

Oligodendrocytes in sulfatide-null optic nerve

References

- 1) Dupree, J. L., Coetzee, T., Blight, A., Suzuki, K. and Popko, B. (1998) Myelin galactolipids are essential for proper node of Ranvier formation in the CNS. *J. Neurosci.* **18**, 1642-1649.
- 2) Bosio, A., Bussow, H., Adam, J. and Stoffel, W. (1998) Galactosphingolipids and axono-glial interaction in myelin of the central nervous system. *Cell Tissue Res.* **292**, 199-210.
- 3) Honke, K., Hirahara, Y., Dupree, J., Suzuki, K., Popko, B., Fukushima, K., Fukushima, J., Nagasawa, T., Yoshida, N., Wada, Y. and Taniguchi, N. (2002) Paranodal junction formation and spermatogenesis require sulfoglycolipids. *Proc. Natl. Acad. Sci. USA.* **99**, 4227-4232.
- 4) Ishibashi, T., Dupree, J. L., Ikenaka, K., Hirahara, Y., Honke, K., Peles, E., Popko, B., Suzuki, K., Nishino, H. and Baba, H. (2002) A myelin galactolipid, sulfatide, is essential for maintenance of ion channels on myelinated axon but not essential for initial cluster formation. *J. Neurosci.* **22**, 6507-6514.
- 5) Coetzee, T., Fujita, N., Dupree, J., Shi, R., Blight, A., Suzuki, K., Suzuki, K. and Popko, B. (1996) Myelination in the absence of galactocerebroside and sulfatide: normal structure with abnormal function and regional instability. *Cell* **86**, 209-219.
- 6) Marcus, J., Honigbaum, S., Shroff, S., Honke, K., Rosenbluth, J., Dupree, J. L. (2006) Sulfatide is essential for the maintenance of CNS myelin and axon structure. *Glia* **53**, 372-381.
- 7) Bansal, R., Winkler, S. and Bheddah, S. (1999) Negative regulation of oligodendrocyte differentiation by galactosphingolipids. *J. Neurosci.* **19**, 7913-7924.

Oligodendrocytes in sulfatide-null optic nerve

- 8) Hirahara, Y., Bansal, R., Honke K., Ikenaka, K. and Wada, Y. (2004) Sulfatide is a negative regulator of oligodendrocyte differentiation: development in sulfatide-null mice. *Glia* **45**, 269-277.
- 9) Marcus, J., Dupree, J. L. and Popko, B. (2000) Effects of galactolipid elimination on oligodendrocyte development and myelination. *Glia* **30**, 319-328.
- 10) Shroff, S. M., Pomicter, A. D., Chow, W. N., Fox, M. A., Colello, R. J., Henderson, S. C. and Dupree, J. L. (2009) Adult CST-null mice maintain an increased number of oligodendrocytes. *J. Neurosci. Res.* **87**, 3403-3414.
- 11) Baba, H., Akita, H., Ishibashi, T., Inoue, Y., Nakahira, K. and Ikenaka, K. (1999) Completion of myelin compaction, but not the attachment of oligodendroglial processes triggers K⁺ channel clustering. *J. Neurosci. Res.* **58**, 752-764.
- 12) Barres, B. A., Hart, I. K., Coles, H. S. R., Burne, J. F., Voyvodic, J. T., Richardson, W. D. and Raff, M. C. (1992) Cell death and control of cell survival in the oligodendrocyte lineage. *Cell* **70**, 31-46.
- 13) Trapp, B. D., Nishiyama, A., Cheng, D. and Macklin, W. (1997) Differentiation and death of premyelinating oligodendrocytes in developing rodent brain. *J. Cell Biol.* **137**, 459-468.
- 14) Nishiyama, A., Lin, X. H., Giese, N., Heldin, C. H. and Stalcup, W. B. (1996) Co-localization of NG2 proteoglycan and PDGF alpha-receptor on O2A progenitor cells in the developing rat brain. *J. Neurosci. Res.* **43**, 299-314.
- 15) Nishiyama, A., Lin, X. H., Giese, N., Heldin, C. H. and Stalcup, W. B. (1996) Interaction between NG2 proteoglycan and PDGF alpha-receptor on O2A progenitor cells

Oligodendrocytes in sulfatide-null optic nerve

is required for optimal response to PDGF. *J. Neurosci. Res.* 1996b **43**, 315-330.

