INTERNATIONAL JOURNAL OF STUDENTS' RESEARCH
Volume 5 Issue 2 Year 2015 **www.ijsronline.net**

EDITORIAL

Noteworthy apprising in neuroregeneration

Utkarsh Gupta[1], Fariah Asha Haque[2]

Prologue to Neuroregeneration

It is well known that tissues within our nervous system possess minimal regenerative capacity when compared to other tissues of the human body. This actuality begets many neuroscientists to comprehend deeper into various mechanism that forms the underlying basis of this trait and find ways to increase the regenerative potential. Over 90,000 individuals are affected by traumatic brain injury and spinal cord injury alone, and 5.3 million people in the United States are affected by traumatic brain injury-related disabilities [1]. It constitutes as one of the most debilitating events along with many other neurodegenerative processes in various pathology causing neurological ailment [1]. Regeneration can be either structural or functional. Even if the anatomical or physiological structures are restored, it is not necessary for it to have complete functional restoration. Functional regeneration tends to restore in time with compensatory mechanism explained best by neuroplasticity. The multiple spectrum approach involving medical, surgical, and rehabilitation procedures is utilized for repair and regeneration of neural tissues.

Regenerative potential varies remarkably between peripheral nervous system (PNS) and central nervous system (CNS). CNS has poorer regenerative capacity than PNS attributing mostly to the inhibitory factors. In PNS, chemotactic factors amid the injury debris mobilize Schwann cells, macrophages, and phagocytes to clear the debris and initiate the process of regeneration and repair. Regeneration is possible only if the soma of neurons is intact. The distal segment goes under Wallerian degeneration. On the contrary, CNS has influx of oligodendrocytes, myelin-associated inhibitors, astrocytes, and others to create an inhibitory environment that rapidly produces glial scars further inhibiting the regeneration process.

Currently Practiced Approaches for Repair

Surgical peripheral nerve reconstruction is applicable for injured peripheral nerve injury. The severed parts are reapproximated by sutures after assessing the viability of the parts of neuron [2]. Following surgical correction, healthy padding is carried out by skin or muscle. Anesthesia used is decided by assessing the complexity of injury. The outcome of surgery depends on various factors such as age, mechanism of injury, and level of energy [2]. Regenerative ability decreases with age. Crush injury is more difficult to regain function as compared to sharp injuries. Distance plays a major role as well with regeneration being better in injuries more distal [2].

Nerve grafting is an epoch-making procedure in attempts toward nerve repair and regeneration. Autologous nerve grafting serves as the gold standard for injury of nerves with large gap between the proximal and distal parts of neurons [2,3]. Allograft and xenograft hold greater disadvantage of graft rejection due to immune process. Recently, nerve guidance conduit, stem cell therapy, immunization targets, and gene therapy are making benchmark progress in repair and regeneration process.

Recent Findings Contributing to Better Understanding

Research in neuronal regeneration is one of the most enthralling topics discussed by scientists. There have been various important findings demonstrated in the last decade. The most common subjects of the study of neural mechanism for regeneration are *Drosophila* (fruit fly), *Caenorhabditis elegans* (free-living transparent nematode), and rodents. It is worth noting a few of the works recently done.

Studies in *Drosophila* show that both dendrite and axon display regenerative capacity with slight developmental differences. Both cell intrinsic and cell extrinsic pathways are involved. Activation of phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase/protein kinase-B (PTEN/AKT) pathway enhances regeneration, but mostly in PNS [4]. Reversed microtubule polarity is seen in the regeneration of both dendrites and axon [4].

Recent studies in rodent model suggest that inactivation of glycogen synthase kinase 3 beta (GSK3β)-collapsin response mediator protein-2 pathway leads to increased microtubule growth speed which eventually increases the rate of axonal growth [5]. Microtubule dynamics is very important for the regeneration process of axons [5]. Another study showed that in neuronal soma, microRNA-26a-GSK3β plays major role in regulation of regeneration, in which microRNA-26a suppresses GSK3β activity and upregulates regeneration [6]. Furthermore, activation of mechanistic target of rapamycin-C1 (mTORC1) and inhibition of mTORC2 along with inhibition of GSK3β support regeneration through AKT3 in mature axons of CNS [7].

