


Polycaprolactone/Gelatin Nanofibrous Scaffolds for Tissue Engineering

Saeed Farzamfar¹ , Mehdi Aleahmad² , Gholamreza Savari Kouzehkonan³ , Majid Salehi^{4,5,6*} , Niloofar Nazeri^{3,*} 

¹ Department of Tissue Engineering and Cell Therapy, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran; saeed.tums1991@gmail.com (S.F.);

² Department of Immunology, Faculty of Public Health, Tehran University of Medical Sciences, Tehran, Iran; mehdi_aleahmad@live.com (M.A.);

³ Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran; g.savary69@yahoo.com (G.S.K.);

⁴ Department of Tissue Engineering, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran

⁵ Tissue Engineering and Stem Cells Research Center, Shahroud University of Medical Sciences, Shahroud, Iran

⁶ Sexual Health and Fertility Research Center, Shahroud University of Medical Sciences, Shahroud, Iran; msalehi.te1392@gmail.com (M.S.);

* Correspondence: nina_1366_nazeri@yahoo.com (N.N.); msalehi.te1392@gmail.com (M.S.);

Scopus Author ID 55915356900

Received: 17.10.2020; Revised: 2.12.2020; Accepted: 4.12.2020; Published: 8.12.2020

Abstract: The combined use of polycaprolactone and gelatin has obviated many drawbacks associated with applying them alone. Polycaprolactone provides mechanical strength and buys sufficient time for tissue regeneration without degradation. Simultaneously, gelatin regulates the surface wettability of the composite scaffold. It makes the structure more cytocompatible by its cell recognition sites. Furthermore, these low polymers' cost, biocompatibility, and tuning of degradation time have added to their therapeutic appeal. In the current study, we have reviewed the application of polycaprolactone/gelatin scaffolds in tissue engineering and drug delivery fields, hoping to translate these scaffolds into medicine.

Keywords: polycaprolactone; gelatin; nanofibers; tissue engineering.

© 2020 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Regenerative medicine seeks to develop alternative solutions for organ transplantation using various approaches. In this regard, cell-based therapies and tissue engineering are the two most studied methods [1,2]. Tissue engineering exploits the combination of cells, scaffolds, and growth factors to build implantable tissues *in vitro* settings [3,4]. Scaffolds can be fabricated using natural and/or synthetic materials using different fabrication techniques [5]. It has been shown that material selection and optimization are key elements determining the success of tissue tissue-engineered tissue implantation [6]. Indeed, cells favor natural polymers since they have optimal hydrophobicity and numerous cell attachment sites for cellular adhesion, migration, and proliferation. Also, polymers derived from the extracellular matrix of native tissues have abundant growth factor attachment sites that can serve as a temporary reservoir for signaling molecules [7,8]. However, lack of sufficient mechanical strength, batch to batch variations, and pathogen transmission risk have driven efforts to search for alternatives for natural polymers application in tissue engineering [9,10].

On the other hand, synthetic polymers have acceptable mechanical properties and can be processed via various solvents or thermal treatment [11, 12]. These polymers lack many of the drawbacks of synthetic polymers; however, due to high hydrophobicity and lack of cell recognition sites, cell affinity towards synthetic polymers is relatively low [13,14]. Therefore, researchers have proposed the combined use of synthetic and natural polymers. Synthetic polymers build the backbone and withstand mechanical forces, and natural polymers provide cytocompatibility [15]. Among various candidates, polycaprolactone (PCL) and gelatin have gained significant attention in the biomedical field [16]. PCL is a biodegradable and biocompatible aliphatic polyester that has FDA approval for biomedical applications [17]. Gelatin is a natural biomaterial produced by either acid or alkaline hydrolysis of collagen [18]. Due to their low cost, lack of cytotoxicity, and non-immunogenicity, they have numerous potential applications in tissue engineering and drug delivery [19]. The combined use of PCL and gelatin has resulted in a potent drug delivery vehicle and a favorable scaffold for tissue engineering. In this study, we have reviewed the current research regarding PCL/gelatin scaffolds' application to repair various tissue injury models.

2. General Characteristics of PCL

Among various synthetic biomaterials, PCL is particularly appealing in the biomedical field and has been successfully tested in various disease models and applications [20]. It is an aliphatic polyester with a semicrystalline structure and a relatively low degradation time. Furthermore, its ease of processability, FDA approval for biomedical applications, and cost-effectiveness have added to its therapeutic appeal [21,22]. PCL is mainly obtained by polymerization of ϵ -caprolactone via ring-opening polymerization method [23]. Its degree of crystallinity and molecular weight can be degraded within months to a couple of years [24]. Since PCL has ester links between its monomers, it cannot be degraded by bodily enzymes. Instead, it is degraded by random hydrolysis by water molecules, and this process is autocatalyzed by released carboxylic acids [25,26]. Due to its high hydrophobicity, PCL has poor interaction with cellular materials. Therefore, researchers have tried to functionalize PCL's surface using various chemicals such as NHS-EDC and NaOH, which provide carboxyl groups on the PCL surface, rendering it more suitable for tissue engineering applications [27,28].

Table 1. The summary of PCL's application in different fields of tissue engineering.

Biomaterial type	Application	Reference
Chitosan and PCL blend	Delivery of Ofloxacin	[31]
PCL	Delivery of cyclodextrin-naproxen	[32]
PCL	Cardiac tissue engineering	[33]
poly (ethylene glycol)/PCL	Heart valve tissue engineering	[34]
PCL/Hydroxyapatite	Bone tissue engineering	[35]
PCL/Alginate	Cartilage tissue engineering	[36]
PCL/chitosan	Cornea tissue engineering	[37]
PCL/collagen	Peripheral nerve tissue engineering	[38]
PCL/starch	Spinal cord tissue engineering	[39]
PCL	Vascular tissue engineering	[40]
PCL/collagen	To drive stem cell fate into neural lineage	[41]
Mineralized PCL	Odontogenesis of human dental pulp cells	[42]
PCL/Silver nanoparticles	Wound dressing	[43]
PCL/P3HB	Ligament tissue engineering	[44]
PCL/ multiwalled carbon nanotubes/ polyacrylic acid/polyvinyl alcohol	Skeletal muscle tissue engineering	[45]

PCL has been widely used in various biomedical fields, from tissue engineering to drug delivery and the packing industry [29,30]. The summary of PCL's application in different fields has been shown in table 1.

3. General Characteristics of Gelatin

Gelatin is a biomaterial that has gained significant attention in the biomedical field due to its ease of extraction, low cost, biocompatibility, and non-immunogenicity [46]. This material is produced from collagen's denaturation process and largely preserves its amino acid composition [47]. However, the source of collagen and denaturation method have a profound effect on the properties of produced gelatin [48]. Proline, Hydroxyproline, and Glycine make up most gelatin's amino acid composition [49]. To produce gelatin from collagen, thermal treatment and hydrolysis are performed [50]. In the first method, collagen is heated up to 40°C, and as a result, Wonderwall bonds between collagen fibrils break [51, 52]. In the latter method, which is performed as an adjunct method with thermal treatment, the extraction is performed by incubation of non-soluble collagen with acidic or basic solutions, which results in the breakage of strong covalent bonds between amino acids of collagen [47, 53]. Gelatin type A is produced when collagen is soaked into acidic solutions. In contrast, Gelatin type B is extracted under alkaline conditions [54].