- 16) Trapp, B. D., Pfeiffer, S. E., Anitei, M. and Kidd, G. J. (2004) Cell biology of myelin assembly; *In Myelin biology and disorders* vol. 1 (ed. Lazzarini, R. A.) Elsevier Academic Press, San Diego, pp 29-55.
- 17) Naruse, I., Keino, H. and Kawarada, Y. (1994) Antibody against single-stranded DNA detects both programmed cell death and drug-induced apoptosis. *Histochem.* **101**, 73-78.
- 18) Kagawa, T., Ikenaka K., Inoue. Y., Kuriyama, S., Tsuji, T., Nakao, J., Nakajima, K., Aruga, J., Okano, H. and Mikoshiba, K. (1994) Glial cell degeneration and hypomyelination caused by overexpression of myelin proteolipid protein gene. *Neuron* **13**, 427-442.
- 19) Tanaka, K. (1993) Cloning and expression of a glutamate transporter from mouse brain. *Neurosci. Lett.* **159**, 183-186.
- 20) Ma, J., Matsumoto, M., Tanaka, K. F., Takebayashi, H. and Ikenaka, K. (2006) An animal model for late onset chronic demyelination disease caused by failed terminal differentiation of oligodendrocytes. *Neuron Glia Biol.* **2**, 81-91.
- 21) Hoshi, T., Suzuki, A., Hayashi, S., Tohyama, K., Hayashi, A., Yamaguchi, Y., Takeuchi, K. and Baba, H. (2007) Nodal protrusions, increased Schmidt-Lanterman incisures, and paranodal disorganization are characteristic features of sulfatide-deficient peripheral nerves. *Glia* **55**, 584-594.
- 22) Gardinier, M. V., Macklin, W. B., Diniak, A. J. and Deininger, P. L. (1986) Characterization of myelin proteolipid mRNAs in normal and jimpy mice. *Mol. Cell. Biol.* **6**, 3755-3762.

Oligodendrocytes in sulfatide-null optic nerve

- 23) Verity, A. N. and Campagnoni, A. T. (1988) Regional expression of myelin protein genes in the developing mouse brain: *in situ* hybridization studies. *J. Neurosci. Res.* **21**, 238-248.
- 24) Berntson Z., Hansson E., Roennbaeck L. and Fredman P. (1998) Intracellular sulfatide expression in a subpopulation of astrocytes in primary cultures. *J. Neurosci. Res.* **52**, 559-568.
- 25) Simons, M. and Trajkovic, K. (2006) Neuron-glia communication in the control of oligodendrocyte function and myelin biogenesis. *J. Cell Sci.* **119**, 4381-4389.
- 26) Bansal, R., Stefansson, K. and Pfeiffer, S. E. (1992) Proligodendroblast antigen (POA), a developmental antigen expressed by A007/04-positive oligodendrocyte progenitors prior to the appearance of sulfatide and galactocerebroside. *J. Neurochem.* **58**, 2221-2229.
- 27) Demerens, C., Stankoff, B., Logak, M., Anglade, P., Allinquant, B., Couraud, F., Zalc, B. and Lebetzki, C. (1996) Induction of myelination in the central nervous system by electrical activity. *Proc. Natl. Acad. Sci. USA* **93**, 9887-9892.
- 28) Wang, S., Sdrulla, A. D., diSibio, G., Bush, G., Nofziger, D., Hicks, C., Weinmaster, G. and Barres, B. A. (1998) Notch receptor activation inhibits oligodendrocyte differentiation. *Neuron* **21**, 63-75.
- 29) Charles, P., Hernandez, M. P., Stankoff, B., Aigrot, M. S., Colin, C., Rougon, G., Zalc, B. and Lubetzki, C. (2000) Negative regulation of central nervous system myelination by polysialylated-neural cell adhesion molecule. *Proc. Natl. Acad. Sci. USA* **97**, 7585-7590.
- 30) Park, S-K., Miller, R., Krane, I. and Vartanian, T. (2001) The erbB2 gene is required for the development of terminally differentiated spinal cord oligodendrocytes. *J. Cell Biol.* **154**, 1245-1258.

