

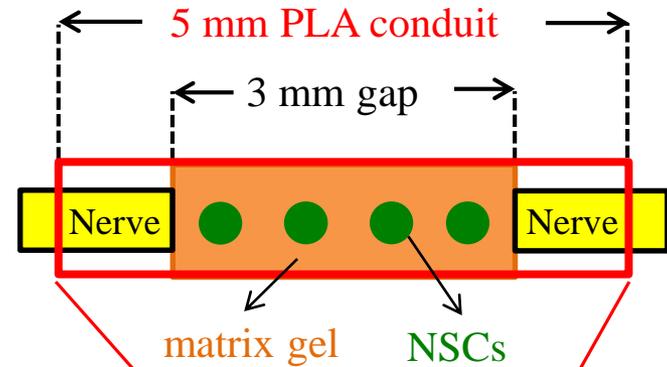
利用神經幹細胞與IL12p40 以增強神經再生的方法

Methods to Enhance Nerve Regeneration Utilizing Neural Stem Cells and IL12p40

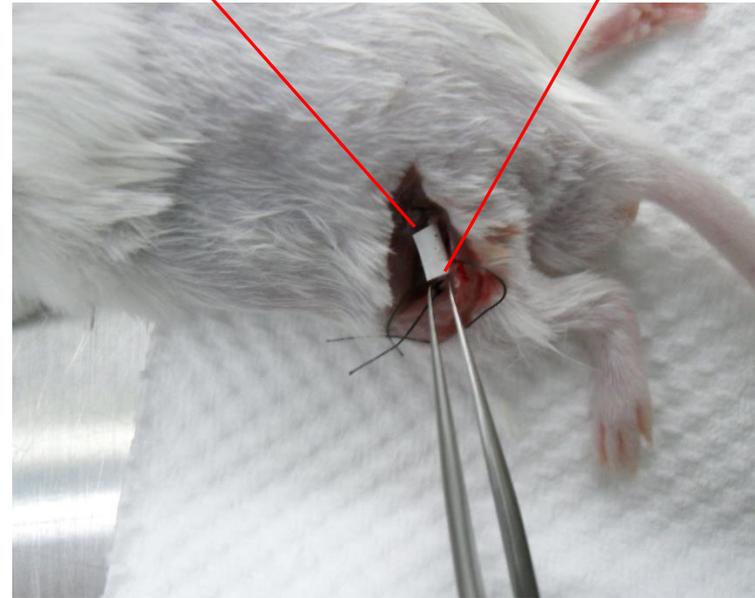
邱英明特聘研究員
Ing-Ming Chiu

Company Name: National Health Research Institutes
Contact Person: Hua-Hsuan Liang
Tel: +886-37-246-166 ext. 33206
E-mail: huahsuan@nhri.org.tw
Address: 35 Keyan Road, Zhunan, Miaoli County 35053, Taiwan
Website: <http://www.nhri.org.tw/>

