# CHAPTER 5
# DISSCUSSION AND CONCLUSION

This study examines the time course of sensory and motor neuron loss after axotomy only and axotomy with ligation in adult rats. It seems likely that the difference between axotomy only and axotomy with ligation may reflect the deprivation of trophic support from target tissue [39] associated with peripheral nerve axotomy with ligation. This source of trophic support would remain following axotomy but would be decreased following axotomy with ligation.

Following axotomy with ligation, the C7 DRGs appear to be similar to the axotomy only in that both die at time periods examined (1 to 6 weeks) following the lesion, but at the later time periods (8 to 32 weeks) the sensory neurons loss following axotomy with ligation is more than the axotomy only (Figure 22, 16). In contrast to the T1 DRGs, at an early time period examined (1 to 6 weeks) sensory neuron loss following axotomy with ligation is more than axotomy only. But at the later time period axotomy with ligation is similar to neuronal loss of axotomy only (Figure 24, 18).

In C8 DRGs appear to die of neurons at any time period examined (1 to 32 weeks) following axotomy with ligation which is more than the axotomy only (Figure 23, 17). In motor neurons, it was found that neuronal loss only at first week after axotomy only and axotomy with ligation and the loss of motor neuron after axotomy with ligation was more than the axotomy only. However, sensory and motor neuron loss following axotomy with ligation was more than that following axotomy in the same period. The reason for the difference in percent loss of sensory and motor neuron after axotomy with ligation and axotomy only in the same period is not clear. In previous reports in adult rats and mice, axotomy of the C7 nerve at a point 3 mm. distal to the spinal cord, did not cause any significant motor neuron loss 3 weeks after axotomy. [40,41] In contrast, in this result, the loss of motor neuron appeared in every level in 1 week after axotomy and axotomy with ligation. However, a detailed

examination of the peripheral stump following axotomy could perhaps provide some clues regarding the putative role of nonneuronal cells (e.g. Schwann cells) in the peripheral nerve in promoting neuron survival following axotomy and axotomy with ligation.

The Leukemia inhibitory factor has shown that applied to the proximal nerve stump in neonatal rat, it promote the survival of both sensory neurons in the dorsal root ganglion and motor neurons in the spinal cord.[32,33] LIF dramatically helps in non-neuronal cells following injury.[42] The mechanism and action of LIF remains unclear. However the capacity of both sensory and motor neuron to retrogradely transport LIF has been confirm in vivo using $^{125}$I-LIF in both adult and newborn mice and rats.[13,43]

Anterograde transport of LIF has been demonstrated in motor neurons following local application at the lesion site. Similarly this anterograde LIF transport rate is raised following nerve lesion.[42] The ability of LIF to rescue sensory and motor neuron when placed at the lesion site suggested that retrograde transport might be important in mediating this effect.

In the adult rats, LIFR mRNA is found throughout the central nervous system including the cerebral cortex, hippocampas, thalamus, hypothalamus, cerebellum, spinal cord and DRG.[44] LIF act indirectly via the cells such as Schwann cells and macrophages in the vicinity of the nerve stump given that the latter express the LIFR.[45]

This result support this concept and it appears that the action of LIF in gelfoam has its effect within 1, 2, and 4 weeks after axotomy, after which neuronal loss proceeds at the same rate as in PBS controls. Sensory neuron in the DRG of the PBS group at the C7, C8, and T1 levels are 84 , 87 , and 88 percent after 1 week period , 85 , 88 , and 86 percent after 2 weeks period, and 86 , 87 , and 86 percent after 4 weeks period. LIF increases the sensory neuron survival at same levels are 89 , 89 , and 93 percent after 1 week period, 89, 89, and 90 after 2 weeks period, and 100, 100, and 100 after 4 weeks period.

The motor neurons of the PBS group at the same levels are 90, 90, and 92 percent after 1 week period. When the axotomized nerves were treated with LIF the motor neuron survival was increased at the same levels: to 95, 92, and 94 after 1 week. We found that there was the motor neuron loss within the first week after axotomy. This shows that the survival cells in the LIF- treated groups is higher than the PBS group at every levels. However, a significant differences is shown only at the level of T1 after 1 week period, C7 and T1 after 2 weeks period, and all level after 4 weeks period of the DRG, and C7 after 1 week period of the motor neuron.

The present findings show that the survival of axotomized sensory and motor neurons is greatly increased by the application of LIF at the peripheral stump. The efficacy of LIF suggests that the signal which delays the death of these neurons is mediated by retrograde axonal process. The next step in this study would be to find the molecule instant LIF for prevent the loss of neurons which cause injury in adult rats.