Oligodendrocytes in sulfatide-null optic nerve

- 31) Genoud, S., Lappe-Siefke, C., Goebbels, S., Radtke, F., Aguet, M., Scherer, S. S., Suter, U., Nave, K. A. and Mantei, N. (2002) Notch1 control of oligodendrocyte differentiation in the spinal cord. *J. Cell Biol.* **158**, 709-718.
- 32) Stevens, B., Porta, S., Haak, L. L., Gallo, V. and Fields, R. D. (2002) Adenosine: a neuron-glial transmitter promoting myelination in the CNS in response to action potentials. *Neuron* **36**, 855-868.
- 33) Ishibashi, T., Dakin, K. A., Stevens, B., Lee, P. R., Kozlov, S. V., Stewart, C.L. and Fields, R. D. (2006) Astrocytes promote myelination in response to electrical impulses. *Neuron* **49**, 823-832.
- 34) Li, S., Liquari, P., McKee, K. K., Harrison, D., Patel, R., Lee, S. and Yurchenco, P. D. (2005) Laminin-sulfatide binding initiates basement membrane assembly and enables receptor signaling in Schwann cells and fibroblasts. *J. Cell Biol.* **169**, 179-189.
- 35) Pesheva, P., Gloor, S., Schachner, M. and Probstmeier, R. (1997) Tenascin-R is an intrinsic autocrine factor for oligodendrocyte differentiation and promotes cell adhesion by a sulfatide-mediated mechanism. *J. Neurosci.* **17**, 4642-4651.
- 36) Shao, K., Hou, Q., Go, M. L., Duan, W., Cheung, N. S., Feng, S. S., Wong, K. P., Yoram, A., Zhang, W., Huang, Z. and Li, Q. T. (2007) Sulfatide-tenascin interaction mediates binding to the extracellular matrix and endocytic uptake of liposomes in glioma cells. *Cell. Mol. Life Sci.* **64**, 506-515.
- 37) Schafer, D. P., Bansal, R., Hedstrom, K. L., Pfeiffer, S. E. and Rasband, M. N. (2004) Does paranode formation and maintenance require partitioning of neurofascin 155 into lipid rafts? *J. Neurosci.* **24**, 3176-3185.

Oligodendrocytes in sulfatide-null optic nerve

- 37) Dyer, C. A. and Benjamins, J. A. (1991) Galactocerebroside and sulfatide independently mediate Ca^{2+} responses in oligodendrocytes. *J. Neurosci. Res.* **30**, 699–711.

Oligodendrocytes in sulfatide-null optic nerve

Figure legends

Fig. 1. PLP-positive cells in adult optic nerves of wild-type and CST-deficient mice. (A-D) The mRNA expression pattern of the oligodendrocyte marker PLP in 4- (A, B) and 22-week-old (C, D) wild-type (WT; +/+) and CST-deficient (CSTKO; -/-) mice were examined by *in situ* hybridization. Scale bar indicates 100 μ m. (E) Comparative cell densities of PLP mRNA-positive cells in the optic nerves are shown. Each value represents the mean \pm SEM of the data obtained from four animals. *, P < 0.05; ***, P < 0.001 vs. control.

