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Abstract

Traumatic peripheral nerve injuries are caused by traffic accidents, sports, and occupational incidents. While it is said that recovery after peripheral nerve damage shows much better outcomes than central nervous system damage, satisfactory therapeutic consequences are not often obtained. As prolonged therapy duration is suggested, physical and exercise therapies are often chosen to facilitate functional recovery. Therefore, improvements in therapeutic methods based on molecular mechanisms and consequently improved rehabilitation methods are expected. Peripheral nerves are composed of many nerve axons that are bundled together, and nerve axons are encompassed by myelin sheaths, which are constructed by Schwann cells. Schwann cells degenerate following peripheral nerve injury and immature Schwann cells proliferate, differentiate, and support axonal regeneration and extension during recovery. Thus, Schwann cells play an important role in peripheral myelination, and dysfunction of these cells leads to axonal damage. Although Heller et al (J Cell Biol, 2014) have reported that serum- and glucocorticoid- inducible kinase 1 (SGK1) in Schwann cells is involved in developmental myelination, its significance during peripheral nerve injury and repair remains unknown. In this study, we examined the dynamics of SGK1 during peripheral nerve repair and the potential role of SGK in the process. Axonal crush injury was first generated in the right sciatic nerve under anesthesia in mice, which exhibited apparent paralysis and subsequent recovery of the injured hindlimbs. Immunohistochemical analysis revealed the appearance of glial fibrillary acidic protein-positive immature Schwann cells around injured nerves, and SGK1 was present in these cells. Next, we employed S16 cells, a Schwann cell line, to explore the impact of SGK1 on Schwann cells, as SGK1 is expressed primarily in these cells. Administration of the SGK inhibitor gsk650394 decreased cell proliferation and increased cell size. SGK inhibition did not cause cellular injury, suggesting that it suppresses proliferation and enlarges Schwann cells without causing cell death. Furthermore, quantitative PCR and immunoblotting revealed that SGK inhibition upregulated the gene expression of BDNF, MBP, and Krox20, which are facilitating factors for myelination and neural regeneration, and downregulated that of Sox10, a marker of immature Schwan cells. Taken together, these findings indicate that SGK1 inactivation in Schwann cells diverts cell fate from proliferation to differentiation.