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Injury to the Spinal Cord is helped by a Reactive Oxygen: A Short Communication

David Jhonson*

Department of Medicine, New York Presbyterian Hospital–Weill/Cornell Medical School, Paris, France

Introduction

By reducing the production of endogenous reactive oxygen species (ROS), attenuating ROS-mediated oxidative damage, and downregulating inflammatory cytokines like interleukin-1 beta (IL-1), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-), the hydrogel was able to effectively encapsulate BMSCs and played a remarkable role in vivo as a neuroprotective agent. The motor functional recovery of SCI rats was significantly enhanced by the ROS-scavenging hydrogel that was encapsulated in BMSCs. It also reduced the formation of scars and enhanced the neurogenesis of the spinal cord tissue. A combinational strategy against ROS-mediated oxidative stress is provided by our work, which has the potential to be utilized not only in SCI but also in other diseases of the central nervous system that share similar pathological conditions.

Description

The application of biocompatible polymers to reduce secondary inflammation, the creation of patterned hydrogels or oriented scaffolds to guide the regenerated axons, immune cells polarization-regulating nanoparticles or hydrogels, and cell transplantation have all played major roles in the treatment of SCI to this point. In a rat SCI model, for instance, a hyaluronic acid (HA) and poly(ethylene glycol) diacrylate (PEGDA)-modified polycaprolactone (PCL) nanofiber-modified hydrogel promotes macrophage polarization, resulting in an increase in the number of immature neurons and axons. SCI therapy also utilizes other types of scaffolds, such as chitosan micro-hydrogels and an imidazole-conjugated poly(organophosphazenes) hydrogel for macrophage targeting. However, the efficacy of these biomaterials on motor recovery is still insufficient without the specific addition or encapsulation of neurogenesis-promoting biomolecules or stem cells [1].

However, despite the fact that damaged neurons can be replaced with stem cells like mesenchymal stem cells (MSCs), their application is still limited by their low bioavailability in the lesion site and insufficient behavior restoration efficacy in cases of severe paraplegia. However, a promising treatment for SCI is stem cell transplantation using hydrogels, which provide an artificial extracellular matrix (ECM) for the implanted cells, serve as a physical barrier to prevent unfavorable diffusion, and reduce secondary inflammation caused by mechanical mismatch. However, the majority of implanted cells may not survive in the cytotoxic and inhibitory microenvironment, so the therapeutic effect of non-stimuli responsive hydrogels is insufficient. Because they cause oxidative stress, cytotoxic neuro-excitement, and a new round of severe inflammatory response, the overproduction of reactive oxygen species (ROS) is thought to be one of the main causes. Coenzyme Q10 has been shown to regulate apoptosis and oxidative stress, protect transplanted BMSCs, and increase the effectiveness of SCI treatment. However, its chemically unstable nature and relative slow adsorption may result in low bioavailability and, consequently, low protection in vivo [2,3].

Traumatic spinal cord injury (SCI) is a catastrophic event that can result in impairment or dysfunction of the locomotor and sensory systems, resulting in life-altering paralysis, severe complications, and even death for patients. There have been 27 million SCI cases worldwide up to this point, with 93.8 thousand new cases occurring annually. However, the current clinical treatments for SCI are unable to restore motor function or axon regeneration with sufficient efficacy. Numerous severe secondary injuries occur around the lesion site after trauma-caused primary injuries, including uncontrolled oxidative stress and inflammation, tissue remodeling, and cytotoxic neural excitement caused by a rapid and large influx of calcium ions and glutamate, which causes the necrosis and apoptosis of neurons and glial cells, both of which contribute to the loss of neurons.