Fig. 2. NG2-positive cells in the optic nerve of 4-week-old wild-type and CST-deficient mice. (A, B) The expression pattern of the oligodendrocyte precursor cell marker, NG2, in wild-type (WT; +/+) and CST-deficient (CSTKO; -/-) mouse optic nerves were examined using an antibody specific to NG2. Scale bar indicates 50 μ m. (C) Comparative cell densities of NG2-positive cells are shown. (D) The total cell number and number of NG2-positive cells were counted in each nerve area and the percentage of NG2-positive cells was calculated. Each value represents the mean \pm SEM of the data obtained from four animals. *, P < 0.05; ***, P < 0.001 vs. control.

Fig. 3. GLAST- and *c-fms*-positive cells in optic nerves of wild-type and CST-deficient adult mice. The cell densities of astrocytes and microglia were examined by *in situ* hybridization using the cell-specific markers, GLAST (A) and *c-fms* (B), respectively. Each value represents the mean \pm SEM of the data obtained from four animals.

Fig. 4. Number of OPCs and the proportion of dying or proliferating cells in 5-day-old optic nerves of wild-type and CST-deficient mice. (A-F) Double labeling of NG2 (green)/PI (red) was performed on optic nerves from 5-day-old wild-type (+/++; A-C) and CST-deficient (-/-; D-F) mice. Scale bar represent 25 μ m. (G-I) Total cell numbers (G) or the number of NG2-positive cells (H) per area, and percentages of NG2-positive cells (I) in both wild-type (WT) and CST-deficient (CSTKO) optic nerves are shown. (J, K) One day after BrdU injection, the densities of dying cells (J) and proliferating cells (K) were

Oligodendrocytes in sulfatide-null optic nerve

examined using specific antibodies against ssDNA or BrdU, respectively. Each value represents the mean \pm SEM of the data obtained from three individual animals of each genotype. *, P < 0.05; ***, P < 0.001 vs. control.

Fig. 5. Regional differences in OPC numbers during early development of optic nerves in wild-type and CST-deficient mice. Transverse serial cryosections (10 μ m) were prepared by cutting 1-day-old (H-J) and 3-day-old (B-G; K-M) optic nerves of wild-type and CST-deficient mice from the retinal to the chiasmal side. (A) A schematic representation of the optic nerve regions (positions 1 to 6) is illustrated. Optic nerves of wild-type (+/+) and CST-deficient (-/-) mice were divided into six regions (250 μ m each, for a total of 1.5 mm; see the materials and methods for details). (B-G) The 10- μ m-thick sections from each region were triple stained with NG2 (red), BrdU (green) and DAPI (blue). Representative pictures in B/C, D/E, and F/G were obtained from positions 1, 3 and 6, respectively. (H- M) The average number of NG2-positive cells per nerve area (H, K), percentages of NG2-positive cells (I, L) and percentages of BrdU-positive cells in NG2-positive cell populations (J, M) from three sections at each optic nerve position are represented as mean \pm SEM. Each value represents the mean of the data obtained from two individual animals (H-J; 1-day-old mice) and three individual animals (K-M; 3-day-old mice) of each genotype. *, P < 0.05; ***, P < 0.001 vs. control.

Fig. 6. Myelinated axons in 10-day-old CST-deficient optic nerves. (A, B) Optic nerves prepared from 10-day-old wild-type (A) and CST-deficient (B) mice were examined by electron microscopy. (C) The percentages of myelinated axons are shown. Each value represents the mean \pm SEM of the data obtained from two animals of each genotype. *, P < 0.001 vs. control.