Establishment of sciatic nerve injury mouse model

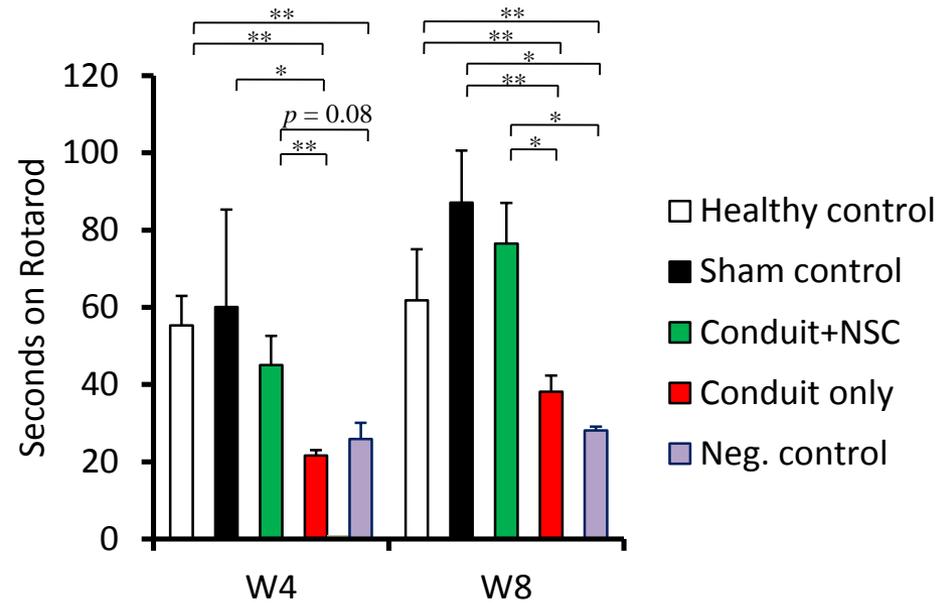
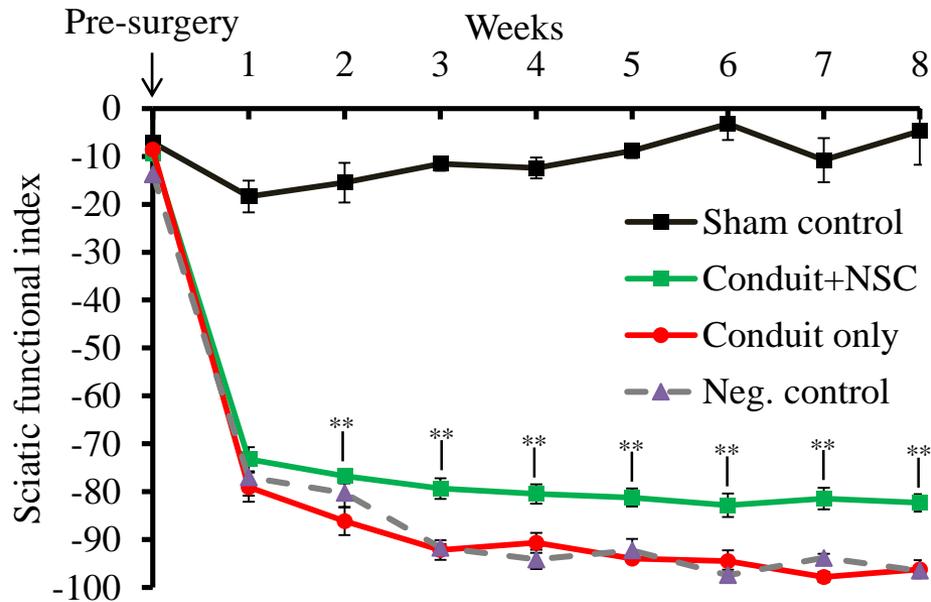