Biomaterials can successfully regulate the hostile environment, protect transplanted cells, and significantly promote neurogenesis by scavenging overproduced ROS. Kim and co. Administered the optimal amount of cerium oxide nanoparticles (CONPs) to the site of the lesion, which decreased the size of the cavity and the number of inflammatory cells, as well as the mRNA expression of inflammatory cytokines and apoptotic proteins. In a similar vein, in the treatment of SCI, selenium nanoparticles (Se NPs), iron oxide NPs, and Mn (III) tetrakis (4-benzoic acid) porphyrin NPs can reduce ROS. In addition, the polymer-based ROS scavenging biomaterials have unique advantages like adjustable degradability and harmless degradable products and are effective in SCI treatment. For the purpose of scavenging ROS in SCI, tetramethylpiperidine 1-oxyl (Tempol)-grafted hydrogel and high-density thioether-containing lipid-polymer nanoparticles have been shown to be effective. Transplanted bone-derived MSCs (BMSCs) into a MnO2 NPs-dotted HA hydrogel and demonstrated that the MnO2 NPs significantly shield the BMSCs from an ROS-rich microenvironment, whereas the BMSCs encapsulated in the undotted hydrogel suffer a significant loss. For SCI treatment, however, the combination of stem cells and ROS-scavenging hydrogels has received little attention. This combination has numerous advantages; including modulating the inflammatory microenvironment and protecting encapsulated stem cells from apoptosis, resulting in a superior in vivo SCI therapy [4,5].

A thioketal-containing hyperbranched polymer (HBPAK) is crosslinked with methacrylate hyaluronic acid (HA-MA) to create a ROS-responsive and scavenging hydrogel in this study. Within this hydrogel, neural-specific CQAASIKVAV peptides (IKVAV for short) are covalently grafted, and rat-derived epidermal growth factor (EGF) and rat-derived basic When transplanted for SCI treatment in vivo, this hydrogel is able to scavenge excess ROS, promote the polarization of M2 macrophages, reduce inflammation, and protect the encapsulated BMSCs from oxidative stress. In vitro, the obtained hydrogel's fundamental physiochemical properties, including its anti-oxidation, anti-inflammatory, and biocompatibility, are characterized. The in vivo therapeutic effect, particularly anti-oxidation and axon regeneration, is evaluated using a rat transection spinal cord injury model at the T10 level (two millimeters) [1].

Therefore, successful SCI treatment relies heavily on the regulation of scar formation. On day 7, the traumatic spinal cord tissue was stained with Masson stain after surgery. The less aniline blue positive area on day 7 indicates that

***Address for Correspondence:** David Jhonson, Department of Medicine, New York Presbyterian Hospital–Weill/Cornell Medical School, Paris, France, E-mail: david.j@hotmail.com*

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the THIEF-Cell group had less collagen deposition and scarring. Both the THIEF-Cell and THI hydrogel groups showed fewer aniline blue-positive areas on day 56 and more purple-colored areas at the site of the lesion, indicating that fewer scars had formed and that more neural fibers had survived. Day 7 saw the appearance of these two distinct scars was then investigated by immunofluorescence staining. GFAP-labeled activated astrocytes play a role in the glial scars that enter the lesion gap and create a harmful cavity. In this case, the fibrotic scar marker PDGFR- was chosen. PDGFR-/GFAP double staining were therefore performed. The seven-day quantitative analysis demonstrates that, in comparison to the PHIEF-cell (14.8 2.1%) and SCI groups, the percentage of PDGFR-+ areas in the THIEF-Cell (10.0 1.2%) and THI hydrogel (10.0 1.5%) groups was significantly lower. Similar to the other two groups, the THIEF-Cell group had a lower percentage of GFAP+ areas (1.8 0.8%) and the THI hydrogel group had a lower percentage of GFAP+ areas (1.9 0.9%). Whether or not BMSCs are encapsulated, the ROS-scavenging hydrogel can significantly reduce the formation of fibrotic and glial scars in the lesion site, which is crucial for axon regeneration.

Conclusion

One-pot synthesis of thioketal-containing hyperbranched polymer (HBPAK), biocompatible HA-MA and IKVAV peptides encapsulated with cell growth factors, and BMSCs produced a BMSC-encapsulated ROS-scavenging hydrogel. This hydrogel could significantly reduce the oxidative microenvironment both in vitro and in vivo and was highly biocompatible. In a rat spinal cord transection model, the BMSC-encapsulated ROS-scavenging hydrogel was applied to the lesion site, significantly reducing oxidation, inflammation, and cell apoptosis.

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Conflict of Interest

There is no conflict of interest by the author.

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