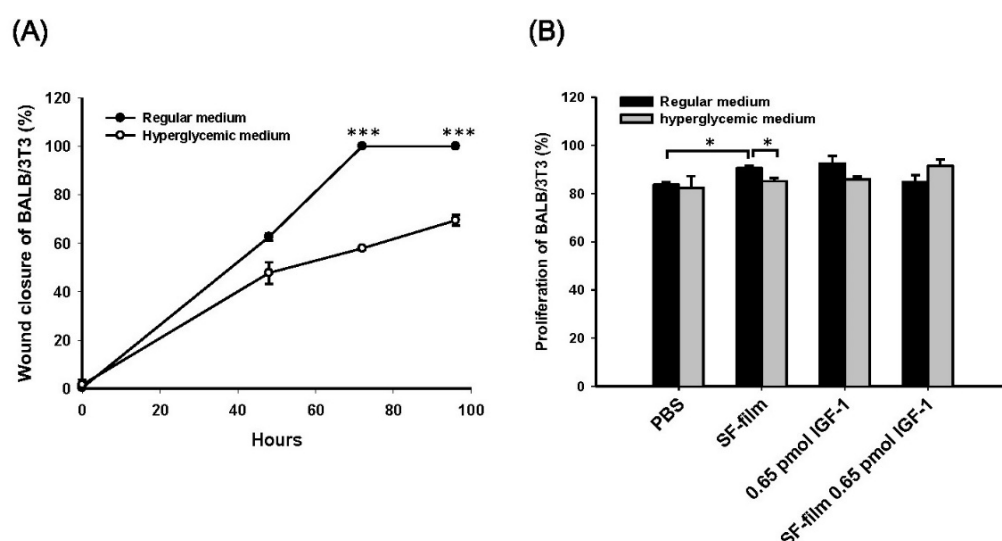
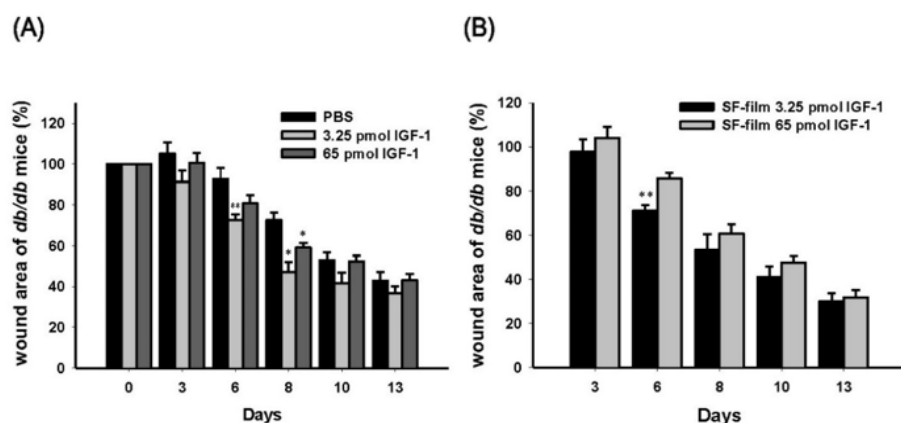


# Supplementary Materials: An Insulin-Like Growth Factor-1 Conjugated Bombyx mori Silk Fibroin Film for Diabetic Wound Healing: Fabrication, Physicochemical Property Characterization, and Dosage Optimization In Vitro and In Vivo

