

**Question/Biological Problem:** Is there a method where it is possible to repair a central nervous system injury by utilizing induced pluripotent stem cells (iPSC) to treat the injury?

Currently, once damage occurs to the central nervous system and a pathway is severed or altered, there is no way to repair this damage in vivo. This often leads to paralysis or even death in many cases. Over the past few decades, much research has been focused on the repair of central nervous system injuries and peripheral nervous system injuries. There has been success with regeneration of peripheral nerves using a nerve conduits with iPSCs and a fibroblast growth factor drug delivery system [1]. However, the peripheral nervous system can regenerate itself while the central nervous system is unable to. In order to regenerate the central nervous system; etiological factors must be removed, inflammatory response must be modulated, cells must be protected from degeneration, and network connections must be rebuilt [2].

**AIM:** The nerve conduit technology will be adapted to the central nervous system in order to apply iPSCs to regenerating central nervous system injuries.

**Research Model and Plan:**

- Create mouse models with lower spinal injuries that at the L4 lumbar vertebrae and ensure loss of function occurs.
- Grow nerve conduits in vitro seeded with iPSCs, fibroblast growth factors, and a compound CLP290 which removes inhibition of neuronal circuits and allows for activation of KCC2 proteins. This compound has previously been successful in spinal cord injuries in previous mouse models [3].
- Implant the nerve conduits into the mice and begin conducting muscle tone, mobility, and sensory response testing daily on the mice.
- Weekly imaging will be performed by fluorescently tagging neuronal growth factors to look for growth in the damaged area. The experiment will be conducted for 2 months.
- Results and data will be compiled to determine if the nerve conduit is successful and autopsy mice at end of study to determine if degeneration or inflammatory responses occurred if the conduits are unsuccessful.

## References

- [1] T. U. T. O. K. T. I. N. Mikiyori Ikeda, "Acceleration of peripheral nerve regeneration using nerve conduits in combination with induced pluripotent stem cell technology and a basic fibroblast growth factor drug delivery system," *Journal of Biomedical Materials Research*, pp. 1370-1378, 2014.
- [2] A. E. W. A. J. B. a. M. R. Xiaohua Xu, "Enhancing Central Nervous System Repair-The Challenges," *CNS Drugs*, vol. 25, no. 7, pp. 555-573, 2011.
- [3] Y. L. B. Y. Z. Z. B. B. P. R. W. Y. L. S. V. H. S. Z. J. Z. H. G. Y. L. Y. Z. X. G. Z. H. Bo Chen, "Reactivation of Dormant Relay Pathways in Injured Spinal Cord by KCC2 Manipulations.," *Cell*, 2018.

