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The involvement of both precursor and mature oligodendrocytes in remyelination following ethidium bromide-induced demyelination in the mouse spinal cord

Yoshihiro Konishi[1)]*, Shigeko Fushimi[2)], Juri Horio[1)], Teruo Shirabe[3)]

1) Department of Clinical Research, NHO Tottori Medical Center

2) Department of Neuropathology, Kawasaki Medical School

3) Faculty of Health Science and Technology, Kawasaki University of Medical Welfare

*Correspondence: ykonishi@tottori-iryo.hosp.go.jp

Abstract

Myelin is produced by oligodendrocytes in the central nervous system (CNS). Disruption of myelin, referred to as demyelination, causes severe diseases, such as multiple sclerosis (MS), in humans. Remyelination can be observed during the early stage of disease. Uncovering the underlying mechanisms of remyelination should provide avenues for future therapeutic strategies for MS; however, it has not yet been determined whether remyelinating oligodendrocytes can arise from mature oligodendrocytes or are generated from the proliferation and differentiation of oligodendrocyte precursor cells (OPCs). To address this issue, 50 mg/kg of 5-bromo-2-deoxyuridine (BrdU) was intraperitoneally administered to 12–17-week-old BALB/*c* male mice, 5, 6, 7 days after ethidium bromide (EBr) injection into the posterior column,to trace cells that were mitotic during demyelination. In this mouse model, focal demyelination was completely induced in the posterior column on the 8th day, and remyelination began to be observed on the 10th day. Four weeks later, the central type of remyelination by oligodendrocytes was seen in the periphery. As a result, some proteolipid protein (PLP)-expressing cells incorporated BrdU in the demyelination stage, subsequently began to participate in remyelination in the early stage of remyelination, and gradually moved into lesions to keep the participation in the subsequent remyelination stage, while platelet-derived growth factor α receptor (PDGFαR)-expressing cells incorporated BrdU in the demyelination stage and began to express PLP to contribute to remyelination 2 weeks after EBr injection, not in the early stage of remyelination. Mature PLP-positive oligodendrocytes as well as OPCs with PDGFαR possibly participate in remyelination following demyelination in the adult mouse spinal cords. Cells expressing PLP that incorporated BrdU, not connected to myelin sheaths, might exist either as a reserve source for myelination or for a function distinct from myelination. *Tottori J. Clin. Res.* 2(2), 245-263, 2009

Key Words: oligodendrocyte precursor cells (OPCs), mature oligodendrocytes, platelet-derived growth factor α receptor (PDGFαR), proteolipid protein (PLP), demyelination, remyelination

Introduction

Myelin is a lipid insulator surrounding individual axons required for the fast conduction of action potentials. Myelin is produced by oligodendrocytes in the central nervous system (CNS), which occurs shortly after birth. Disruption of myelin, referred to as demyelination, occurring later in life, causes severe diseases such as multiple