Sciatic nerve injury mouse model



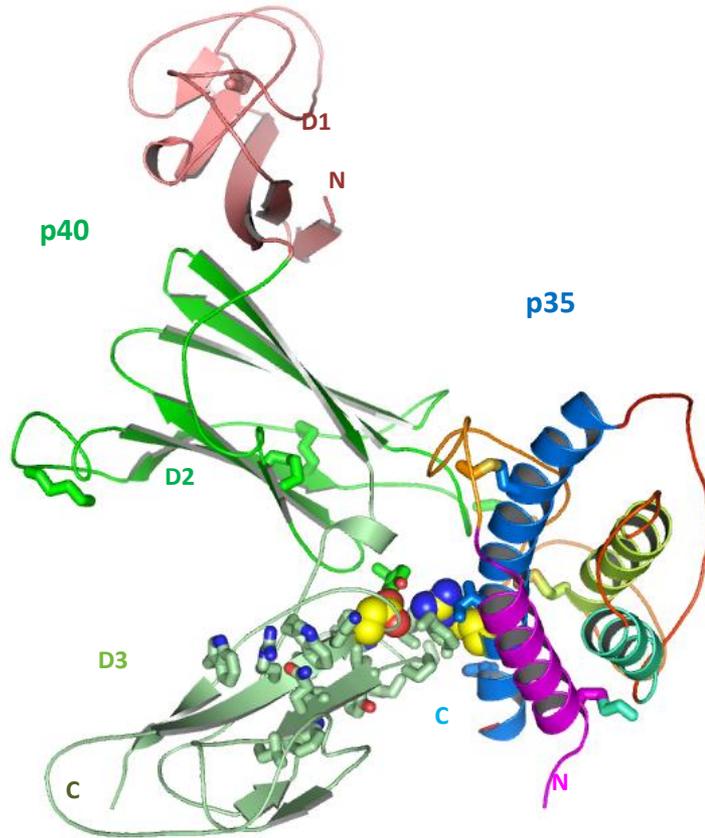
Implantation of NSCs with nerve conduit

Implantation of F1BGFP⁺-NSCs with nerve conduits improved recovery of sciatic nerve injury in mice



Proteomic analysis revealed that **IL12p40** but not p35 was up-regulated in the conduit seeded with NSCs

A.

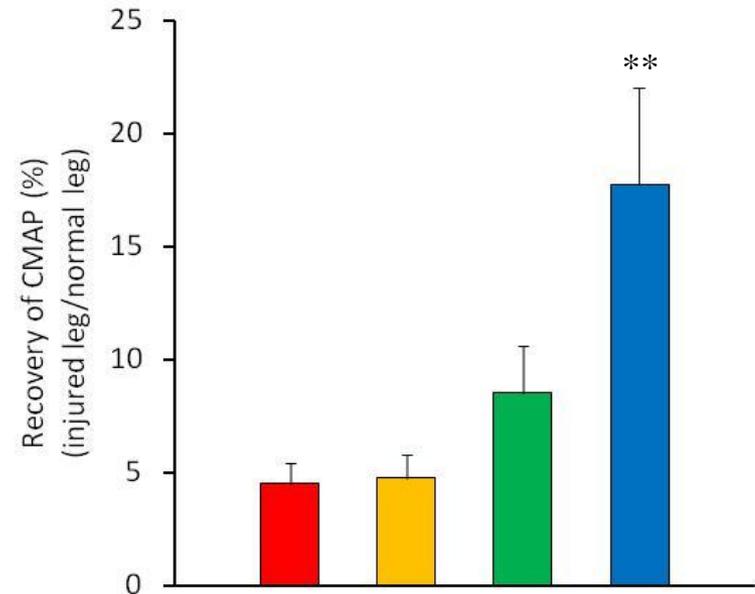
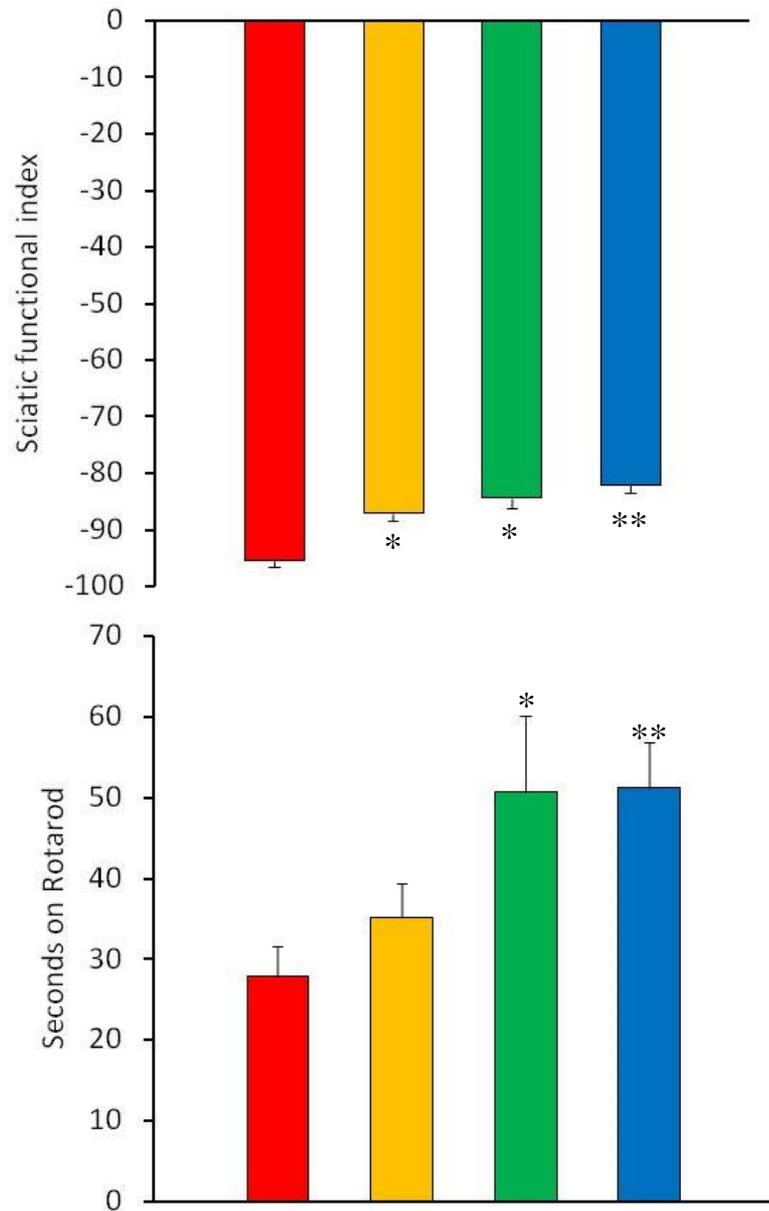


