## **Supplementary Material**

## Acute and chronic demyelinated CNS lesions exhibit opposite elastic properties

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## Supplemental Table 1. Elastic moduli of human MS brain sections

| Sample Type                             |                 | $\mathbf{E} \pm \mathbf{SD}$ |
|---|-----------------|------------------------------|
| Fixed Human Brain, Thick Sections*      | Chronic Lesions | 9.148 ± 18.51                |
|   | Acute Lesions   | $1.314 \pm 1.653$            |
|   | NAWM            | $1.88 \pm 2.54$              |
| Fixed Human Brain, 100µm Cryosections** | Lesion 2        | $3.26 \pm 2.32$              |
|   | Lesion 6        | $2.49 \pm 1.83$              |
|   | NAWM            | $1.93 \pm 1.69$              |

\* n = 1932, 1782 and 2824 for the chronic lesions, acute lesions and NAWM, respectively.

\*\* n = 980, 500 and 1000 for Lesion 2, Lesion 6 and NAWM, respectively.



**Supplemental Figure 1**. AFM of 100  $\mu$ m cryosections of human MS brain samples (**A-B**) Representative images showing MS lesions (stiff – lesion 2 and soft – lesion 6) and adjacent normal-appearing white matter (NAWM). The extent of myelin loss (fluoromyelin), presence of a reactive astrocytes (GFAP) and monocyte /microglia infiltration (lba1) are shown. (Scale bars 100  $\mu$ m) (**C**) Representative 90 x 90  $\mu$ m AFM force maps from the lesions shown in A and B. Changes in elasticity are detectable within each lesion compared to adjacent NAWM. (**D**) Quantitation of AFM stiffness measurements from MS lesions (stiff lesion in red; soft in blue), with data from 100 $\mu$ m cryosections shown in the left panel, and data from the original thick sections (Fig. 5) on the right. Values are expressed as lesion stiffness relative to adjacent NAWM. Dotted line indicates two-fold increase in stiffness compared to NAWM. Bars indicate the mean value from all measurements (for 100  $\mu$ m cryosections, n = 980 for lesion 2 and 500 for lesion 6; for thick sections, n = 693 for lesion 2 and 384 for lesion 6; \*\*\*\*p < 0.0001, Mann-Whitney test).