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The promoter region of 46-kDa CNPase is sufficient for its expression in corpus callosum

Myelin is formed by oligodendrocytes in the central nervous system (CNS) or by Schwann cells in the peripheral nervous system (PNS). It is composed of many bioorganic components such as lipids, proteins and amino acids, as well as nucleotides [1,2]. Growing evidence indicates that myelin diseases represented by genetic hypomyelinating leukodystrophies (HLDs) are related to the failure of the metabolism [3,4].

2',3'-Cyclic nucleotide phosphodiesterase (CNPase) is one of the major myelin component proteins in the CNS. CNPase participates not only in nucleotide metabolism as intracellular phosphodiesterase but also in linking actin cytoskeletons to the intracellular side of myelin membranes [1]. The *cnpase* gene encodes two isoforms of 48- and 46-kDa, which are regulated by different promoters [5]. Despite the important role of CNPase in myelin membrane homeostasis, the question of whether the isolated 1-kilobase upstream unit from mRNA encoding the smaller isoform actually contributes to protein expression remains to be unanswered. In contrast, the longer isoform uses the specific promoter upstream of the isolated 1-kilobase unit [5].

We have succeeded in getting one line of transgenic mice harboring the isolated 1-kilobase unit of the mouse *cnpase* gene and *cre* [6,7] (Figs. S1 and S2). The mice were crossbred with ROSA26-β-galactosidase (ROSA26-BGAL, JAX's strain No. 003474) mice, identifying Cre recombinase-positive cells. We thus immunostained neonatal transgenic mouse brain tissues sliced vertically for myelinated axons in corpus callosum, which contains high-dense myelin sheaths. BGAL staining

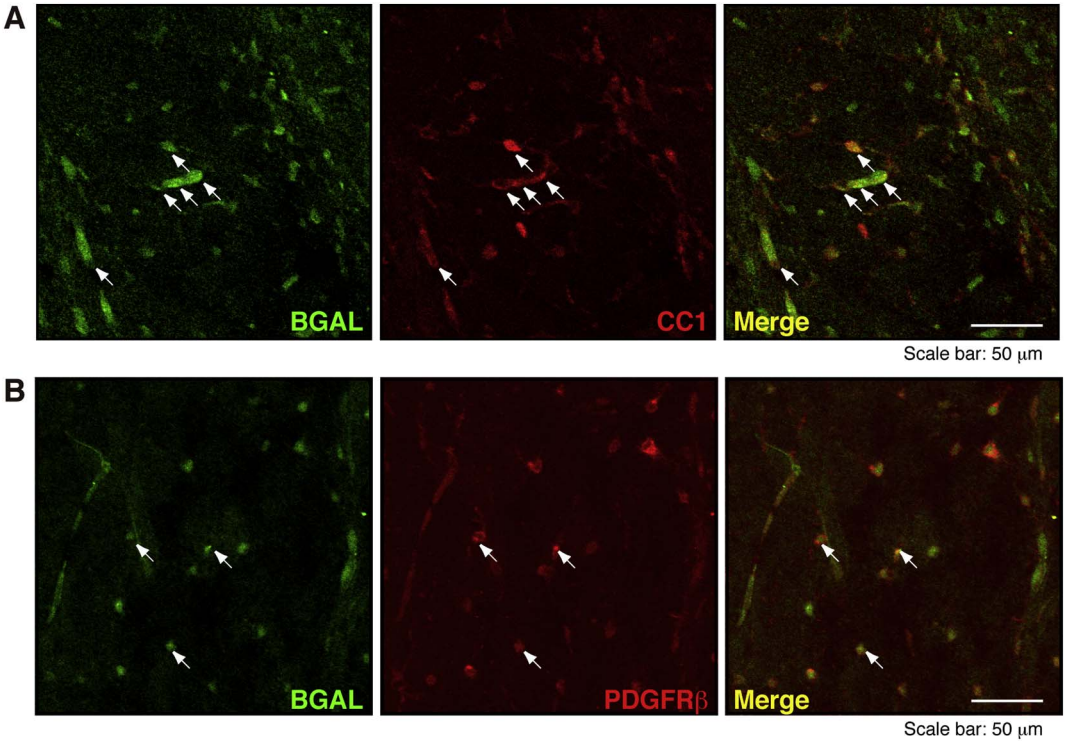

Fig. 1. Staining of β-Galactosidase (BGAL) and an oligodendrocyte marker in transgenic mouse corpus callosum. Transgenic mice of 46-kDa CNPase promoter-driven Cre recombinase were crossbred with ROSA26-BGAL mice. BGAL activities were detected in corpus callosum sections. In (A), BGAL (green) and CC1 (red, oligodendrocyte marker) were co-stained. In (B), BGAL (green) and PDGFRβ (red, oligodendrocyte precursor cell marker) were co-stained. Arrows indicate the representative colocalization positions of BGAL and an oligodendrocyte marker. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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corresponded to the oligodendrocyte marker CC1, as well as to the oligodendrocyte precursor cell marker PDGFRβ (Fig. 1, A and B). We also sliced along an anterior and posterior axis in brain and performed BGAL staining (Fig. S3). Further studies allow us to understand not only its promoter activity but also studies on mechanisms underlying myelin development and diseases by using Cre mice.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ymgmr.2018.03.003.

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