IL12 p40-p35 Heterodimer

B.

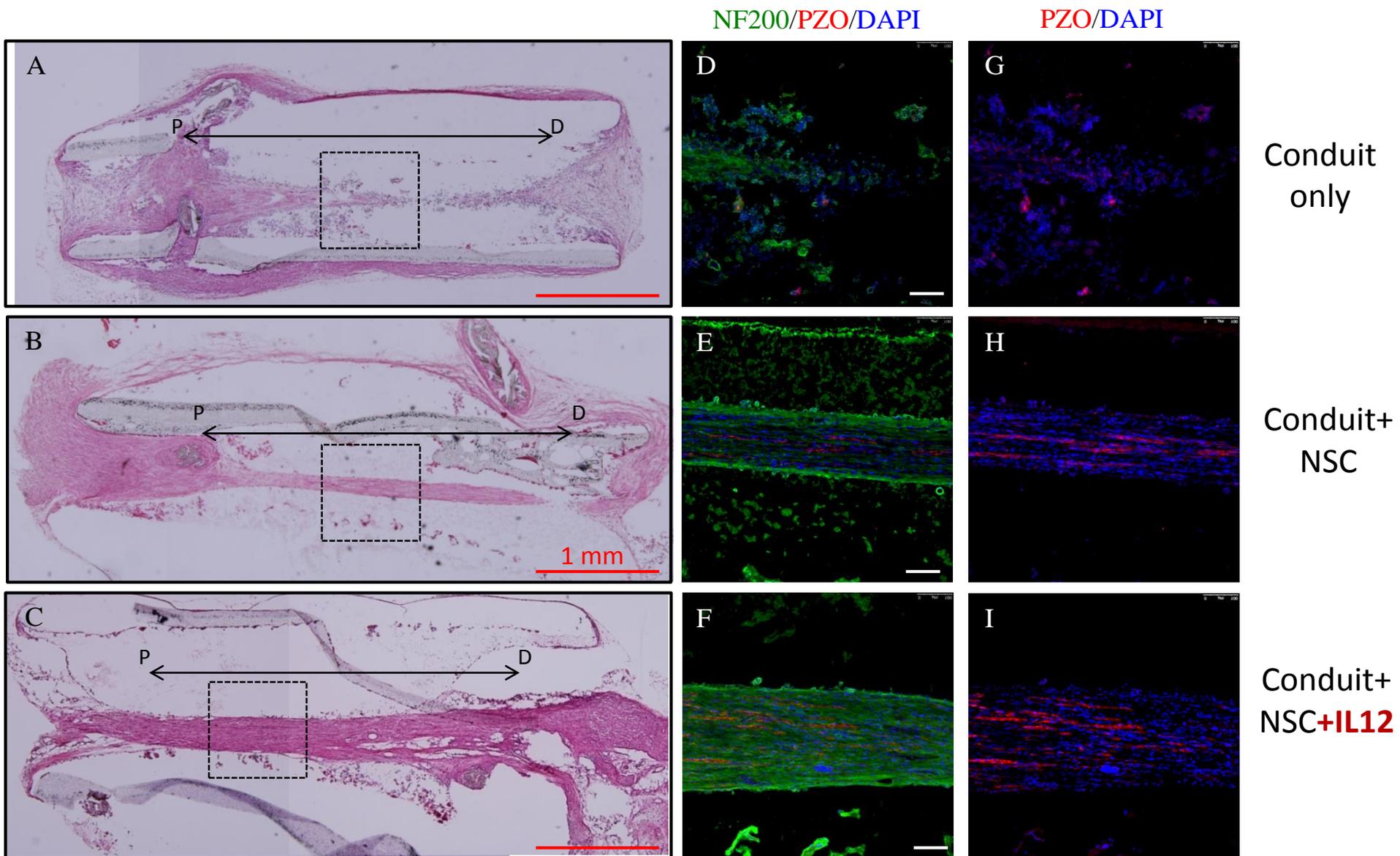
..... Suggesting that the Neurotrophic Protein is IL12 p40-p40 Homodimer

