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Effect of substrate stiffenss and nanotophographic cue in mouse tendon derived stem cell

Byungchan LEE[1*], Sangjun KIM[1†]

Samsung Medical Center, Department of Rehabilitation Medicine[1]

Tendon-derived stem cells (TDSCs) are key factors associated with regeneration and healing in tendinopathy and tendon injury. Mechanical stimulation, topographic signals, biochemical factors, and their combinations have been attempted to regulate stem cell differentiation into teno-lineage. We compared TDSCs from normal tendon with TDSCs from tendinopathic tendon and compared characteristics of TDSCs according to the nanotopographic-cues and surface stiffness. TDSCs from 5-week normal tendon showed high expression of type III collagen and tenomodulin on the flat NOA86 substrate. In TDSCs from 5-week tendinopathy and 15-week normal tendon, type III collagen and tenomodulin were high expressed on the 800 nm NOA86 substrate. Gene expression of scleraxis increased on the 800 nm PUA substrate in TDSCs from 5-week normal tendon. In TDSCs from 15-week normal tendon, scleraxis was prominently expressed on the 800 nm nanotopographic signals. However, the expression of type I collagen was not different. These results show therapeutic application needs to be diverse because the effects of substrate stiffness and nanotopographic cues on the TDSCs were different based on the mechanism of tendinopathy. Further in-vivo studies should be conducted to determine how stiffness and nanotopographic cues can be delivered to the TDSCs in the animal model or patients with tendinopathy.

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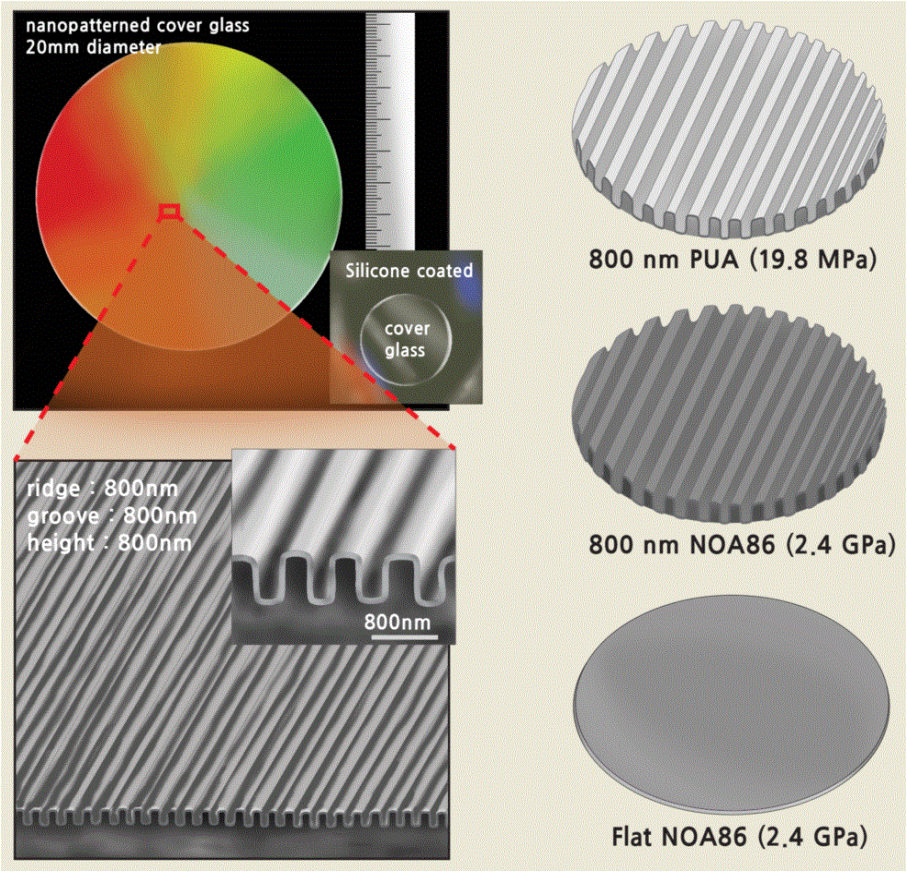
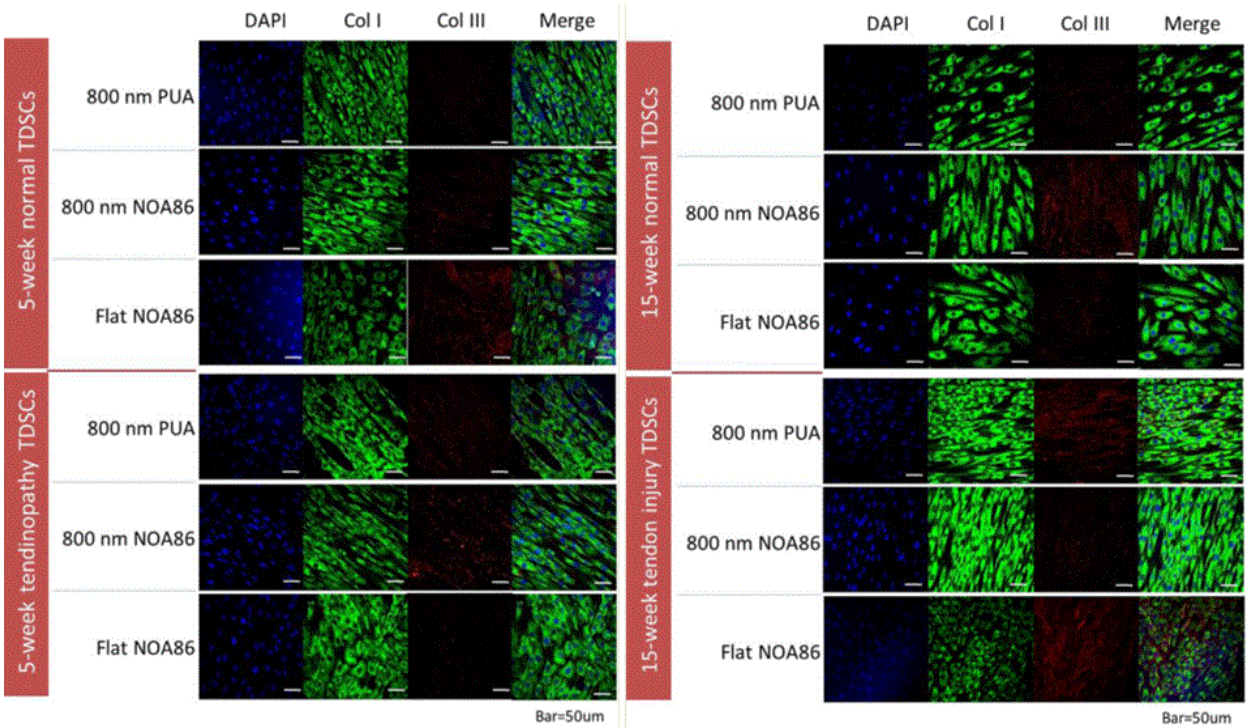
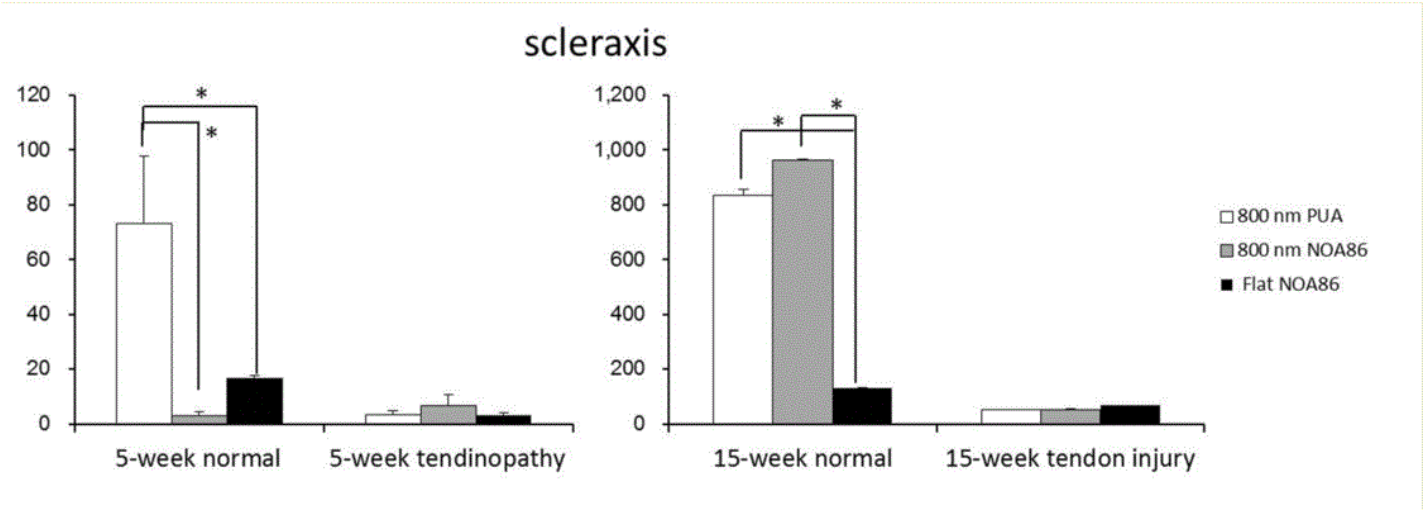