[1]Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, [2]Department of Medicine, Jawaharlal Nehru Medical College, Wardha (Sawangi), India

Corresponding Author:
Utkarsh Gupta, E-mail: utkarshgupta.neuro@gmail.com

Selective suppression of neurite outgrowth inhibitor-A (Nogo-A) in oligodendrocyte and myelin while preserving its function in neurons enhances regeneration process and hence suggests dual function of Nogo-A, which is a well-known myelin-enriched inhibitory factor [8].

Studies done on *C. elegans* discuss that axons form growth cone but fail to grow extensions in the presence of mutated RNA-binding protein UNC-75 (unc stands for uncoordinated), supporting the presence of role of UNC-75 of CUBP and Etr-3 like factor family in neuronal regeneration [9]. Alternative splicing of Soluble NSF Attachment Protein Receptor syntaxin is regulated by UNC-75 [9]. Dual leucine zipper kinase signaling pathway has role in both axonal regeneration and degeneration [10].

Conclusion

Vast majority of human population is affected by nerve injury and neurodegenerative disease. Minimal potential of regeneration in nervous tissues makes it a challenge for us to find novel methods to rehabilitate affected individuals and promote research for its better repair and regeneration. Major research works done are on *Drosophila*, rodents, and C. *elegans* to find the underlying mechanisms. CNS exhibits less regenerative potential than PNS explained by the inhibitory environment in CNS. Surgical repair and nerve grafts are mostly used. Newer modalities such as gene therapy and stem cell therapy can play a vital role.

References

1. Stabenfeldt SE, García AJ, LaPlaca MC. Thermoreversible laminin-functionalized hydrogel for neural tissue engineering. *J Biomed Mater Res A* 2006;77(4):718-25.
2. The Southern Orthopaedic Association > Patient Education: Nerve Repair and Grafting in the Upper Extremity; 2006. The Southern Orthopaedic Association > Patient Education: Nerve Repair and Grafting in the Upper Extremity 2006. Available from: http://www.orthopaediccare.net/ [Last retrieved on 2009 Jan 12].
3. Kalantarian B, Rice DC, Tiangco DA, et. al. Gains and losses of the XII-VII component of the "baby-sitter" procedure: a morphometric analysis. *J Reconstr Microsurg* 1998;14(7):459-71.
4. Song Y, Ori-McKenney KM, Zheng Y, et. al. Regeneration of *Drosophila* sensory neuron axons and dendrites is regulated by the AKT pathway involving PTEN and microRNA bantam. *Genes Dev* 2012;26(14):1612-25.
5. Liz MA, Mar FM, Santos TE, et. al. Neuronal deletion of GSK3ß increases microtubule speed in the growth cone and enhances axon regeneration via CRMP-2 and independently of MAP1B and CLASP2. *BMC Biol* 2014;12:47.
6. Jiang JJ, Liu CM, Zhang BY, et. al. MicroRNA-a supports mammalian axon regeneration *in vivo* by suppressing GSKß expression. *Cell Death Dis* 2015;6(8):e1865.
7. Miao L, Yang L, Huang H, et. al. mTORC1 is necessary but mTORC2 and GSK3ß are inhibitory for AKT3-induced axon regeneration in the central nervous system. *Elife* 2016;5:e14908.
8. Vajda F, Jordi N, Dalkara D, et. al. Cell type-specific Nogo-A gene ablation promotes axonal regeneration in the injured adult optic nerve. *Cell Death Differ* 2015;22(2):323-35.
9. Chen L, Liu Z, Zhou B, et. al. CELF RNA binding proteins promote axon regeneration in *C. elegans* and mammals through alternative splicing of Syntaxins. *Elife* 2016;5. pii: E16072.
10. Tedeschi A, Bradke F. The DLK signalling pathway – A double-edged sword in neural development and regeneration. *EMBO Rep* 2013;14(7):605-14.

Author's Contributions

Editorial theme, defining of intellectual content, literature review and manuscript preparation and editing were done by both the authors Utkarsh Gupta and Fariah Asha Haque.

Competing Interest

The authors declare that they have no competing interests

Funding

Sources of Funding: None

Please cite this paper as: Gupta U, Haque FA. Noteworthy apprising in neuroregeneration. *Int J Stud Res* 2015;5(2):19-20.

Received: 13 Dec 2016, Accepted: 9 Jan 2017

Access this article online	
Quick Response Code:	Website: www.ijsronline.net
	DOI: 10.4103/ijsr.Int_J_Stud_Res_14_16