In vivo wound healing using biocompatible nanofibers immobilized with epidermal growth factor (EGF)

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Statement of Purpose: In order to facilitate wound healing process, many attempts have been made including associating growth factors to biocompatible materials. Eletrospun nanofibers are received a great attention because of their unique structure and potentials as a novel biomaterials. In the current study, we electrospun biocompatible nanofibers and chemically conjugated epidermal growth factor on the surface of the nanofiber to enhance wound healing efficiency in diabetic animals.

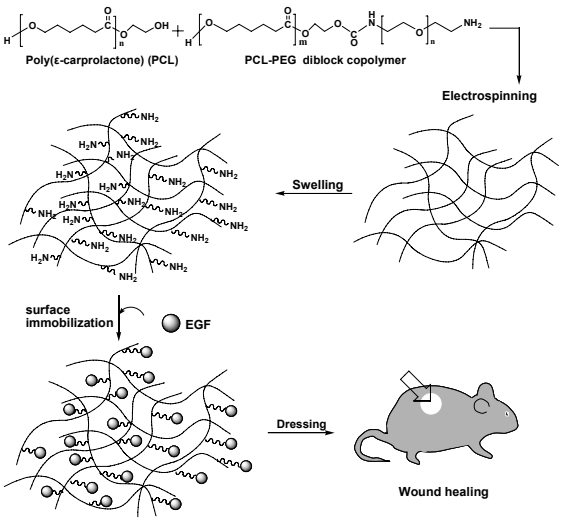

Figure 1. Schematic preparation diagram EGF-immobilized nanofibers and wound healing process.

Table 1. Preparation of EGF nanofibers for *in vivo* wound healing study

	(a)	*(b)*	*(c)*	*(d)*
blend ratio of PCL /PCL-PEG (%, w/w)	10	0	0	-
The amount of in corporated epider mal growth factor (EGF) (%, w/w)	10 (conjugation)	10 (blend)	-	-

Methods: Amine-terminated PCL-PEG was synthesized as described previously. Briefly, hydroxyl group of PCL in methylene chloride was activated by p-nitrophenyl chloroformate and the activated PCL was slowly dropped into PEG diamine in methylene chloride. The synthesized polymer was precipitated in cold diethyl ether twice. Twenty percents PCL/PCL-PEG solution in methanol/chloroform mixture was electrospinned at 15 kV of an applied voltage and 1ml/h of a flow rate. Pre-wetted nanofiber containing PCL-PEG block copolymer was incubated with EGF in phosphate buffered saline (PBS) at pH 6.0 in the presence of EDC and HOBt. After completely washing off unreacted EGF, nanofiber immobilized with EGF was dried. C57B/6 female mouse at 5 weeks was intraperitoneally administered with streptozotocin (50mg/kg). After confirming diabetes symptoms in animals, a round-shape wound was made on shaved dorsal area. The wounds of the diabetic animals was covered with nanofibers and 3M Tegaderm® was used to affix the nanofibers.

Results/Discussion: Fig 1 shows schematic diagram of wound healing process using EGF-immobilized nanofibers. Because amine groups are exposed on the surface of nanofibers via PEG linkers, EGF was chemically immobilized on the surface of nanofibers. Table 1 summarizes nanofibers used for treating wounded animals. The blend ratio of PCL-PEG block copolymer was kept at 10% (w/w) to immobilize EGF. The amount of immobilized EGF was quantitated by electron spectroscopy for chemical analysis (ESCA). In order to compared effects of immobilized EGF on nanofibers and those with physically-mixed EGF, 10% (w/w) of EGF was simultaneously applied on PCL nanofibers when wound dressing was made (b). Fig 2 shows results from treated mouse with EGF blended or immobilized nanofibers. Fig 2(a) indicates diabetic animals treated with nanofibers chemically immobilized with EGF and Fig 2(b) indicates that treated with physical mixtures of PCL nanofibers and EGF. This result clearly shows that animals treated with EGF-immobilized nanofibers showed superior recovery rate compared to that treated with physical mixtures of PCL nanofibers and EGF.

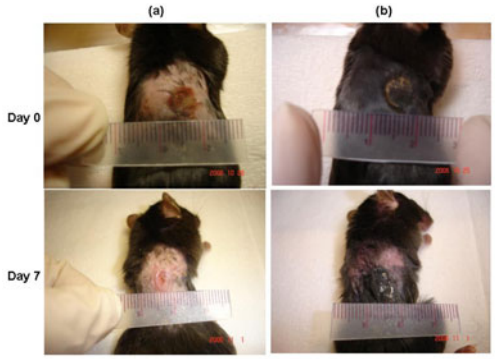

Figure 2. Wound healing using EGF nanofibers

Conclusions: For diabetic wounded animals, EGF-immobilized nanofibers enhanced treatment efficacy compared to unconjugated one.

References: Yoo HS et al., Biomaterials 2005;26:1925-1933