Figure 1. A Norland Optical Adhesive 2.48 GPa stiffness (NOA86) and a polyurethane acrylamide 19.8 MPa (PUA) substrates were prepared to provide an environment with mechanical properties comparable to a developing tendon. The NOA86 and PUA were coated with silicone and carved to create 800-nm-wide nanogrooves for nanotopographic cues. Flat NOA86 with the same stiffness was prepared to determine the effects of nanotopographic cues



Expression of type I and type III collagen was observed in the TDSCs extracted from 5-week normal and 5-week tendinopathy models cultured on the 800 nm NOA86 (2.4 GPa), flat NOA86, and 800 nm PUA (19.8 MPa) substrates. In the 5-week normal condition, high expression of type III collagen was found on the flat NOA86, while this expression was increased on the 800 nm NOA86 in the 5-week tendinopathy model. There was no difference in expression of type I collagen between the substrates. Expression of type I and type III collagen was observed in the TDSCs extracted from 15-week normal and 15-week tendon injury

models cultured on the 800 nm NOA86 (2.4 GPa), flat NOA86, and 800 nm PUA (19.8 MPa) substrates. In the 15-week normal tendonmodel, expression of type III collagen was highly expressed in TDSCs cultured on the 800 nm NOA86 substrates. However, in the 15-week tendon injury model, type III collagen was highly expressed in TDSCs cultured on the 800 nm PUA and flat NOA86 substrate. The expression of type I collagen was not different between the substrates.



Gene expression of scleraxis increased in TDSCs cultured on the 800 nm PUA substrate in the 5-week normal tendon model (P<0.01). In the 15-week normal tendon model, scleraxis was highly expressed in TDSCs cultured on the 800 nm PUA and 800 nm NOA86 substrate (P<0.01). However, the gene expression was not significantly different between the substrates in the 5-week tendinopathy and 15-week tendon injury models.