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Concerted interactions of neurogenesis and myelinogenesis in promoting neuroregeneration

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Regeneration of injured peripheral nerves and spinal cord is a slow and complicated process that could be improved by implantation of neural stem cells (NSCs) or nerve conduit. We previously showed that implantation of NSCs along with conduits promotes the regeneration of damaged nerve. The improvement is likely due to conduit supports and guides axonal growth from the proximal nerve stump to the distal one, while preventing fibrous tissue ingrowth and retaining neurotrophic factors; and implanted NSCs differentiate into Schwann cells and maintain a growth factor-enriched microenvironment, which promotes nerve regeneration. We identified IL12p80 (homodimer of IL12p40) in the cell extracts of implanted nerve conduit combined with NSCs by using protein antibody array and western blotting analyses. Levels of IL12p80 in these conduits are 1.6-fold higher than those in conduits without NSCs. In the sciatic nerve injury mouse model, implantation of NSCs combined with nerve conduit and IL12p80 improves motor recovery and increases the diameter up to 4.5-fold, at the medial site of the regenerated nerve. *In vitro* studies further revealed that IL12p80 stimulates the Schwann cell differentiation of mouse NSCs. Moreover, the cellular differentiation is enhanced through phosphorylation of signal transducer and activator of transcription 3 (Stat3). Our results suggest that IL12p80 could trigger Schwann cell differentiation of NSCs through Stat3 phosphorylation. Differentiation of myelinating Schwann cells increases the diameter of regenerated nerves and, in turn, enhances the functional recovery in a mouse sciatic nerve injury model.

Biography

Ing-Ming Chiu is currently a Distinguished Investigator and Professor at the National Health Research Institutes in Taiwan. He is the Group Leader of a multidisciplinary research group in Stem Cell and Regenerative Medicine. He has earned his PhD in Biochemistry at Florida State University. He did Post-Doctoral training in National Cancer Institute in Bethesda, Maryland before joining as the Faculty in The Ohio State University in Columbus, Ohio in 1986. He served as the Director of the Brain Tumor Gene Therapy Program at The Ohio State University. In the National Health Research Institutes, his group developed a method to combine the use of nerve conduits, FGF1 and neural stem cells in the repair of sciatic nerve injury. He has published more than 140 papers and have received 14 patents.

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