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### Using Crosslinked Hyaluronic Acid (HA) and Collagen Scaffolds with Sustained Brain-Derived Neurotrophic Factor (BDNF) Release for Post-SCI Nerve Regeneration

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Panth Doshi

Average BBB scores of rats with different treatment methods

(4 weeks post-SCI)

10 12

**BBB Score** 

8

## Using Crosslinked Hyaluronic Acid (HA) and Collagen Scaffolds with Sustained Brain-Derived Neurotrophic Factor (BDNF) Release for Post-SCI Nerve Regeneration

#### BACKGROUND

 Traumatic events resulting in spinal cord injuries (SCIs) often leave people paralyzed or with partial loss of motor function below the site of injury. The physical disabilities arising from traumatic events prevent people from functioning at the same level as pre-injury.

> Figure 1: Most common traumatic events that result in spinal cord injury.

The immune response after SCIs protects the blood brain barrier. Astrocyte hypertrophy and release of chondroitin sulfate proteoglycans (CSPGs) are chemical barriers to regeneration. Meanwhile, the formation of the glia limitans is a physical barrier to regeneration.

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Figure 3: Rupture of the blood brain barrier results in a physical barrier to nerve regeneration

### **METHODS**

REFERENCES

doi:10.1016/j.ymeth.2015.03.023

A literature review on the inhibitory post-SCI environment and the efficacy of currently used hyaluronic acid (HA) and collagen scaffolds was completed to propose a viable scaffold polymer to regenerate tissue and restore neural function.

Chen, Y., Tang, Y., Vogel, L. C., & DeVivo, M. J. (2013). Causes of spinal cord injury. Topics in

injectable hyaluronic acid hydrogel is safe and biocompatible in the intrathecal space for

ordered collagen scaffolds loaded with collagen-binding brain-derived neurotrophic factor

improve the recovery of spinal cord injury in rats. Tissue Engineering Part A, 15(10), 2927-2935. doi:10.1089/ten.tea.2008.0506

ultimate use in regenerative strategies of the injured spinal cord. Methods, 84, 60-69.

Han O. Sun W. Lin H. Zhao W. Gao Y. Zhao Y. Chen B. Dai J. (2009) Linear

Spinal Cord Injury Rehabilitation, 19(1), 1-8. doi:10.1310/sci1901-1 Führmann, T., Obermeyer, J.M., Tator, C.H., & Shoichet, M.S. (2015). Click-crosslinked

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### RESULTS

- HA scaffolds and collagen scaffolds reduce leukocyte extravasation, decreasing inflammation, to counteract the inhibitory post-SCI environment. HA scaffold implants resulted in less inflammation, lower GFAP intensity, and level of CSPGs
- Immune response, signified by inflammatory cells and different leukocyte types, shifted away from the center of injury to the periphery
- Implanting HA scaffolds and collagen scaffolds into injured spinal cords resulted in more neurofilaments than the natural healing process
- Regenerating neurons had more linear longitudinal growth and more myelinated axons
- Linear aligned nerve regeneration is correlated with better functional recovery than random regeneration

HA + BDNF 10

Collagen + BDNF

**BDNF** alone

Collagen alone

HA alone

Untreated

Uninjured

**Freatment Method** 

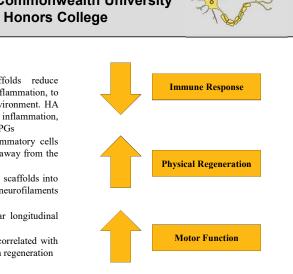
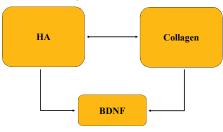


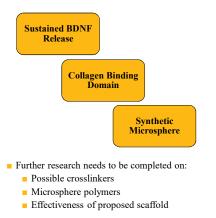
Figure 4: On average, scaffolds alone or growth factors alone are unable to restore much motor function in rats. However, by combining a scaffold polymer with BDNF, functional recovery increases greatly

### PROPOSAL

- HA scaffold with sustained BDNF release through synthetic microspheres and linear ordered collagen scaffold with sustained BDNF release through collagen binding domain both have high levels of functional recovery
- Combine effective HA + BDNF scaffold with effective collagen + BDNF scaffold



Crosslink HA and collagen for base scaffold polymer, then adding in collagen binding domain and embedding in synthetic microspheres for sustained BDNF release



### **FURTHER INFORMATION**

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- Park, J., Lim, E., Back, S., Na, H., Park, Y., & Sun, K. (2009). Nerve regeneration following spinal cord injury using matrix metalloproteinase-sensitive, hvaluronic acid-based biomimetic hydrogel scaffold containing brain-derived neurotrophic factor. Journal of Biomedical Materials Research Part A, 93(3), 1091-1099. doi:10.1002/jbm.a.32519
- Shearer, M. C., & Fawcett, J. W. (2001). The astrocyte/ meningeal cell interface A barrier to successful nerve regeneration? Cell and Tissue Research, 305(2), 267-273. doi:10.1007/s004410100384

Siebert, J. R., Steencken, A. C., & Osterhout, D. J. (2014). Chondroitin sulfate proteoglycans in the nervous system: Inhibitors to repair. *Biomed Research International*, 2014, 1-15. doi:10.1155/2014/845323

Wen, Y., Yu, S., Wu, Y., Ju, R., Wang, H., Liu, Y., Wang, Y., & Xu, Q. (2016). Spinal cord injury repair by implantation of structured hyaluronic acid scaffold with PLGA microspheres in the rat. Cell and Tissue Research, 364(1), 17-28. doi:10.1007/s00441-015-2298-1

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