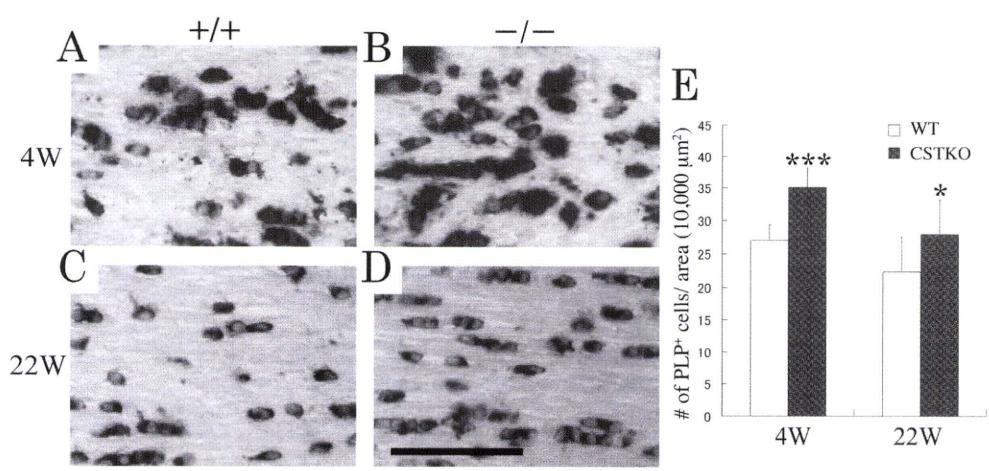


Fig.1 Kajigaya et al. Oligodendrocytes in sulfatide-null optic nerve. black and white

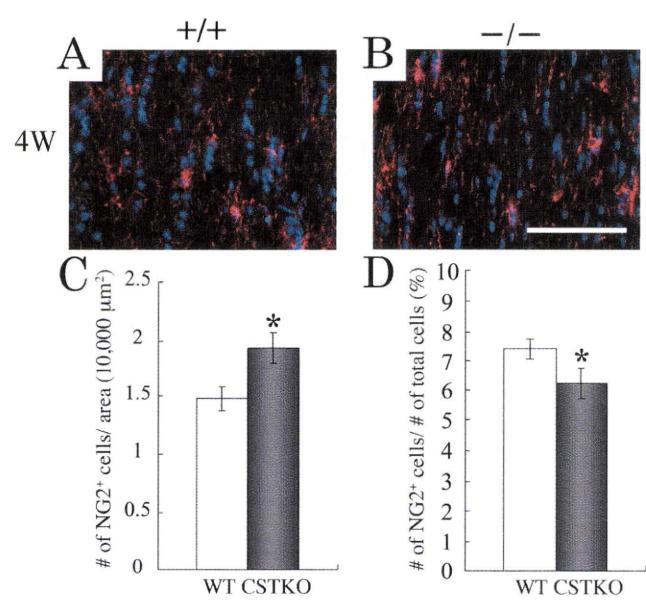


Fig. 2 kajigaya et al. Oligodendrocytes in sulfatide-null optic nerve
color

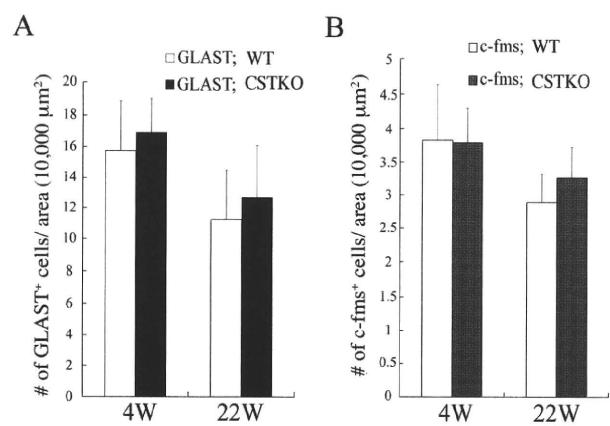


Fig. 3 Kajigaya et al, Oligodendrocytes in sulfatide-null optic nerve
black and white