Contrary to collagen, which has an orderly structure, gelatin demonstrates a random and heterogeneous molecular structure; therefore, there is a high batch to batch variation in marketed gelatin [50, 55]. In terms of physical properties, gelatin's characteristics vary according to the pH and supplement electrolytes. To obtain a structure with sufficient mechanical properties, gelatin can be cross-linked using various materials such as glutaraldehyde, formaldehyde, carbodiimide, and hexamethylene diisocyanate [56,57]. However, the risk of cytotoxicity rises as the amount of crosslinker or time of incubation with crosslinker increases [58,59]. Gelatin has been widely used in various biomedical fields such as tissue engineering, drug delivery, and cosmetics [60]. The summary of gelatin's application in the biomedical field is shown in table 2.

Table 2. The summary of gelatin application in different fields of tissue engineering.

Biomaterial type	Application	Reference
Polyaniline/gelatin	Engineering of conductive tissues	[61]
Gelatin/hydroxyapatite	Bone tissue engineering	[62]
Gelatin/hyaluronic acid/chondroitin	Cartilage tissue engineering	[63]
Photocrosslinkable gelatin	Epidermal tissue engineering	[64]
Gelatin microspheres	Basic fibroblast growth factor delivery for adipose tissue engineering	[65]
Chitosan/gelatin/bioglass	Alveolar bone tissue engineering	[65]
PLGA/gelatin	Fenbufen drug delivery	[66]
Pectin/gelatin	Metronidazole drug delivery	[67]
Lactose cross-linked gelatin	Dexamethasone drug delivery	[68]
Gelatin patterned hydrogel	Cardiac tissue engineering	[18]
PCL/gelatin/graphen oxide	Neural tissue engineering	[16]
Gelatin/chitosan/polyurethane	Heart valve tissue engineering	[69]
PLGA/gelatin	Vascular tissue engineering	[70]
Chitosan/gelatin	Skin tissue engineering	[71]
Gelatin/silk fibroin	Ligament tissue engineering	[72]
Gelatin nanoparticles	Didanosine drug delivery	[73]

4. Application of PCL/Gelatin Scaffolds to Treat Tissue Injuries

As the largest organ in the body, the skin comprises 8% of the total body mass. It serves as a barrier against environmental hazards, protects the body from dehydration, plays a crucial role in vitamin D synthesis, and regulates body temperature [74,75]. Although it has an inherent potential to repair after injury, in case of critical-sized defects, skin damages turn into non-healing chronic wounds or scar tissue [76,77]. To tackle this dilemma, the gold standard of treatment is autologous skin grafting. However, this treatment modality is associated with several shortcomings, such as the need for a second surgery for donor tissue harvest with its accompanying complications and unavailability of donor tissue in case of extensive skin injuries [78, 79]. Therefore, studies are trying to find an alternative strategy for the treatment of large skin defects. During the past decade, skin tissue engineering has opened new frontiers for wound patients [80, 81]. A tissue-engineered skin construct should meet certain criteria for successful wound repair. It should be biodegradable and biocompatible on which fibroblasts can adhere and populate [82]. Chong *et al.* proposed an effective composite consisting of PCL/gelatin electrospun nanofibers embedded on Tegaderm TM, 3M Medical wound dressing. They hypothesized that this system would form a fibroblast-populated dermal matrix that will provide a temporary artificial dermis before re-epithelialization. Fibroblast adhesion and proliferation were studied on both sides. Results showed that the construct supported successful adhesion and proliferation of fibroblasts and built a cell-populated 3-dimensional dermal matrix [83]. Farzamfar *et al.* incorporated cerium oxide nanoparticles into PCL/gelatin nanofibrous matrices to fabricate a fibrillar wound care product. Various cerium oxide nanoparticles' concentrations were added to the blend solution of PCL and gelatin, and the resulting mixture was transferred to an electrospinning device. The produced scaffolds were studied regarding their microstructure, hydrophobicity, the ability to uptake water, the rate of water vapor transmission, cytotoxicity assay, and mechanical properties. According to cytotoxicity assay, the optimal scaffold was selected for *in vivo* study on full-thickness excisional wound model in rat. Results showed that after 14 days, the wounds covered with cerium oxide nanoparticle-incorporated dressing could significantly close the wounds than the control group (100% vs. 63%). The histopathological study also confirmed the higher healing potential of the produced wound dressing. Their results suggested the possible applicability of cerium oxide nanoparticle-containing dressing to treat skin wounds in the clinic [84]. In another study, Farzamfar *et al.* used electrospun PCL/gelatin nanofibrous yarns as a delivery vehicle for taurine (2-aminoethane sulfonic acid) to treat the excisional wound. The composite matrices containing 3%, 5%, and 10% of taurine were produced by the electrospinning method. The physicochemical and biological properties of the scaffolds were studied. The scaffolds embedded with 5% taurine were selected to treat the excisional wound in the rat model. The macroscopic analysis and histopathological examinations showed that taurine loaded scaffolds outperformed the control and taurine free scaffolds [85]. Gautam *et al.* modified electrospun PCL/ gelatin nanofibrous scaffolds with type one collagen for skin tissue engineering and wound healing applications. Microstructure analysis by scanning electron microscopy showed that the fiber diameter increased. The scaffold's pore size was decreased by increased collagen concentration. Infrared spectroscopy and the thermogravimetric study confirmed successful grafting of collagen molecules on PCL/gelatin yarns. Cytotoxicity assay was studied using MTT analysis. The results showed that scaffolds could support the successful proliferation of L929 mouse fibroblast cells. Cell adhesion study on L929 mouse fibroblasts showed that cells

could adhere to matrices with numerous filopodia indicating proper interaction of scaffolds with seeded cells [85]. Fu *et al.* investigated the healing effects of human urine-derived stem cells (HUSCs) combined with PCL/gelatin nanofibrous scaffolds to promote wound healing. A two nozzle electrospinning device was used to fabricate PCL/gelatin nanofibrous yarns. The morphology and surface wettability study was performed on the scaffolds. The attachment, cytotoxicity, and proliferation assays were conducted on seeded HUSCs on the matrices. HUSCs were seeded onto the PCL/gelatin composite scaffold and implanted into a rabbit model of a full-thickness excisional wound. Results showed that the wounds treated with HUSCs and PCL/gelatin scaffolds could significantly improve wound healing compared to sterile gauze and PCL/gelatin only scaffolds, evidenced by enhanced re-epithelialization, increased angiogenesis, and collagen deposition [86].

