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GDNF-secreting Schwann cells in multichannel OPF+scaffolds promote ascending axonal regeneration and locomotor recovery following complete spinal cord transaction in rats

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Improving neurologic function in patients after spinal cord injury will require combinations of interventions that are concurrently applied. Polymer scaffold technologies may be particularly useful for multimodal approaches in the treatment of SCI. Our work has focused on the implantation of cell-loaded, multichannel scaffolds fabricated from the positively-charged polymer oligo[poly(ethylene glycol) fumarate] (OPF$^+$). Photo-cross linked OPF$^+$ forms a soft, porous, biodegradable hydrogel with biomechanical properties similar to spinal cord tissue. In this study, we compared the regenerative capacity of multichannel OPF+ scaffolds containing primary unmodified Schwann cells (SCs) with OPF$^+$ scaffolds delivering Schwann cells that have been genetically modified to secrete glial cell-derived neurotrophic factor (GDNF-SCs). OPF$^+$ scaffolds containing SCs or GDNF-SCs were implanted into completely transected rat spinal cords at the T9/10levelin 10 animals per group.GDNF-SCs promoted the regeneration of significantly higher numbers of axons (2773.0±396.0, mean±SEM) into OPF$^+$ scaffolds than into scaffolds with primary SCs (1666.0±352.2) ($p<0.05$). A central and ventral midline axon growth orientation was observed through the GDNF-SC scaffolds. The cell body origin of axons which traversed through OPF$^+$ scaffolds and out into the distal cord was identified by retrograde fast blue (FB) axonal tracing studies. The mean number of neuron cell bodies labeled in caudal spinal cord segments by FB injection 5 mm rostral to the scaffold (ascending axons) was significantly higher (111.80±28.64) in animals with GDNF-SC OPF$^+$ scaffolds than in animals with primary SC OPF$^+$ scaffolds (12.60±2.60 per section) ($p<0.001$). No significant difference in the mean number of FB-labeled neuronal cell bodies was observed between SC and GDNF-SC groups when the FB injection site was 5 mm caudal to the scaffold (descending axons) (19.90±1.68 in SC and 19.60±3.42 in GDNF-SC OPF$^+$ scaffold animals). Animals transplanted with GDNF-SC OPF$^+$ scaffolds demonstrated a significant degree of functional locomotor recovery at weeks 3 and 4 following surgery which was not seen with primary SC scaffold implantation.

Biography

Bingkun K Chen is an Assistant Professor of Medicine, Mayo Clinic College of Medicine. He graduated with an MD in China, further studied in Germany, and later received his PhD in Japan. He focuses on spinal cord injury and regeneration. He developed and optimized bidirectional axonal tracing with DiI and DiO, and retrograde axonal tracing with Fast Blue. By using tissue engineered technology with biodegradable polymer scaffolds loaded with growth-promoting cells (Schwann cells) to bridge transection, it might aim to shift the balance in injured spinal cord towards healing and functional regeneration in patients. He has authored and published more than 50 peer-reviewed articles; as well as serving as Editor, Associate editor and Editor-in-chief for several books and bulletins, and as Reviewer for a number of journals in neuroscience.

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