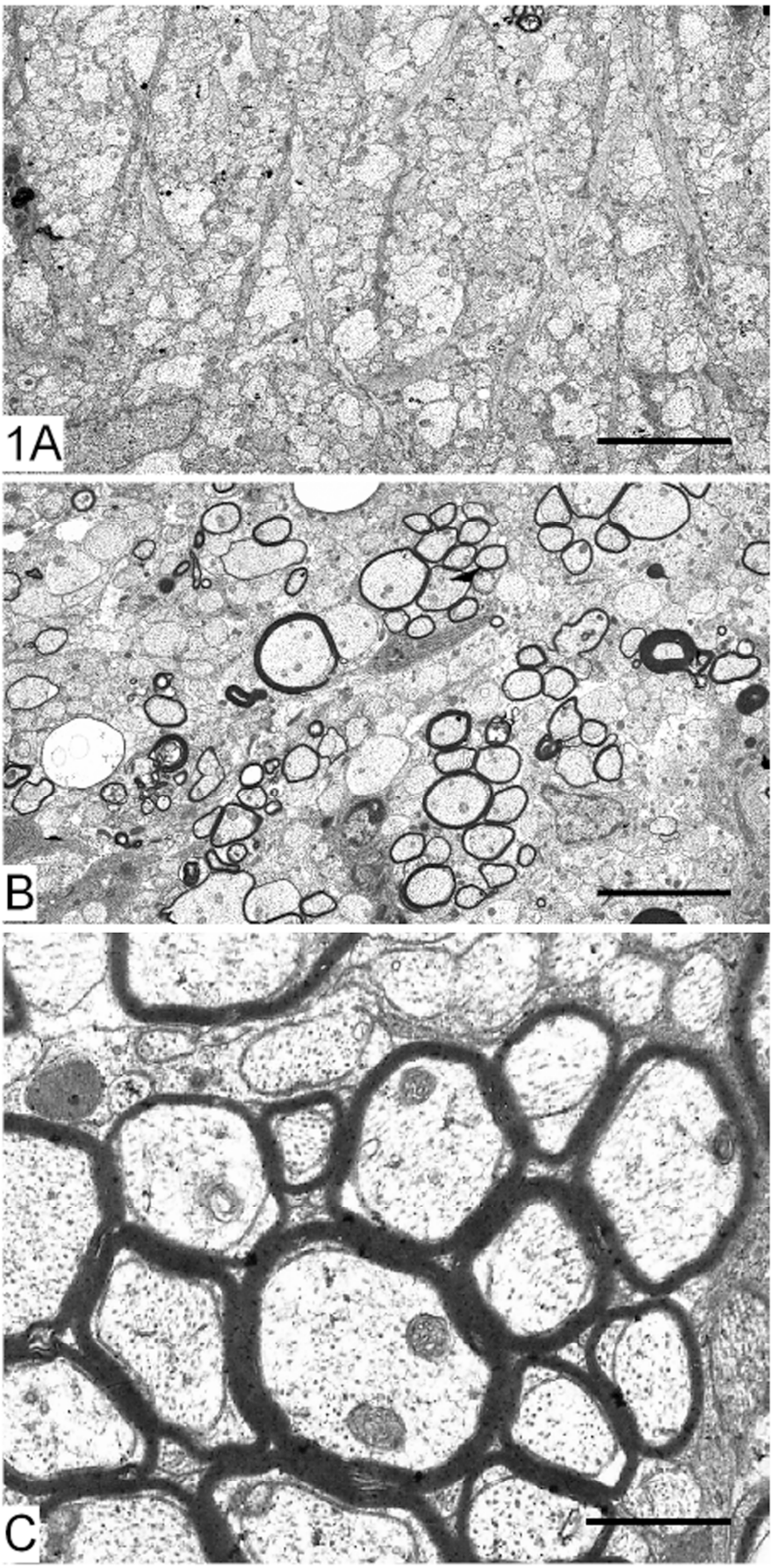
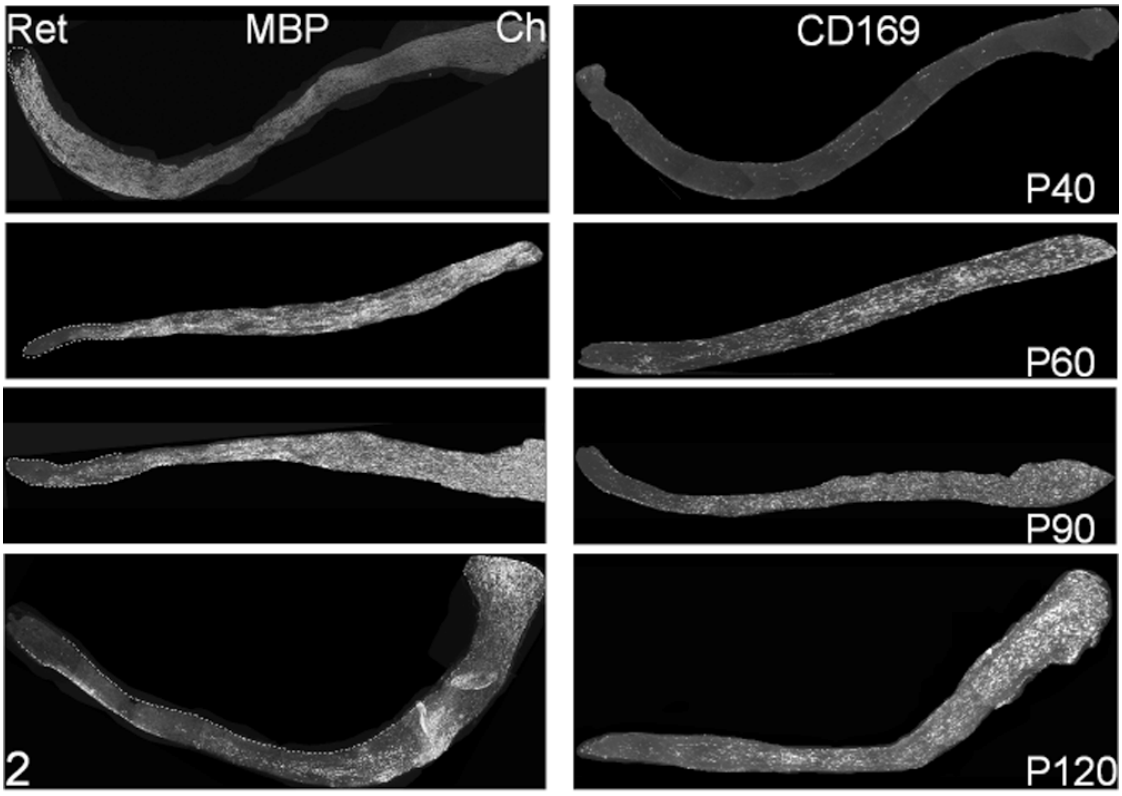
