Supplementary Information

An RNAi nanotherapy for fibrosis: Highly durable knockdown of CTGF/CCN-2 by using siRNA-DegradaBALL (LEM-S401) to treat skin fibrotic diseases

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Supplementary figures

**Figure S1.** siCTGF loading capacity and dynamic light scattering (DLS) analysis of DegradaBALL. (A) 1 μg of Cy5 conjugated siCTGF was incubated with various concentration of DegradaBALL (0, 1.25, 2.5, 5.0, 10.0 and 15.0 μg). The loaded amount of siCTGF was calculated by fluorescence in the supernatant. (B) DLS analysis of DegradaBALL.
Figure S2. Viability of A549 and HaCaT cells after treatment of DegradaBALL. After treating various doses of DegradaBALL to A549 and HaCaT cells, cell viability was measured by CCK-8 assay.
Figure S3. **Time-dependent CTGF expression induced by TGF-β.** (A) A549 and (B) HaCaT cells were treated with 2 ng/mL of TGF-β for 24 hr. The cells were harvested at different time points and the CTGF expression level was analyzed by RT-PCR.
Figure S4. Histopathological photograph of LEM-S401 treated mouse skin during tissue remodeling process in vivo. (A) LEM-S401 was intradermally injected at the wound site on day 10, 14, 18, and 22 post wound formation. The mouse was sacrificed on day 28. (A) the skin tissue was harvested and trichrome stained. (B) Quantitative analysis of skin thickness data based on the images shown in (A). (C) CTGF, Col I and Col III mRNA expression levels in the injection sites were measured by RT-PCR. (D) Fluorescent images of CTGF, Col I and Col III in the harvested mouse skin were examined by immunohistochemistry. Scale bar: 100 μm. (E) Quantitative analysis of immunohistochemistry data based on the images shown in (D). *P<0.05, **P<0.01, ***P<0.001
Figure S5. Sequence information of siRNA and RT-PCR primers. (A) Human and mouse targeted siRNA sequences. (B) Human and mouse RT-PCR primer sequences.