IL12p80 promotes functional recovery

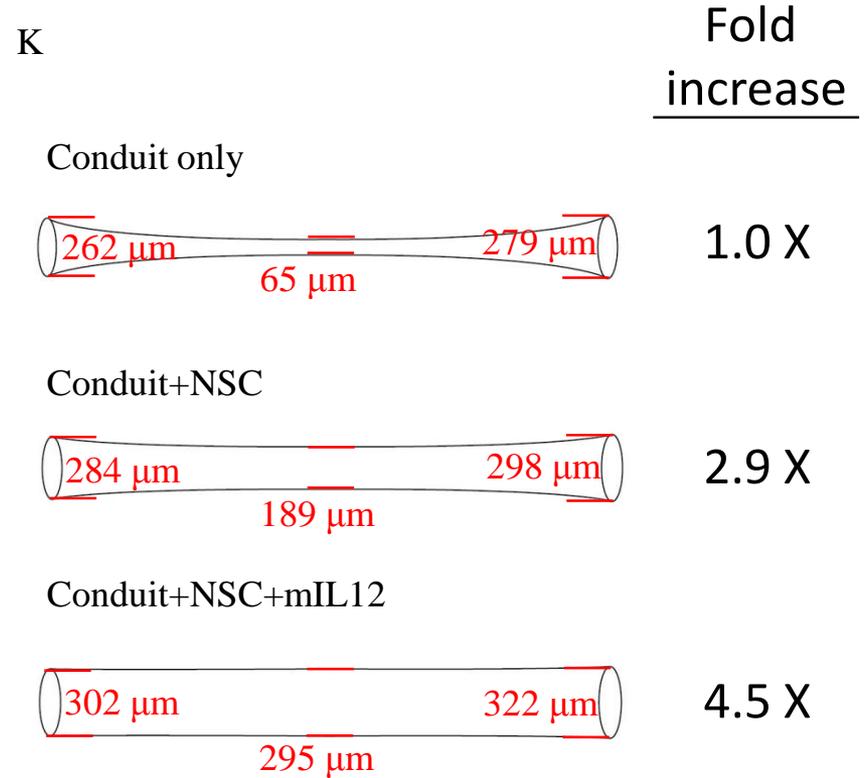
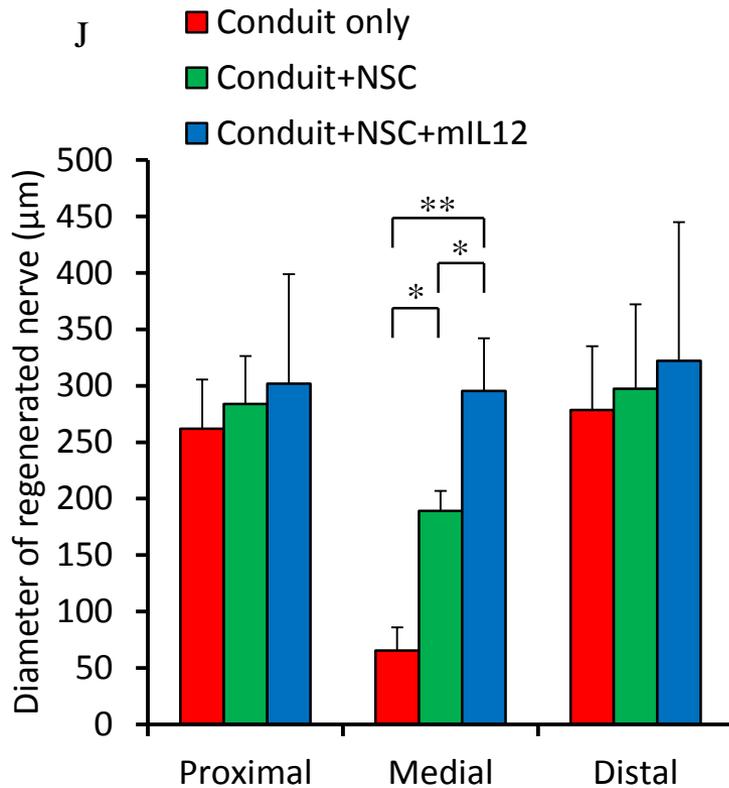