To treat peripheral nerve injuries in cases that the gap is larger than 5mm, autologous nerve grafting is often performed in the clinic. However, this treatment strategy has several shortcomings, such as unavailability of donor tissue, donor site morbidity, and the possibility of neuroma formation [87,88]. To obviate these drawbacks, neural channels have been introduced due to their favorable properties, such as the possibility of mass production and tailorable properties [89]. In this regard, PCL and gelatin have been widely used as scaffolding materials for neural channel fabrication. Farzamfar *et al.* produced neural guidance channels using electrospun PCL/gelatin nanofibrous sheets. After detaching the aluminum foil sheets, they rolled up the yarns to shape them into channel-like structures. The biological and physicochemical properties of the scaffolds were studied *in vitro*. Then, humane menstrual blood stem cells were seeded into the neural channel before implanting them into a sciatic nerve defect rat model. After 14 weeks, the results of histopathological examinations and functional assessment studies showed that the PCL/gelatin composite scaffolds could successfully deliver menstrual blood stem cells to the injured site. No sign of hematoma or tissue injury was observed around the implantation site indicating good tissue compatibility of the produced scaffolds [90]. In another study, Farzamfar *et al.* used PCL/gelatin nanofibrous yarns to implant unrestricted somatic stem cells into a rat model of sciatic nerve defect. They found that the scaffolds had no toxicity towards PC-12 cell line *in vitro* and provided a favorable environment for Schwann cells adhesion and proliferation. The results of *in vivo* study also confirmed the cytocompatibility of the fabricated matrices [91]. Babaloo *et al.* used the PCL/gelatin nanofibrous scaffolds combined with endometrial stem cells and Schwann cells to treat spinal cord injury. They co-cultured human endometrial stem cells with human Schwann cells for 10 days. They found that endometrial stem cells could differentiate into nerve-like cells, evidenced by a real-time reverse transcription-polymerase chain reaction and immunocytochemistry studies. The differentiated cells were then grafted onto the PCL/gelatin yarns followed by implantation into hemisected spinal cords in the rat model. Neural outgrowth was analyzed by an immunohistochemical technique, which dyed NF-H as a neuronal marker. For functional analysis, the Basso, Beattie, and Bresnahan (BBB) were exploited. The results showed that the designed system could successfully enhance motor and sensory function recovery. No case of immunogenicity or tissue injury was observed in any of the animals, following previous studies that confirmed the tissue compatibility of PCL and gelatin [92].

Bone morphogenic proteins (BMPs) play a vital role in distinguishing mesenchymal stem cells into chondrocytes and osteoblasts [93]. Therefore, it has been used in a variety of delivery vehicles in bone tissue engineering. In one study, Kim *et al.* used a composite of PCL/gelatin nanofibers and biphasic calcium phosphate to deliver BMP-2 for bone

regeneration. The matrices were prepared by electrospinning method that could produce a network of extracellular matrix resembling structure. BMP release profile analysis showed that it experienced a burst release within the first 10 hours then slowed down to a sustained release manner within the next 31 days. Cellular behavior studies on different scaffolds proved that cells cultured on BMP-containing yarns significantly enhanced cellular proliferation and attachment. The *in vivo* healing potential of the fabricated composite was studied in a rat model of critical-sized skull bone defect. It was shown that a marked difference was noticeable in bone healing in rats treated with BMP loaded nanofibers indicating its huge potential for bone tissue engineering applications [94]. Binulal *et al.* used a stem cell-populated electrospun PCL/gelatin nanofibrous scaffold for bone tissue engineering. Various weight ratios of PCL:gelatin were tested for optimum scaffold fabrication concentration. A diluted acetic and ethyl acetate mixture was exploited for solution preparation. The effects of this solvent system on the matrices structure and solution properties were studied. Degradation rate measurement and surface wettability analysis showed that the yarns containing 30 and 40 wt.% gelatin showed a desired hydrophilicity and degradability. Mesenchymal stem cells were cultured on the composite scaffold. They differentiated successfully into osteoblast cells suggesting proper bio-functionality of this system for bone healing applications [95].

Infection is a major deterrent factor for the success of guided tissue/bone regeneration [96]. Therefore, strategies seek to develop membranes with anti-infection capabilities. A study conducted by Xue *et al.* Metronidazole was loaded into PCL/gelatin membranes to develop a smart scaffold for guided bone regeneration. The scaffolds demonstrated a tensile strength, suitable degradation rate, and barrier function. Drug release profile study showed that metronidazole had a sustained release and could successfully mitigate anaerobic bacteria colonization. The scaffolds imparted no toxicity towards seeded cells. The matrices were implanted into subcutaneous tissue in a rat model for 8 months. Results showed that the scaffolds had triggered a negligible inflammatory response, which depended on the loaded drug dose [97]. Another study conducted by Ke *et al.* PCL and gelatin was blended to produce a membrane for guided bone regeneration. The scaffolds were produced by electrospinning method and then cross-linked with genipin. Scanning electron microscopy study showed that the fibers had smooth and random morphology. The mechanical strength analysis showed that the scaffolds had suitable tensile strength. CCK-8 study revealed that the yarns imparted no toxicity towards MC3T3-e1 cells. Furthermore, the *in vitro* osteogenesis study showed that the nanofibrous scaffold promoted bone formation as evidenced by alizarin red staining [98]. Schematic illustration of PCL/gelatin scaffold's application in various disease models has been shown in figure 1.

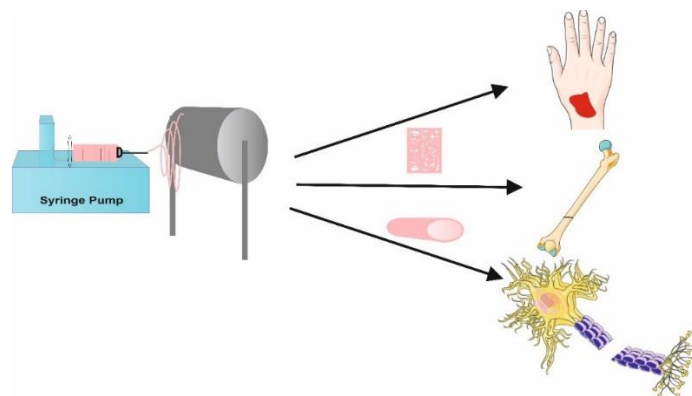


Figure 1. Summary of PCL/gelatin nanofibrous scaffolds application in the skin, bone, and neural tissue engineering.

5. Concluding remarks

PCL and gelatin in the form of combined or single-use have been widely studied in different fields. It seems that by blending PCL and gelatin, we can produce a new biomaterial with more appealing characteristics. Nevertheless, more studies with term follow-ups are needed to ensure that the combined use of PCL and gelatin has no adverse effects on living organisms.

Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Keshtkar, S.; Azarpira, N.; Ghahremani, M.H. Mesenchymal stem cell-derived extracellular vesicles: novel frontiers in regenerative medicine. *Stem cell research & therapy* **2018**, *9*, <https://doi.org/10.1186/s13287-018-0791-7>.
2. Nazeri, N.; Karimi, R.; Ghanbari, H. The effect of surface modification of poly-lactide-co-glycolide/carbon nanotube nanofibrous scaffolds by laminin protein on nerve tissue engineering. *Journal of Biomedical Materials Research Part A* **2020**, <https://doi.org/10.1002/jbm.a.37013>.
3. Ahsan, S.M.; Thomas, M.; Reddy, K.K.; Sooraparaju, S.G.; Asthana, A.; Bhatnagar, I. Chitosan as biomaterial in drug delivery and tissue engineering. *International journal of biological macromolecules* **2018**, *110*, 97-109, <https://doi.org/10.1016/j.ijbiomac.2017.08.140>.
4. Turnbull, G.; Clarke, J.; Picard, F.; Riches, P.; Jia, L.; Han, F.; Li, B.; Shu, W. 3D bioactive composite scaffolds for bone tissue engineering. *Bioactive materials* **2018**, *3*, 278-314, <https://doi.org/10.1016/j.bioactmat.2017.10.001>.
5. Jammalamadaka, U.; Tappa, K. Recent advances in biomaterials for 3D printing and tissue engineering. *Journal of functional biomaterials* **2018**, *9*, <https://doi.org/10.3390/jfb9010022>.
6. Armiento, A.; Stoddart, M.; Alini, M.; Eglin, D. Biomaterials for articular cartilage tissue engineering: Learning from biology. *Acta biomaterialia* **2018**, *65*, 1-20, <https://doi.org/10.1016/j.actbio.2017.11.021>.
7. Palchesko, R.N.; Carrasquilla, S.D.; Feinberg, A.W. Natural biomaterials for corneal tissue engineering, repair, and regeneration. *Advanced healthcare materials* **2018**, *7*, <https://doi.org/10.1002/adhm.201701434>.
8. Ranganathan, S.; Balagangadharan, K.; Selvamurugan, N. Chitosan and gelatin-based electrospun fibers for bone tissue engineering. *International journal of biological macromolecules* **2019**, *133*, 354-364, <https://doi.org/10.1016/j.ijbiomac.2019.04.115>.
9. Pollot, B.E.; Rathbone, C.R.; Wenke, J.C.; Guda, T. Natural polymeric hydrogel evaluation for skeletal muscle tissue engineering. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **2018**, *106*, 672-679, <https://doi.org/10.1002/jbm.b.33859>.
10. Steffens, D.; Braghirolli, D.I.; Maurmann, N.; Pranke, P. Update on the main use of biomaterials and techniques associated with tissue engineering. *Drug discovery today* **2018**, *23*, 1474-1488, <https://doi.org/10.1016/j.drudis.2018.03.013>.
11. Galler, K.M.; Brandl, F.P.; Kirchhof, S.; Widbiller, M.; Eidt, A.; Buchalla, W.; Göpferich, A.; Schmalz, G. Suitability of different natural and synthetic biomaterials for dental pulp tissue engineering. *Tissue Engineering Part A* **2018**, *24*, 234-244, <https://doi.org/10.1089/ten.tea.2016.0555>.
12. Kelly, C.N.; Miller, A.T.; Hollister, S.J.; Guldberg, R.E.; Gall, K. Design and structure-function characterization of 3D printed synthetic porous biomaterials for tissue engineering. *Advanced healthcare materials* **2018**, *7*, <https://doi.org/10.1002/adhm.201701095>.
13. Sharif, S.; Ai, J.; Azami, M.; Verdi, J.; Atlasi, M.A.; Shirian, S.; Samadikuchaksaraei, A. Collagen-coated nano-electrospun PCL seeded with human endometrial stem cells for skin tissue engineering applications.