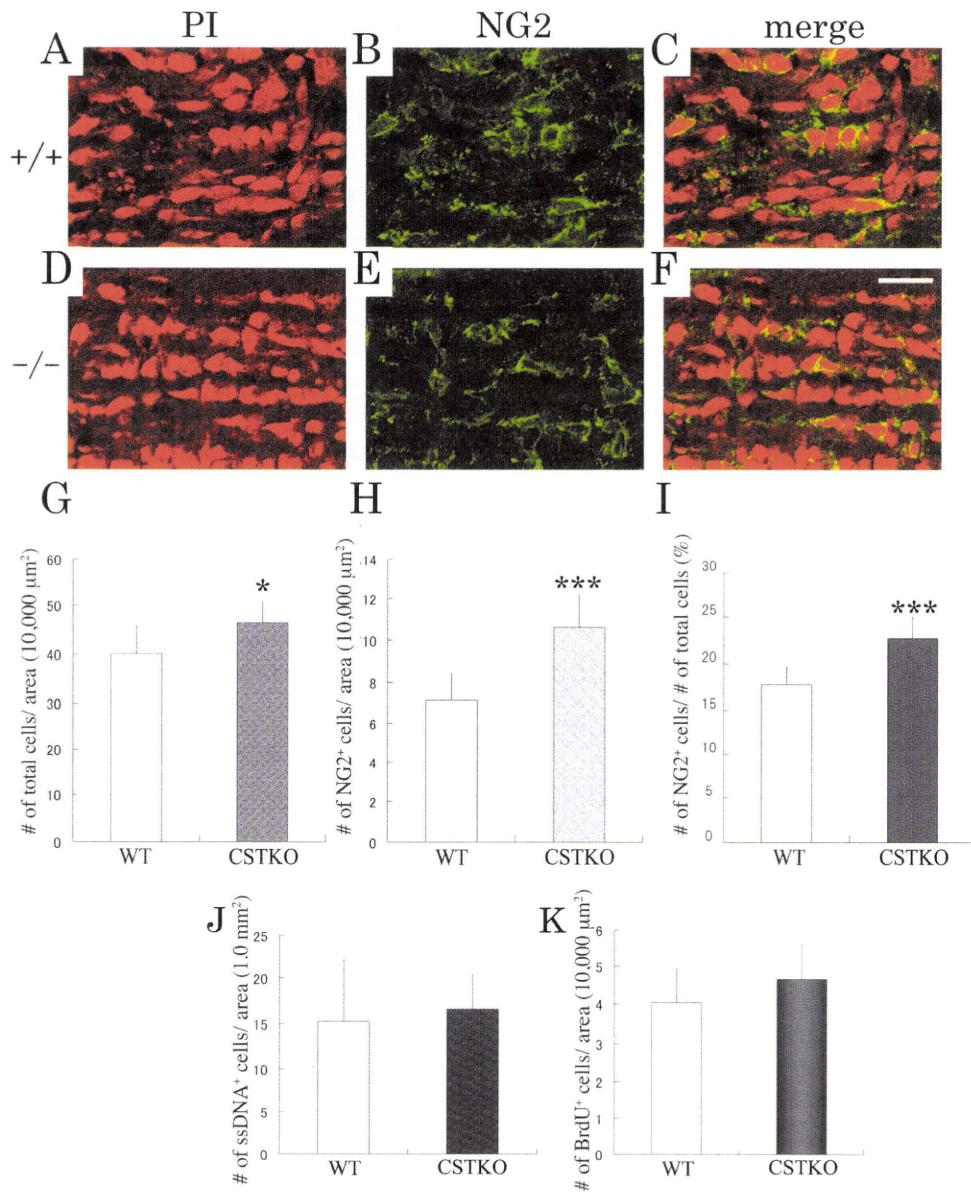
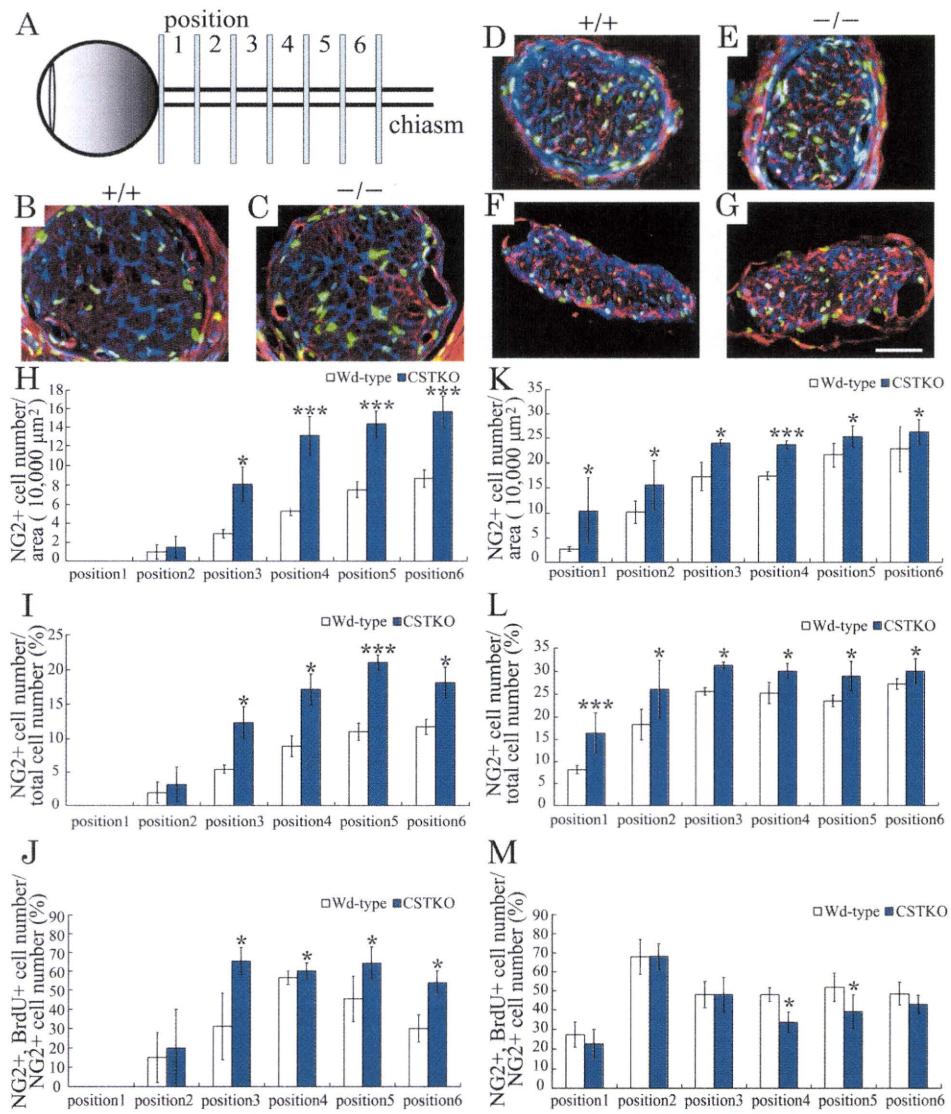