- Conduit only
- Conduit+mIL12
- Conduit+NSC
- Conduit+NSC+mIL12

IL12 facilitates nerve regeneration *in vivo*



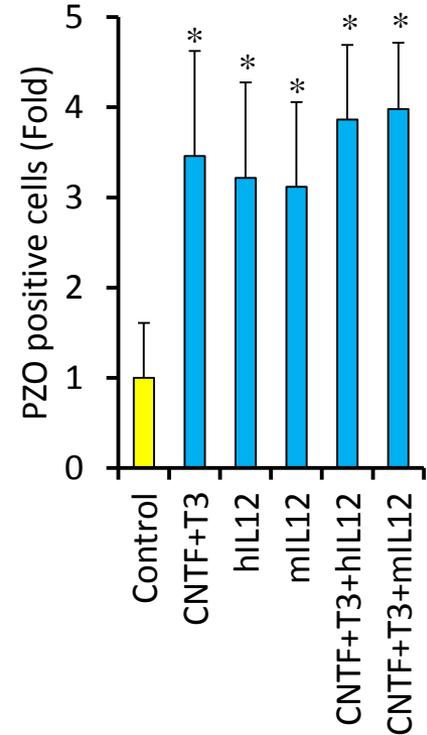
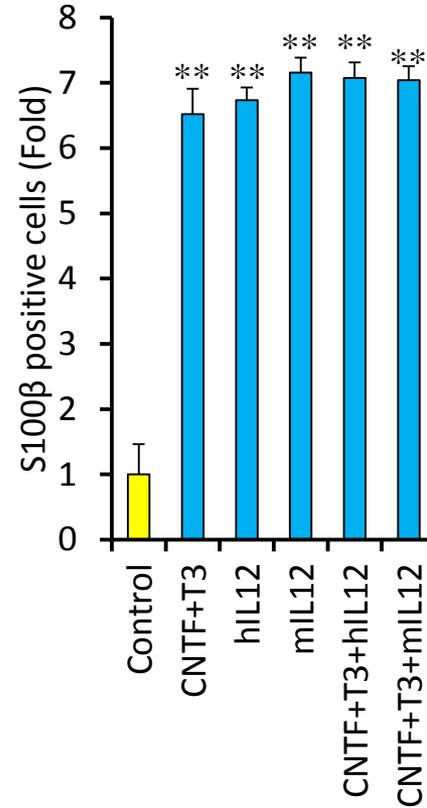
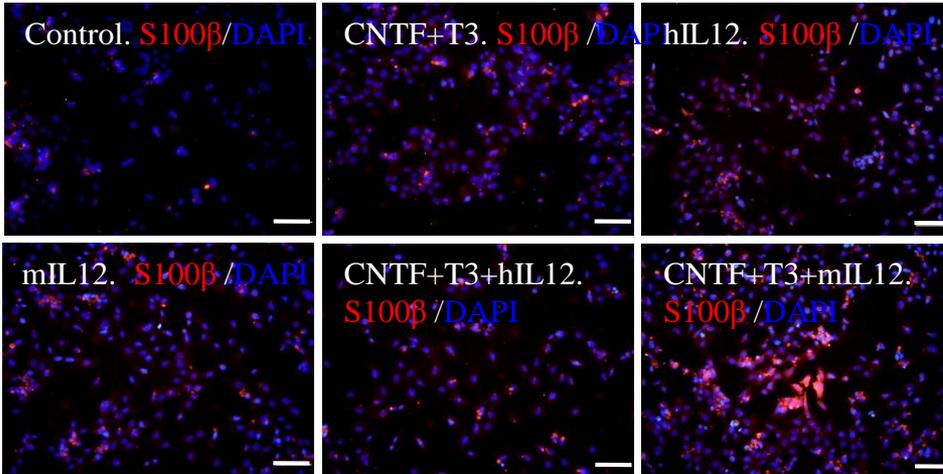
IL12 facilitates nerve regeneration (cont.)