- Journal of Biomedical Materials Research Part B: Applied Biomaterials* **2018**, *106*, 1578-1586, <https://doi.org/10.1002/jbm.b.33966>.
14. Cruz, Y.; Muñoz, E.; Gomez-Pachón, E.; Morales-Corona, J.; Olayo-Lortia, J.; Olayo, R.; Olayo-Valles, R. Electrospun PCL-protein scaffolds coated by pyrrole plasma polymerization. *Journal of Biomaterials Science, Polymer Edition* **2019**, *30*, 832-845, <https://doi.org/10.1080/09205063.2019.1603338>.
15. Salehi, M.; Naseri-Nosar, M.; Ebrahimi-Barough, S.; Nourani, M.; Khojasteh, A.; Farzamfar, S.; Mansouri, K.; Ai, J. Polyurethane/gelatin nanofibrils neural guidance conduit containing platelet-rich plasma and melatonin for transplantation of Schwann cells. *Cellular and molecular neurobiology* **2018**, *38*, 703-713, <https://doi.org/10.1007/s10571-017-0535-8>.
16. Heidari, M.; Bahrami, S.H.; Ranjbar-Mohammadi, M.; Milan, P. Smart electrospun nanofibers containing PCL/gelatin/graphene oxide for application in nerve tissue engineering. *Materials Science and Engineering: C* **2019**, *103*, <https://doi.org/10.1016/j.msec.2019.109768>.
17. Xiang, P.; Wang, S.-S.; He, M.; Han, Y.-H.; Zhou, Z.-H.; Chen, D.-L.; Li, M.; Ma, L.Q. The in vitro and in vivo biocompatibility evaluation of electrospun recombinant spider silk protein/PCL/gelatin for small caliber vascular tissue engineering scaffolds. *Colloids and Surfaces B: Biointerfaces* **2018**, *163*, 19-28, <https://doi.org/10.1016/j.colsurfb.2017.12.020>.
18. Tijore, A.; Irvine, S.A.; Sarig, U.; Mhaisalkar, P.; Baisane, V.; Venkatraman, S. Contact guidance for cardiac tissue engineering using 3D bioprinted gelatin patterned hydrogel. *Biofabrication* **2018**, *10*.
19. Rahmani, S.; Tabandeh, F.; Faghihi, S.; Amoabediny, G.; Shakibaie, M.; Noorani, B.; Yazdian, F. Fabrication and characterization of poly (ϵ -caprolactone)/gelatin nanofibrous scaffolds for retinal tissue engineering. *International Journal of Polymeric Materials and Polymeric Biomaterials* **2018**, *67*, 27-35, <https://doi.org/10.1080/00914037.2017.1297939>.
20. Wisel, S.; Faleo, G.; Conkling, N.; Chang, R.; Stock, P.; Desai, T.; Tang, Q. Optimization of a Polycaprolactone (PCL) Scaffold for Islet and Cellular Transplantation. *Transplantation* **2018**, *102*, <https://doi.org/10.1097/01.tp.0000543019.47831.40>.
21. Ramos, D.M.; Abdulmalik, S.; Arul, M.R.; Rudraiah, S.; Laurencin, C.T.; Mazzocca, A.D.; Kumbar, S.G. Insulin immobilized PCL-cellulose acetate micro-nanostructured fibrous scaffolds for tendon tissue engineering. *Polymers for advanced technologies* **2019**, *30*, 1205-1215, <https://doi.org/10.1002/pat.4553>.
22. Malikmammadov, E.; Tanir, T.E.; Kiziltay, A.; Hasirci, V.; Hasirci, N. PCL-TCP wet spun scaffolds carrying antibiotic-loaded microspheres for bone tissue engineering. *Journal of Biomaterials science, Polymer edition* **2018**, *29*, 805-824, <https://doi.org/10.1080/09205063.2017.1354671>.
23. Soni, R.; Kumar, N.V.; Chameettachal, S.; Pati, F.; Rath, S.N. Synthesis and Optimization of PCL-Bioactive Glass Composite Scaffold for Bone Tissue Engineering. *Materials Today: Proceedings* **2019**, *15*, 294-299, <https://doi.org/10.1016/j.matpr.2019.05.008>.
24. Lin, W.-C.; Yao, C.; Huang, T.-Y.; Cheng, S.-J.; Tang, C.-M. Long-term in vitro degradation behavior and biocompatibility of polycaprolactone/cobalt-substituted hydroxyapatite composite for bone tissue engineering. *Dental Materials* **2019**, *35*, 751-762, <https://doi.org/10.1016/j.dental.2019.02.023>.
25. Munir, N.; Callanan, A. Novel phase separated polycaprolactone/collagen scaffolds for cartilage tissue engineering. *Biomedical Materials* **2018**, *13*,
26. Bruyas, A.; Lou, F.; Stahl, A.M.; Gardner, M.; Maloney, W.; Goodman, S.; Yang, Y.P. Systematic characterization of 3D-printed PCL/ β -TCP scaffolds for biomedical devices and bone tissue engineering: influence of composition and porosity. *Journal of materials research* **2018**, *33*, 1948-1959, <https://doi.org/10.1557/jmr.2018.112>.
27. Lancuški, A.; Fort, S.B.; Bossard, F.D.R. Electrospun azido-PCL nanofibers for enhanced surface functionalization by click chemistry. *ACS applied materials & interfaces* **2012**, *4*, 6499-6504, <https://doi.org/10.1021/am301458y>.
28. Xu, F.; Wang, Z.; Yang, W. Surface functionalization of polycaprolactone films via surface-initiated atom transfer radical polymerization for covalently coupling cell-adhesive biomolecules. *Biomaterials* **2010**, *31*, 3139-3147, <https://doi.org/10.1016/j.biomaterials.2010.01.032>.
29. Chang, S.H.; Lee, H.J.; Park, S.; Kim, Y.; Jeong, B. Fast degradable polycaprolactone for drug delivery. *Biomacromolecules* **2018**, *19*, 2302-2307, <https://doi.org/10.1021/acs.biomac.8b00266>.
30. Bose, S.; Vu, A.A.; Emshadi, K.; Bandyopadhyay, A. Effects of polycaprolactone on alendronate drug release from Mg-doped hydroxyapatite coating on titanium. *Materials Science and Engineering: C* **2018**, *88*, 166-171, <https://doi.org/10.1016/j.msec.2018.02.019>.
31. Sahoo, S.; Sasmal, A.; Nanda, R.; Phani, A.; Nayak, P. Synthesis of chitosan-polycaprolactone blend for control delivery of ofloxacin drug. *Carbohydrate Polymers* **2010**, *79*, 106-113, <https://doi.org/10.1016/j.carbpol.2009.07.042>.
32. Canbolat, M.F.; Celebioglu, A.; Uyar, T. Drug delivery system based on cyclodextrin-naproxen inclusion complex incorporated in electrospun polycaprolactone nanofibers. *Colloids and Surfaces B: Biointerfaces* **2014**, *115*, 15-21, <https://doi.org/10.1016/j.colsurfb.2013.11.021>.
33. Yeong, W.; Sudarmadji, N.; Yu, H.; Chua, C.; Leong, K.; Venkatraman, S.; Boey, Y.; Tan, L. Porous polycaprolactone scaffold for cardiac tissue engineering fabricated by selective laser sintering. *Acta biomaterialia* **2010**, *6*, 2028-2034, <https://doi.org/10.1016/j.actbio.2009.12.033>.