Fig 4 Kajigaya et al. Oligodendrocytes in sulfatide-null optic nerve. color



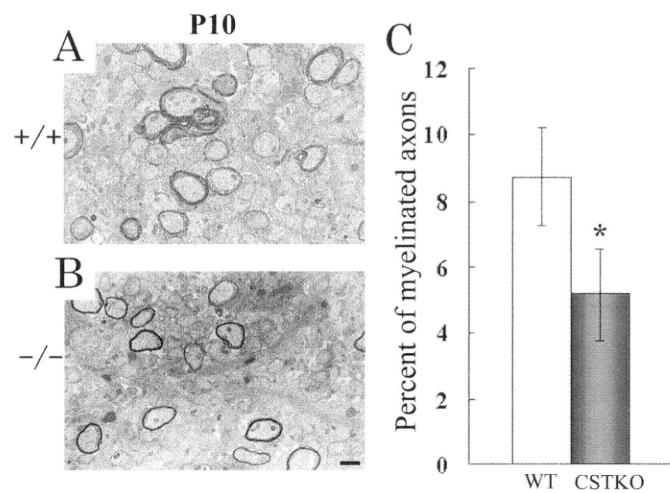


Fig. 6 Kajigaya et al. Oligodendrocytes in sulfatide-null optic nerve.
black and white

