Supporting Information:

Zwitterionic Poly(Sulfobetaine Methacrylate) Hydrogels with Optimal Mechanical Properties for Improving Wound Healing *In Vivo*

Huacheng He[1#], Zecong Xiao[2#], Yajiao Zhou[2], Anqi Chen[2], Xuan Xuan[2], Yanyan Li[2], Xin Guo[2], Jie Zheng[3]*, Jian Xiao[2]*, Jiang Wu[1]*

[1]College of Chemistry and Materials Engineering
Wenzhou University, Wenzhou, Zhejiang 325027, P.R. China

[2]School of Pharmaceutical Sciences
Wenzhou Medical University, Wenzhou, Zhejiang 325035, P.R. China

[3]Department of Chemical and Biomolecular Engineering
The University of Akron, Akron, OH 44325, USA

***Corresponding Author:** J.Z: zhengj@uakron.edu; J.X: xfxj2000@126.com; J.W. (woody870402@hotmail.com)

The authors contribute equally to this work

Hydrogel biocompatibility in vitro: To study the biocompatibility of the hydrogel, cell viability and growth in each hydrogel for Hacat cells were observed using live/dead staining. In brief, the Hacat cell were seeded in 24-well plate at a density of 1×10^4 in each well at DMEM medium supplement with 10% FBS for 24 h, then 0.1g hydrogel were added into each well incubated cell for 24 h, the medium was replaced with 1ml 3μg/ml fluorescein diacetate (FDA) at 37 ℃ for 30 min in 24 h. The samples were photographed at Nikon Eclipse TE2000U microscope. Cell proliferation was observed using the cell counting kit-8 (CCK-8) assay when co-culture with each hydrogel, the Hacat cell were seeded in 96-were plate at a debsity of 1×10^5 cell/well then hydrogel were added into each well co-culture 24 h at 37 °C, CCK-8 solution incubated with cell in the last 4 hours in the dark. The absorbance was measured at 450nm using an ELISA reader.

Cell toxicity and viability： we also conducted cell toxicity experiments, when co-cultured with polySBMA hydrogels, to verify their biocompatibility. As shown in Fig. S1 A, as compared to the control group, four hydrogel groups showed no obvious differences in terms of the morphology and proliferation of Hacat cells. Furthermore, CCK-8 assay in Fig. S1B showed that upon 24 h incubation, cell viability for all hydrogels groups and the control group displayed no obvious difference. Both cell toxicity and viability results indicate the good biocompatibility of polySBMA hydrogels.

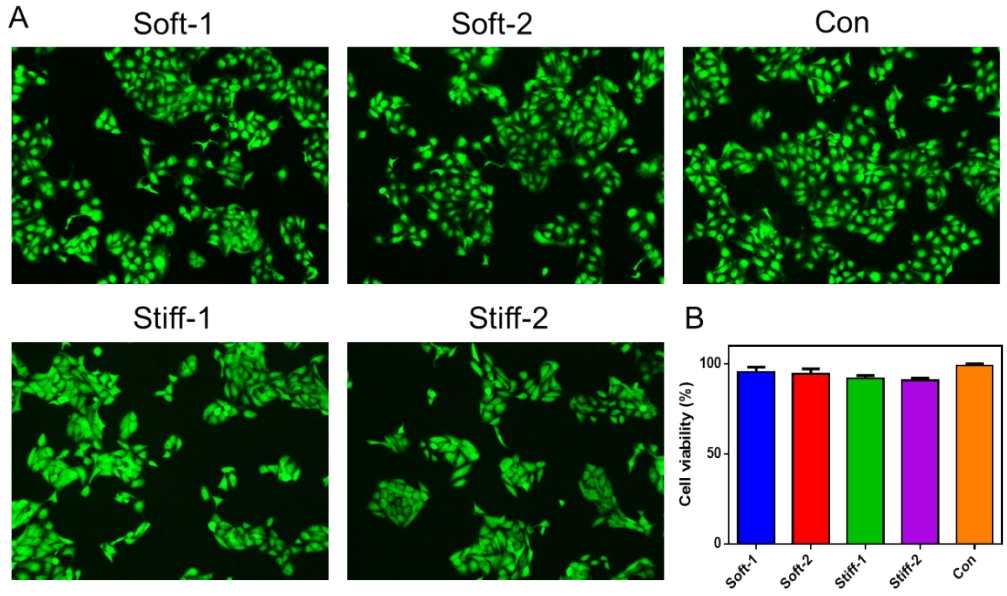

Figure S1. (A) In vitro cell cytotoxicity and proliferation of Hacat cells on soft-1, soft-2, stiff-1 and stiff-2 hydrogels and the control group upon 24-hour incubation. (B) Biocompatibility

assessment of soft-1, soft-2, stiff-1 and stiff-2 hydrogels and the control group using CCK-8 assay upon 24-hour incubation.