34. Tseng, H.; Puperi, D.S.; Kim, E.J.; Ayoub, S.; Shah, J.V.; Cuchiara, M.L.; West, J.L.; Grande-Allen, K.J. Anisotropic poly (ethylene glycol)/polycaprolactone hydrogel–fiber composites for heart valve tissue engineering. *Tissue Engineering Part A* **2014**, *20*, 2634–2645, <https://doi.org/10.1089/ten.tea.2013.0397>.
35. Park, S.A.; Lee, S.H.; Kim, W.D. Fabrication of porous polycaprolactone/hydroxyapatite (PCL/HA) blend scaffolds using a 3D plotting system for bone tissue engineering. *Bioprocess and biosystems engineering* **2011**, *34*, 505–513, <https://doi.org/10.1007/s00449-010-0499-2>.
36. Kundu, J.; Shim, J.H.; Jang, J.; Kim, S.W.; Cho, D.W. An additive manufacturing-based PCL–alginate–chondrocyte bioprinted scaffold for cartilage tissue engineering. *Journal of tissue engineering and regenerative medicine* **2015**, *9*, 1286–1297, <https://doi.org/10.1002/term.1682>.
37. Wang, T.-J.; Wang, I.-J.; Lu, J.-N.; Young, T.-H. Novel chitosan-polycaprolactone blends as potential scaffold and carrier for corneal endothelial transplantation. *Molecular vision* **2012**, *18*.
38. Lee, B.-K.; Ju, Y.M.; Cho, J.-G.; Jackson, J.D.; Lee, S.J.; Atala, A.; Yoo, J.J. End-to-side neurorrhaphy using an electrospun PCL/collagen nerve conduit for complex peripheral motor nerve regeneration. *Biomaterials* **2012**, *33*, 9027–9036, <https://doi.org/10.1016/j.biomaterials.2012.09.008>.
39. Salgado, A.; Sousa, R.; Fraga, J.; Pêgo, J.M.; Silva, B.; Malva, J.; Neves, N.; Reis, R.; Sousa, N. Effects of starch/polycaprolactone-based blends for spinal cord injury regeneration in neurons/glia cells viability and proliferation. *Journal of Bioactive and Compatible Polymers* **2009**, *24*, 235–248, <https://doi.org/10.1177/0883911509104081>.
40. Venugopal, J.; Zhang, Y.; Ramakrishna, S. Fabrication of modified and functionalized polycaprolactone nanofibre scaffolds for vascular tissue engineering. *Nanotechnology* **2005**, *16*, 2138–42, <https://doi.org/10.1088/0957-4484/16/10/028>.
41. Hackett, J.; Dang, T.; Tsai, E.; Cao, X. Electrospun biocomposite polycaprolactone/collagen tubes as scaffolds for neural stem cell differentiation. *Materials* **2010**, *3*, 3714–3728, <https://doi.org/10.3390/ma3063714>.
42. Kim, J.-J.; Bae, W.-J.; Kim, J.-M.; Kim, J.-J.; Lee, E.-J.; Kim, H.-W.; Kim, E.-C. Mineralized polycaprolactone nanofibrous matrix for odontogenesis of human dental pulp cells. *Journal of biomaterials applications* **2014**, *28*, 1069–1078, <https://doi.org/10.1177/0885328213495903>.
43. Thomas, R.; Soumya, K.; Mathew, J.; Radhakrishnan, E. Electrospun polycaprolactone membrane incorporated with biosynthesized silver nanoparticles as effective wound dressing material. *Applied biochemistry and biotechnology* **2015**, *176*, 2213–2224, <https://doi.org/10.1007/s12010-015-1709-9>.
44. Naghashzargar, E.; Farè, S.; Catto, V.; Bertoldi, S.; Semnani, D.; Karbasi, S.; Tanzi, M.C. Nano/micro hybrid scaffold of PCL or P3HB nanofibers combined with silk fibroin for tendon and ligament tissue engineering. *Journal of applied biomaterials & functional materials* **2015**, *13*, 156–168, <https://doi.org/10.5301/jabfm.5000216>.
45. McKeon-Fischer, K.; Flagg, D.; Freeman, J. Coaxial electrospun poly (ϵ -caprolactone), multiwalled carbon nanotubes, and polyacrylic acid/polyvinyl alcohol scaffold for skeletal muscle tissue engineering. *Journal of biomedical materials research Part A* **2011**, *99*, 493–499, <https://doi.org/10.1002/jbm.a.33116>.
46. Oppenheim, R.C. Nanoparticulate drug delivery systems based on gelatin and albumin. In: *Polymeric nanoparticles and microspheres*. CRC Press: **2018**; pp. 1–27.
47. Salerno, A.; Verdolotti, L.; Raucci, M.; Saurina, J.; Domingo, C.; Lamanna, R.; Iozzino, V.; Lavorgna, M. Hybrid gelatin-based porous materials with a tunable multiscale morphology for tissue engineering and drug delivery. *European Polymer Journal* **2018**, *99*, 230–239. <https://doi.org/10.1016/j.eurpolymj.2017.12.024>.
48. Kang, M.G.; Lee, M.Y.; Cha, J.M.; Lee, J.K.; Lee, S.C.; Kim, J.; Hwang, Y.-S.; Bae, H. Nanogels Derived from Fish Gelatin: Application to Drug Delivery System. *Marine drugs* **2019**, *17*, <https://doi.org/10.3390/md17040246>.
49. Su, K.; Wang, C. Recent advances in the use of gelatin in biomedical research. *Biotechnology letters* **2015**, *37*, 2139–2145, <https://doi.org/10.1007/s10529-015-1907-0>.
50. C Echave, M.; S Burgo, L.; L Pedraz, J.; Orive, G. Gelatin as biomaterial for tissue engineering. *Current pharmaceutical design* **2017**, *23*, 3567–3584, <https://doi.org/10.2174/0929867324666170511123101>.
51. Sharifi, E.; Azami, M.; Kajbafzadeh, A.-M.; Moztaaradeh, F.; Faridi-Majidi, R.; Shamousi, A.; Karimi, R.; Ai, J. Preparation of a biomimetic composite scaffold from gelatin/collagen and bioactive glass fibers for bone tissue engineering. *Materials Science and Engineering: C* **2016**, *59*, 533–541, <https://doi.org/10.1016/j.msec.2015.09.037>.
52. Kirdponpattara, S.; Phisalaphong, M.; Kongruang, S. Gelatin-bacterial cellulose composite sponges thermally cross-linked with glucose for tissue engineering applications. *Carbohydrate polymers* **2017**, *177*, 361–368, <https://doi.org/10.1016/j.carbpol.2017.08.094>.
53. Jalaja, K.; Naskar, D.; Kundu, S.C.; James, N.R. Potential of electrospun core–shell structured gelatin–chitosan nanofibers for biomedical applications. *Carbohydrate polymers* **2016**, *136*, 1098–1107, <https://doi.org/10.1016/j.carbpol.2015.10.014>.
54. Foox, M.; Zilberman, M. Drug delivery from gelatin-based systems. *Expert opinion on drug delivery* **2015**, *12*, 1547–1563, <https://doi.org/10.1517/17425247.2015.1037272>.
55. Babaei, J.; Mohammadian, M.; Madadlou, A. Gelatin as texture modifier and porogen in egg white hydrogel. *Food chemistry* **2019**, *270*, 189–195, <https://doi.org/10.1016/j.foodchem.2018.07.109>.

