Poster
Number

72 **Instructive roles of DRG neurons in directing the fate choice of bone marrow derived Schwann cells**

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(Supervisor: Professor YS Chan, HKU)

The bone marrow offers an autologous source of progenitor cells for use in remyelination therapy. Our success in deriving Schwann cells from bone marrow stromal cells suggests juxtacrine signals provided by dorsal root ganglia (DRG) neurons in the switch of Schwann cell-like cells (SCLCs) to fate commitment.

In our search for the signals, immunocytochemical analysis found the Notch ligands,DLL-1 and Jagged-1, localized on the surface of DRG neurons whereas the receptor, Notch-1, was on bone marrow-derived SCLCs. In cocultures with DRG neurons, SCLCs indicated nuclear localization of the Notch intracellular domain (NICD), suggestive of ligand-activated Notch signaling. Concomitantly, increase in ErbB2/3 expression was revealed among SCLCs by mmunocytochemistry and confirmed by Western blotting. As cells achieved commitment to the Schwann cell fate, nuclear NICD returned to the basal level. When a γ-secretase inhibitor was used to inhibit Notch signaling, the increase inErbB2/3 expression among SCLCs was no longer effected and progress of SCLCs to the Schwann cell fate was significantly retarded. We therefore revealed an emerging role of Notch signaling in the upregulation of ErbB receptors for neuregulin-activated signaling as SCLCs transition into fate commitment.

73 **Chitosan Nanofiber Composed Nerve Conduit for Directing Axonal Growth**

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Schwann cell-seeded guidance channels have been exploited to bridge and guide axonal re-growth across gaps in lesioned nerves. By orienting the Schwann cell growth on aligned nanofibers, we hypothesized that axonal growth can be guided along the designated direction towards the target. Chitosan as the choice scaffold material given its biocompatibility and the tunable susceptibility to biodegradation. Chitosan was dissolved in trifluoroacetic acid/methylene chloride solution and for electrospinning onto a high speed rotating collector drum yielding aligned nanofibers. These aligned chitosan nanofibers directed the growth pattern of Schwann cells. We further seeded dissociated cells of dorsal root ganglia (DRG, E14/15 rats) onto the aligned nanofibers and found that neurons and Schwann cells adapted the uniaxial arrangement of nanofibers. The Schwann cells could also be induced to undergo myelination of the DRG neurons. We then rolled the Schwann cell-seeded or DRG explant-seeded nanofiber sheet into a model of nerve conduit. The Schwann cells remained in alignment and DRG neuron grew along the longitudinal axis of the conduit. These in vitro results provide proof-of-principle for pursuing improvement in post-traumatic recovery from nerve injury with use of Schwann cell-seeded uniaxially aligned chitosan nanofibers as a nerve guidance channel.

Supported by ITS/100/10 of the Innovation and Technology Commission, HK Government