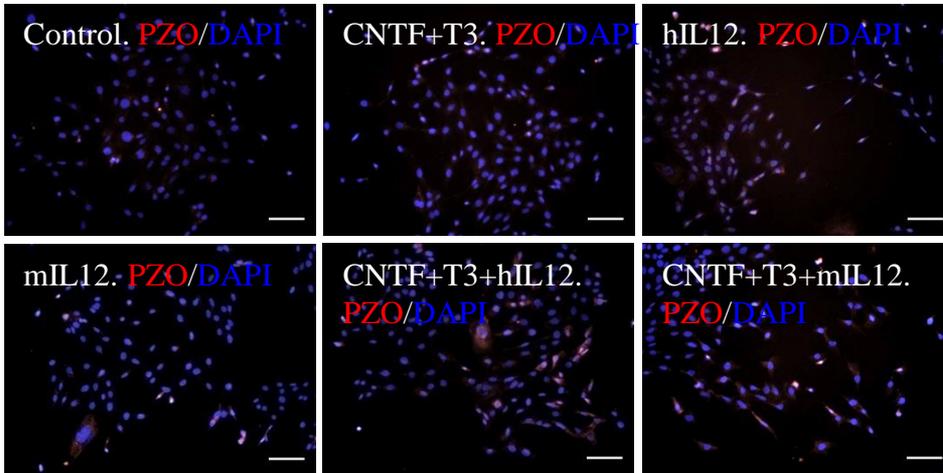
Chiu, Lee and Chi. PCT Patent Submitted (Aug. 2015)
 Chiu, Lee and Chi. TW Patent Submitted (Aug. 2015)
 Lee et al., Mol Cell Neurosci. In press (2017)

Immunocytochemistry showed that IL12p80 induces Schwann cell differentiation *in vitro*