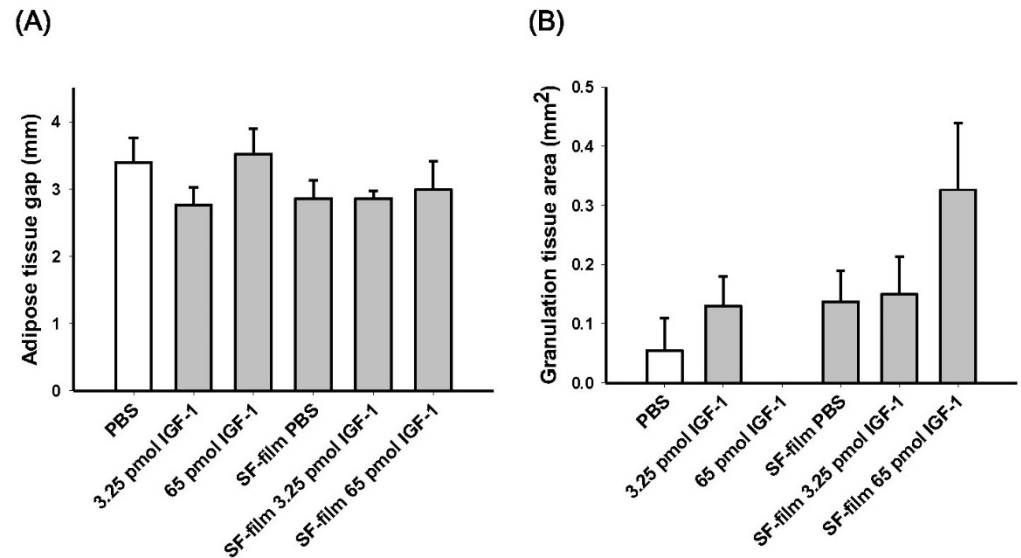
Meng-Jin Lin, Mei-Chun Lu, Yun-Chen Chan, Yu-Fen Huang and Hwan-You Chang



**Figure S1.** Migration and proliferation of BALB/3T3 fibroblasts in response to insulin-like growth factor 1 (IGF-1), silk fibroin (SF)-film, and IGF-1-loaded SF-film treatment. **(A)** Quantification of cell wound closure in regular and hyperglycemic media. Statistically significant differences between regular and hyperglycemic culture medium were determined by Dunnett's multiple comparison post hoc test. \*  $p < 0.05$  and \*\*\*  $p < 0.001$ ;  $n = 4$ ; mean  $\pm$  SEM. **(B)** Cell proliferation after IGF-1 (3.25 pmol), SF-film, or IGF-1 (3.25 pmol) loaded SF-film treatment in regular or hyperglycemic medium. The 100% reduced form of alamarBlue reagent as the 100% of cell proliferation (positive control). Statistically significant differences between PBS and the other treatments were determined by Dunnett's multiple comparison post hoc test. \*  $p < 0.05$ ;  $n = 4$ ; mean  $\pm$  SEM.



**Figure S2.** Time-course analysis of diabetic wound healing after insulin-like growth factor 1 (IGF-1), silk fibroin (SF)-film, and IGF-1-loaded SF-film treatment. **(A)** Quantification of wound closure from day 0 to day 13 post-wounding upon treatment with 65 pmol and 3.25 pmol IGF-1. Statistically significant differences between PBS and other IGF-1 treatments were determined by Dunnett's multiple comparison post hoc test. \*  $p < 0.05$ , and \*\*  $p < 0.01$ ;  $n = 5$ ; mean  $\pm$  SEM. **(B)** Quantification of wound closure from day 0 to day 13 post-wounding upon treatment with 65 pmol and 3.25 pmol doses of IGF-1-loaded SF-films. Five stained sections for each group were evaluated and the average di-iameter was estimated under a light microscope. Statistically significant differences between 65 pmol and 3.25 pmol dose treatments were determined by Dunnett's multiple comparison post hoc test. \*  $p < 0.05$ , and \*\*  $p < 0.01$ ;  $n = 5$ ; mean  $\pm$  SEM.



**Figure S3.** Analysis of tissue regeneration in diabetic wounds after insulin-like growth factor 1 (IGF-1)-loaded silk fibroin (SF)-film treatment. Tissues at day 13 post-wounding were histologically sectioned and subjected to Masson's trichrome staining. Quantification of adipose tissue gaps **(A)** and granulation tissue areas **(B)** are shown. Five stained sections from 10 random fields for each group were evaluated and the average diameter was estimated under a light microscope. No significant differences between PBS and other treatments were determined by Dunnett's multiple comparison post hoc test ( $n = 5$ ); mean  $\pm$  SEM.