56. Stevenson, M.; Long, J.; Seyfoddin, A.; Guerrero, P.; de la Caba, K.; Etxabide, A. Characterization of ribose-induced cross-linking extension in gelatin films. *Food Hydrocolloids* **2020**, *99*, <https://doi.org/10.1016/j.foodhyd.2019.105324>.
57. Koshy, S.T.; Desai, R.M.; Joly, P.; Li, J.; Bagrodia, R.K.; Lewin, S.A.; Joshi, N.S.; Mooney, D.J. Click-Crosslinked Injectable Gelatin Hydrogels. *Advanced healthcare materials* **2016**, *5*, 541-547, <https://doi.org/10.1002/adhm.201500757>.
58. Nieto-Suárez, M.; López-Quintela, M.A.; Lazzari, M. Preparation and characterization of cross-linked chitosan/gelatin scaffolds by ice segregation induced self-assembly. *Carbohydrate polymers* **2016**, *141*, 175-183, <https://doi.org/10.1016/j.carbpol.2015.12.064>.
59. De Clercq, K.; Schelfhout, C.; Bracke, M.; De Wever, O.; Van Bockstal, M.; Ceelen, W.; Remon, J.P.; Vervaeke, C. Genipin-crosslinked gelatin microspheres as a strategy to prevent postsurgical peritoneal adhesions: In vitro and in vivo characterization. *Biomaterials* **2016**, *96*, 33-46, <https://doi.org/10.1016/j.biomaterials.2016.04.012>.
60. Piao, Y.; Chen, B. Synthesis and mechanical properties of double cross-linked gelatin-graphene oxide hydrogels. *International journal of biological macromolecules* **2017**, *101*, 791-798, <https://doi.org/10.1016/j.ijbiomac.2017.03.155>.
61. Li, M.; Guo, Y.; Wei, Y.; MacDiarmid, A.G.; Lelkes, P.I. Electrospinning polyaniline-contained gelatin nanofibers for tissue engineering applications. *Biomaterials* **2006**, *27*, 2705-2715, <https://doi.org/10.1016/j.biomaterials.2005.11.037>.
62. Liu, X.; Smith, L.A.; Hu, J.; Ma, P.X. Biomimetic nanofibrous gelatin/apatite composite scaffolds for bone tissue engineering. *Biomaterials* **2009**, *30*, 2252-2258, <https://doi.org/10.1016/j.biomaterials.2008.12.068>.
63. Chang, C.-H.; Liu, H.-C.; Lin, C.-C.; Chou, C.-H.; Lin, F.-H. Gelatin-chondroitin-hyaluronan tri-copolymer scaffold for cartilage tissue engineering. *Biomaterials* **2003**, *24*, 4853-4858, [https://doi.org/10.1016/S0142-9612\(03\)00383-1](https://doi.org/10.1016/S0142-9612(03)00383-1).
64. Zhao, X.; Lang, Q.; Yildirim, L.; Lin, Z.Y.; Cui, W.; Annabi, N.; Ng, K.W.; Dokmeci, M.R.; Ghaemmaghami, A.M.; Khademhosseini, A. Photocrosslinkable gelatin hydrogel for epidermal tissue engineering. *Advanced healthcare materials* **2016**, *5*, 108-118, <https://doi.org/10.1002/adhm.201500005>.
65. Kimura, Y.; Ozeki, M.; Inamoto, T.; Tabata, Y. Adipose tissue engineering based on human preadipocytes combined with gelatin microspheres containing basic fibroblast growth factor. *Biomaterials* **2003**, *24*, 2513-2521, [https://doi.org/10.1016/S0142-9612\(03\)00049-8](https://doi.org/10.1016/S0142-9612(03)00049-8).
66. Meng, Z.; Xu, X.; Zheng, W.; Zhou, H.; Li, L.; Zheng, Y.; Lou, X. Preparation and characterization of electrospun PLGA/gelatin nanofibers as a potential drug delivery system. *Colloids and Surfaces B: Biointerfaces* **2011**, *84*, 97-102, <https://doi.org/10.1016/j.colsurfb.2010.12.022>.
67. Saravanan, M.; Rao, K.P. Pectin-gelatin and alginate-gelatin complex coacervation for controlled drug delivery: Influence of anionic polysaccharides and drugs being encapsulated on physicochemical properties of microcapsules. *Carbohydrate Polymers* **2010**, *80*, 808-816, <https://doi.org/10.1016/j.carbpol.2009.12.036>.
68. Etxabide, A.; Long, J.; Guerrero, P.; de la Caba, K.; Seyfoddin, A. 3D printed lactose-crosslinked gelatin scaffolds as a drug delivery system for dexamethasone. *European Polymer Journal* **2019**, *114*, 90-97, <https://doi.org/10.1016/j.eurpolymj.2019.02.019>.
69. Wong, C.; Shital, P.; Chen, R.; Owida, A.; Morsi, Y. Biomimetic electrospun gelatin-chitosan polyurethane for heart valve leaflets. *Journal of Mechanics in Medicine and Biology* **2010**, *10*, 563-576, <https://doi.org/10.1142/S0219519410003551>.
70. Hajiali, H.; Shahgasempour, S.; Naimi-Jamal, M.R.; Peirovi, H. Electrospun PGA/gelatin nanofibrous scaffolds and their potential application in vascular tissue engineering. *International journal of nanomedicine* **2011**, *6*, 2133-2141, <https://doi.org/10.2147/IJN.S24312>.
71. Dhandayuthapani, B.; Krishnan, U.M.; Sethuraman, S. Fabrication and characterization of chitosan-gelatin blend nanofibers for skin tissue engineering. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **2010**, *94*, 264-272, <https://doi.org/10.1002/jbm.b.31651>.
72. Fan, H.; Liu, H.; Wang, Y.; Toh, S.L.; Goh, J.C.H. Development of a silk cable-reinforced gelatin/silk fibroin hybrid scaffold for ligament tissue engineering. *Cell transplantation* **2008**, *17*, 1389-1401, <https://doi.org/10.3727/096368908787648047>.
73. Jain, S.K.; Gupta, Y.; Jain, A.; Saxena, A.R.; Khare, P.; Jain, A. Mannosylated gelatin nanoparticles bearing an anti-HIV drug didanosine for site-specific delivery. *Nanomedicine: Nanotechnology, Biology and Medicine* **2008**, *4*, 41-48, <https://doi.org/10.1016/j.nano.2007.11.004>.
74. Pereira, R.F.; Bartolo, P.J. Traditional therapies for skin wound healing. *Advances in wound care* **2016**, *5*, 208-229, <https://doi.org/10.1089/wound.2013.0506>.
75. Sorg, H.; Tilkorn, D.J.; Hager, S.; Hauser, J.; Mirastschijski, U. Skin wound healing: an update on the current knowledge and concepts. *European Surgical Research* **2017**, *58*, 81-94, <https://doi.org/10.1159/000454919>.
76. Qu, J.; Zhao, X.; Liang, Y.; Zhang, T.; Ma, P.X.; Guo, B. Antibacterial adhesive injectable hydrogels with rapid self-healing, extensibility and compressibility as wound dressing for joints skin wound healing. *Biomaterials* **2018**, *183*, 185-199, <https://doi.org/10.1016/j.biomaterials.2018.08.044>.
77. Zomer, H.D.; Trentin, A.G. Skin wound healing in humans and mice: Challenges in translational research. *Journal of dermatological science* **2018**, *90*, 3-12, <https://doi.org/10.1016/j.jdermsci.2017.12.009>.

