Facilitation of Schwann cell differentiation can be a novel approach to suppress paclitaxel-induced peripheral neuropathy

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We have previously demonstrated that paclitaxel reduces myelin-forming Schwann cells due to dedifferentiation of mature Schwann cells, prior to the induction of cytotoxicity against peripheral neurons. This cytotoxic process should be a causative pathogenesis of taxane-related chemotherapy-induced peripheral neuropathy (CIPN). To find the causal treatment of CIPN, we screened approved drugs with the ability to promote Schwann cell differentiation. Among numerous medicines,the most effective compounds identified was a PDE inhibitor, which promoted differentiation of immature Schwann cells, as indicated by increased expression of a mature Schwann cell marker, MBP. In a mixed culture of Schwann cells and DRG neurons, the co-treatment with a PDE inhibitor (30 mM) significantly suppressed paclitaxel (10
nM)-induced loss of myelin-forming Schwann cells (i.e. demyelination). In addition, the long-term administration of a PDE inhibitor (0.3% in chow diets) during the paclitaxel injection-period, paclitaxel (5 mg/kg, i.p.) twice a week for 8 weeks, reduced mechanical hypersensitivity in mice. Thus, we propose here that a PDE inhibitor, which prevents paclitaxel-induced Schwann cell dedifferentiation and demyelination, can be a therapeutic candidate to suppress paclitaxel-related CIPN.