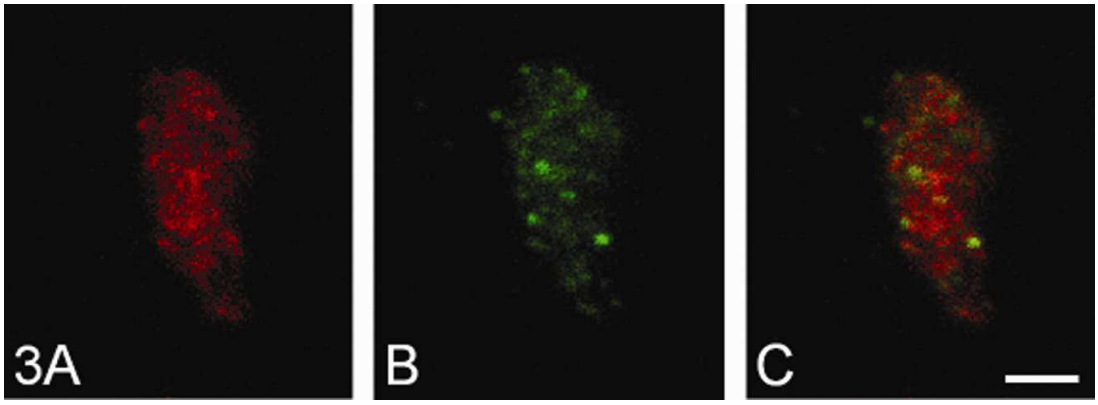