78. Kucharzewski, M.; Rojczyk, E.; Wilemska-Kucharzewska, K.; Wilk, R.; Hudecki, J.; Los, M.J. Novel trends in application of stem cells in skin wound healing. *European journal of pharmacology* **2018**, *843*, 307-315, <https://doi.org/10.1016/j.ejphar.2018.12.012>.
79. Bakhtyar, N.; Jeschke, M.G.; Herer, E.; Sheikholeslam, M.; Amini-Nik, S. Exosomes from acellular Wharton's jelly of the human umbilical cord promotes skin wound healing. *Stem cell research & therapy* **2018**, *9*, <https://doi.org/10.1186/s13287-018-0921-2>.
80. Kim, B.S.; Kwon, Y.W.; Kong, J.-S.; Park, G.T.; Gao, G.; Han, W.; Kim, M.-B.; Lee, H.; Kim, J.H.; Cho, D.-W. 3D cell printing of in vitro stabilized skin model and in vivo pre-vascularized skin patch using tissue-specific extracellular matrix bioink: a step towards advanced skin tissue engineering. *Biomaterials* **2018**, *168*, 38-53, <https://doi.org/10.1016/j.biomaterials.2018.03.040>.
81. Tarassoli, S.P.; Jessop, Z.M.; Al-Sabah, A.; Gao, N.; Whitaker, S.; Doak, S.; Whitaker, I.S. Skin tissue engineering using 3D bioprinting: an evolving research field. *Journal of Plastic, Reconstructive & Aesthetic Surgery* **2018**, *71*, 615-623, <https://doi.org/10.1016/j.bjps.2017.12.006>.
82. Lin, Z.; Gao, W.; Ma, L.; Xia, H.; Xie, W.; Zhang, Y.; Chen, X. Preparation and properties of poly (ϵ -caprolactone)/bioactive glass nanofibre membranes for skin tissue engineering. *Journal of Bioactive and Compatible Polymers* **2018**, *33*, 195-209.
83. Chong, E.J.; Phan, T.T.; Lim, I.J.; Zhang, Y.; Bay, B.H.; Ramakrishna, S.; Lim, C.T. Evaluation of electrospun PCL/gelatin nanofibrous scaffold for wound healing and layered dermal reconstitution. *Acta biomaterialia* **2007**, *3*, 321-330, <https://doi.org/10.1016/j.actbio.2007.01.002>.
84. Naseri-Nosar, M.; Farzamfar, S.; Sahrapeyma, H.; Ghorbani, S.; Bastami, F.; Vaez, A.; Salehi, M. Cerium oxide nanoparticle-containing poly (ϵ -caprolactone)/gelatin electrospun film as a potential wound dressing material: in vitro and in vivo evaluation. *Materials Science and Engineering: C* **2017**, *81*, 366-372, <https://doi.org/10.1016/j.msec.2017.08.013>.
85. Farzamfar, S.; Naseri-Nosar, M.; Samadian, H.; Mahakizadeh, S.; Tajerian, R.; Rahmati, M.; Vaez, A.; Salehi, M. Taurine-loaded poly (ϵ -caprolactone)/gelatin electrospun mat as a potential wound dressing material: In vitro and in vivo evaluation. *Journal of Bioactive and Compatible Polymers* **2018**, *33*, 282-294.
86. Fu, Y.; Guan, J.; Guo, S.; Guo, F.; Niu, X.; Liu, Q.; Zhang, C.; Nie, H.; Wang, Y. Human urine-derived stem cells in combination with polycaprolactone/gelatin nanofibrous membranes enhance wound healing by promoting angiogenesis. *Journal of translational medicine* **2014**, *12*, <https://doi.org/10.1186/s12967-014-0274-2>.
87. Syu, W.-Z.; Hueng, D.-Y.; Chen, W.-L.; Chan, J.Y.-H.; Chen, S.-G.; Huang, S.-M. Adipose-Derived Neural Stem Cells Combined with Acellular Dermal Matrix as a Neural Conduit Enhances Peripheral Nerve Repair. *Cell transplantation* **2019**, 0963689719853512. <https://doi.org/10.1177/0963689719853512>.
88. Jones, I.; Novikova, L.N.; Novikov, L.N.; Renardy, M.; Ullrich, A.; Wiberg, M.; Carlsson, L.; Kingham, P.J. Regenerative effects of human embryonic stem cell-derived neural crest cells for treatment of peripheral nerve injury. *Journal of tissue engineering and regenerative medicine* **2018**, *12*, e2099-e2109, <https://doi.org/10.1002/term.2642>.
89. Yen, C.-M.; Shen, C.-C.; Yang, Y.-C.; Liu, B.-S.; Lee, H.-T.; Sheu, M.-L.; Tsai, M.-H.; Cheng, W.-Y. Novel electrospun poly (ϵ -caprolactone)/type I collagen nanofiber conduits for repair of peripheral nerve injury. *Neural regeneration research* **2019**, *14*, <https://doi.org/10.4103/1673-5374.255997>.
90. Salehi, M.; Naseri-Nosar, M.; Ebrahimi-Barough, S.; Nourani, M.; Khojasteh, A.; Hamidieh, A.A.; Amani, A.; Farzamfar, S.; Ai, J. Sciatic nerve regeneration by transplantation of Schwann cells via erythropoietin controlled-releasing polylactic acid/multiwalled carbon nanotubes/gelatin nanofibrils neural guidance conduit. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **2018**, *106*, 1463-1476, <https://doi.org/10.1002/jbm.b.33952>.
91. Farzamfar, S.; Ehterami, A.; Salehi, M.; Vaez, A.; Atashi, A.; Sahrapeyma, H. Unrestricted somatic stem cells loaded in nanofibrous conduit as potential candidate for sciatic nerve regeneration. *Journal of Molecular Neuroscience* **2019**, *67*, 48-61, <https://doi.org/10.1007/s12031-018-1209-9>.
92. Babaloo, H.; Ebrahimi-Barough, S.; Derakhshan, M.A.; Yazdankhah, M.; Lotfibakhshaiesh, N.; Soleimani, M.; Joghataei, M.T.; Ai, J. PCL/gelatin nanofibrous scaffolds with human endometrial stem cells/Schwann cells facilitate axon regeneration in spinal cord injury. *Journal of cellular physiology* **2019**, *234*, 11060-11069, <https://doi.org/10.1002/jcp.27936>.
93. Aslani, S.; Abhari, A.; Sakhinia, E.; Sanajou, D.; Rajabi, H.; Rahimzadeh, S. Interplay between microRNAs and Wnt, transforming growth factor- β , and bone morphogenic protein signaling pathways promote osteoblastic differentiation of mesenchymal stem cells. *Journal of cellular physiology* **2019**, *234*, 8082-8093, <https://doi.org/10.1002/jcp.27582>.
94. Kim, B.-R.; Nguyen, T.B.L.; Min, Y.-K.; Lee, B.-T. In vitro and in vivo studies of BMP-2-loaded PCL-gelatin-BCP electrospun scaffolds. *Tissue Engineering Part A* **2014**, *20*, 3279-3289, <https://doi.org/10.1089/ten.tea.2014.0081>.
95. Binulal, N.; Natarajan, A.; Menon, D.; Bhaskaran, V.; Mony, U.; Nair, S.V. PCL-gelatin composite nanofibers electrospun using diluted acetic acid-ethyl acetate solvent system for stem cell-based bone tissue engineering. *Journal of Biomaterials Science, Polymer Edition* **2014**, *25*, 325-340, <https://doi.org/10.1080/09205063.2013.859872>.

96. Shi, R.; Ye, J.; Li, W.; Zhang, J.; Li, J.; Wu, C.; Xue, J.; Zhang, L. Infection-responsive electrospun nanofiber mat for antibacterial guided tissue regeneration membrane. *Materials Science and Engineering: C* **2019**, *100*, 523-534, <https://doi.org/10.1016/j.msec.2019.03.039>.
97. Yang, L.; Jiang, Z.; Zhou, L.; Zhao, K.; Ma, X.; Cheng, G. Hydrophilic cell-derived extracellular matrix as a niche to promote adhesion and differentiation of neural progenitor cells. *RSC Advances* **2017**, *7*, 45587-45594, <https://doi.org/10.1039/C7RA08273H>.
98. Ren, K.; Wang, Y.; Sun, T.; Yue, W.; Zhang, H. Electrospun PCL/gelatin composite nanofiber structures for effective guided bone regeneration membranes. *Materials Science and Engineering: C* **2017**, *78*, 324-332, <https://doi.org/10.1016/j.msec.2017.04.084>.