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Surgical Intervention Associated with Multiple Complications and Side Effects

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Description

Peripheral nerve injury (PNI) and its regeneration continue to remain a significant medical burden worldwide. The current treatment strategies used to treat PNI are often associated with multiple complications and yet do not achieve complete motor and sensory functions. Recently, synthetic biodegradable nerve conduits have become one the most commonly used conduits to repair small gaps in nerve injury. But they have not shown better results than nerve grafts possibly because of the lack of biological microenvironment required for axonal growth. Schwann cells play a very crucial role in peripheral nerve regeneration where activated SCs produce multiple neurotrophic factors that help in demyelination and immune modulation during nerve repair. Studies have shown that Nano fibrous scaffolds have better bioactivity and more closely mimic the native structure of the extracellular matrix. Therefore, the present study was focused on designing a Nano fibrous scaffold that would cover the roles of both structural support for the cells that can provide a microenvironment with biological cues for nerve growth and regeneration. Schwann cells displayed growth in the direction of the aligned PCL nanofibers and ACM treated exhibited appropriate bipolar morphology indicating that these modified fibers could provide directional cues making them highly suitable for neuronal cell growth.

Medical Technology

Peripheral Nerve Injury (PNI) continues to be one of the most common medical burdens worldwide. Even with the advancement in medical technology, treatment and management of nerve injuries remain expensive and ineffective. Most traumatic PNIs need surgical intervention which is often associated with multiple complications and side effects. Even then none of the current therapeutic options can fully achieve complete recovery of motor and sensory functions. Nerve grafting even though has proven to be one of the most effective treatments currently available, is not completely devoid of shortcomings. Nerve grafts are often associated with transplant rejections thus making the patient prone to more risks and complications. Therefore, it calls for an urgent need for new therapeutic options for the treatment of peripheral nerve injury. Healing during peripheral nerve injury is a complicated biological process that concerns replacing damaged tissue with a living one. Thus, restoring tissue integrity is quite difficult by itself. In the self-healing process, the interaction of immune cells, as well as neural extracellular matrices (ECM) components such as fibronectin, glycosaminoglycan's, proteoglycans, thrombospondins, tenascin, vitronectin, or collagens, takes place. The mentioned cell interactions with neural ECM components are subject to the regulation of biochemical mediators, numerous cytokines, and growth factors.

The ECM in our body with which cells interact has topography at the nanoscale that guides axonal growth and regeneration. Thus, ECM-based biomaterials are proposed to quickly regain healing cues and suppress or halt immune reactions to implant sites. In the peripheral nervous system, Schwann cells play a very important role in nerve regeneration. Activated Schwann cells during an injury produce multiple neurotrophic factors such as Nerve Growth Factor (NGF), brain-derived growth factor, ciliary neurotrophic factor, and neuropeptide Y all of which play a crucial role in axonal regeneration and myelin formation. In addition to secreting neurotrophic factors, SCs are also responsible for secreting the extracellular matrix (ECM) components thus providing a platform for neuronal cell growth and regeneration. Recently, nerve conduits are being developed as a possible therapy for nerve damage that acts as the scaffolding platform for bridging the gap between the proximal and distal ends of the injured nerves. Synthetic, biodegradable nerve conduits have become one the most commonly used conduits to repair small gaps. Some of the biomaterials used for this purpose are commonly made from polymers like Poly-caprolactone (PCL), Polyglycolic acid (PGA), and Poly Lactic acid (PLA). PCL is FDA approved (non-toxic), has a low melting point and its semi-crystalline form is a rubbery state that provides it excellent mechanical properties thus, making it highly suitable for application in regenerative therapy. The electro spinning technique produces fibrous scaffolds that can provide high surface area for attachment of cells, the porous network for cell migration, and a 3D environment for cell-to-cell interaction. This technique can produce aligned fibers that provide topographical cues for the alignment of cells for the regeneration of axons. This also ensures to help in the unidirectional conduction of nerve impulses. This method can consistently produce nanofibers while also being economical. Thus, the nanofibers formed by electrospinning mimic the ECM forming a similar microenvironment around the cells.

Decellularized Matrix

Even though synthetic conduits are cost-effective and are associated with fewer complications, in terms of nerve regeneration, they have not shown better results than nerve grafts possibly because of the lack of biological microenvironment required for axonal growth. Therefore, in order to provide nerve cells with both structural support and a microenvironment with biological cues for growth and regeneration, in this study we fabricated electro spun poly-caprolactone nanofibers coated with decellularized extracellular matrix (ACM) of Schwann cells to use as a nerve conduit for the treatment of peripheral nerve injury that would potentially be financially feasible, with fewer side effects and highly effective for filling large nerve gaps. Cytochemical staining for different components of the extracellular matrix was carried out. To visualize glycoproteins, the ACM was stained using Alcian blue and picrosirius red and to visualize collagen, the scaffolds were treated with Mason's trichome and safranin O. To visualize the total protein content, the ACM-coated scaffolds, and the control were treated with Coomassie

blue. Since an ideal decellularized matrix should not contain any cells, the scaffolds were treated with methylene blue to check for any left-over cells by staining DNA. For all the staining, scaffolds treated with PBS were used as a control. Analog regimen compared with patients treated with a premixed insulin analog regimen is limited or nearly unavailable. Because of ethical constraints, this issue is not easy to address in a prospective study. The causal relationship between insulin regimens and acute complications such as severe hypoglycemia and DKA is difficult to identify, due to low DKA event rate. Thus, we conducted a retrospective study via review of a longitudinal follow-up system. We hypothesized that a basal-bolus insulin regimen may lead to a lower event rate of DKA than a premixed regimen.