



Tuesday, September 4, 2018

LSC 3 | 11:00 - 12:00PM

Anand Krishnan PhD

Senior Postdoctoral Fellow
Division of Neurology
University of Alberta

"Tumor suppressors as critical targets for peripheral nerve regeneration"

Peripheral nerves are essential connections of the body. Without them, there is no movement or sensation. Damage to peripheral nerves is common, can occur through major accidents, sports injuries, etc, but the disability it renders is often devastating. Successful regeneration of injured nerves is often problematic due to poor growth rate and impaired directionality and currently no effective treatments are in place for complete restoration of damaged nerves. We identified that molecular pathways involved in tumorigenesis, nonetheless expressed in neurons, critically regulate peripheral nerve regeneration. For example, selective manipulation of the tumor suppressor proteins Rb1 (Retinoblastoma 1) or BRCA1 (breast cancer susceptibility gene 1) modified growth pattern of injured rodent sciatic nerve. Knockdown of Rb1 was associated with dramatic rise in axon outgrowth and partial functional recovery, through mechanisms dependent and independent of E2F pathway. In contrast, nuclear localization of BRCA1 was found to be essential for nerve regeneration. We found that a distant injury to axons elicits DNA breaks in neuronal soma in dorsal root ganglia (DRG) and BRCA1 participates in DNA Damage Response (DDR) and maintain neuronal integrity, which is essential for nerve regeneration. Finally, we also identified a population of DRG resident cycling cells (DRCCs) in DRG, the dynamics of which is ramped up after distal axotomy at a controlled rate. We characterized DRCCs as satellite glial cells and resident macrophages. The role of tumor suppressors in controlling the turnover of DRCCs and their functional implications on nerve regeneration are under current investigation. Collectively, the regulatory role of tumor suppressors over the changes in cellular and molecular dynamics in the peripheral nerve regenerative milieu is promising and of therapeutic advantage.

Live Online Seminar Viewing:
<http://tinyurl.com/cbrseminaronline>