Dedifferentiation of Schwann cells by taxanes participates in the chemotherapy-induced peripheral neuropathy pathogenesis

Satoshi Imai

Dept. Clin. Pharmacol. & Therap., Kyoto Univ. Hosp.

Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent side effect of taxanes. CIPN is a serious impediment in effective cancer treatment, because aggravation of symptoms results in discontinuation of taxane treatment or dose reduction, which can increase cancer related mortality and morbidity. Although impairment of neuroaxis of peripheral neurons by taxanes has been considered to be a major cause of CIPN, however, the precise underlying mechanisms are unknown. To address this issue, we have focused on the role of Schwann cells in supporting the maintenance of the peripheral nervous system, and have examined the direct effects of taxanes on these cells. We demonstrated for the first time that taxanes preferentially impair Schwann cells, rather than induce neurotoxicity in sensory neurons. Furthermore, the novelty of our study lies in the finding that paclitaxel induces dedifferentiation of myelin-forming Schwann cells characterized by increased expression of low affinity nerve growth factor receptor p75 (immature Schwann cell marker) and decreased expression of myelin-associated molecule (MBP, mature Schwann cell marker).
In this presentation, I will talk about our research on the mechanisms underlying CIPN pathogenesis, focusing on Schwann cells.