1A
B
C

Supplementary Fig. 1. Temporal and spatial evolution of demyelination in optic pathway of *Plp1*-transgenic mice. **A.** Retinal end of optic nerve from P120 mouse showing complete loss of myelin with axonal preservation and an increase in astrocytic processes. **B.** Optic tract from P120 mouse showing active demyelination and increased numbers of microglia. **C.** Optic tract from P60 mouse prior to demyelination showing that the majority of axons have a structurally normal myelin sheath. Some non-myelinated axons (top of image) probably represent the low level dysmyelination that is present throughout development. Bars A, B = 5μm, C = 1μm.



Supplementary Fig. 2. Demyelination and inflammation progresses rostro-caudally in the *Plp1* transgenic mouse optic nerve. MBP and CD169 stained sections of P40, P60, P90 and P120 optic nerve showing the rostral to caudal progression of myelin loss and inflammation. The 'patchy' appearance of the MBP staining is indicative of myelin breakdown.



Supplementary Fig. 3. Anterogradely and retrogradely transported CtB co-localise in axonal spheroids in the *Plp1* transgenic mouse optic nerve. Confocal image of a single z position of **A.** FITC- and **B.** TRITC-labelled CtB demonstrating that both are present in the same axonal swelling. **C**. Overlay shows that the anterogradely and retrogradely transported tracers have unique profiles. Bar = 2 μm.

Supplementary Materials and Methods

Genotyping: Hemizygous *Plp1* transgenic males and females were bred to generate wild type, hemizygous and homozygous offspring. Mice carrying the transgene were identified by PCR genotyping (Readhead *et al.*, 1994). At P120, homozygotes could be distinguished from hemizygotes by neurological signs, such as seizures, which are absent in the hemizygote. At earlier ages we used morphological criteria (Anderson *et al.*, 1999) or quantitative real time PCR (Identigene, Houston, U.S.A.) to ascertain transgene copy number.

Heterozygous *rumpshaker* female mice were crossed with wild type males (C3H/101 background) to generate *rumpshaker* (*rsh*/y) and wild type (+/y) male offspring. These were distinguished on the basis of the neurological phenotype of *rumpshaker,* which exhibit a mild tremor.

Tissue processing for immunohistochemistry.
For immunohistochemistry with CD3, CD45, sialoadhesin and MBP antibodies, mice were perfusion fixed with periodate-lysine-paraformaldehyde (McLean and Nakane, 1974), optic nerves were post-fixed for 1-2 hours then cryoprotected in 20% sucrose and flattened between frozen discs of OCT embedding medium (Fintek Europe, Zoeterwoude, The Netherlands). For immunohistochemistry with SMI32 or for examination of cholera toxin B subunit in the optic nerve, mice were perfused with 0.9% saline and the optic nerve immersion fixed for 1-2 hours in buffered neutral formalin (BNF), and frozen as above. For the B cell marker (CD45R/B220), unfixed tissue was frozen between OCT discs. For Olig2 immunohistochemistry, mice were perfused with 4% paraformaldehyde and nerves were post-fixed for 20 minutes before cryoprotecting and freezing.

Artificial cerebrospinal fluid (ACSF) for electrophysiology.
ACSF contained (in mM): NaCl 126, KCl 3.0, $CaCl_2$ 2.0, $MgCl_2$ 2.0, NaH_2PO_4 1.2, $NaHCO_3$ 26 and glucose 10.

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