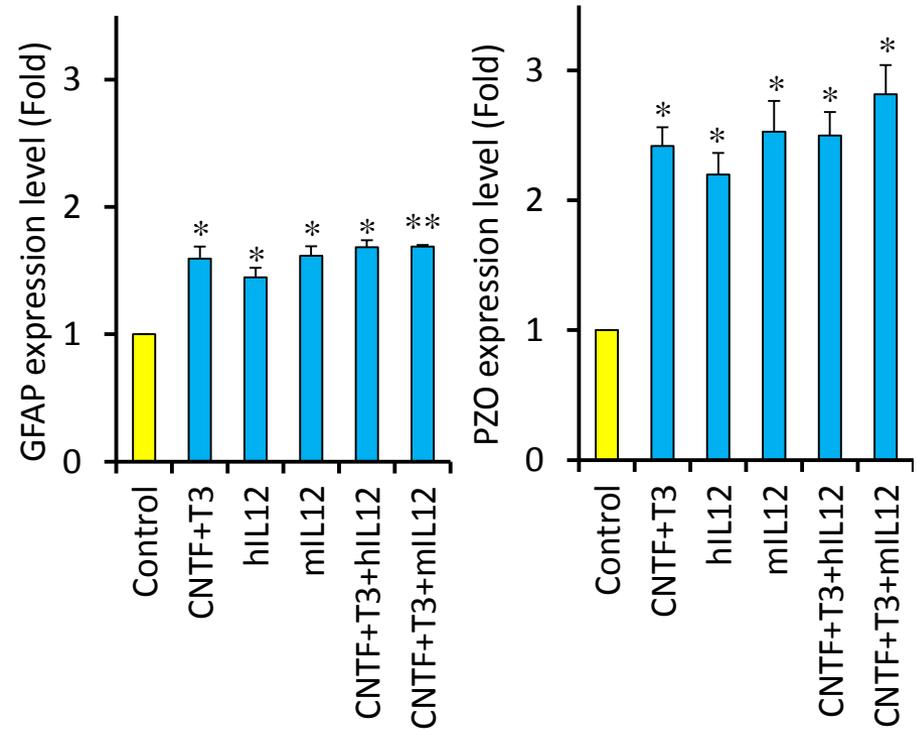
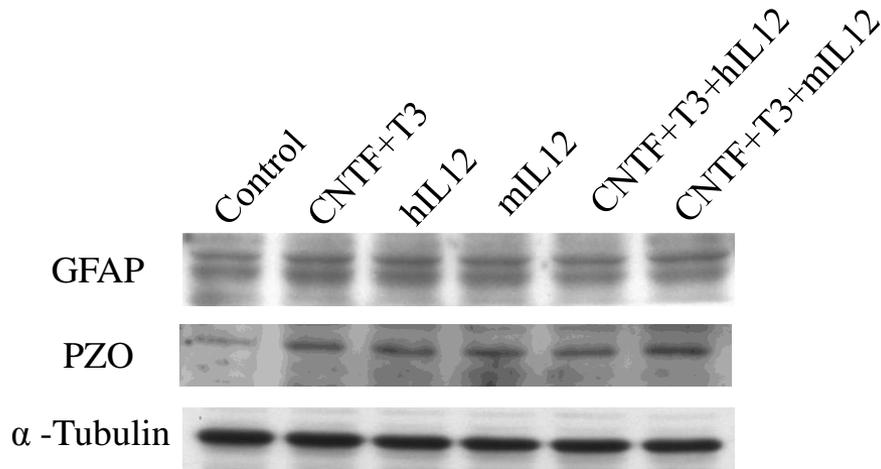
A



B



Western blotting showed that IL12p80 induces Schwann cell differentiation *in vitro*



Conclusion

- We discovered that IL12p80 is present in the mouse cell extracts of implanted nerve conduit combined with NSCs.
- In the sciatic nerve injury mouse model, implantation of NSCs combined with nerve conduit and IL12p80 improves motor recovery and increases the regenerated nerve diameter up to 4.5-fold.
- Our *in vitro* study showed that IL12p80 stimulates the Schwann cell differentiation of mouse NSCs.
- We further showed that this differentiation is activated through the phosphorylation of Stat3.
- The Executive Yuan of Taiwan is funding TWD \$95 million dollars per year to setup Biologics Program in National Health Research Institutes.
- We are targeting to submit IND (Investigational New Drug) application to Taiwan FDA for IL12 as a novel biologic drug by 2018.
- We will consider exclusive licensing or non-exclusive licensing for the use of IL12.

Chiu, Lee and Chi. PCT Patent Submitted (Aug. 2015)

Chiu, Lee and Chi. TW Patent Submitted (Aug. 2015)

Lee et al., Mol Cell Neurosci. Mar. 2017