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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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## 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.**

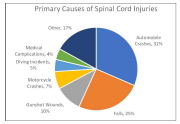



**Figure 1:** Most common traumatic events that result in spinal cord injury.

- 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.

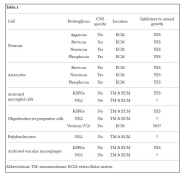


**Figure 2:** Common CSPGs act as chemical inhibitors to nerve regeneration

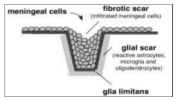


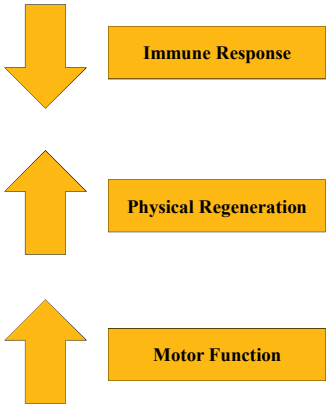

**Figure 3:** Rupture of the blood brain barrier results in a physical barrier to nerve regeneration

## Methods

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.

## 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



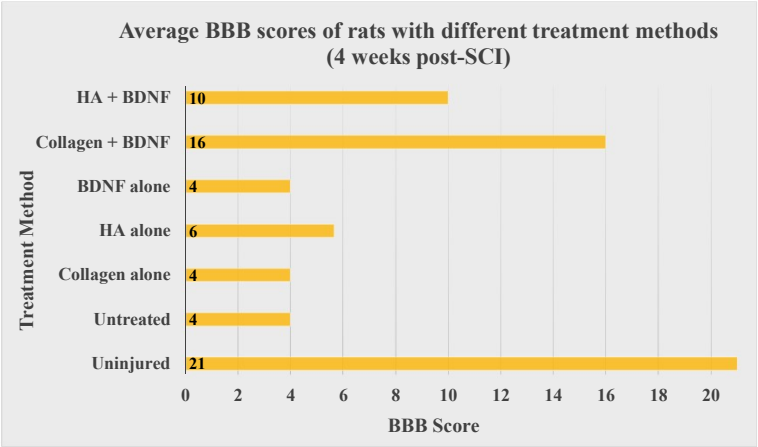
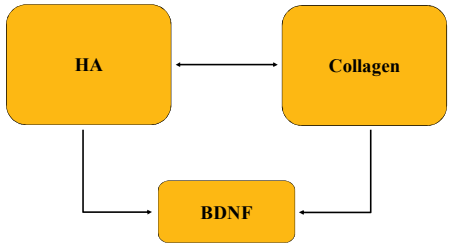



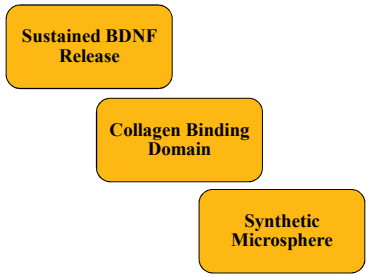

**Figure 4:** On average, scaffolds alone or growth factors alone are unable to restore much motor function in rats. However, by combining a scaffold polymer with BDNF, functional recovery increases greatly

## 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 research needs to be completed on:
  - Possible crosslinkers
  - Microsphere polymers
  - Effectiveness of proposed scaffold

## References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## Further Information


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